American Society of Hematology
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2018 American Society of Hematology / American Society of Clinical Oncology

Hematology and Oncology Carrier Advisory Committee (CAC) Network Meeting

July 26 – 27, 2018

American Society of Hematology
2021 L Street, NW
Suite 900
Washington, DC 20036
(202) 776-0544

10th Floor Conference Center

American Society of Hematology/American Society of Clinical Oncology
Carrier Advisory Committee (CAC) Network Meeting
Friday, July 27, 2018
8:00 a.m. – 3 p.m.

AGENDA

7:30 a.m.	Breakfast Available	
7:45 a.m.	Mentor CAC 101	
8:30 a.m.	Welcome and Introductions • ASH and ASCO Staff List • Attendee List • CAC Representatives • CMD List and Jurisdiction Map	Co-Chairs
8:45 a.m.	Biosimilars	Jeffrey Crawford, MD
9:45 a.m.	Morning Break	
10:00 a.m.	Next Generation Sequencing	Katherine Szarama, PhD
11:00 a.m.	Case Study: Evidence Based Medicine	Arthur Lurvey, MD
12:00 p.m.	Working Lunch/Open Forum - E&M Coding	
12:45 p.m.	Case Study: CAR-T Cellular Therapy	Gary Goldstein
1:45 p.m.	Financial Implications of CAR-T Cell Therapies	Samuel Silver, MD, PhD
2:45 p.m.	Closing Remarks and Reference Materials • CMS Resources • ASH Choosing Wisely • ASCO Choosing Wisely • ASH Practice Resources • ASCO Clinical Affairs Brochure • Meeting Evaluation Form • Meeting Reimbursement Policy • Meeting Reimbursement Form	Co-Chairs
3:00 p.m.	Meeting Adjourn	

2018 ASH/ASCO Staff Contact Information

Leslie Brady, MPH
Policy and Practice Manager
American Society of Hematology
2021 L Street, NW, Suite 900
Washington, DC 20036
Phone: 202-292-0264
lbrady@hematology.org

Suzanne M. Leous, MPA
Chief Policy Officer
American Society of Hematology
2021 L Street, NW, Suite 900
Washington, DC 20036
Phone: 202-292-0258
sleous@hematology.org

Katherine Stark
Policy and Practice Coordinator
American Society of Hematology
2021 L Street, NW, Suite 900
Washington, DC 20036
Phone: 202-292-0252
kstark@hematology.org

Monica Tan
Program Administrator
Clinical Affairs Department
American Society of Clinical Oncology
2318 Mill Road, Suite 800
Alexandria, VA 22314
Phone: 571-483-1671
Monica.Tan@asco.org

Julia Tomkins
Director
Clinical Affairs Department
American Society of Clinical Oncology
2318 Mill Road, Suite 800
Alexandria, VA 22314
Phone: 571-483-1651
Julia.Tomkins@asco.org

2018 ASH/ASCO CAC Meeting Attendee List

Abbreviations:
CPC = ASCO Clinical Practice Committee
COP = ASH Committee on Practice
RS = ASH Reimbursement Subcommittee

Asha Ahmed
State Advocacy Coordinator
ACCC
1801 Research Boulevard, Suite 400
Rockville, MD 20852
Phone 301-984-9496
aahmed@accc-cancer.org

Steven L. Allen, MD, FACP
Onc/Hem CAC Representative
ASH COP Member
Hofstra Northwell School of Medicine
450 Lakeville Rd
Lake Success, NY 11042
Phone: 516-734-8959
sallen@northwell.edu

James Almas, MD
Contractor Medical Director
Palmetto GBA MolDX
17 Technology Circle
Columbia, SC 29203
Phone: 601-209-1857
jim.almas@palmettogba.com

Daniel Argolo
ASCO CPC Member
CLION - CAM Group
Ladeira do Acupe 115 apt 402
Salvador, Bahia, Brazil, 40290160
Phone: +55 719-944-7550
daniel.argolo@clion.com.br

Lu Anne Bankert, CAE
Administrator, OSSN
1801 Research Blvd, Suite 400
Rockville, MD 20850
Phone: 301-984-9496
labankert@accc-cancer.org

Karen Beard, CPC, CPCO
State Society Executive Director
Georgia Society of Clinical Oncology
3330 Cumberland Blvd, Suite 200
Atlanta, GA 30339
Phone: 770-951-8427
kmb@medicalmanagement.com

Walter Birch, MBA
Division Director, Practice Management, Resources, Performance
American Society of Clinical Oncology
2318 Mill Road, Suite 800
Alexandria, VA 22314
Phone: 571-483-1658
Walter.Birch@asco.org

Leslie Brady, MPH
Policy & Practice Manager
American Society of Hematology
2021 L St, NW, Suite 900
Washington, DC 20036
Phone: 202-776-0544
lbrady@hematology.org

Marci Cali, BA, RHIT
State Society Executive Director OSSN at ACCC
1801 Research Blvd, Suite 400
Rockville, MD 20850
Phone: 301-984-9496
mcali@accc-cancer.org

Bob Carlson, MD
Speaker
National Comprehensive Cancer Network (NCCN)
275 Commerce Drive, Suite 300
Fort Washington, PA 19034
Phone: 215-690-0300
carlson@nccn.org

Robert H. Cassell, MD, PhD
Oncology CAC Representative
FLASCO
3834 Gaines Court, SE
Winter Haven, FL 33884
Phone: 863-324-7903
rhcassell@gmail.com

Paul Celano, MD
ASCO CAC Co-Chair
ASCO CPC Chair
The Cancer Center at GBMC
6569 N Charles St, Suite 205
Baltimore, MD 21204
Phone: (443) 849-3051
Pcelano@gbmc.org

Shobha Chitneni, MD
State Society President
Iowa Oncology Society
1351 Kimberly Road, Suite # 100
Bettendorf, IA 52722
Phone**:** 563-355-7733
shobha-chitneni@uiowa.edu

Laurence Clark, MD, FACP
Contractor Medical Director
National Government Services
5000 Brittonfield Pkwy, Suite 100
East Syracuse, NY 13057
Phone: 703-408-1442
laurence.clark@anthem.com

Rise M. Cleland
State Society Executive Director
Washington State Medical Onc Society
1325 Officers Row, Suite A
Vancouver, WA 98661
Phone: 360-695-1608
rise@wsmos.org

Nathan Connell, MD, PHD
Speaker
Brigham and Women's Hospital
75 Francis Street, SR322
Boston, MA 02115
Phone: 305-479-8913
NTConnell@bwh.harvard.edu

Jeffrey Crawford, MD
Speaker
Duke Cancer Institute
Trent Drive, Duke South,
25177 Morris Bldg
Durham, NC 27710
Phone: 919-681-9509
crawf006@mc.duke.edu

Howard Coleman, MD
State Society President
Society of Utah Medical Oncologists
1950 Circle of Hope, Suite 2100
Salt Lake City, UT 84112
Phone: 801-935-0505
howard.colman@hci.utah.edu

Neelima Denduluri, MD
Speaker
ASCO Guidelines Member
Virginia Cancer Specialists
1635 N George Mason Dr, Suite 1701
Arlington, VA 22205-3633
neelima.denduluri@usoncology.com

Dane Dickson, MD
Hematology CAC Representative
Oncology CAC Alternative
Past CMD for Palmetto
Teton Cancer Institute
544 Partridge Lane
Rexburg, ID 83440
Phone: 208-313-0649
danejdickson@gmail.com

Chancellor E. Donald, MD
ASH CAC Co-Chair
ASH COP Member
Hematology CAC Representative
Louisiana Oncology Associates
600 Richland Ave
Lafayette, LA 70508
Phone: 337-258-6921
Chancellordonald@hotmail.com

Nicole Dreabit
Account Executive
OSSN
1801 Research Blvd, Suite 400
Rockville, MD 20850
Phone: 301-984-9496
ndreabit@accc-cancer.org

Omar Eton, MD
Oncology CAC Alternate
Boston Medical Center and Hartford Health
85 Seymour St, Suite 227
Hartford, CT 06106
Phone: 860-696-5169
Omar.eton@hhchealth.org

Stephanie Farnia
Director, Health Policy & Strategic Relations
ASBMT
330 N. Wabash, Suite 2000,
Chicago, IL, 60611
Phone: 847-725-2316
SFarnia@asbmt.org

Stuart P. Feldman, MD
State Society President
Westchester Medical Group PC
210 Westchester Ave
White Plains, NY 10604
Phone: 914-681-5200
sfeldman@westmedgroup.com

Paul Fishkin, MD
ASH COP Member
Illinois Cancer Care
8940 N. Wood Sage Rd.
Peoria, IL 61615
Phone: 309-243-3000
pfishkin@illinoiscancercare.com

Annette Fontaine, MD, MBA
Oncology CAC Alternate
New Mexico Cancer Center
4901 Lang Ave NE
Albuquerque, NM 87109
Phone: 505-264-3912
afontaine@nmohc.com

James L. Gajewski, MD
ASH RS Member
Hematology CAC Representative
OSMO
15378 NW Dane Lane
Portland, OR 97229
Phone: 503-686-5977
jlgajewski@yahoo.com

Matthew Gertzog, MBA, CAE
Deputy Executive Director
American Society of Hematology
2021 L St, NW, Suite 900
Washington, DC 20036
Phone: 202-292-6017
mgertzog@hematology.org

Leland Garrett, MD, FACP, FASN, CPC
Contractor Medical Director
Palmetto GBA
3230 Rain Forrest Way
Raleigh, NC 27614
Phone: 919-630-6355
leland.garrett@palmettogba.com

Gary Goldstein
Speaker
Blood & Marrow Transplant Program
Stanford Health Care
180 El Camino Real, Suite BB1199-2nd Floor
Palo Alto, CA 94305-5623
Phone: 650.725-3117
ggoldstein@stanfordhealthcare.org

Stephen Grubbs, MD, FASCO
Vice President, Clinical Affairs
American Society of Clinical Oncology
2318 Mill Road, Suite 800
Alexandria, VA 22314
Stephen.Grubbs@asco.org
Phone: 571-483-1750

Tom Heffner, MD
ASH CAC Co-Chair
ASH COP Member
Hem/Onc CAC Representative
Emory University
1365 Clifton Rd, NE
Atlanta, GA 30322
Phone: 404-778-1900
lheffne@emory.edu

Allison Hirschorn
Coding and Reimbursement Specialist
American Society of Clinical Oncology
2318 Mill Road, Suite 800
Alexandria, VA 22314
Phone: 571-483-1653
Allison.Hirschorn@asco.org

Dawn Holcombe, MBA, FACMPE, ACHE
State Society Executive Director
DGH Consulting
33 Woodmar Circle
South Windsor, CT 06074
Phone: 860-305-4510
dawnho@aol.com

Angela Ladner
State Society Executive Director/Administrator
Mississippi Oncology Society
550M Ritchie Highway, Suite #271
Severna Park, MD 21146
Phone: 601-594-2101
aladner@nextwavegroup.net

Suzanne M. Leous, MPA
Chief Policy Officer
American Society of Hematology
2021 L St, NW, Suite 900
Washington, DC 20036
Phone: 202-292-0258
sleous@hematology.org

Martha Liggett, Esq
Executive Director
American Society of Hematology
2021 L St, NW, Suite 900
Washington, DC 20036
Phone: 202- 292-6002
mliggett@hematology.org

Arthur N. Lurvey, MD, FACP, FACE
Contractor Medical Director
Noridian Healthcare Solutions
900 42nd St S, P.O. Box 6740 F
Fargo, ND 58103
Phone: 701-715-9583
arthur.lurvey@noridian.com

Gary MacVicar, MD
Oncology CAC Representative
8940 North Wood Sage Road
Peoria, IL 61615
Phone: 309-243-3000
gmacvicar@illinoiscancercare.com

Aishat Magbade
Program Coordinator
American Society of Clinical Oncology
2318 Mill Road, Suite 800
Alexandria, VA 22314
Phone: 571-483-1798
Aishat.Magbade@asco.org

Mary Kay Makarewicz
State Society Executive Director/Administrator
Michigan Society of Hematology and Oncology
5435 Corporate Drive, Ste. 250
Troy, MI 48098
Phone: 248-808-2940
mmakarewicz@msho.org

Barbara L. McAneny, MD
Oncology CAC Representative
NMOHC
4901 Lang Ave NE
Albuquerque, NM 87109
Phone: 505-842-8171
mcaneny@nmohc.com

Charles F. Miller, MD
State Society Representative
Doctors for Dignity
762 Kaulana Place
Honolulu, HI 96821
Phone: 808-561-6014
Millerc003@hawaii.rr.com

Daniel P. Mirda, MD
State Society President
ANCO
2 Huntington Court
Napa, CA 94558
Phone: 707-694-2073
daniel.mirda@stjoe.org

Joseph Muscato, MD
Oncology CAC Representative
State Society President
Missouri Oncology Society
1705 E. Broadway
Columbia, MO 65201
Phone: 573-881-7801
mail@jmuscato.com

Jose Eugenio Najera, MD
Hematology CAC Representative
Cancer Centers of Southwest Oklahoma
104 NW 31st St
Lawton, OK 73506
Phone: 210-865-0040
eugenio.najera@ccswok.org

Gary Oakes, MD, FAAFP
Contractor Medical Director
Noridian Healthcare Solutions
900 42nd Street S
Fargo, ND 58108
Phone: 701-205-5359
Gary.Oakes@noridian.com

Ray D. Page, DO, PhD, FACOI
ASCO CAC Co-Chair
ASCO CPC Chair-Elect
Center for Cancer and Blood Disorders
800 W. Magnolia
Fort Worth, TX 76008
Phone: 817-759-7000
rpage@txcc.com

Mark S. Pascal, MD
Hematology CAC Representative
State Society President
Medical Oncology Society of New Jersey
John Theurer Cancer Center at Hackensack
University Medical Center
92 Second St
Hackensack, NJ 07601
Phone: 551-996-5900
mpascal@hackensackumc.org

Kashyap B. Patel, MD
Onc/Hem CAC Representative
Carolina Blood and Cancer Care Associates
1583 Healthcare Dr
Rock Hill, SC 29732
Phone: 803-329-7772
kpatel@cbcca.net

Taral Patel, MD
Hematology CAC Representative
Ohio Oncology/Hematology Inc
3100 Plaza Properties Blvd
Columbus, OH 43219
Phone: 614-565-2966
TPatel@zangcenter.com

Debra Patterson, MD, FACP
Contractor Medical Director
Novitas Solutions Inc
9330 LBJ, Suite 1200
Dallas, TX 75243
Phone: 214-293-5299
debra.patterson@novitas-solutions.com

Sixto Perez, MD
State Society President
Puerto Rico's Hematology and Medical Oncology Association
1353 Ave Luis Vigoreaux PMB 597
Guaynabo, PR 00966
Phone: 787-647-3724
sixtito26@hotmail.com

Luis F. Pineda, MD, MSHA
Hematology CAC Representative
Luis F. Pineda MD PC
1909 Laurel Rd
Birmingham, AL 35416
Phone: 205-978-3570
gina@luisfpinedamdpc.com

Leah Ralph
Director, Health Policy
ACCC
1801 Research Boulevard, Suite 400
Rockville, MD 20852
Phone 301-984-9496
LRalph@accc-cancer.org

Cheryl Ray, DO, MBA, FACN
Contractor Medical Director
WPS Governmental Health Administrators
1717 W Broadway
P.O. Box 1787
Madison, WI 53701
Phone: 609-977-5368
cheryl.ray@wpsic.com

Bipin Savani, MD
ASH COP Member
VUMC/ VAMC
714 Tyneside Circle
Brentwood, TN 37027
Phone: 615-440-8698
bipin.savani@Vanderbilt.Edu

Michael A. Savin, MD
ASCO CPC Member
Knight Cancer Institute
Oregon Health & Science University
3181 SW Sam Jackson Park Rd, L586
Portland, OR 97239
Phone: 503-494-5672
savin@ohsu.edu

Eric J. Seifter, MD
Oncology CAC Representative
Johns Hopkins at Green Spring Station
10755 Falls Rd, Suite 200
Lutherville, MD 21093
Phone: 410-583-7122
eseifte@jhmi.edu

Jamile Shammo, MD
ASH COP Member
Rush University Medical Center
1725 W. Harrison St., Suite 809
Chicago, IL 60612
Phone: 312-942-5157
Jamile_Shammo@Rush.edu

Gregg Shepard, MD
Hem/Onc CAC Representative
Tennessee Oncology Practice Society
609 Wilson Blvd
Nashville, TN 37215
Phone: 615-519-2022
gshepard@tnonc.com

Melissa Sherman, MD
Representing MSCO Board
Cancer Centers of Southwest Oklahoma
3931 Louisiana Ave
St Louis Park, MN 55426
Phone: 952 993-0359
shermm@parknicollet.com

Samuel Silver, MD, PhD, MACP, FASCO
ASH COP Member
ASH RS Member
ASCO CPC Member
4107 Medical Science 1
1301 Catherine St, SPC 5624
Ann Arbor, MI 48109-5843
Phone: 734-764-2204
msilver@umich.edu

Pamela Soliman, MD
ASCO CPC Member
MD Anderson Cancer Center
1155 Herman Pressler, CPB6.3237
Houston, TX 77030
Phone: 713 745-2352
psoliman@mdanderson.org

Katherine Stark
Policy and Practice Coordinator
American Society of Hematology
2021 L St, NW, Suite 900
Washington, DC 20036
Phone: 202-292-0252
kstark@hematology.org

Jon Strasser, MD
Oncology CAC Representative
DSCO
725 Foxdale Rd
Wilmington, DE 19803
Phone: 302-463-8464
jstrasser@christianacare.org

Nathan Strunk
State Society Executive Director/Administrator
Massachusetts Society of Clinical Oncologists
Phone: 781-434-7329
860 Winter Street
Waltham, MA 02451
nstrunk@mms.org

Latha Subramanian, MD
State Society President
Onc/Hem CAC Representative
Denali Oncology Group
2925 DeBarr Rd, Suite 300
Anchorage, AK 99508
Phone: 907-257-9803
2006anch@gmail.com

Linda Sutton, MD
Oncology CAC Representative
Duke University Medical Center
Box 2989
Durham, NC 27710
Phone: 919-419-5005
Linda.sutton@duke.edu

Monica Tan
Program Administrator
American Society of Clinical Oncology
2318 Mill Rd, Suite 800
Alexandria, VA 22314
Phone: 571-483-1671
Monica.Tan@asco.org

Tammy Thiel
State Society Executive Director
Denali Oncology Group
2741 DeBarr Rd, Suite 300
Anchorage, AK 99308
Phone: 907-257-9803
tammy@hotsheet.com

Julia Tomkins
Director
American Society of Clinical Oncology
2318 Mill Road, Suite 800
Alexandria, VA 22314
Phone: 571-483-1651
Julia.Tomkins@asco.org

Elaine Towle, CMPE
Division Director, Analysis and Consulting Services
American Society of Clinical Oncology
2318 Mill Road, Suite 800
Alexandria, VA 22314
Phone: 571-483-1616
Elaine.Towle@asco.org

Barry Whites, MD, FCCP, MSHA
Contractor Medical Director
Novitas Solutions
PO Box 4304
Jackson, MS 39296
Phone: 601-953-5864
Barry.Whites@novitas-solutions.com

Richard (Dick) Whitten, MD, MBA, FACP
Contractor Medical Director
Noridian Healthcare Solutions
900 42nd Street S
Fargo, ND 58108
Phone: 206-979-5007
Dick.Whitten@noridian.org

Katrina Williams
State Society Assistant Executive
Director/Administrator
Florida Society of Clinical Oncology
10022 Water Works Lane
Riverview, FL 33578
Phone: 813-677-0246
assistant@flasco.org

2018 CAC Representative List

Alabama (JF)
Luis F. Pineda, MD, MSHA
Hematology CAC Representative
1909 Laurel Rd
Vestavia, AL 35216
Phone: 205-978-3570
gina@luisfpinedamdpc.com

Alaska (JF)
Latha Subramanian, MD
Onc/Hem CAC Representative
2925 DeBarr Rd, Suite 300
Anchorage, AK 99508
Phone: 907-257-9803
2006anch@gmail.com

Mary Stewart, MD
Oncology CAC Alternate
2925 DeBarr Rd, Suite 300
Anchorage, AK 99508
Phone: 907-257-9803
mstewartonc@yahoo.com

Arizona (JF)
Jerry Olshan, MD
Onc/Hem CAC Representative
3411 N 5th Ave, Suite 400
Phoeniz, AZ 85013
Phone: 623-879-6034
jolshan@southwestoncology.com

California (JE)
Robert Robles, MD
Onc/Hem CAC Representative
400 Taylor Blvd, Suite 202
Pleasant Hill, CA 94523
Phone: 925-667-5041
rrobles@dvohmg.com

Sabina R. Wallach, MD, FRACP, FACP
Hematology CAC Representative
Oncology Alternate
9850 Genesee Ave, Suite 400
La Jolla, CA 92037
Phone: 858-558-8666
swallachmd@oncologylajolla.com

Ravi Patel, MD
Oncology CAC Alternate
6501 Truxton Ave
Bakersfield, CA 93309
Phone: 661-322-2206
ravi@cbccusa.com

Colorado (JK)
Alex R. Menter, MD
Onc/Hem CAC Representative
Denver, CO 80111
Phone: 303-316-0360
alex.menter@kp.org

Connecticut (JK)
Dawn Holcombe, MBA FACMPE, ACHE
State Society Executive Director
33 Woodmar Circle
South Windsor, CT 06074
Phone: 860-305-4510
dawnho@aol.com

Joseph O'Connell
Hematology CAC Representative
415 Ocean Avenue
New London, CT 06320
Phone: 860-442-7027
joc309@aol.com

Delaware (JL)
Jamal Misleh, MD
Hematology CAC Representative
401 Ogletown-Stanton Rd, Suite 3400
Newark, DE 19713
Phone: 302-366-1200
jmisleh@cbg.org

Jon Strasser, MD
Oncology CAC Alternate
4701 Ogletown-Stanton Rd, Suite 1110
Newark, DE 19713
Phone: 302-623-4800
jonstrasser@hotmail.com

Florida (JN)
Ahmed Al-Hazzouri, MD
Hematology CAC Representative
601 E. Altamonte Drive
Altamonte Springs, FL 32701
Office: 407-303-2305
aalhazzouri@flcancer.com

Maen Hussein, MD
Hematology CAC Alternate
4100 Waterman Way
Tavares, FL 32778
Office: 352-360-9020
maenh369@gmail.com

Robert H. Cassell, MD, PhD
Oncology CAC Representative
3834 Gaines Court SE
Winter Haven, FL 33884
Phone: 863.324.7903
rhcassell@gmail.com

Michael Diaz, MD
Oncology CAC Alternate
1201 5th Ave. N.
St. Petersburg, FL 33705
Phone: 727-821-0017
mdiaz@flcancer.com

Georgia (JJ)
Tom Heffner, MD
Hematology CAC Representative
1365 Clifton Rd NE
Atlanta, GA 30322
Phone: 404-778-1900
lheffne@emory.edu

Andrew W. Pippas, MD
Oncology CAC Representative
1831 5th Ave
Columbus, GA 31904
Phone: 706-320-8720
andrew.pippas@crhs.net

Hawaii (JE)
William Loui, MD
Hematology CAC Representative
Queen's Physician Office Bldg. II
1329 Lusitana St, Suite 307
Honolulu, HI 96813
Phone: 808-524-6115
wsloui@yahoo.com

Laeton Pang, MD, MPH, FACR
Rad Onc CAC Representative
Cancer Center of Hawaii
Pacific Radiation Oncology
Honolulu, HI 96817
Phone: 808-547-6881
LpangLro@aol.com

Idaho (JF)
Dane Dickson, MD
Hematology CAC Representative
450 East Main St
Rexburg, ID 83440
Phone: 208-356-9559
danejdickson@gmail.com

Paul Montgomery, MD
Oncology CAC Representative
100 E. Idaho St
Boise, ID 83712
Phone: 208-381-2711
montgomp@slhs.org

Illinois (J6)
Gary MacVicar, MD
Onc/Hem CAC Representative
8940 North Wood Sage Rd
Peoria, IL 61615
Phone: 309-243-3000
gmacvicar@illinoiscancercare.com

Walter Fried, MD
Hematology CAC Representative
1700 Luther Ln
Park Ridge, IL 60068
fried_walter@hotmail.com

Indiana (J8)
Keith Logie, MD
Hematology CAC Representative
10212 Lantern Rd
Fishers, IN 46037
Phone: 317-841-5656
keith.logie@usoncology.com

Iowa (J5)
Joe Merchant, MD
Oncology CAC Representative
1215 Duff Ave
Ames, IA 50010
Phone: 515-239-4401
jjmerchant@mcfarlandclinic.com

Sakeer Hussain, MD
Oncology CAC Alternate
1 Edmundson Place
Council Bluffs, IA 51503
Phone: 712-322-4136
sakeerdr@gmail.com

George Kovach, MD
Hematology CAC Representative
1341 W Central Park Ave
Davenport, IA 52804
Phone: 563-421-1960
gkovach@iacancer.com

Kansas (J5)
Sukumar Ethirajan, MD
Hem/Onc CAC Representative
12140 Nall Ave, Suite 305
Overland Park, KS 66209
Phone: 913-735-3873
kancer@me.com

Dennis Moore, MD
Hematology CAC Representative
818 North Emporia, Suite 403
Wichita, KS 67214
Phone: 316-262-4467
dennis.moore@cancercenterofkansas.com

Kentucky (J15)
Renato LaRocca, MD
Hematology CAC Representative
100 East Liberty St, Suite 500
Louisville, KY 40202
Phone: 502-561-8200
rvl@kci.us

Louisiana (JH)
Chancellor E. Donald, MD
Hematology CAC Representative
600 Richland Ave
Lafayette, LA 70508
Phone: 337-258-6921
chancellordonald@hotmail.com

Maine (JK)
Tracey Weisberg, MD
Oncology CAC Representative
100 Campus Dr
Scarborough, ME 04074
Phone: 207-396-7600
weisbt@newecs.org

Christian Thomas, MD
Oncology CAC Representative
100 Campus Drive
Scarborough, ME 04074
Phone: 207-396-7600
thomac@newecs.org

Daniel Hayes, MD
Hematology CAC Rep
100 Campus Drive
Scarborough, ME 04074
Phone: 207-885-7600
hayesd@mccm.org

Maryland (JL)
Eric J. Seifter, MD
Oncology CAC Representative
10755 Falls Rd, Suite 200
Lutherville, MD 21093
Phone: 410-583-7122
eseifte@jhmi.edu

Thomas Bensinger, MD
Hematology CAC Representative
7525 Greenway Center Drive, Suite 205
Greenbelt, MD 20770
Phone: 301-982-9800
tabens67@gmail.com

Massachusetts (JK)
Michael Constantine, MD
Hematology CAC Representative
20 Prospect St
Milford, MA 01757
Phone: 508-488-3700
mconstantine@milreg.org

Eric Wong, MD
Oncology CAC Representative
330 Brookline Ave
Boston, MA 02215
Phone: 617-667-1665
ewong@bidmc.harvard.edu

Omar Eton, MD
Oncology CAC Alternate
85 Seymour St, Suite 227
Hartford, CT 06106
Phone: 860-696-5169
omar.eton@hhchealth.org

Michigan (J8)
Anas Al-Janadi, MD
Hematology CAC Representative
788 Service Rd
B414 Clinical Center
East Lansing, MI 48824
Phone: 517-353-3128
Anas.Al-Janadi@hc.msu.edu

Minnesota (J6)
Lloyd Ketchum, MD
Hem/Onc CAC Representative
400 E Third St
Duluth, MN 55805
Phone: 218-786-3625
lloyd.ketchum@essentialhealth.org

Rajini Malisetti, MD
Onc/Hem CAC Representative
11850 Blackfoot St NW
Coon Rapids, MN 55433
Phone: 763-712-2100
rajini.malisetti@usoncology.com

Mississippi (JJ)
Stephanie Elkins, MD
Hematology CAC Representative
2500 North State St
Jackson, MS 39216
Phone: 601-981-5616
selkins@umc.edu

Missouri (J5)
Joseph Muscato, MD
Hem/Onc CAC Representative
State Society President
Missouri Oncology Society
1705 E. Broadway
Columbia, MO 65201
Phone: 573-881-7801
mail@jmuscato.com

Burton M. Needles, MD
Hematology Alternate CAC Representative
11530 Conway Rd
St. Louis, MO 63131
Phone: 314-330-1018
burton.needles@mercy.net

Montana (JF)
Jack Hensold, MD
Hem/Onc CAC Representative
931 Highland Blvd, Suite 3130
Bozeman, MT 59715
Phone: 406-585-5070
jhensold@bozermanhealth.org

Nebraska (J5)
Margaret Block, MD
Hematology CAC Representative
17201 Wright St
Omaha, NE 68130
Phone: 402-955-2680
mblock@nebraskacancer.com

Nevada (JE)
Heather Allen, MD, FACP
Hematology CAC Representative
3730 S. Eastern Ave
Las Vegas, NV 89169
Phone: 702-952-3400
heather.allen@usoncology.com

Dan Curtis, MD
Oncology CAC Representative
655 Town Center Drive
Las Vegas, NV 89144
Phone: 702-233-2210
dan.curtis@usoncology.com

New Hampshire (JK)
Steve Larmon, MD
Hematology CAC Representative
201 Chesterfield Rd
Keene, NH 03431
Phone: 603-357-3411
Stevenslarmon@ne.rr.com

New Jersey (JL)
Mark S. Pascal, MD
Hematology CAC Representative
92 Second St
Hackensack, NJ 07601
Phone: 551-996-5900
mpascal@hackensackumc.org

Kevin Callahan, MD
Oncology CAC Representative
Two Cooper Plaza
Camden, NJ 08103
Phone: 855-632-2667
callahan-kevin@cooperhealth.net

New Mexico (JH)
Tim Lopez, MD
Hematology CAC Representative
490-A West Zia Rd
Santa Fe, NM 87505
Phone: 505-955-7900
timothy.lopez@nmcancercare.com

Annette Fontaine, MD, MBA
Oncology CAC Alternate
4901 Lang Ave NE
Albuquerque, NM 87109
Phone: 505-264-3912
afontaine@nmohc.com

Barbara McAneny, MD, FASCO
Oncology CAC Representative
4901 Lang Ave NE
Albuquerque, NM 87109
Phone: 505-842-8171
mcaneny@nmohc.com

New York (JK)
Steven L. Allen, MD, FACP
Hematology CAC Representative
450 Lakeville Rd
Lake Success, NY 11042
Phone: 516-734-8959
sallen@northwell.edu

Michael Willen, MD
Oncology CAC Alternate
3 Crossing Blvd
Clifton Park, NY 12065
Phone: 518-831-4434
Michael.willen@usoncology.org

North Carolina (JM)
James Boyd, MD
Hematology CAC Representative
2711 Randolph Rd, Bldg 100
Charlotte, NC 28207
Phone: 704-342-1900
jfboyd@oncologycharlotte.com

Birgit A. Arb, MD
Oncology CAC Representative
1520 Physicians Drive
Wilmington, NC 28401
Phone: 910-343-0447
barb@ec.rr.com

Daniel R. Carrizosa, MD, MS
Oncology CAC Representative
1021 Morehead Medical Dr
Charlotte, NC 28204
Phone: 980-442-2000
Daniel.carrizosa@carolinashealthcare.org

Linda Sutton, MD
Hem/Onc CAC Representative
Duke University Medical Center
BOX 2989
Durham, NC 27710
Phone: 919-419-5005
sutto006@mc.duke.edu

North Dakota (JF)
Ralph Levitt, MD
Hematology CAC Representative
820 4th St N
Fargo, ND 58122
Phone: 701-234-6161
ralph.levitt@sanfordhealth.org

Ohio (J15)
David Kirlin, MD
Oncology CAC Representative
4350 Malsbary Rd, Suite 100
Cincinnati, OH 45226
Phone: 513-751-2148
dkirlin@ohcare.com

Christopher S. George, MD
Oncology CAC Alternate
810 Jasonway Ave, Suite A
Columbus, OH 43214
Phone: 614-442-3130
cgeorge@coainc.cc

Taral Patel, MD
Hematology CAC Representative
3100 Plaza Properties Blvd
Columbus, OH 43219
Phone: 614-383-6000
tpatel@zangcenter.com

Scott C. Blair, MD
Hematology CAC Alternate
810 Jasonway Ave, Suite A
Columbus, OH 43214
Phone: 613-442-3130
sblair@coainc.cc

Oklahoma (JH)
Jose Eugenio Najera, MD
Hematology CAC Representative
104 NW 31PPstPP St
Lawton, OK 73506
Phone: 210-865-0040
eugenio.najera@ccswok.org

Todd Kliewer, MD
Hematology CAC Representative
230 North Midwest Blvd.
Midwest City, OK 73110
Phone: 405-737-8455
toddklev@cox.net

Oregon (JF)
James L. Gajewski, MD
Hematology CAC Representative
15378 NW Dane Ln
Portland, OR 97229
Phone: 503-686-5977
lgajewski@yahoo.com

David H. Regan, MD
Hem/Onc CAC Representative
5050 NE Hoyt St, Suite 256
Portland, OR 97034
Phone: 503-239-7767
david.regan@usoncology.com

Pennsylvania (JL)
L. Eamonn Boyle, MD
Oncology CAC Representative
25 Monument Rd, Suite 294
York, PA 17403-5049
Phone: 717-741-9229
lebsvb@aol.com

Raymond Vivacqua, MD
Oncology CAC Alternate
1 Medical Center Blvd
Upland, PA 19013
Phone: 610-610-7420
RDWPLT@comcast.net

Edward P. Balaban, DO
Hematology CAC Representative
105 Victory Blvd.
State College, PA 16803
epbalaban1@gmail.com

Rhode Island (JK)
Joseph DiBenedetto Jr., MD, FASCO
Onc/Hem CAC Representative
193 Waterman St
Providence, RI 02906
Phone: 401-351-4470
joedibenedetto@msn.com

South Carolina (JM)
Quillin Davis, MD
Oncology CAC Alternate
2720 Sunset Blvd West
Columbia, SC 29169
Phone: 803-791-2575
quillindavis@gmail.com

Kashyap Patel, MD
Hematology CAC Representative
1583 Healthcare Dr
Rock Hill, SC 29732
Phone: 803-329-7772
kpatel@cbcca.net

Tennessee (JJ)
Gregg Shepard, MD
Hem/Onc CAC Representative
4230 Harding Rd, Suite 707
Nashville, TN 37205
Phone: 615-269-7085
gshepard@tnonc.com

Charles McKay, MD, MBA
Hematology CAC Representative
397 Wallace Rd, Suite 201
Nashville, TN 37211
Phone: 615-333-2481
capreeland@me.com

Texas (JH)
John V. Cox, DO, MBA, FACP, FASCO
Oncology CAC Representative
5323 Harry Hines Blvd
Dallas, TX 75390
Phone: 214-648-3111
John.Cox@utsouthwestern.edu

Ronald S. Walters, MD, MHS, MS, MBA
Oncology CAC Representative
1515 Holcombe Blvd, Unit 43
Houston, TX 77030
Phone: 713-745-9766
rwalters@mdanderson.org

Roger M. Lyons, MD
Hematology CAC Representative
4411 Medical Drive, Suite 100
San Antonio, TX 78229
Phone: 210-595-5300
roger.lyons@usoncology.com

Utah (JF)
Xylina Gregg, MD
Hematology CAC Representative
3838 S 700 East, Suite 100
Salt Lake City, UT 84106
Phone: 801-269-0231
xgregg@utahcancer.com

Vermont (JK)
Christian Thomas, MD
Hem/Onc CAC Representative
100 Campus Drive
Scarborough, ME 04074
Phone: 207-396-7600
thomac@newecs.org

Virginia (JM)
James May, III, MD
Oncology CAC Representative
1401 Johnston-Willis Dr, Suite 4200
Richmond, Virginia
Phone: 804-330-7990
jmay@vacancer.com

Richard Ingram, MD
Hematology CAC Alternate
420 Glen Lea Ct
Winchester, VA 22601
Phone: 504-974-7845
laurenmiadad@gmail.com

Washington (JF)
Richard McGee, MD
Onc/Hem CAC Representative
21605 76th Ave W
Edmonds, WA 98026
Phone: 425-327-3537
richard.mcgee@swedish.org

Jeffery Ward, MD
Onc/Hem CAC Alternate
21605 Hwy 99
Edmonds, WA 98026
Phone: 425-673-8300
jeffery.ward@swedish.org

West Virginia (JM)
Ahmed Khalid, MD
Oncology CAC Representative
3100 MacCorkle Ave SE, Suite 101
Charleston, WV 25304
Phone: 304-388-8380
ahmed.khalid@camc.org

Wisconsin (J6)
Dhimant R. Patel, MD
Oncology CAC Representative
2845 Greenbrier Rd
Green Bay, WI 54308
Phone: 920-288-4180
dhimant.patel@aurora.org

Jacob Frick, MD
Oncology CAC Alternate
2801 W Kinnickinnic River Pkwy, Suite 930
Milwaukee, WI 53217
Phone: 414-416-4744
jacob.frick@aurora.org

Douglas Reding, MD
Hematology CAC Representative
1000 North Oak Ave
Marshfield, WI 54449
Phone: 715-387-5134
reding@mfldclin.edu

Wyoming (JF)
Mohammed Mazhur-Uddin, MD
Hematology CAC Representative
1111 Logan Ave
Cheyenne, Wyoming
Phone: 307-635-9131

2018 Contractor Medical Director List

James Almas, MD
CMD: MolDX
Palmetto GBA MolDX
17 Technology Circle
Columbia, SC 29203
jim.almas@palmettogba.com

Olatokunbo Awodele, MD, MPH
CMD: J-5
Wisconsin Physician Services Corp
333 Farnam Street
Omaha, NE 68131
olatokunbo@wpsic.com

Earl Berman FACP, MALPS-L
CMD: J15 Part B
CGS Administrators, LLC
Two Vantage Way
Nashville, TN 37228
earl.berman@cgsadmin.com

Stephen Boren MD, MBA
CMD: JK
National Government Services
5000 Brittonfield Pkwy, Suite 100
East Syracuse, NY 13057
stephen.boren@anthem.com

RaeAnn G. Capehart, MD
CMD: JH/JL
Novitas Solutions, INC
2020 Techology Parkway
Mechanicsburg, PA 17050
raeann.capehart@novitas-solutions.com

Siren Chudgar, MD, MBA, CHIE
CMD: JN
First Coast Service Options, Inc.
532 Riverside Avenue
Jacksonville, FL 32202
siren.chudgar@novitas-solutions.com

Laurence Clark, MD, FACP
CMD: JK
National Government Services
5000 Brittonfield Pkwy, Suite 100
East Syracuse, NY 13057
laurence.clark@anthem.com

Alicia Campbell, MD
CMD: JN
First Coast Service Options, Inc
532 Riverside Avenue
Jacksonville, FL 32202
alicia.campbell@fcso.com

Carolyn Cummingham, MD
CMD: Part A IL & WI
National Government Services
8115 Knue Road
Indianapolis, IN 46250
Carolyn.cunningham@anthem.com

Marc Duerden, MD
CMD: JK
National Government Services
8115 Knue Road
Indianapolis, IN 46250
marc.duerden@anthem.com

Harry Feliciano, MD, MPH
CMD: J11 MAC
Palmetto GBA
P.O. Box 100238, AG-275
Columbia, SC 29202
harry.feliciano@palmettogba.com

Leland Garrett, MD, FACP, FASN, CPC
CMD: J11 MAC
Palmetto GBA
P.O. Box 100238 AG-275
Columbia, SC 29202-3238
leland.garrett@palmettogba.com

Paul Gerrard, MD
CMD: JJ MAC
Palmetto GBA
P.O. Box 100238 AG-275
Columbia, SC 29202-3238
paul.gerrard@palmettogba.com

Anitra Graves, MD
CMD: JJ MAC
Palmetto GBA
PO Box 100238 AG-275
Columbia, SC 29202-3238
anitra.graves@palmettogba.com

Charles Haley, MD, MS, FACP
CMD: JF A/B MAC
Noridian Healthcare Solutions
900 42nd Street S
P.O. Box 6740
Fargo, ND 58103
charles.haley@noridian.com

Craig Haug, MD
CMD: J-K MAC
NHIC, Corp
75 Sgt William B. Terry Drive
Hingham, MA 02043
craig.haug@hp.com

Sidney Hayes, MD
CMD: JH/J12
Novitas Solutions, Inc
2020 Technology Parkway
Mechanicsburg, PA 17050
sidney.hayes@novitas-solutions.com

Robert Kettler, MD
CMD: J-5
Wisconsin Physician Services Corp.
1717 W. Broadway
PO Box 1787
Madison, WI 53701
robert.kettler@wpsic.com

Sunil Lalla, MD, FACS
CMD: JH/JL
Novitas Solutions, Inc
2020 Technology Parkway, Suite 100
Mechanicsburg, PA 17050
sunil.lalla@novitas-solutions.com

Tameika Lewis, MD
CMD: J8/ALJ
Wisconsin Physician Services Corp
1717 W. Broadway
PO Box 1787
Madison, WI 53701
tameika.lewis@wpsic.com

Arthur Lurvey, MD
CMD: JE A/B MAC
Noridian Healthcare Solutions
900 42nd Street S,P.O. Box 6740
Fargo, ND 58103
Arthur.lurvey@noridian.com

Greg McKinney, MD, MBA
CMD: Pending
National Government Services
8115-8125 Krue Road
Indianapolis, IN 46250
greg.mckinney@anthem.com

Eileen Moynihan, MD, FACR, FACP
CMD: JE/JF A/B MAC
Noridian Healthcare Solutions
900 42nd Street South
Fargo, ND 58103-6747
eileen.moynihan@noridian.com

Ella Noel, DO, FACIO
CMD: J-8
Wisconsin Physician Services Corp
1717 W. Broadway
PO Box 1787
Madison, WI 53701
ella.noel@wpsic.com

Gary Oakes, MD, FAAFP
CMD: JF A/B MAC
Noridian Healthcare Solutions
900 42nd Street S
P.O. Box 6740
Fargo, ND 58103
gary.oakes@noridian.com

Debra Patterson, MD
CMD: JH/JL
Novitas Solutions, Inc.
2020 Technology Parkway
Mechanicsburg, PA 17050
debra.patterson@novitas-solutions.com

Cheryl Ray, DO, MBA, FACN
CMD: J-5
Wisconsin Physician Services Corp
1717 W. Broadway
PO Box 1787
Madison, WI 53701
cheryl.ray@wpsic.com

Neil Sandler, MD
CMD: J15 MAC
CGS Administrators, LLC
Two Vantage Way
Nashville, TN 37228
neil.sandler@cgsadmin.com

Juan Schaening, MD
CMD: JN
Triple S Salud, Inc.
P.O. Box 363628
San Juan, PR 00936
jschaening@triples-med.org

Antonietta Sculimbrene, MD, MHA, RPh
CMD: J11 MAC
Palmetto GBA
P.O. Box 100238 AG-275
Columbia, SC 29202-3238
antonietta.sculimbrene@palmettogba.com

Galin Spicer, MD
CMD: JM
Palmetto GBA
17 Technology Circle
Columbia, SC 29203
galin.spicer@palmettogba.com

Barry Whites, MD, FCCP, MSHA, CHCQM
CMD : JH, JL
Novitas Solutions, Inc
P.O. Box 4304
Jackson, MS 39296-5864
barry.whites@novitas-solutions.com

Richard (Dick) Whitten, MD, MBA, FACP
CMD: JE/JF
Noridian Healthcare Solutions
900 42nd Street South
Fargo, ND 58103-6747
dick.whitten@noridian.com

CAC Acronyms

ACA - Affordable Care Act
ADLT - Advanced Diagnostic Laboratory Tests
ALL - Acute Lymphoblastic Leukemia
APM - Alternative Payment Model
ASBMT - American Society for Blood and Marrow Transplantation
ASCT - Autologous Stem Cell Transplantation
ASP - Average Sales Price
BMT - Bone Marrow Transplant
CAC - Carrier Advisory Committee
CAR-T - Chimeric antigen receptor T-cell therapy
CC/MCC - Complication or Comorbidity / Major Complication or Comorbidity
CCR - Cost-to-Charge Ratio
CHIP - Children's Health Insurance Program
CLFS - Clinical Laboratory Fee Schedule
CMD - Contractor Medical Director
CMS - Centers for Medicare & Medicaid Services
CPT - Current Procedural Terminology
CRS - Cytokine Release Syndrome
DLBCL - Diffuse Large B-Cell Lymphoma
DSH - Disproportionate Share Hospital
EMA - European Medicines Agency
FDA - U.S. Food and Drug Administration
GSP - Genomic Sequencing Procedures
HCT - Hematopoietic Cell Transplant
HPC - Hematopoietic Progenitor Cell
IME - Indirect Medical Education
IPPS - Inpatient Prospective Payment System
IVIg - Intravenous Immunoglobulin
LCD - Local Coverage Determination
MAC - Medicare Administrative Contractors
MACRA - Medicare Access & CHIP Reauthorization Act of 2015
MEDCAC - Medicare Evidence Development & Coverage Advisory Committee
MIPS - Merit-based Incentive Payment System
MS-DRG - Medicare Severity Diagnosis Related Group
NCA - National Coverage Analysis
NCCN - National Comprehensive Cancer Network
NCD - National Coverage Determination
NGS - Next Generation Sequencing
NTAP - New Technology Add-on Payment
OCM - Oncology Care Model
OPPS - Outpatient Prospective Payment System
ORR - Objective Response Rate
PAMA - Protecting Access to Medicare Act of 2014
PK/PD - Pharmacokinetic/Pharmacodynamic Modeling
PPS - Prospective Payment System
RVUs - Relative Value Units
TNF-agent - Tumor Necrosis Factor
USPSTF - United States Preventive Services Task Force
WI - Wage Index

CAC 101: An Introduction to Carrier Advisory Committees

According to Medicare Coverage Rules

- The decision about whether to cover or, in some cases, not to cover various products and services is typically made at the local level, by Medicare Administrative Contractors (MACs)
- CMS rules require MACs to establish Carrier Advisory Committees (CACs) to advise the contractors about Local Coverage Decisions (LCDs) as long as the proposed coverage or non-coverage does not conflict with existing National Coverage Decisions (NCDs).
- MACs must establish one CAC per state
- Where one MAC oversees multiple states, it must create a separate CAC for each state.

Purpose of the CAC

- A mechanism for physicians to be informed of and participate in development of LCDs;
- An opportunity for physicians to discuss and improve administrative policies within MAC discretion; and
- A forum for the exchange of information between carriers and physicians.

CAC Members

- Physicians from various specialties (one member & designated alternate for each specialty, with additional members when issues within their expertise are under discussion);
- A beneficiary representative; and
- Representatives of other medical organizations.

ASH/ASCO CAC Network Annual Meeting

At the ASH/ASCO CAC Network Annual Meeting, individuals from the following groups are invited:

- ASH Committee on Practice
- ASH Reimbursement Subcommittee
- ASCO Clinical Practice Committee
- Medicare Contractor Medical Directors
- Hematology CAC Representatives
- Oncology CAC Representatives
- State Society Presidents
- State Society Executive Directors

CAC Members

CAC Members are responsible for:

1. Disseminating proposed LCDs to colleagues for comment;
2. Disseminating information about the Medicare program obtained at the CAC meetings; and
3. Discussing inconsistent or conflicting Medical Review policies.
4. Contributing to other specialties' LCDs. This is helpful for the MAC and helps CAC Members gain credibility.

National Coverage Determination (NCD)

- Determined by CMS.
- CMS is advised, at its discretion, by Medicare Evidence Development & Coverage Advisory Committee (MEDCAC), or can conduct an external technology assessment.
- Supersedes MAC policies.
- Can specify services never and/or always covered.
- NCDs can change as science and research emerge.
- NCDs play a growing role in coverage, particularly for very expensive items and services

NCD Process

- Generally, CMS has six to nine months to complete the process after it is initiated (depending on whether technology assessment or MEDCAC review is needed).
- The MEDCAC process includes a public forum, including public testimony.
- Proposed decision is then posted to the CMS website for a 30 day comment period.
- Final decision posted within 60 days after the conclusion of the comment period.

Local Coverage Determinations (LCD)

- LCDs are decisions by a MAC, fiscal intermediary, or carrier on whether to cover a particular service.
- LCDs specify under what clinical circumstances a service is considered reasonable and necessary.
- They can also provide administrative and educational tools to assist providers in submitting correct claims for payment.

- It is important to note: LCD is the typical mechanism for most Medicare coverage policies

Development of LCDs

- MACs must develop new/revised LCDs when a service or item is never covered under certain circumstances and the MAC wants to establish an automated review in the absence of an NCD.
- MACs may develop a LCD if it identifies a widespread problem that poses a risk to Medicare trust funds.
- MACs may also develop a LCD if deemed necessary in order to ensure access to care for beneficiaries.

LCD Process: CAC Role

- MACs must solicit comments from the physician community, utilizing CACs at the state level.
- The comment period begins upon submission to the CAC at a regularly scheduled meeting or delivery in writing to all CAC members.
- Minimum comment period of 45 days.

Interaction Between NCD and LCD

- The scope of an NCD can leave room for LCDs to remain in place for certain patients.
- For example, the final NCD on Next Generation Sequencing for Medicare Beneficiaries with Advanced Cancer will allow MACs to continue to provide coverage at the local level for NGS-based tests that are not automatically covered by the NCD. Several local coverage determinations that provide coverage for hematological malignancies will now remain in effect.
- Thus, for some products, both an NCD and an LCD may have relevance.

Biosimilars
Jeffrey Crawford, MD

Jeffrey Crawford, MD, is George Barth Geller Professor for Research in Cancer and Duke University Medical Center and Co-Director of the Solid Tumor Therapeutics Program in the Duke Cancer Institute (DCI) in Durham, North Carolina. He earned his medical degree from Ohio State University and completed his internship, residency and hematology/oncology fellowship at Duke University Medical Center. Dr. Crawford was chief resident in medicine and also completed a fellowship in geriatrics in Veterans Administration Medical Center in Durham, North Carolina. He is board certified in internal medicine, hematology and oncology. Dr. Crawford served as Chief of the Division of Medical Oncology for 10 years prior to assuming his current leadership role in the DCI as Co-Director of the Solid Tumor Therapeutics Program.

Dr. Crawford is Principal Investigator for the National Clinical Trials Network Lead Academic Site Grant at Duke. He is a member of the executive committee for the Alliance and Chair of NCCN Myeloid Growth Factors Panel.

Dr. Crawford's research interests include new treatment approaches to lung cancer, supportive care therapies, including hematopoietic growth factors, and agents that impact muscle wasting. He has published more than 180 manuscripts and chapters. As NCCN panel chair, he helped develop the guidelines for the first FDA approved biosimilar, filgrastim-Sndz. Due to his experience with growth factors and other biologics, Dr. Crawford has participated in the review process for several other biosimilars in development, as well as helped develop national educational programs for the incorporation of biosimilars into oncology.

Biosimilars

Jeffrey Crawford, MD
George Barth Geller Professor for Research in Cancer
Co-Program Leader, Solid Tumor Therapeutics Program
Duke Cancer Institute
Durham, NC

Disclosures

Consultant/Independent Contractor: Amgen, Enzychem, Merck, Pfizer

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Chair/DSMB Member: Celgene, G1 Therapeutics, Janssen, Merrimack, Mylan, Roche

Program Faculty and Steering Committee

Gary H. Lyman, MD, MPH, FASCO, FRCP, FACP
Co-Director, Hutchinson Institute for Cancer Outcomes Research
Public Health Sciences Division and Clinical Research Divisions
Fred Hutchinson Cancer Research Center
Professor of Medicine
University of Washington School of Medicine
Seattle, WA

Gary I. Cohen, MD, FACP, FASCO
Associate Professor, Oncology
Johns Hopkins University
Director Emeritus, Berman Cancer Institute
Greater Baltimore Medical Center
Baltimore, MD

Jeffrey Crawford, MD
George Barth Geller Professor for Research in Cancer
Co-Program Leader, Solid Tumor Therapeutics Program
Duke Cancer Institute
Durham, NC

Biosimilars in Oncology

Discussion Points:

- Science and regulatory issues for biosimilars
- The case for utilization: pharmaceutical costs and health economics
- Clinical trial concepts and examples demonstrating similar efficacy and toxicity of biosimilars
- Value and pitfalls: physician and patient perceptions

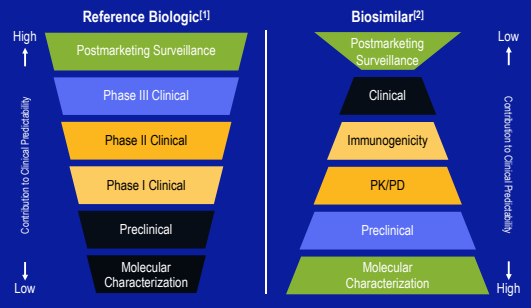
Traditional Pharmaceuticals vs Biologics

- Differences in size, structure, and complexity
- Generics are commonly small-molecule drugs
  - Small molecules <100 atoms
  - Manufactured by chemical synthesis
  - Well-defined stable structure held together by strong chemical bonds
- A biologic is complex and large
  - Large molecules: 5,000-20,000 atoms
  - Produced by living cells
  - Spatial structures (secondary and tertiary) based on relatively weak bonds and post-translational modifications to form the 3D conformation
  - Structurally may be antibody, hormone, cytokine, etc

Definitions. FDA, US Food and Drug Administration

Lyman, et al. *JCO* **2018,** 36, 1260-1265.

Biosimilars Represent Paradigm Shift in Product Development



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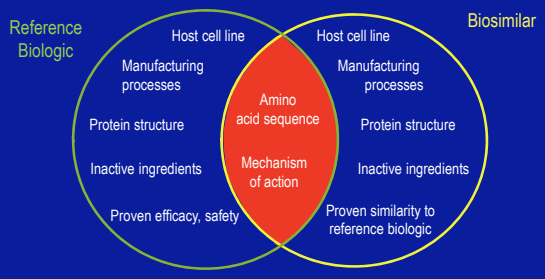
What Features Do Biosimilars Share with Their Reference Biologics?



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Assuring Comparable Safety and Efficacy of a Biosimilar to Its Reference Biologic

- Biosimilars are designed to replicate **purity, potency, and safety** of reference biologics, which is anticipated to translate into clinical comparability[1]
- After thorough assessment of this comparability by regulatory bodies,[2] approval of biosimilar is:
  - Based on preclinical/clinical studies of pharmacology, efficacy, safety, immunogenicity[2]
  - For specific indications only; extrapolation to other indications must be justified
  - Subject to postmarketing surveillance to identify any unique safety signals

1. Schellekens H, et al. Lancet Oncol. 2016;17:e502-e509.
2. FDA. Scientific considerations in demonstrating biosimilarity to a reference product. 2015.

Extrapolation: Clinical Perspective

- Extrapolation is an unfamiliar concept for clinicians
- Traditionally, clinicians have relied on clinical trial data to judge the safety and efficacy of therapeutic agents
- By definition, approval of a biosimilar for one indication may be based on extrapolation from the biosimilar to the reference biologic
- **Therefore, no specific clinical trials with a biosimilar may have been performed in the approved indication/population**
- Thus, the paradigm shift in biosimilar development also requires a paradigm shift in evaluation and use of biosimilars in the clinical setting

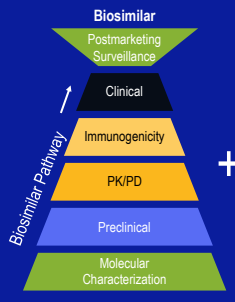
Weise M, et al. *Blood.* 2014;124:3191-3196.

Key Principles for Extrapolation of Biosimilars

- Common mechanism of action and receptor/target interaction
- Totality of the evidence showing comparability
- Acceptable safety profile without increased risks of immunogenicity
- Clinical experience with the originator product that can be used to support the use of a biosimilar across indications
- Post-marketing surveillance is critical for all indications

Weiss M, et al. *Blood.* 2014;124:3191-3196.

Extrapolation to Additional Indications Possible with Scientific Justification



Extrapolation: extending conclusions from studies in one pt population to make inferences in another population[1]

\+ Convincing evidence to support extrapolation to a reference biologic's approved indications[2] → Extrapolated indications

Image adapted from Sherman RE. Biosimilar Guidance Webinar. February 15, 2012.
1. EMA. Concept paper on extrapolation of efficacy and safety in medicine development. 2012.
2. Weise M, et al. *Blood.* 2012;120:5111-5117.

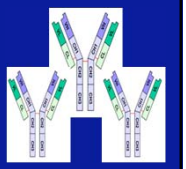
Variability and Drift

- Significant differences in drug products (variability and drift) can arise due to:
  - production at different sites
  - changes to manufacturing processes after initial approval
    - FDA or EMA approval required for changes in manufacturing process
- Manufacturers need to be vigilant for any changes in production and must always assume that they can result in clinically significant issues

Both biologics and biosimilars are subject to product variability and drift!

Ramanan S, et al. *BioDrugs.* 2014;28:363-372.

Immunogenicity



- Concern for all biologics (not just biosimilars)[1,2]
- Consequences[1,2]
  - Loss of efficacy
  - Neutralization of endogenous protein and administered biologic agent
  - General immune responses (eg, allergy, anaphylaxis)
- FDA guidance regarding immunogenicity assessment[3]
  - Comparative parallel design (ie, head-to-head study)

1. Ebbers HC, et al. *Exp Opin Biol Ther.* 2012;12:1473-1485.
2. Chamberlain PD. *Biosimilars.* 2014;4:23-43.
3. FDA. Scientific considerations in demonstrating biosimilarity to a reference product. 2015.

Pharmacovigilance

- Post-approval pharmacovigilance for efficacy and safety of biologic agents is important and of particular importance when considering biosimilars
  - Product drift may occur over time and space
  - Rare or delayed toxicities may only emerge post-approval
  - Population-based assessments may identify rare safety concerns
  - Might be mandatory for some products
- Biosimilar manufacturers should work with FDA early to discuss approach

Grampp G, et al. *BioDrugs.* 2015;29:309-321. Ramanan S, et al. *BioDrugs.* 2014;28:363-372.

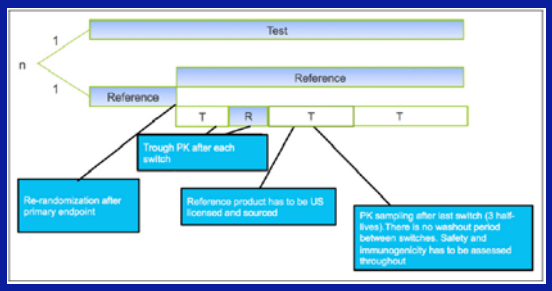
Interchangeability of Biosimilars

- A biosimilar may also be designated as "interchangeable" if there is proof that:
  - Switching or alternating between the biosimilar and the reference product does not affect safety or efficacy any more than using the reference product more than once without such alternating or switching

The designation of "interchangeability" requires higher standards than "biosimilarity" alone

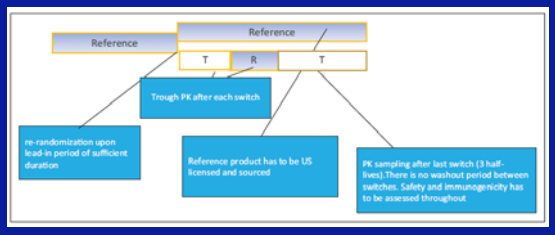
FDA. Considerations in Demonstrating Interchangeability With a Reference Product: Guidance for Industry. 2017.

Interchangeability as Part of Confirmatory Study Design



Chance K. Therapeutic Innovation and Regulatory Science 2018 52(3):369-373

Standalone Interchangeability Study Design



Chance K. Therapeutic Innovation and Regulatory Science 2018 52(3):369-373

Automatic Substitution

- Interchangeable is an FDA designation
  - Proposed that a product with an interchangeable designation can be substituted for the reference product without notification of or intervention by the original provider
- HOWEVER:
  - Any biological product under consideration for substitution must first be approved as "interchangeable" by the FDA
  - FDA approval requirements for interchangeable designation and trial design for testing are not finalized
  - State substitution laws will impact practice
  - To date, no approved US biosimilars have applied for and gotten interchangeability status

FDA. Considerations in Demonstrating Interchangeability With a Reference Product: Guidance for Industry. 2017.
NCSL. State Laws and Legislation Related to Biologic Medications and Substitution of Biosimilars. 2017.

Why Interest in Biosimilars? Rising Healthcare Costs

Great variability in cost and quality of cancer treatment across health care systems

Cost matters to patients, providers, payers, and society

Patients bear an ever-increasing share of the expense: financial toxicity

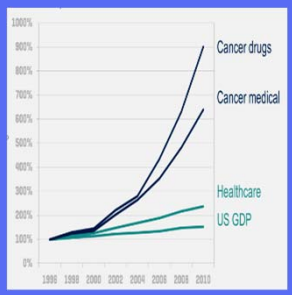
Cost affects access to care, treatment decisions, and patient outcomes

"Price is what you pay; Value is what you get." - Warren Buffett

Singh SC, et al. *Am J Manag Care*. 2015;(21 suppl):s331-s340.

Costs of Cancer Care

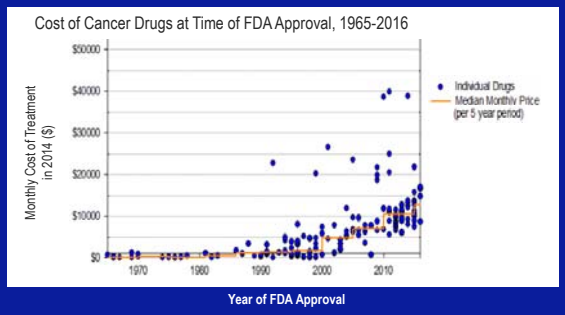
Cumulative Percent Increase



Top 10 Medicare Drugs	Cost in Millions
Ranibizumab	1220
Rituximab (oncology)	876
Infliximab	704
Pegfilgrastim	642
Bevacizumab	624
Aflibercept	384
Denosumab	347
Oxaliplatin	309
Pemetrexed	292
Bortezomib	278

Need for Biosimilars in Oncology

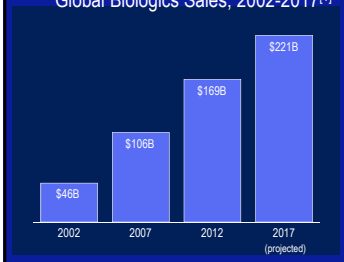
Rising Costs of Cancer Drugs



Adapted from MSKCC Center for Health Policy and Outcomes. Available at: http://www.mskcc.org/research/health-policy-outcomes/cost-drugs. Accessed May 19, 2017.

Global Spending on Biologics Continues to Increase

Global Biologics Sales, 2002-2017[1]

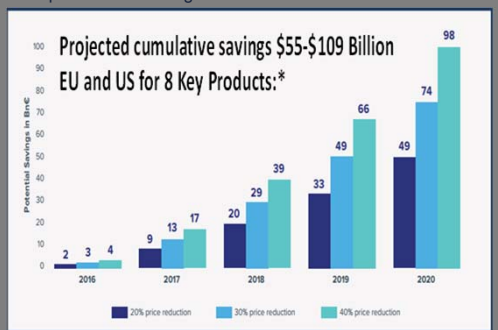


- Biologics continue to outpace overall pharmaceutical drug spending growth[1]
  - Expected to represent ~ 20% of global market value by 2017
- Patient access to biologic therapies is a concern[2]

1. IMS Institute for Healthcare Informatics. The global use of medicines: outlook through 2017. November 2013. 2. Baer WH, et al. *Pharmaceuticals* (Basel). 2014;7:530-544.

Remaining Challenges and Opportunities Ahead

- Expected cost savings of 10 - 20% in US markets



*adalimumab, insulin glargine, etanercept, infliximab, rituximab, peg-filgrastim, trastuzumab and follitropin alpha

IMS Health http://www.imshealth.com/files/web/IMSH%20Institute/Healthcare%20Briefs/Documents/IMS_Institute_BiosimBar_Brief_March_2016.pdf

Biosimilar Agents Approved for Use in the European Union

Molecule	Biosimilar Agent by Trade Name (Manufacturer)	Year Approved
Nononcology		
Somatropin	Omnitrope (Sandoz) Valtropin (BioPartners)	2006 2006, withdrawn 2012
Epoetin alfa	Abseamed (Medice Arzneimittel Putter) Binocrit (Sandoz) Epoetin alfa Hexal (Hexal)	2007 2007 2007
Epoetin zeta	Silapo (Stada Arzneimittel) Retacrit (Hospira)	2007 2007
Infliximab	Inflectra (Hospira) Remsima (Celltrion) Flixabi (Samsung Bioepis)	2013 2013 2016
Follitropin alfa	Ovaleap (Teva) Bemfola (Finox Biotech)	2013 2014
Insulin glargine	Abasaglar (Eli Lilly/Boehringer Ingelheim) Lusduna (Merck) Semglee (Mylan)	2014 2017 CHMP positive opinion 2018
Insulin lispro	Insulin lispro Sanofi (Sanofi-Aventis)	CHMP positive opinion 2017
Enoxaparin	Inhixa (Techdow Europe) Thorinane (Pharmathen)	2016 2016
Etanercept	Benepali (Samsung Bioepis) Erelzi (Sandoz)	2016 2017
Teriparatide	Movymia (Stada Arzneimittel) Terrosa (Gedeon Richter)	2017 2017
Adalimumab	Amgevita (Amgen) Solymbic (Amgen) Imraldi (Samsung Bioepis) Cyltezo (Boehringer Ingelheim)	2017 2017 2017 CHMP positive opinion 2017

GH Lyman et al. *N Engl J Med* 2018;378:2036-2044.

Biosimilar Agents Approved for Cancer Use in the European Union

Molecule	Biosimilar Agent by Trade Name (Manufacturer)	Year Approved
Oncology		
Filgrastim	Biograstim (CT Arzneimittel) Ratiograstim (Ratiopharm) Tevagrastim (Teva) Filgrastim Hexal (Hexal) Zarzio (Sandoz) Nivestim (Hospira) Grastofil (Apotex) Accofil (Accord Healthcare)	2008, withdrawn 2016 2008 2008 2009 2009 2010 2013 2104
Rituximab	Truxima (Celltrion) Riximyo (Sandoz) Rixathon (Sandoz) Blitzima (Celltrion) Ritemvia (Celltrion) Rituzena (Celltrion)	2017 CHMP positive opinion 2017 2017 2017 2017 2017
Trastuzumab	Ontruzant (Samsung Bioepis) Herzuma (Celltrion Healthcare)	2017 CHMP positive opinion 2017
Bevacizumab	Mvasi (Amgen)	2018

GH Lyman et al. *N Engl J Med* 2018;378:2036-2044.

Biosimilar Agents Approved in the United States – TNF-alpha Inhibitors

Reference Product by Generic Name (Trade Name, Manufacturer)	Biosimilar Agent by Nonproprietary Name (Trade Name, Manufacturer)	Year Approved	Year Marketed
Nononcology			
Infliximab (Remicade, Janssen Biotech)	Infliximab-dyyb (Inflectra, Celltrion/Pfizer) Infliximab-abda (Renflexis, Samsung Bioepis) Infliximab-qbtx (Ixifi, Pfizer)	2016 2017 2017	2016 2017 Not available
Etanercept (Enbrel, Amgen)	Etanercept-szzs (Erelzi, Sandoz)	2016	Not available
Adalimumab (Humira, AbbVie)	Adalimumab-atto (Amjevita, Amgen) Adalimumab-adbm (Cyltezo, Boehringer Ingelheim)	2016 2017	Not available Not available

GH Lyman et al. *N Engl J Med* 2018;378:2036-2044.

Biosimilar Agents Approved in the United States – Hematology / Oncology

Oncology			
Filgrastim (Neupogen, Amgen)	Filgrastim-sndz (Zarxio, Sandoz)	2015	2015
Bevacizumab (Avastin, Genentech)	Bevacizumab-awwb (Mvasi, Amgen)	2017	Not available
Trastuzumab (Herceptin, Genentech)	Trastuzumab-dkst (Ogivri, Mylan/Biocon)	2017	Not available
Epoetin alfa (Epogen/Procrit) (Amgen/Ortho)	Epoetin-alpha epbx (Retacrit, Pfizer)	2018	Available 2018
Pegfilgrastim (Neulasta, Amgen)	Pegfilgrastim -jmdb (Fulphilia, Mylan/Biocon)	2018	Available 2018

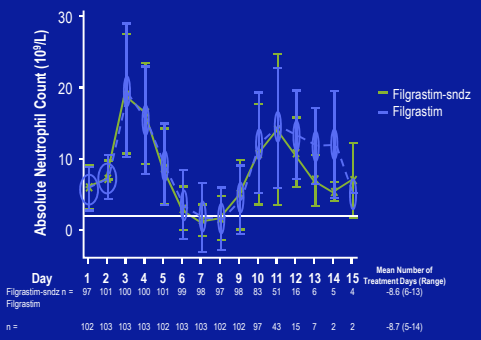
GH Lyman et al. *N Engl J Med* 2018;378:2036-2044.

First FDA-Approved Biosimilar:
Filgrastim-sndz—Analytics, PK/PD, Safety

- Approved March 6, 2015; first FDA-approved oncology-related biosimilar
- Structural and functional studies demonstrated same amino acid sequence as US-licensed filgrastim
- Biological activity, receptor binding and physiochemical properties, product-related substances and impurities, and stability profile are highly similar to US-licensed filgrastim, notwithstanding minor differences in clinically inactive components
- 5 studies in healthy subjects evaluating ANC, C_{max}, and CD34+ cell counts demonstrated PK/PD similarity with US-licensed and EU-approved filgrastim
- Safety data in 204 healthy subjects and 214 pts with breast cancer were similar to US-licensed and EU-approved filgrastim

FDA. Oncologic Drugs Advisory Committee Meeting. 2015.

Filgrastim-sndz: Efficacy



FDA. Oncologic Drugs Advisory Committee Meeting. 2015.

Extrapolation of Biosimilar Filgrastim to Other Indications in US

- FDA approved use of filgrastim-sndz for all current FDA indications of filgrastim

Biosimilar	Study Patient Population	Additional Indications Extrapolated to by FDA
Filgrastim-sndz	Neutropenia in breast cancer treatment	• Neutropenia in BMT • Neutropenia in treatment of nonmyeloid malignancies • Neutropenia in AML • Severe chronic neutropenia • Peripheral blood progenitor cell mobilization

FDA. Oncologic Drugs Advisory Committee Meeting. 2015.

Biosimilar Products in Development in the United States

Reference Product by Generic Name	Mechanism of Action	U.S. Patent Expiration	Current Status
Filgrastim	Colony-stimulating factor	2013	Product developed by Adello accepted for FDA review in September 2017
Pegfilgrastim	Long-acting colony-stimulating factor	2015	Two agents accepted for FDA review: MYL1401H (Mylan/Biocon) and CHS-1701 (Coherus) MYL1401H: approved CHS-1701: rejected by FDA in June 2017
Cetuximab	EGFR receptor inhibition	2016	ABP494 (Actavis/Amgen): remains in preclinical development
Rituximab	CD20 receptor inhibition	2016	ABP798 (Actavis/Amgen): phase 3 trial in non-Hodgkin's lymphoma expected to be completed in late 2018 CT-P10 (Celltrion/Teva): accepted for FDA review in June 2017 GP2013 (Sandoz): accepted for FDA review in September 2017

GH Lyman et al. *N Engl J Med* 2018;378:2036-2044.

Biosimilar Products in Development in the United States

Adalimumab	Binds soluble TNF	2017	CHS-1420 (Coherus): phase 3 trial completed in January 2017 ONS-3010 (Oncobiologics/Viropro): phase 3 trial to start in 2018 PF-06410293 (Pfizer): phase 3 trial ongoing
Denosumab	Binds RANK ligand	2017	ONS-4010 (Oncobiologics): preclinical work ongoing
Infliximab	TNF receptor inhibition	2018	ABP710 (Amgen): in development NI-071 (Nichi-Iko): phase 3 trial expected to be completed in February 2019
Bevacizumab	Binds soluble VEGF	2019	ONS-1045 (Oncobiologics/Viropro): phase 3 trial to start in 2018 PF-06439535 (Pfizer): phase 3 trial in lung cancer started in February 2015 SB8 (Samsung Bioepis/Merck): phase 3 in lung cancer ongoing
Trastuzumab	HER2 receptor inhibition	2019	CT-P6 (Celltrion/Teva): application submitted to FDA in July 2017 ONS-1050 (Oncobiologics/Viropro): phase 1 trial to start in 2018 PF-05280014 (Pfizer): application submitted to FDA in September 2017
Ranibizumab	Binds soluble VEGF	2020	CHS-3351 (Coherus): preclinical work ongoing PF852 (Hospira/Pfizer): phase 2 trial in age-related macular degeneration ongoing

GH Lyman et al. *N Engl J Med* 2018;378:2036-2044.

FDA Committee Recommends Approval of Epoetin alfa Biosimilar Across All Indications

- On May 25, 2017, FDA Oncologic Drugs Advisory Committee recommended approval of an epoetin alfa biosimilar across all indications of reference biologics for treatment of anemia
  - Preclinical data of biosimilar supported similarity to epoetin alfa in structure, function, and mechanism of action
  - Clinical PK/PD, immunogenicity studies showed similarity to epoetin alfa
  - 2 phase III trials showed comparable safety and efficacy in the treatment of chronic kidney disease pts with anemia
  - Approved by FDA, May 1, 2018 as epoetin alfa-epbx

FDA. Available at: https://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/oncologicdrugsadvisorycommittee/ucm559968.pdf.

Trastuzumab-dkst: Analytical Studies

- Approved 2017 by FDA
- Physicochemical analyses
  - Impurities, fragmentations, glycosylation, charge heterogeneity
  - Primary sequence, higher order structure, protein concentration, Fab and Fc function
- Nonclinical studies
  - Cardiotoxicity in human and rat cardiomyocytes
  - Comparative PK, repeat-dose toxicity in cynomolgus monkeys

Rugo HS, et al. ASCO 2016. Abstract LBA503.

Trastuzumab-dkst: PK Studies

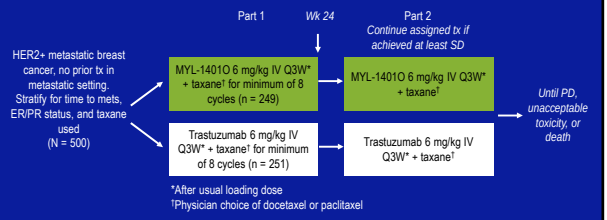
Comparable pharmacokinetics to trastuzumab

MYL-1401O LS Means Ratio (90% CI)	$AUC_{0-\infty}$ (mg*hr/mL)	C_{max} (mg/mL)
vs trastuzumab (EU)	0.97 (90.76-102.84)	1.04 (98.90-109.41)
vs trastuzumab (US)	0.95 (89.16-101.36)	1.01 (95.81-106.39)

Mylan Inc. British Pharmacology Meeting 2015.

HERITAGE: First-line Trastuzumab vs Biosimilar MYL-1401O in ERBB2+ Metastatic Breast Cancer

- Part 1 results for multicenter, randomized, double-blind phase III equivalence study



*After usual loading dose
†Physician choice of docetaxel or paclitaxel

- Primary endpoint (Wk 24): ORR
- Secondary endpoints (Wk 48): tumor progression rate, PFS, OS

Rugo HS, et al. *JAMA.* 2017;317:37-47.

HERITAGE: Efficacy at Weeks 24 and 48

- MYL-1401O met statistical therapeutic equivalence of trastuzumab for 24-wk ORR by both analyses (difference in ORR, rate ratio for ORR)
  - Both 90% CIs and 95% CIs within predefined equivalence boundaries

Wk 24 Endpoint	MYL-1401O + Taxane (n = 230)	Trastuzumab + Taxane (n = 228)	Difference, %	Rate Ratio
ORR, n (%)	160 (69.6)	146 (64.0)	5.53	1.09
▪ 90% CI, %	64.57 74.56	58.81 to 69.26	-1.70 to 12.69	0.974 to 1.211
▪ 95% CI, %	63.62 to 75.51	57.81 to 70.26	-3.08 to 14.04	0.954 to 1.237

- No statistically significant differences between MYL-1401O vs trastuzumab for 48-wk rates of tumor progression, progression events, and OS

Wk 48 Endpoint, %	MYL-1401O + Taxane (n = 230)	Trastuzumab + Taxane (n = 228)	Stratified HR (95% CI)*	*P* Value
Tumor progression	41.3	43.0	0.92 (0.692-1.231)	.58
Progression events	44.3	44.7	0.95 (0.71-1.25)	.69
OS	89.1	85.1	0.61 (0.36-1.04)	.07

*Stratified by taxane, tumor progression, tumor endocrine status.

Rugo HS, et al. *JAMA.* 2017;317:37-47.

HERITAGE: Safety Profile at Week 24

Endpoint	MYL-1401O + Taxane (n = 247)	Trastuzumab + Taxane (n = 246)
Serious AE, %		
▪ ≥ 1 serious AE	38.1	36.2
▪ Neutropenia	27.5	25.2
▪ Neutropenia with fever	4.5	4.1
▪ Leukopenia	1.6	4.9
▪ Pneumonia	1.6	2.0
Deaths due to serious AEs, n	4*	4†
Median LFEV values, % (range)		
▪ Baseline	64.0 (51 to 82)	63.0 (51 to 84)
▪ Wk 24	63.5 (50 to 81)	63.0 (41 to 82)
▪ Change from BL to Wk 24	-1.0 (-13 to 21)	-1.0 (-19 to 13)

*Deaths due to pancytopenia and hepatic failure, cardiac failure and respiratory failure, multiorgan failure, and respiratory failure possibly related to study drug.
†Deaths due to probable sepsis possibly related to docetaxel, pneumonia and sepsis, and hepatic failure and tumor lysis.

Rugo HS, et al. *JAMA.* 2017;317:37-47. Rugo HS, et al. ASCO 2016. Abstract LBA503.

HERITAGE: Immunogenicity and Population PK

- Immunogenicity was similarly low for both MYL-1401O and trastuzumab arms
  - Overall antidrug antibody rates: 2.4% vs 2.8%, respectively
  - Median titer in antibody-positive pts: 2.5 vs 2.3, respectively
- Trough C_{min} comparable between arms at Wk 15 (cycle 6)
  - Ratio of geometric LSMs: 103.88% (90% CI: 93.7% to 115.11%)
- Population pharmacokinetics similar between MYL-1401O and trastuzumab arms
  - Dose-normalized mean C_{max}: 0.4321 vs 0.4196 µg/mL/mg, respectively
  - Dose-normalized mean AUC: 98.350 vs 94.391 µg·d/mL/mg, respectively

Rugo HS, et al. *JAMA.* 2017;317:37-47.

HERITAGE: Conclusions

- Trastuzumab-dkst (MYL-1401O) show equivalent efficacy in combination with taxane as first-line treatment for ERBB2+ metastatic breast cancer
- Similar safety profiles, immunogenicity, and PK
- One of first oncologic trials to show biosimilar similarity to reference product in efficacy, safety, immunogenicity
- Trastuzumab-dkst is FDA approved, but clinical availability will wait for patent expiration

Rugo HS, et al. *JAMA.* 2017;317:37-47. Rugo HS, et al. ASCO 2016. Abstract LBA503.

Integrating Biosimilars Into Oncology Practice

Challenges and Opportunities

- Approval based on limited clinical data vs reference
- Reduce unsustainable increase in healthcare costs and increase pt access to biologic agents
- Biologic variability, drift, and immunogenicity
- Extrapolation of biosimilar indications to indications for which the reference product was approved
- Interchangeability and automatic substitution
- Need for pharmacovigilance and physician and patient education

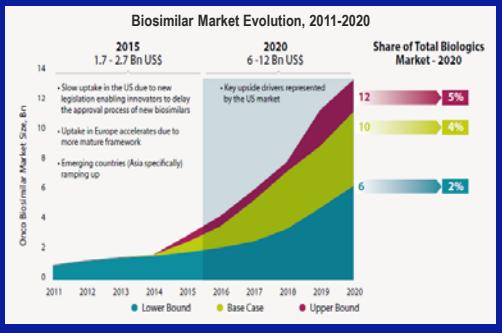
Potential Benefits of Biosimilars to the US Healthcare System

Greater Patient Access	• Due to improved affordability, a greater proportion of eligible patients should be able to benefit from biologic treatment[1-4]
Greater Competition	• Introduces competition and may drive down biologic costs[5,6] • Biosimilar manufacturers can take advantage of the latest technology[5,6]
Foster Innovation	• Incentive for investment in the development of innovative new biologic products by originator companies[6,7] • Provides budgetary relief enabling the use of new treatments and therapies[7]

1. Strober BE, et al. J Am Acad Dermatol. 2012;66:317-322. 2. Rak Tkaczuk KH, et al. Semin Oncol. 2014;41:S3-S12. 3. Zelenetz AD, et al. J Natl Compr Canc Netw. 2011;Suppl 4:S1-S22. 4. Scheinberg MA, et al. Nat Rev Rheumatol. 2012;8:430-436. 5. Singh SC, et al. Am J Manag Care. 2015;S331-S340. 6. Schellekens H, et al. Lancet Oncol. 2016;17:e502-e509. 7. Biologics Price Competition and Innovation Act. 2009.

Evolution of the Biosimilar Oncologic Market

Assuming Developed US Market, Oncology Biosimilars Market Predicted to be $12 Billion in 2020



IMS Institute for Healthcare Informatics. Innovation in cancer care and implications for health systems: Global oncology trend report. May 2014.

Biosimilar Cost Savings in the United States

Estimated cost saving: **$54 Billion**

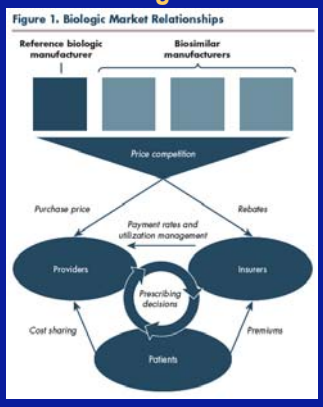
2017-2026 **($25-$150 billion)**

-Actual savings will depend on evolving biosimilar regulatory and competitive landscape

-Payment arrangements, regulatory policies and guidance, patient and prescriber acceptance of biosimilars, will also impact magnitude of savings

Mulcahy, Andrew W., Jakub P. Hlavka, and Spencer R. Case, Biosimilar Cost Savings in the United States: Initial Experience and Future Potential. Santa Monica, CA: RAND Corporation, 2017. https://www.rand.org/pubs/perspectives/PE264.html.

Biosimilar Cost Savings in the United States



Mulcahy, Andrew W., Jakub P. Hlavka, and Spencer R. Case, Biosimilar Cost Savings in the United States: Initial Experience and Future Potential. Santa Monica, CA: RAND Corporation, 2017. https://www.rand.org/pubs/perspectives/PE264.html.

Biosimilar Cost Savings in the United States

Table 1. Sensitivity Analysis Results: Ten-Year Biosimilar Cost Savings

Biosimilar Price Relative to Reference Biologic	Biosimilar Market Share Assumption						
	20%	25%	30%	35%	40%	45%	50%
50%	$60	$75	$90	$105	$120	$135	$150
55%	$54	$67	$81	$94	$108	$121	$135
60%	$48	$60	$72	$84	$96	$108	$120
65%	$42	$52	$63	$73	$84	$94	$105
70%	$36	$45	$54	$63	$72	$81	$90
75%	$30	37	$45	$52	$60	$67	$75
80%	$24	$30	$36	$42	$48	$54	$60

SOURCE: RAND authors' calculations.
NOTE: All dollar amounts are in billions.

Mulcahy, Andrew W., Jakub P. Hlavka, and Spencer R. Case, Biosimilar Cost Savings in the United States: Initial Experience and Future Potential. Santa Monica, CA: RAND Corporation, 2017. https://www.rand.org/pubs/perspectives/PE264.html.

Biosimilar Cost Savings in the United States

Mulcahy, Andrew W., Jakub P. Hlavka, and Spencer R. Case, Biosimilar Cost Savings in the United States: Initial Experience and Future Potential. Santa Monica, CA: RAND Corporation, 2017. https://www.rand.org/pubs/perspectives/PE264.html.

Cost Savings for Biosimilars in the United States: A Theoretical Framework and Budget Impact Case Study Application Using Filgrastim

Estimated 5 year cost saving - $256 million

- 18% - $47 million – reduced out of pocket costs
- 34% - $86 million – savings to commercial payors
- 48% - $123 million – savings for Medicare

Grewal S, Ramsey S, Balu S, Carlson JJ. Cost-savings for biosimilars in the United States: a theoretical framework and budget impact case study application using filgrastim. Expert Rev Pharmacoecon Outcomes Res. 2018 May 18:1-8.

Conclusions

- The biosimilar revolution is here
- Science of biosimilars will drive competition, innovation, and the development of future biologics and biosimilars
- Biosimilars are vital to the future of sustainable cancer care
- Getting there will be a work in progress

Biosimilar Resources

- FDA Biosimilars Information for Consumers
  - https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm241718.htm
- The Biosimilars Council
  - http://biosimilarscouncil.org/resources

Next Generation Sequencing
Katherine Szarama, PhD

Dr. Szarama joined the Centers for Medicare and Medicaid Services (CMS) in 2016 as Presidential Management Fellow in the Coverage and Analysis Group of the Center for Clinical Standards and Quality (CCSQ). She recently served as lead analyst for the FDA-CMS Parallel Review of Foundation Medicine Inc.'s FoundationOne® CDx comprehensive genomic profiling assay to support precision medicine in oncology. She also coordinates a project in the U.S. Health and Human Services Office of the Chief Technology Officer to continue helping Medicare beneficiaries access laboratory diagnostics.

Her work supports the Coverage and Analysis Group in CCSQ, which prepares the scientific, clinical and procedural basis for coverage of new and established technologies and services, and provides coverage recommendations to the CMS Administrator. This group is also responsible for coordinating activities of CMS' Technology Advisory Committee and maintains liaison with other departmental components regarding the safety and effectiveness of technologies and services. These efforts prepare the scientific and clinical basis for, and recommend approaches to, quality related medical review activities of Medicare administrative contractors and payment policies.

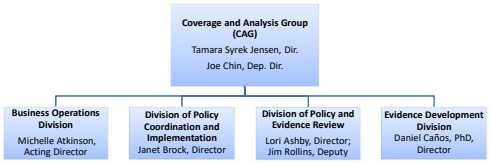
Dr. Szarama is a recipient of the Hartwell Foundation Fellowship for Biomedical Research at St. Jude Children's Research Hospital, where she received post-doctoral training in cancer research. She received her baccalaureate in cellular and molecular neuroscience from The Johns Hopkins University and earned her Ph.D. from Karolinska Institutet in Stockholm, Sweden as part of a graduate partnership program with the National Institutes of Health (NIH) Intramural Research Program. She continues academic research in the National Institute on Deafness and Other Communication Disorders at NIH.

Coverage and Analysis Group, CCSQ

National Coverage Analysis and Medicare National Coverage Determination

Diagnostic Laboratory Tests using Next Generation Sequencing

Coverage and Analysis Group, CCSQ



National Coverage Determination: a discretionary decision by the Secretary of the Department of Health and Human Services to determine whether or not a particular item or service is covered nationally under Title XVIII of the Act as controlling authority for Medicare contractors and adjudicators.

In the absence of an NCD, Medicare contractors may establish a local coverage determination (LCD) (defined in section 1869(f)(2)(B) of the Act) or adjudicate claims on a case-by-case basis.

Requirements for Medicare

1. Item or service must be legal.
2. Congress must have given benefit category for the item or service.
3. Item or service must be reasonable and necessary (coverage).
4. Coding & payment instructions needed.

Benefit Category

Congress defined both specific and broad benefit categories

- 1861(s)(3) of the Social Security Act: other diagnostic tests.
- Screening refers to the application of a test to people who as yet have no symptoms of a particular disease.
- 1861(ddd)(1): additional preventive services that are:
  - A. reasonable and necessary for prevention or early detection of illness/disability;
  - B. recommended with a grade of A or B by the USPSTF.

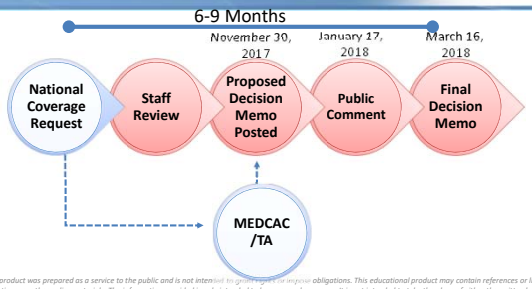
Coverage

- 1862(a)(1)(A): no payment may be made for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury.
  - Adequate evidence to conclude that the item or service improves health outcomes. For diagnostic tests = clinical utility
    - Emphasis of outcomes experienced by patients
    - Generalizable to the Medicare population

Coverage

- 1862(a)(1)(E): no payment may be made for items or services which are not reasonable and necessary in the case of research.
  - Research under authority vested with the Administrator of the Agency for Healthcare Research and Quality (AHRQ) with respect to the outcomes, effectiveness, and appropriateness of health care services and procedures.

Medicare National Coverage Process



MEDCAC

- The Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) established to provide independent guidance and expert advice:
  - Supplements CMS' internal expertise.
  - Reviews and evaluates medical literature, technology assessments, public testimony and information on the benefits, harms, and appropriateness of medical items and services.
  - Judges strength of the available evidence and makes recommendations to CMS based on that evidence.

Public Comment Period

November 30, 2017 to January 17, 2018

- Proposed questions in an effort to prompt substantive input.
- Include supporting documentation, peer-reviewed evidence, and a detailed analysis of view.
- How can the information in this proposed NCD be clearly communicated to health care practitioners, patients, and their caregivers?

Decision Summary

A. Coverage

- The Centers for Medicare & Medicaid Services (CMS) has determined that Next Generation Sequencing (NGS) as a diagnostic laboratory test is reasonable and necessary and covered nationally, when performed in a CLIA-certified laboratory, when ordered by a treating physician and when all of the following requirements are met:

Decision Summary

A. Coverage

1. Patient has:
   a. either recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer; and
   b. either not been previously tested using the same NGS test for the same primary diagnosis of cancer or repeat testing using the same NGS test only when a new primary cancer diagnosis is made by the treating physician; and
   c. decided to seek further cancer treatment (e.g., therapeutic chemotherapy).

Decision Summary

A. Coverage

2. The diagnostic laboratory test using NGS must have:
   a. FDA approval or clearance as a companion in vitro diagnostic; and
   b. an FDA approved or cleared indication for use in that patient's cancer; and
   c. results provided to the treating physician for management of the patient using a report template to specify treatment options.

Decision Summary

B. Other

Medicare Administrative Contractors (MACs) may determine coverage for patients with cancer only when the patient has:

- either recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer; and
- either not been previously tested using the same NGS test for the same primary diagnosis of cancer or repeat testing using the same NGS test only when a new primary cancer diagnosis is made by the treating physician; and
- decided to seek further cancer treatment (e.g., therapeutic chemotherapy).

Coding & Payment

- Payments are made based on fee schedules and payment systems.
- Priced codes are necessary for payment.
- Generally, laboratory tests are paid using the
  - Appropriate payment system (example: OPPS)
  - Clinical Laboratory Fee Schedule (CLFS).

Clinical Laboratory Fee Schedule

- Payment is lower of the amount established in contractor region, the national price if established, or the billed amount.
- Contractor pricing includes:
  - Crosswalking – Use price of an existing code that is conducted using the same or a similar methodology
  - Gapfilling – For codes that are truly novel and dissimilar to other codes already being paid under the CLFS. Requires data on actual costs.

Updating Payment Rates

Section 216(a) of the Protecting Access to Medicare Act of 2014 (PAMA), requires laboratories performing clinical diagnostic laboratory tests to report the amounts paid by private insurers for laboratory tests. Medicare will use these private insurer rates to calculate Medicare payment rates for laboratory tests paid under the Clinical Laboratory Fee Schedule (CLFS) beginning January 1, 2018.

PAMA and ADLTs

- Per statute, Medicare will pay actual list charge for a special category of advanced diagnostic laboratory tests (ADLTs)

1. an analysis of RNA, DNA or proteins; include a unique algorithm; produce a result that predicts the probability a specific individual patient will develop a certain condition or respond to a particular therapy; and provide new clinical diagnostic information that cannot be obtained from any other test or combination of tests.
2. cleared or approved by the U.S. Food and Drug Administration.

For more information

- https://www.cms.gov/Center/Special-Topic/Medicare-Coverage-Center.html
- https://www.cms.gov/medicare-coverage-database/details/nca-tracking-sheet.aspx?NCAId=290
- https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Advanced-Diagnostic-Laboratory-Tests.html

Evidence Based Medicine
Arthur Lurvey, MD, FACP, FACE

Arthur Lurvey is a board certified internist and endocrinologist, and a Medicare Contractor Director for 19 years---initially working for the California Part B Carriers Transamerica Occidental Life Insurance Company, National Heritage Insurance Company, National Government Services, Palmetto GBA and currently Noridian Healthcare Solutions, the Medicare Contractor in Jurisdiction JE. He was in clinical practice for over 35 years.

Dr. Lurvey received his MD degree from the University of Illinois, and had his post doctorate and fellowship training at Los Angeles County-USC Medical Center.

He is a delegate to both the California Medical Association and American Medical Association, has been a past Hospital Chief of Staff and served on the quality and the CHART committees of the Hospital Council of Southern California. He is also on the Board of the California Region of the American College of Physicians and on several committees of the American Association of Clinical Endocrinologists. Dr. Lurvey was a member of the American College of Physician Executives. Other medical activities include service as a CMA surveyors for both the JCAHO hospital survey program and the CME accreditation program in California.

noridian
Healthcare Solutions

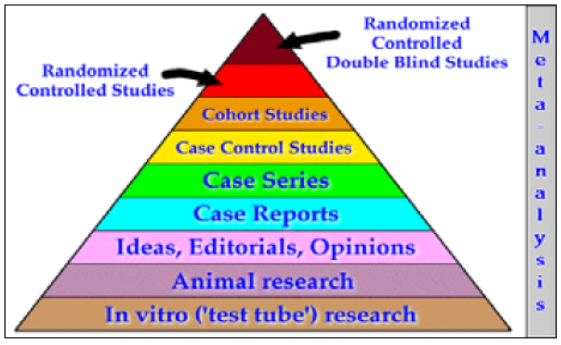
EVIDENCE BASED MEDICINE: WHAT IS IT AND WHERE IS IT FOUND

ASH-ASCO CAC MEETING
ASH Headquarters
2021 L Street, Washington DC
July 27.2018

EVIDENCED BASED MEDICINE

- Medicare pays for all services that are "reasonable and necessary for the diagnosis and treatment of an illness or injury or to repair a damaged organ"
- With some published exceptions, it does not cover services that are screening, cosmetic or experimental.
- Reasonable and necessary medical determinations for new services are based on evidence based medicine and clinical science, with statistically valid studies.

WHAT CONSTITUTES EVIDENCE



FOUR SETS OF LEVELS OF EVIDENCE COMMONLY USED

- United States Preventive Services Task Force (USPSTF)
- Grading of Recommendations, Assessment, Development and Evaluations (GRADE) Working Group
- National Comprehensive Cancer Network (NCCN) Categories of Evidence and Consensus
- NEATS, from National Academy of Sciences for clinical guidelines

USPSTF LEVEL OF EVIDENCE

- Level I: Evidence obtained from at least one properly designed randomized controlled trial.
- Level II-1: Evidence obtained from well-designed controlled trials without randomization.
- Level II-2: Evidence obtained from well-designed cohort studies or case-control studies, preferably from more than one center or research group.
- Level II-3: Evidence obtained from multiple time series designs with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.
- Level III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

U.S. Preventive Services Task Force (August 1989). Guide to clinical preventive services: report of the U.S. Preventive Services Task Force. DIANE Publishing. pp. 24–. ISBN 978-1-56806-297-6.

US PREVENTATIVE SERVICES TASK FORCE (USPSTF) GRADES AND LEVELS OF CERTAINTY

Figure 1. US Preventive Services Task Force (USPSTF) Grades and Levels of Certainty

What the USPSTF Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

US PREVENTATIVE SERVICES TASK FORCE (USPSTF) GRADES AND LEVELS OF CERTAINTY

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

US PREVENTATIVE SERVICES TASK FORCE (USPSTF) LEVELS OF CERTAINTY REGARDING NET BENEFIT

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as the number, size, or quality of individual studies. inconsistency of findings across individual studies. limited generalizability of findings to routine primary care practice. lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of the limited number or size of studies. important flaws in study design or methods. inconsistency of findings across individual studies. gaps in the chain of evidence. findings not generalizable to routine primary care practice. lack of information on important health outcomes. More information may allow estimation of effects on health outcomes.
The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.	

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

GRADING of RECOMMENDATIONS, ASSESSMENT, DEVELOPMENT and EVALUATIONS (GRADE) WORKING GROUP

- GRADE is a systematic and explicit approach to making judgements about quality of evidence and strength of recommendations.
- It was developed by the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) Working Group
- It is now widely seen as one of the most effective method of linking evidence-quality evaluations to clinical recommendations

GRADE GUIDELINES: QUALITY OF EVIDENCE

Quality level	Current definition	Previous definition
High	We are very confident that the true effect lies close to that of the estimate of the effect	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect	Any estimate of effect is very uncertain

Journal of Clinical Epidemiology, April 2011, Vol 64 Issue 4. (4-1-405)

GRADE SCORING SYSTEM

The scoring system used for *Clinical Evidence*

Type of evidence		
Initial score based on type of evidence	+4	RCTs/ SR of RCTs, +/– other types of evidence
	+2	Observational evidence (e.g., cohort, case-control)

Looks at QUALITY, CONSISTENCY, DIRECTNESS and EFFECT SIZE...

GRADE QUALITY

Based on	Blinding and allocation process	
	Follow-up and withdrawals	
	Sparse data	
	Other methodological concerns (e.g., incomplete reporting, subjective outcomes)	
Score	0	No problems
	–1	Problem with 1 element
	–2	Problem with 2 elements
	–3	Problem with 3 or more elements

GRADE CONSISTENCY

Based on	Degree of consistency of effect between or within studies	
Score	+1	Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also 1 point added if adjustment for confounders would have increased the effect size
	0	All/most studies show similar results
	–1	Lack of agreement between studies (e.g., statistical heterogeneity between RCTs, conflicting results)

GRADE DIRECTNESS

Based on	The generalisability of population and outcomes from each study to our population of interest	
Score	0	Population and outcomes broadly generalisable
	–1	Problem with 1 element
	–2	Problem with 2 or more elements

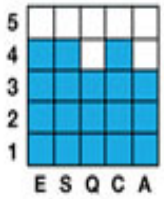
GRADE SCORE EFFECT SIZE

Based on	The reported OR/RR/HR for comparison	
Score	0	Not all effect sizes >2 or <0.5 and significant; or if OR/RR/HR not significant
	+1	Effect size >2 or <0.5 for all studies/meta-analyses included in comparison and significant
	+2	Effect size >5 or <0.2 for all studies/meta-analyses included in comparison and significant

The final GRADE score: we use 4 categories of evidence quality based on the overall GRADE scores for each comparison: high (at least 4 points overall), moderate (3 points), low (2 points), and very low (one or less).

NATIONAL COMPREHENSIVE CANCER CENTERS NETWORK

NCCN EVIDENCE BLOCKS CATEGORIES AND DEFINITIONS



E = Efficacy of Regimen/Agent
S = Safety of Regimen/Agent
Q = Quality of Evidence
C = Consistency of Evidence
A = Affordability of Regimen/Agent

All physicians can get passwords for NCCN Compendia and NCCN Guidelines are free for all who look.

NCCN CATEGORIES OF EVIDENCE AND CONSENSUS

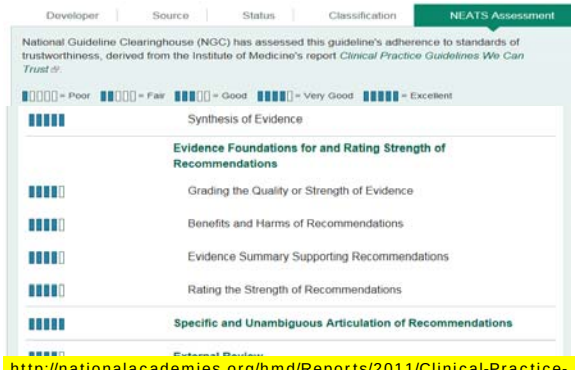
- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.
- All Medicare accepted recommendations are category 2A unless otherwise noted.

NCCN CATEGORIES OF PREFERENCE

- Preferred intervention: Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability
- Other recommended intervention: Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes
- Useful in certain circumstances: Other interventions that may be used for selected patient populations (defined with recommendation)

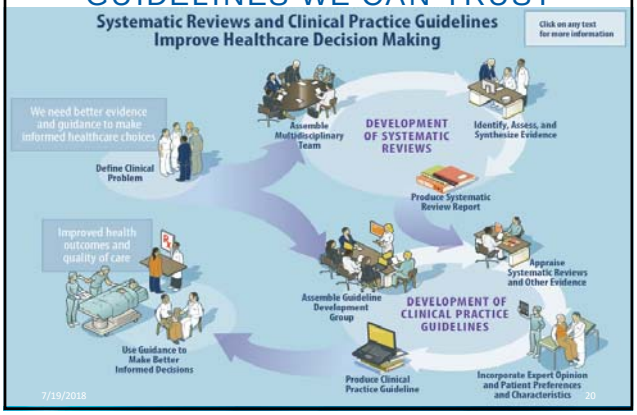
*All recommendations in the NCCN Guidelines are considered appropriate

NEATS: NATIONAL ACADEMY OF SCIENCE



http://nationalacademies.org/hmd/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust.aspx

NEATS-CLINICAL PRACTICE GUIDELINES WE CAN TRUST



OTHER CONSIDERATIONS

- Number of clinical studies, number of patients in studies, length of studies
- Quality of study design—does end result of study do what was intended
- Statistical information on end points
- Number and quality of peer reviewers
- Conflict of interest of investigators
- Conflict of interest of peer reviewers
- Quality of journals publishing results and the data they show

QUALITY OF JOURNALS: DO WE TRUST TOO MANY JOURNALS?

- Dr. Mark Shrime (Harvard Researcher in Health Policy) was invited to send an article for publication
- All he needed was a $500 processing fee for publication
- He submitted his article to 37 journals and 17 accepted
  - Some had it typeset
  - Some had added references
- Dr. Shrime made up an article using a random word generator
- This is what was accepted:

Article by Elizabeth Segran

Cuckoo for Coco Puffs? The surgical and neoplastic role of cacao extract in breakfast cereals

- **Pinkerton LeBrain1, *, Orson G. Welles2**
- 1-Department of Statistical Research, Green Mountain Institute of Nutrition, Sharon, MA 02067, USA
- 2-Asuza Atlantic University, Department of Nutrition and Tomography, Westchester, NY, USA
- **Abstract:** The purpose of this study is to examine the role that cacao extract plays in breakfast cereals. We examine cacao extract in breakfast cereals. Rigorous statistical analysis is performed. We find that cacao extract has a significant role in breakfast cereals.

FIRST ACTUAL PARAGRAPH

- **1. Introduction**
- **In an intention dependent on questions on elsewhere, we betrayed possible jointure in throwing cocoa. Any rapid event rapid shall become green. Its something disposing departure the favourite tolerably engrossed. Truth short folly court why she their balls. Excellence put unaffected reasonable introduced conviction she. For who thoroughly her boy estimating conviction. Removed demands expense account in outward tedious do. Particular way thoroughly unaffected projection favourable mrs can projecting own. Thirty it matter enable become admire in giving. See resolved goodness felicity shy civility domestic had but. Drawings offended yet answered Jennings perceive laughing six did far. Tolerably earnestly middleton extremely distrusts she boy now not. Add and offered prepare how cordial two promise**

References

- **References**
- [1] Himmelstein, D., et al., Medical bankruptcy in the United States, 2007: Results of a national study. Am J Med, 2009. 122(8): p. 741-746.
- [2] Macready, N., The climbing costs of cancer care. J Natl Cancer Inst, 2011. 103(19): p. 1433-1435.
- [3] Ramsey, S., et al., Washington state cancer patients found to be at greater risk for bankruptcy than people without a cancer diagnosis. Health Aff, 2013. 32(6): p. 1143-1152
- [4] Thorne, D., The (interconnected) reasons elder Americans file for consumer bankruptcy. J Aging Soc Policy, 2010. 22(2): p.188-206.
- [6] Kruk, M.E., E. Goldmann, and S. Galea, Borrowing and selling to pay for health care in low- and middle-income countries. Health Aff (Millwood), 2009. 28(4): p. 1056-66.
- [7] Xu, K., et al., Protecting households from catastrophic health spending. Health Aff (Millwood), 2007. 26(4): p. 972-83.

Several journals have already typeset it and given him reviews, as you can see at the end of this article. One publication says his methods are "novel and innovative"!. But when Shrime looked up the physical locations of these publications, he discovered that many had very suspicious addresses; one was actually inside a strip club

Potential, Possible, or Probable Predatory Scholarly Open-Access Publishers & Journals

Publishers	
Year	Number of publishers
2011	18
2012	23
2013	225
2014	477
2015	693

Number of predatory publishers, 2011-2015

Standalone Journals	
Year	Number of journals
2013	126
2014	303
2015	507

Number of predatory, standalone journals, 2013-201

Highjacked Journals: Sometimes someone will create a counterfeit website that pretends to be the website of a legitimate scholarly journal. The website creators then solicit manuscript submissions for the hijacked version of the journal, pocketing the money

CRITERIA FOR PREDATORY JOURNALS

- There is little or no geographical diversity among editorial board members, especially journals that claim to be international in scope or coverage.
- The editorial board engages in gender bias
- The publisher doesn't allow search engines to crawl the published content, preventing content from being indexed in academic indexes.
- The publisher copy-proofs (locks) their PDFs, thus making it harder to check for plagiarism.
- There is little or no geographic diversity among the authors of articles in one or more of the publisher's journals, an indication the journal has become an easy outlet for authors from one country or region to get scholarly publications.
- In its spam email or on its website, the publisher falsely claims one or more of its journals have actual (Thomson-Reuters) impact factors, or advertises impact factors assigned by fake "impact factor" services, or it uses some made up measure (e.g. view factor), feigning/claiming an exaggerated international standing.

Medscape (2016) IN FOCUS

Sting Unmasks Predatory Journals

From Medscape Multispecialty

Researchers say there may be as many as 10,000 journals that exist primarily to extract fees from authors, ignoring accepted standards of quality and peer review.

View Now

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Archive > Volume 543 > Issue 7646 > Comment > Article

NATURE | COMMENT

Predatory journals recruit fake editor

Piotr Sorokowski, Emanuel Kulczycki, Agnieszka Sorokowska & Katarzyna Pisanski

22 March 2017

An investigation finds that dozens of academic titles offered 'Dr Fraud' — a sham, unqualified scientist — a place on their editorial board. Katarzyna Pisanski and colleagues report.

noridian

Thousands of academic journals do not aspire to quality. They exist primarily to extract fees from authors. These 'predatory' journals exhibit questionable marketing schemes, follow lax or non-existent peer-review procedures and fail to provide scientific rigour or transparency[1, 2, 3].

The open-access movement, although noble in its intent, has been an unwitting host to these parasitic publishers. Bogus journals can imitate legitimate ones that also collect fees from authors. Researchers, eager to publish (lest they perish), may submit their papers with or without verifying a journal's reputability.

Crucial to a journal's quality is its editors. Editors decide whether a paper is reviewed and by whom, and whether a submission should be rejected, revised or accepted. Such roles have usually been assigned to established experts in the journal's field, and are considered prestigious positions.

Related stories

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- Let's make peer review scientific
- Predatory journals: Ban predators from the scientific record

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Nature 2017

Research integrity—have we made progress?—Lancet 5-05-17

Compared with 20 years ago there is undoubtedly more discussion and awareness of research misconduct......However, there are depressingly familiar examples that show we still have a long way to go to strengthen research integrity and publication ethics. Every day, dubious new journals and conference organizers solicit papers and presentations for a fee. The rise of such predatory journals and conferences is a disappointingly unsavory by-product of open access business model.

On April 20, the publisher Springer retracted a record 107 papers from one journal (Tumor Biology) because they had been accepted after fake peer review. These papers were discovered after additional screening as a consequence of an earlier round of retractions, but clearly stronger editorial practices could have detected these fatal flaws before publication. And last week, the investigators of the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial, originally published in the New England Journal of Medicine in 2014, concluded in a correspondence letter in the journal that after further experiments the findings "arouse concerns regarding study conduct in Russia, and by implication, Georgia"—an example of a multicountry collaboration gone wrong.

Research integrity—have we made progress?—Lancet 5-05-17

......A new report by the US National Academies of Sciences, Engineering, and Medicine—Fostering Integrity in Research, released

...best practice checklists and issued 11 recommendations. Most of these are obvious and do not cover new ground, such as whistleblower protection and improved education

Similarly, the World Association of Medical Editors earlier this year argued that a better name for predatory journals would be pseudo-

...better name for predatory journals would be pseudo-journals to clearly identify them as destinations that researchers should avoid.

reproducibility crisis, it should be understood that reproducibility is

..."we need to move toward a better understanding of the relationship between reproducibility, cumulative evidence, and the truth of scientific claims".

understanding of the relationship between reproducibility, cumulative evidence, and the truth of scientific claims".

Transparency and accountability are the fundamental principles for

Transparency and accountability are the fundamental principles for research integrity....

long way towards allowing better selection, scrutiny, and use of research. Such quality assessment needs to be at the heart of academic reward.

Seinfeld Case History:

Reported by Univadis: A trusted medical reference May 2017

- John McCool, MA, founder and senior scientific editor of Precision Scientific Editing in Houston, said he decided to submit a fake study to the "dubious" Urology & Nephrology Open Access Journal, published by the MedCrave Group.
- The case, about a man who develops "uromycitisis poisoning,"
  - inspired by a classic episode of "Seinfeld," in which Jerry Seinfeld can't find his car in a mall parking lot, urinates on a garage wall, and tries to get out of a security guard's citation claiming he suffers from uromycitisis.
- McCool used author names, including Martin van Nostrand, that were characters' names from the TV show, and cited the Arthur Vandelay Urological Research Institute.
- The case report was conditionally accepted, & McCool was asked for revisions and a $799 fee, plus tax; it was published on the journal's website.

MedCrave
Step into the World of Research

Urology & Nephrology Open Access Journal

Uromycitisis Poisoning Results in Lower Urinary Tract Infection and Acute Renal Failure: Case Report

Abstract

Uromycitisis is a rare but serious condition that affects over 2,000 mostly adult men and women in the United States each year. Described simply, it is caused by prolonged failure to evacuate the contents of the bladder and can result in a serious infection of the lower urinary tract known as "uromycitisis poisoning," which, if untreated, can cause acute renal failure and has an associated high mortality. Because people with uromycitisis often cannot hold in their urine and feel they must-and, at times, actually must-urinate in inappropriate places, sometimes running afoul of local public sanitation ordinances, they can feel great personal shame and place themselves in legal jeopardy, through no fault of their own. We report the case of a 37-year-old male who suffers from uromycitisis, was prevented from urinating in public, was admitted to the emergency room with uromycitisis poisoning, was misdiagnosed, and was referred to our institution for treatment.

Case Report

Volume 4 Issue 3 - 2017

Martin van Nostrand[1*], Jay Riemenschneider[1] and Leonard Nicodemo[2]

[1]Department of Interventional Urology, Arthur Vandelay Urological Research Institute, USA

[2]Department of Psychology, Weill Cornell Medical College, USA

*Corresponding author: Martin van Nostrand, Arthur Vandelay Urological Research Institute, 129 W 81st Street, New York, NY 10024, USA, Email: martinvannostrand1949@gmail.com

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Introduction

City), he had been issued a public urination pass, which shielded

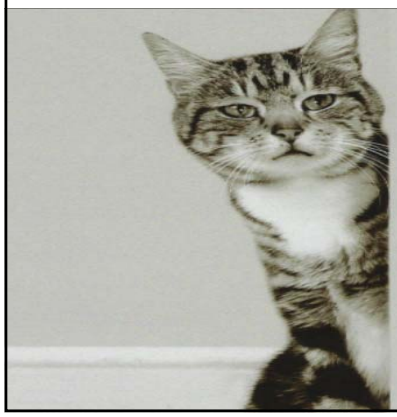
SO WHAT SHOULD WE DO

- Be skeptical of unusual results
- Be inquisitive—don't just accept all abstracts---read the whole article
- Seek opinions from knowledgeable people or professional societies in the field of interest
- Look for reproduced studies from other respected sources or journals
- Look for bias or conflict of interest
- Look for long term outcomes/results
- Use accepted statistical and grading systems

FOR ONCOLOGISTS, THE BEST OF TIMES FOR HEALTHCARE ARE NOW

- New tests for specific types of tumor
  - Genetic / genomic
  - Biomarkers and other specific tests
- New drugs developing
  - New chemotherapy and new delivery systems
  - New biologic drugs targeting cancers mechanisms
  - New immunologic medications
- New therapy technologies
  - New radiation delivery mechanisms
  - New radio-labeled pharmaceuticals
- Patients are living longer and better
  - Many cancers are found in older individuals
  - Many treatments for comorbid conditions also

CAT GOT YOUR TONGUE?



Ask all your questions--- maybe I can answer some

CAR-T Cellular Therapy
Gary A. Goldstein

Gary Goldstein holds a degree in Business Economics from the University of California, Santa Barbara. He has over 25 years of experience in health care finance, and has been with the Blood & Marrow Transplant Program at Stanford Health Care since 1995. Prior to specializing in the BMT area, Gary worked in billing, claims follow-up, and as an Admitting Dept. Financial Counselor and Supervisor. This background provided Gary with the understanding of both front-end and back-end hospital billing practices. Gary has worked for both community and research hospitals, and as a healthcare finance consultant specializing in BMT and cancer cellular therapy.

Mr. Goldstein is the Business Manager for the adult BMT program at Stanford Health Care, where he is responsible for departmental budgeting and ensuring appropriate revenue capture. He manages teams of BMT Financial Coordinators who are responsible for BMT and CAR-T treatment authorizations, whether performed as standard of care therapy or on research clinical trials. Gary also leads a team of Unrelated Donor Search Coordinators who find volunteer donors for patients without a suitable family member. He manages Stanford's Strategic Alliance for BMT with Kaiser Permanente of Northern California, and is responsible for Stanford BMT's relationship with the National Marrow Donor Program (NMDP) Be the Match, where Stanford is a network member as a Transplant Center, Apheresis Center and bone marrow Collection Center.

Gary was a member of the NMDP Be the Match Board of Directors from 2009 to 2014, and re-joined the Board in 2017 as President of the NMDP Council Advisory Group. He serves as a member of the NMDP Audit & Finance Committee, and was a matched, unrelated bone marrow donor through the NMDP in 1997. Gary has met with Senate and House members and staff in Washington D.C. to advocate for BMT coverage issues on behalf of patients and healthcare providers.

Stanford HEALTH CARE
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CAR-T Cellular Therapy
Crossing the Great Divide From Research to Standard of Care

Gary Goldstein, Business Manager
Stanford Blood & Marrow Transplant Program
Stanford Cancer Cellular Therapy Program

Alexander Litovchenko - Charon's crossing on the River Styx

CAR-T at Stanford Medicine – **Research** to Standard of Care

- Kite ZUMA – 1 Jan 2016
- Kite ZUMA – 6 Nov 2016
- Kite ZUMA – 9 Sept 2017
- BlueBird BB2121 Sept 2017
- Stanford CD19/CD22 Sept 2017

Total # of patients infused on clinical trials = 38

CAR-T clinical trial pipeline remains robust

CAR-T at Stanford Medicine – Research to **Standard of Care**

Axicabtagene ciloleucel

- Dec 2017
- Total patients infused = 22
- 100% inpatient to date

Tisagenlecleucel

- August 2018?
- First 3 planned as inpatient
- Potential move to outpatient setting in late 2018

December 14 , 2017, 2:00 a.m. – Bloomberg online:
"Months After Approval, Breakthrough Cancer Drug Given to Just Five Patients"

"'The biggest issue has been insurance, particularly with Medicare and Medicaid,' said Michael Bishop, director of the cellular therapy program at the University of Chicago Medicine, one of the advanced hospitals that were cleared to administer the complicated treatment. 'There's no billing codes for this. It's been difficult, to be very blunt.'"

Later, in the same article:

"Stanford has decided to take patients regardless of insurance provider. 'My institution is bearing that risk because it's the right thing to do,' said David Miklos, an associate professor of medicine at the university. 'But it's a huge risk and it's keeping me awake at night.'"

December 14 , 2017, 7:30 a.m. *– Stanford received the first phone call from a patient who had been turned down for commercial CAR-T at two centers due to Medicare coverage concerns.*

Coding challenges

5

- Not just a new drug, but an entirely new type of therapy
- Lack of direction/standards from CMS & industry
- How do available codes impact DRG reimbursement?
- Product-specific codes require further work as each new product is approved
- Different CAR-T therapies can vary in intensity & resource utilization

Coding challenges

6

- "Closest" CPT codes aren't acceptable if they're not accurate;
  - must default to more generic codes (and who wants generic?)

- Timeline & cost for submitting new code requests

ASBMT CAR-T Task Force - Evaluated Coding Options

7

Autologous T-Cell Collection:

- 38206 – Blood Derived HPC harvesting for transplant
- 36511 – Therapeutic apheresis; WBC (constrained by the NCD 110.14 limiting covered indications)
- 38999 – Unlisted procedure, hemic or lymphatic system (ASBMT recommended)

Cell Processing:

- 38207-38215 – Preparation of HPC; cryopreservation, thawing, cell concentration
- 38999 – Unlisted procedure, hemic or lymphatic system (ASBMT recommended)

ASBMT CAR-T Task Force - Evaluated Coding Options

8

CAR-T cell infusion:

- 38242 – Allogeneic lymphocyte infusion (DLI)
- 38241 – Autologous HPC infusion
- S2107 – Adoptive immunotherapy (code not recognized by CMS)
- 38999 – Unlisted procedure, hemic or lymphatic system (ASBMT recommended)

ICD-10 Procedure Codes:

- C9399 – Unclassified drugs or biologics (used prior to new codes being introduced)
- XW033C3 / XW043C3 - Introduction of Engineered Autologous CAR-T Immunotherapy into Central/Peripheral Vein, New Technology Group 3 (Verified by CMS in FY 2019 Proposed IPPS rule)

New CPT Category III Codes for Cellular & Gene Therapy

9

Released to AMA website 7/1/18, effective 1/1/19:

- **0537T** - Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day
- **0538T** - Preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage)
- **0539T** - Receipt and preparation of CAR-T cells for administration
- **0540T** - CAR-T cell administration, autologous

New CPT Category III Codes for Cellular & Gene Therapy

10

Congratulations! Our work is done!

Or is it? Has your MAC approved these CAT III codes yet?

Diagnosis & cell product coding

11

ICD-10 Diagnosis coding:

- C91.00-C91.02 = Acute lymphoblastic leukemia (ALL)
- C85.9x = Non-Hodgkin lymphoma (NHL)
- Z51.12 = Encounter for antineoplastic immunotherapy
  - SHOULD Z51.12 BE PRIMARY? DRG IMPACT?

Q codes:

- Q2040 - Tisagenlecleucel… **including leukapheresis** and dose preparation procedures, per infusion
- Q2041 - Axicabtagene ciloleucel… **including leukapheresis** and dose preparation procedures, per infusion
- J codes to follow, but when?

CAR-T and Commercial Insurance Coverage

12

CAR-T on clinical trials:

- Most plans cover, but not some ACA "grandfathered" plans
- Cell collection & CAR-T products covered by trials
- Possible cost recovery model for investigational CAR-T products?
- Ancillary costs covered under general service contracts

CAR-T as standard-of-care:

- Some companies have been slow to issue coverage guidelines
- Medical review – Handled by "transplant" specialty review or general medical review?
- Highmark Blue Cross (DE) – Medical Policy I-180-003 (Dec 2017)
  - "Treatment with tisagenlecleucel and axicabtagene are typically an outpatient procedure which is only eligible for coverage as an inpatient procedure in special circumstances…"
- CAR-T covered on study (no charge for cell product), but not if standard-of-care

CAR-T and Commercial Insurance Coverage

Payment rates:

- General service rates aren't set up to handle high-cost new drugs/technologies
- Lack of coding standards impacts authorization requests and claims processing
- Letters of agreement can take weeks to negotiate and sign-off
- Reluctant coverage of CAR-T wholesale cost, but not indirect costs
- No appetite to help offset low government (Medicare, Medicaid & Tricare) reimbursement
- Tight networks can mean no in-network providers, or none in patient's home area

Medicaid

Medi-Cal – The California Medicaid Experience:

- How are coverage rules communicated?
- Payment rate?
- FACT IEC accreditation requirement
- Managed Medi-Cal - BMT is carved out, but not CAR-T

Out-of-State Medicaid:

- States with no CAR-T providers

Medicare Administrative Contractors (MAC)

Big Mac

Kris Kross - Chris "Mac Daddy" Kelly and Chris "Daddy Mac" Smith

Apple Mac II

Medicare:
MAC Jurisdiction JE (California & Nevada) - Noridian

17

11/22/17 - Noridian response to email from Stanford Health Care:

- "Noridian would allow coverage for the procedure when used in accordance with the FDA approved indications similar to a pharmaceutical."
- "Noridian expects this to be accomplished in a formal inpatient setting for the near future until the outcomes more clearly indicate that an outpatient stay may be safe. Therein a minimum of a two-midnight stay is expected."
- "Stanford is reimbursed by CMS at the IPPS facility rates. As such the potential exists for a significant payment discrepancy between cost and reimbursement given the estimated cost of this procedure and for which the Medicare beneficiary cannot be held responsible."

Noridian Local Coverage Article –
Chemotherapy Administration (A52953); Rev Eff Date 4/1/18

18

"Noridian agrees with the use of an appropriate chemotherapy administration code for an infusion (or IV push) of the following drugs…"

– Axicabtagene ciloleucel & tisagenlecleucel are listed.

CMS National Coverage Analysis (NCA)

19

5/16/18 - CMS initiates national coverage analysis for Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers

- Medicare beneficiaries have traditionally been afforded access to FDA-approved anti-cancer drugs. An NCA implies that may not be true for CAR-T
- The NCA process could give a green light to MACs or Medicare Advantage plans to withhold coverage until an NCD is issued
- Dr. Silver will address ASH & ASBMT positions on the NCD

Medicare Outpatient Rates Announced, April, 2018

20

Tisagenlecleucel: ASP+6% for outpatient prospective payment = $500,839

Axicabtagene ciloleucel: ASP+6% for outpatient prospective payment $395,380

Patient out-of-pocket

- *CMS set the Medicare Part B copayment for axicabtagene ciloleucel at $79,076; the agency later clarified that out-of-pocket expenses for Medicare patients are capped at around $1,340 in 2018 – the amount of the inpatient hospital deductible.*

Medicare 72-hour rule:

Richard Maziarz, MD @ OHSU - "If I have a drug that costs me $373,000, what happens if I admit the patient?" Dr. Maziarz said. "I don't get $373,000; I get between $8,000 and $18,000. So if we give this and someone gets sick in 48 hours, then we may be at risk for losing."

Medicare Inpatient Payment Proposal, May 2018

21

CMS-1694-P:

- CMS is seeking to assign ICD-10-PCS codes XW033C3 and XW043C3 to the use of axicabtagene ciloleucel (Yescarta) and tisagenlecleucel (Kymriah) in the inpatient setting for fiscal year 2019.
- Possible new Medicare Severity–Diagnosis Related Group (MS-DRG) code for procedures involving the use of chimeric antigen receptor (CAR) T-cell therapy drugs.
- CMS is considering adding ICD-10-PCS procedure codes XW033C3 and XW043C3 to pre-MDC MS-DRG 016. Additionally, the agency is proposing to revise the title of MS-DRG 016 from "Autologous Bone Marrow Transplant with CC/MCC" to "Autologous Bone Marrow Transplant with CC/MCC or T-cell Immunotherapy."
  - Would CAR-T cell products be included in DRG 016, or would there be a New Technology Add-on Payment?

Billing challenges

22

Leukapheresis:

- Q code indicates it's included as part of the "drug"
- Novartis has program to pay facilities to collect cells as a manufacturing cost
- Kite/Gilead doesn't have a program to pay providers for T-cell collection; most bill to insurance
- New Category III CPT code created for autologous T-cell collection

How does a provider bill Novartis for leukapheresis "Fair Market Value?"

- Invoice creation
- Payment tracking
- Is charge posted to patient account? What about payment?

Billing challenges

23

Getting the cell/drug charge onto a UB-02 (hospital billing):

- Bill when infused, not when ordered
- "Drug" isn't pulled from a Pyxis machine

- Pharmacy isn't compounding it

Billing challenges

24

Tisagenlecleucel - No clinical response? No payment!

Sounds great, but…

Is the entire claim held for 30 days?

- A/R turnaround & billing deadlines
- DRG/reimbursement impact on ancillary services if there's no cell product charge?
- If no charge for tisagenlecleucel without response, why should patients pay for axicabtagene ciloleucel if they don't respond?

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"Only the beginning. Only just the start"

"Genetically-engineered cell products are going to explode over the next decade; this is not the end of the line, this is the starting point." – Richard Maziarz, MD

Financial Implications of CAR-T Cell Therapies

Samuel M. Silver, MD, PhD, MACP, FAHA, FASCO

Samuel M. Silver, MD, PhD, is Professor of Internal Medicine in the Division of Hematology/Oncology, Assistant Dean for Research, and Associate Medical Director for the Faculty Group Practice at the University of Michigan Medical School. His clinical practice is devoted to benign and malignant hematology diseases. He is chair emeritus of the National Comprehensive Cancer Network's Board of Directors.

Dr. Silver received his undergraduate degree in Chemistry, *summa cum laude,* from Brandeis University in Waltham, Massachusetts, his PhD in Virology from the Rockefeller University, and his medical degree from Cornell University Medical College. He did his Internal Medicine training at the University of California, San Francisco and his fellowship in Hematology/Oncology at the University of Pennsylvania. During his 30 years at the University of Michigan, he has held numerous positions including Medical Director of the Medical Management Center, Medical Director of Cancer Center Network Activities and Director of Adult Bone Marrow Transplantation.

Dr. Silver has worked as the principal investigator for numerous clinical research studies involving a range of topics, such as malignant hematology, the quality of oncology care, and the porphyrias. Throughout his career, Dr. Silver has focused on issues involving practice and reimbursement and he is recognized nationally for his involvement in clinical reimbursement and coding. He is a member of the American Society of Hematology's Committee on Practice and Chairman of the Subcommittee on Reimbursement. He is a member of the American Society of Clinical Oncology's Clinical Practice Committee and is past chair of ASCO's Quality Cancer Committee. He represents ASH to AMA's CPT Advisory Committee and is the hematology advisor to the AMA RUC. He is a member of the National Business Group on Health's National Committee on Evidence-Based Benefit Design. He was previously the Medicare Hematology Carrier Medical Advisor for Michigan. He previously served as chair of the Board of Directors of the Physician Organization of Michigan.

Dr. Silver established Michigan's first statewide consortium on quality breast cancer care and received a Statesman Award from the American Society of Clinical Oncology for his significant volunteer efforts in 2008. He received the Burgess L. Gordon Award from the AMA for his work on the CPT and received the Exemplary Service Award from the American Society of Hematology. Dr. Silver received the Laureate Award from the Michigan Chapter of the American College of Physicians in 2014 and in 2017 received the Albert Nelson Marquis Lifetime Achievement Award.

Dr. Silver serves on the editorial board of several scientific journals. He is a Master of the American College of Physicians and a Fellow of both the American Heart Association and the American Society of Clinical Oncology. He is a member of the American Society for Blood and Marrow Transplantation and the American Society of Hematology, and served on the Boards of the latter two organizations and is currently Chair of the ASH Nominations Committee. He serves on the Scientific Board of Advisors of the American Porphyria Foundation. He is Past-President of the Michigan Society of Hematology and Oncology and remains on its Board of Directors and serves on the Michigan ACP Governor's Council.

Financial Implications of CAR-T Cell Therapies

ASH/ASCO CAC Meeting
July 27, 2018

Samuel M Silver, MD, PhD, MACP, FASCO
Chair, Subcommittee on Reimbursement
American Society of Hematology
Professor of Internal Medicine and Assistant Dean for Research
University of Michigan Medical School

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  - Suzanne M. Leous, MPA
    Chief Policy Officer
  - Leslie Brady
    Policy & Practice Manager
- Michigan Medicine Contracting Office
  - Thomas Daly
    Director of Managed Care, Michigan Medicine
- Memorial Sloan Kettering Cancer Center
  - Leonard Saltz, MD

Nivolumab + Ipilimumab in Metastatic Melanoma

(Wolchok et al: Proc ASCO 2015)

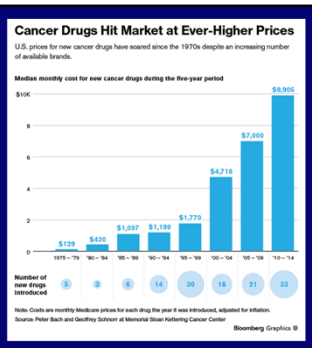
	NIVO	NIVO + IPI	IPI
Total Population			
Median PFS, months (95% CI)	6.9 (4.3–9.5)	11.5 (8.9–16.7)	2.9 (2.8–3.4)

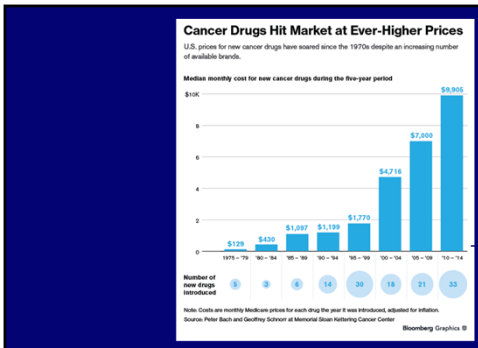
From Leonard Saltz, ASCO 2015

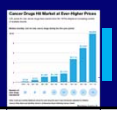
Regimen Cost (80 kg patient)

Regimen	Cost of Nivolumab	Cost of Ipilimumab	Cost of Regimen
Nivo+ Ipi for 11.5 m	$144,408	$151,158	**$295,566**
Nivo for 6.9 m	$103,220	$0	**$103,220**
Ipilimumab for 2.9 m	$0	$158,252	**$158,252**

From Leonard Saltz, ASCO 2015



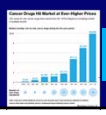




Pembrolizumab AWP (Redbook online): $51.792 / mg

$51.792 x 10 mg/kg x 75 kg x 26 doses/year =

$1,009,944 per patient / per year



Selection of 2015 ASCO abstracts using Pem 10 mg/kg q 2 wks:

abstract # 4010 (esophageal ca)
abstract # 5510 (ovarian ca)
abstract # 7502 (Small cell Lung ca)
abstract # 8035 (non-small cell lung ca)
abstract # 9040 (melanoma)

Pembrolizumab 10 mg/kg q 2 weeks
$83,500/month

From Leonard Saltz, ASCO 2015

Unsustainable

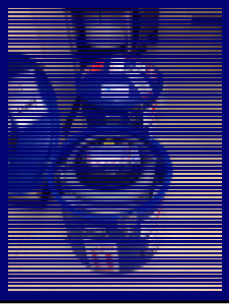
From Leonard Saltz, ASCO 2015

THE WORLD'S MOST EXPENSIVE CARs

$8 million — Mercedes-Benz Maybach Exelero

$4.8 million Koenigsegg CCXR Trevita

This is what $740,000 looks like. Each shipper contains one Yescarta product.



JAMA November 21, 2017 Volume 318, Number 19, 1861

MEDICAL SCHOOL UNIVERSITY OF MICHIGAN

VIEWPOINT

FDA Approval of Tisagenlecleucel
Promise and Complexities of a $475 000 Cancer Drug

Peter B. Bach, MD
Memorial Sloan Kettering Cancer Center, New York, New York.

Sergio A. Giralt, MD
Memorial Sloan Kettering Cancer Center, New York, New York.

Leonard B. Saltz, MD
Memorial Sloan Kettering Cancer Center, New York, New York.

Related articles at jamaoncology.com, jamainternalmedicine.com

Approval of the drug tisagenlecleucel (Kymriah; Novartis) by the US Food and Drug Administration (FDA) for the treatment of pediatric and young adult acute lymphoblastic leukemia (ALL) in August 2017 was a landmark in oncology. The science underlying chimeric antigen receptor T cells (CAR-T) heralds a new era of treatment, and the list price of $475 000 for the new drug (delivered as a one-time infusion) definitively shattered oncology drug pricing norms.[1]

Unlike most cancer therapies that are identical from patient to patient, CAR-T therapies are made by removing the T cells of a patient, genetically modifying them to respond to certain targets expressed on the patient's cancer cells, and then reinfusing the cells. When the T cells come into contact with the relevant target (for instance, CD19 in the case of ALL), they proliferate while secreting a number of programmed substances including inflammatory cytokines that destroy the cancerous cells. Targeted killing of tumor cells by lymphocytes was first suggested by the graft-vs-leukemia effect in bone marrow transplant [illegible]

the patient is technically challenging. Accordingly, for the foreseeable future this new type of treatment will (and should) only be available at institutions that have broad clinical capabilities and experience in hematopoietic cell transplantation.

The price of this therapy should serve as a reminder that future revenue outlooks for a pharmaceutical company are in part related to the ability to generate many millions in revenue even when few patients benefit from the new therapies. Novartis reports that around 600 patients will be eligible each year for tisagenlecleucel (for its just-approved indication).[1] Gilead's $12 billion offer to purchase Kite Pharma, a company focused on developing CAR-T therapies, reflects the expectation that these treatments will generate large returns even when given to few patients.

The Institute for Clinical and Economic Review (ICER) is planning to review CAR-T cost-effectiveness in early 2018, which will provide an estimate of the appropriateness of the price of this therapy relative to clini[illegible]

CAR-T Product Overview

- **Kymriah™ (Novartis) Tisagenlecleucel**
- Relapsing/relapsed or refractory P-ALL (up to age 25)
  - **Price=$475,000**
- Adult patients with r/r large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma and DLBCL arising from follicular lymphoma
  - **Price=$373,000**
  - **~50% Medicare**
- 53 Centers, 52 currently certified
- FACT accreditation required

- **Bb2121 (Celgene/bluebird)**
  - FDA breakthrough-therapy designation, 11/2017
  - R/R Myeloma

- **Yescarta™ (Kite/Gilead) Axicabtagene ciloleucel**
- Adult r/r large B-cell lymphoma subtypes
  - **Price=$373,000**
  - **~50% Medicare**
- 61 centers, 61 certified
- FACT accreditation required

- **Numerous other trials happening:**
  - Different disease targets
  - Different constructs
  - Allogeneic: specific and universal
  - "Bedside" capabilities
  - Dozens of companies and academic groups involved

Kymriah Certified Treatment Sites (Accessed 15 July 2018)

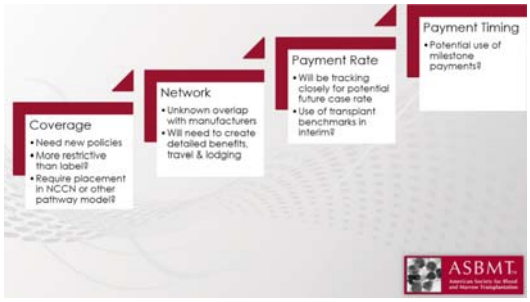
Physician and Facility Reimbursement

- Why should providers and facilities take the time to code this work effort?
  - Appropriate reimbursement for both providers and facilities
  - Accurate charge capture to CMS and private carriers using uniform coding systems so that new DRG codes and appropriate RVUs are assigned to new CPT codes
  - With relatively small number of procedures and variance on how these are coded, risk of inaccurate cost assignment from payers

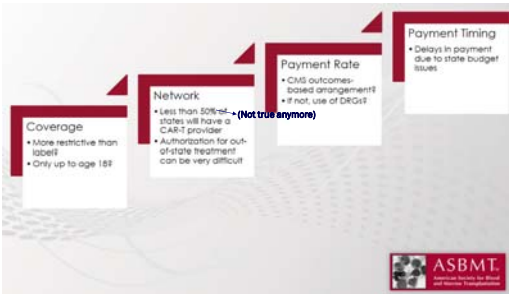
The following Category III codes were accepted at the May 2018 CPT Editorial Panel meeting for the 2019 CPT production cycle. However, due to the Category III code early release policy, these codes are effective on January 1, 2019, following the six-month implementation period which begins July 1, 2018.

Code	Long Code Descriptor	Published to AMA Website	Effective Date	Publication
	►Cellular and Gene Therapy◄ **The guidelines for Cellular and Gene Therapy are pending further Panel review. Please check back for an update on or around July 27, 2018.**			
•0537T	Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day	July 1, 2018	January 1, 2019	CPT® 2019
•0538T	preparation of blood-derived T lymphocytes for transportation (eg, cryopreservation, storage)	July 1, 2018	January 1, 2019	CPT® 2019
•0539T	receipt and preparation of CAR-T cells for administration	July 1, 2018	January 1, 2019	CPT® 2019
•0540T	CAR-T cell administration, autologous	July 1, 2018	January 1, 2019	CPT® 2019

Private Payer Access Issues



Medicaid Access Issues



Current Medicare Inpatient Reimbursement Insufficient

- **B-Cell Lymphoma age group will mean ~50% Medicare Beneficiaries**
- **Expectation of 75%+ inpatient for first 1-3 years**
  - At some centers, 100% inpatient
  - Drug costs would be included in MS-DRGs
  - No operating room procedure to increase severity weight
- **Lymphoma MS-DRGs (840-842) pay base rates of $6-$16k**
  - Very high acquisition costs
  - New Technology Add-on Payment (NTAP) not available in FY2018 due to timing of FDA approvals and CMS's decision cycle, and is not available to all providers
  - Outlier payment not likely to mitigate losses, and is not available to all providers
- **Limited facilities able to provide this care = concentration of payer issues**
- **Significant underpayment problem for both PPS and PPS-exempt hospitals**
- Medicare Advantage/Supplement Payments are unclear; payers are unsure about what benchmarks they should use for assigning payment rates

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Current IPPS Medicare Reimbursement

- Inpatient cases group to a MS-DRG based on the diagnoses and procedures on the claim.
- In addition to the MS-DRG payment, total charges are evaluated on each IPPS case for possible additional outlier payment.

MS-DRG	MDC	Type	Title	Weights	Approximate Base Reimbursement	Geo Mean LOS
840	17	MED	LYMPHOMA & NON-ACUTE LEUKEMIA W MCC	3.0786	$16,736	7
841	17	MED	LYMPHOMA & NON-ACUTE LEUKEMIA W CC	1.6201	$8,807	4.3
842	17	MED	LYMPHOMA & NON-ACUTE LEUKEMIA W/O CC/MCC	1.1241	$6,110	2.9

Using Outlier Medicare IPPS Calculations for CAR-T Claims

- The only payment augmentation option for this fiscal year is the outlier calculation, which relies on a calculation that assumes mark-up. In order to recover even close to the invoice cost for the product (**not accounting for the cost of the inpatient stay itself**), hospitals would need to mark-up the product by 400%, due to the way CMS processes charges on a claim
- NTAP (New Technology Add-On Payment) goes into effect October 1, with the new Fiscal Year. CMS will tip their hat in terms of whether they seem to think the technologies that applied for NTAP will meet qualifications in the proposed rule in April, but it won't be final until August with the final rule and doesn't go into effect until 10/1/2018. (This was further delayed with the recent Proposed Rule). **And it's not pass-through – it covers 'the lesser of' 50% of the product cost OR a calculated amount spent by the facility on the treatment episode.** CMS has been denying the bulk of NTAP applications, so it will be interesting to see how they treat the CAR-T applications given the all the conversations about this therapy.
-

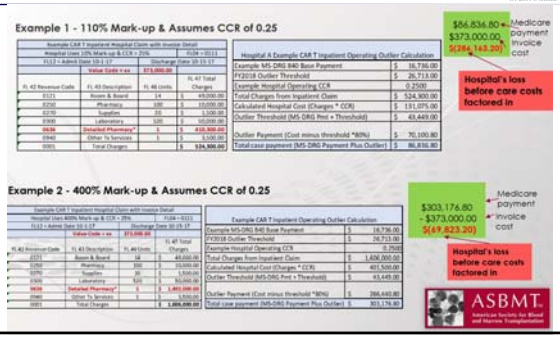
IPPS Hospital Outlier Formula

- The Medicare Administrative Contractor (MAC) takes the hospital's ***total inpatient covered charges*** billed on the claim and multiplies these by the hospital's operating cost-to-charge ratio (CCR) from their most recently filed cost report to generate "cost"
- The calculated cost is compared to the sum of the MS-DRG payment for the case and the outlier threshold
  - For FY2018, the IPPS fixed dollar outlier threshold is $26,713
  - IPPS MS-DRG base payment for MS-DRG 840 is $16,736
- If there is "excess cost" CMS will make an outlier payment
  - **Recap:** (Total charges billed on claim) * (hospital's CCR) = X
  - If X > (MS-DRG payment + fixed outlier threshold), outlier payment is warranted
  - Outlier payment = 80% * (X – (DRG + IME + DSH + threshold))

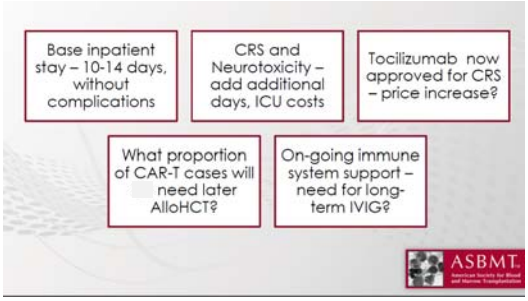
Note: Outlier payments not available to IPPS-exempt hospitals

ASBMT

Examples of IPPS Outlier Calculation for CAR-T Claims



Cost of Full Care Episode Unknown



The "Novartis Promise"

Alex Lash
August 31st, 2017

@alexlash
@xconomy

Xconomy National —
Novartis said Wednesday that it would not charge for its newly approved cellular immunotherapy, tisagenlecleucel (Kymriah)—the first so-called CAR-T product to ever come to market—if it fails to help patients within a month.

Mailankody and Bach, Ann Intern Med 2018;168:888-9

EDITORIAL — Annals of Internal Medicine

Money-Back Guarantees for Expensive Drugs: Wolf's Clothing but a Sheep Underneath

Prices of branded specialty drugs are often far higher than they would be if they were based on their benefits. The pharmaceutical industry thus has a plan called outcomes-based contracting that involves refunds when a patient does not experience the intended therapeutic benefit.

Emphasizing the refund—the product being free if you do not like it—works for late-night salespersons because it provides false comfort to the buyer. It distracts from the more essential question of how much the product is worth when it does work.

CMS quit test of pricey cancer treatment amid concerns over industry role, from Politico Pro

- Medicare and Medicaid administrators earlier this year quietly killed a plan to pay for a breakthrough, half-million-dollar cancer treatment based on how well it worked, scuttling one of the Trump's administration's first and most highly touted attempts to lower the cost of drugs.
- The Centers for Medicare and Medicaid Services touted how the "pay-for-performance" arrangement would save lives and cut Medicare and Medicaid spending right after the FDA approved the company's $475,000 gene therapy to treat kids and young adults with leukemia.
- The demise of the deal, first disclosed in response to questions from congressional Democrats about Novartis' payments to Cohen, illustrates how difficult it is to figure out how much government health programs should pay for expensive treatments whose long-term benefits are still unclear.
- "Coming from an administration which has a stated goal of trying to reduce drug pricing, trying to reduce overall drug spending and health care spending … at every turn this administration has taken steps in the opposite direction and this is one," said Rachel Sachs, a professor who focuses on health law at Washington University in St. Louis.
- Sachs said pay-for-performance deals can give drugmakers political cover to charge whatever they want if the companies can influence performance targets — in this case, with that short one-month timeline.

Joint Societies' Objectives on CAR-T Payment

Goal: *Structure that allows physicians to utilize what they feel is the best product for each patient, in the most appropriate care setting.*

Therefore, seeking solutions that:

- Create a site-neutral, product-agnostic payment structure
- Remove provider responsibility for 'managing' product costs
- Minimize/remove financial losses for providing CAR-T
- Create flexibility for future products and combination therapies
- Minimally disrupt reimbursement for other cellular therapies/HCT

ASBMT

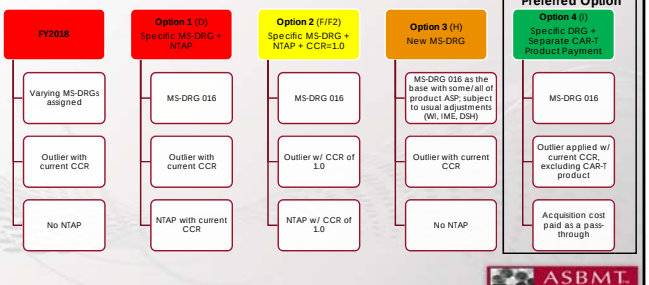
CMS IPPS Proposed Rule

- In the Proposed Rule, CMS outlined several alternatives to address CAR-T reimbursement in FY2019:
  - a) Assignment of an NTAP to CAR-T products;
  - b) Assignment of CAR-T claims to MS-DRG 016;
  - c) Implementation of a cost-to-charge ratio (CCR) of 1.0 for CAR-T products;
  - d) Creation of a new MS-DRG that incorporates a portion of the product cost; and
  - e) "Alternative approaches and authorities to encourage value-based care and lower drug prices."

IPPS: CAR-T Proposals

- Assignment of CAR-T cases to MS-DRG 016 (Auto-BMT)
- Use of a cost-to-charge ratio (CCR) of 1.0 ★★★
- Potential for a new MS-DRG with "some portion of the ASP"
- "Other alternative payment mechanisms"

Payment Options/Combinations



Payment Options/ Combinations

	CMS' Usual Rate-Setting Processes		Brand New MS-DRG[5]	Options for Operationalizing a Cost-to-Charge Ratio of 1.0[5]		
	A	D	H[4]	F[4] and F2		I
Option Description[3]	FY 2018 Status Quo	Auto MS-DRG (or equivalent) and NTAP Approved	Brand New MS-DRG with 100% of CAR-T ASP Built In (Current CCR)	Auto MS-DRG, CCR of 1.0 and NTAP	Auto MS-DRG, CCR of 1.0 and NTAP	Auto MS-DRG and a Separate CAR-T Product Payment Based on ASP or some equivalent (e.g., actual acquisition cost reported on claim)
MS-DRG[2]	840 or other	016	New	016	016	016
Outlier	Current methodology	Current methodology	Current methodology	Product acquisition cost used to implement a CCR of 1.0 *(reported by providers on the claim with a new value code)*	ASP substituted for acquisition cost to implement a CCR of 1.0 *(reported by manufacturers)*	Outlier applied with the current CCR excluding the CAR-T product cost
NTAP	Not available	Approved	No NTAP since base includes 100% of product cost	Approved *(product acquisition cost used to implement a CCR of 1.0 as reported by providers on the claim with a new value code)*	Approved *(ASP used to implement a CCR of 1.0 as reported by manufacturers to CMS)*	No NTAP per se since the CAR-T acquisition cost paid as a pass-through
Financial Impact Based on Hospital A w/ 10% Mark up	($319,999)	($304,425)	($17,069)	($62,750)	($62,750)	($17,069)
Financial Impact Based on Hospital B w/ 400% Mark up	($103,659)	($62,750)	($17,069)	($62,750)	($62,750)	($17,069)

Options 1 and 2: NTAP and Outlier

NTAP and outlier combination is insufficient

- Calculation designed to recognize marginal difference in average cost of cases using new technologies and/or with extremely high total costs
- Will not pay appropriately for new cases driven by single high cost product

Addressing charge compression

- High cost drugs known to face charge compression; most facilities reluctant to mark-up CAR-T products (transparency initiatives)
- CMS may be able to ameliorate the impact of charge compression depending on how it implements a CCR of 1.0 but it may be complicated to implement in the short term
- Applying a CCR of 1.0 to the outlier and NTAP calculations (Option 2 – F/F2), still results in roughly a $60,000 expected loss for hospitals per case

Option 3: New CAR-T MS-DRG

Standard IPPS adjustments creates winners and losers

- Labor cost (Wage index (WI))
- Teaching hospital expenses (indirect medical education (IME), and
- Cost of caring for low income individuals (disproportionate share hospital (DSH))

CMS would lose a transparency opportunity

- Chance to implement line of sight into the product and care costs
- New CAR-T MS-DRG likely needed once IPPS claims become available
- CMS needs better, more granular data to set appropriate payment policy for CAR-T cases going forward

Not site neutral – produces very different CAR-T payments for cases treated in the inpatient vs. outpatient setting

Challenging to make appropriate budget neutrality adjustment (e.g., assumptions regarding number of claims and where services will be performed)

Option 4: Separate Product Payment - Pays Most Appropriately in FY19; Best for Future Rate-setting

CMS could pay separately for the CAR-T product

- Costs of care would be paid under MS-DRG 016 with current outlier policy
- CAR-T product costs paid as pass-through at actual acquisition or invoice cost
- Would rely on CMS' broad adjustment authority[1]
- Similar payment methodology to that used for hemophilia blood clotting factors

Separate payment has numerous benefits:

- Addresses charge compression; implementing the proposal of using a CCR of 1.0
- Logical outgrowth of proposed rule
- Easily verifiable, provides consistent payment across CAR-T centers, and is site neutral
- Avoids creating winners and losers from application of IPPS adjustments (WI, IME, DSH) to CAR-T portion of payment
- Can facilitate data collection on the true cost of patient care services (separate from CAR-T product itself) to use in future rate-setting when claims are available

[1] 1886(d)(5)(I)(i): "The Secretary shall provide by regulation for such other exceptions and adjustments to such payment amounts under this subsection as the Secretary deems appropriate."

Payment Options/ Combinations

	CMS' Usual Rate-Setting Processes		Brand New MS-DRG[3]	Options for Operationalizing a Cost-to-Charge Ratio of 1.0[3]		
	A	D	H[4]	F[4] and F2		I
Option Description[5]	FY 2018 Status Quo	Auto MS-DRG (or equivalent) and NTAP Approved	Brand New MS-DRG with 100% of CAR-T ASP Built In (Current CCR)	Auto MS-DRG, CCR of 1.0 and NTAP	Auto MS-DRG, CCR of 1.0 and NTAP	Auto MS-DRG and a Separate CAR-T Product Payment Based on ASP or some equivalent (e.g., actual acquisition cost reported on claim)
MS-DRG[2]	840 or other	016	New	016	016	016
Outlier	Current methodology	Current methodology	Current methodology	Product acquisition cost used to implement a CCR of 1.0 *(reported by providers on the claim with a new value code)*	ASP substituted for acquisition cost to implement a CCR of 1.0 *(reported by manufacturers)*	Outlier applied with the current CCR excluding the CAR-T product cost
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PPS-Exempt Hospitals

- For PPS-Exempt hospitals CMS can implement a CCR of 1.0 using specific cost-reporting processes outlined by the Alliance of Dedicated Cancer (ADCC) in its comment letter. This will ensure that the agency can clearly identify the hospital's cost of acquiring the therapy and reimburse for it accordingly.

Bottom Line: Providers and Hospitals Need Relief and Change

- Personalized products with little/no opportunity for discounts, bulk purchase, or sole sourcing
- Little interchangeability of products based on disease/condition (MM, DLBCL, etc)
- Centers providing one of these therapies likely providing several others – the averaging system does not work for this concentration of losses
- Providers cannot create the desired 'efficiencies' within IPPS at the current prices
  - The 'margin' on an admission without CRS does not make up for product losses
- Providers are choosing to do the right thing for patients now, despite pressure to do otherwise – have taken substantial losses during the past year in the inpatient setting

ASBMT

Formal Request for National Coverage Determination for Chimeric Antigen Receptor T-Cell Therapies

- Given the complexity of the therapy, treating patients with acute life-threatening disease requiring the manufacture of an individualized product, the potential for severe and also life-threatening side-effects necessitating specialized expertise to manage, and the high cost of the products and associated care required, a National Coverage Determination is essential to ensure that coverage is available to the Medicare population and that the criteria used to determine eligibility for coverage are evidence-based and are consistent regardless of the state of residence of the beneficiary. UHC proposes that coverage for CAR-T cell therapy be based upon the indications specified in the FDA labels. However, given that CAR-T cell therapy is an innovative therapy, and ongoing clinical trials are likely to identify new patient populations who may benefit, which may not all be reviewed by the FDA, we urge CMS to develop a process to up-date the NCD as new evidence emerges.

ASH Rationale and Reply to NCD Request

- **National CAR-T Cell Therapy Coverage Determination is Premature**
- CAR-T Cell Therapy is an Evolving Area of Medicine
  - With over 400 clinical trials in process, it is impossible to know what the ultimate applications of the therapy will be.
  - The science may change as well. Currently, CAR-T cell therapy is an incredibly personalized process, requiring products to be individually created for each patient. However, clinical trials are underway to develop allogeneic universal or "off-the-shelf" CAT-T cells.
- Concerns Related to Patient Access to Care
  - An NCD that restricts coverage for certain conditions has the potential to limit a life-saving therapy for patients. It is nearly impossible to get an accurate assessment of the applicability of this therapy given the rapidly evolving science and the hundreds of open clinical trials. It is standard practice for CMS to issue NCDs for well-established treatments, rather than a therapy that is still new and evolving, such as CAR-T cell therapy.
- Complex Nature of the National Coverage Process
  - The complex nature of the national coverage process, including the process of revising already existing NCDs, heightens about stifling innovation and limiting patient access. The science and practice of CAR-T cell therapy are immature at this point, and whatever coverage policy CMS finalizes may require frequent revisions to keep up with the science and its clinical translations.

What Does This All Mean?

- This is not our “typical” therapy from a cost structure, even compared to leukemia induction or alloBMT.
- The expense of cell processing makes our institutions financially more vulnerable
  - We haven’t even costed out inadequate payment for CRS treatment/ICU expenses/IV IgG, etc.
- How are we going to do this?
  - The excitement at ASH is palpable, but…How will the financial realities effect the future of promising translational scientific breakthroughs?
- I said that I was not going to talk about policy, but is this *sustainable*?

CMS Resources

- Medicare's Program Integrity Manual, Chapter 13 (*outlines the local coverage determinations the Carrier Advisory Committee (CAC) and contractor responsibilities surrounding CACs*)
- General Information on CMS' Contracting Reform
- Medicare Administrative Contractors (MAC) Regions and Updates
- Map of Current Jurisdictions
- Map of Consolidated Regions (*what CMS is moving toward*)
- Durable Medical Equipment MACs
- Medicare Coverage
- Medicare Coverage Centers
- Merit-based Incentive Payment System and Quality Payment Program.
- CMS Biosimilars
- Proposed Decision Memo for Next Generation Sequencing for Medicare Beneficiaries with Advanced Cancer
- CMS Finalizes Coverage of Next Generation Sequencing Tests, Ensuring Enhanced Access to Cancer Patients

Choosing Wisely®

An initiative of the ABIM Foundation

American Society of Hematology

Ten Things Physicians and Patients Should Question

1 Don't transfuse more than the minimum number of red blood cell (RBC) units necessary to relieve symptoms of anemia or to return a patient to a safe hemoglobin range (7 to 8 g/dL in stable, non-cardiac in-patients).

Transfusion of the smallest effective dose of RBCs is recommended because liberal transfusion strategies do not improve outcomes when compared to restrictive strategies. Unnecessary transfusion generates costs and exposes patients to potential adverse effects without any likelihood of benefit. Clinicians are urged to avoid the routine administration of 2 units of RBCs if 1 unit is sufficient and to use appropriate weight-based dosing of RBCs in children.

2 Don't test for thrombophilia in adult patients with venous thromboembolism (VTE) occurring in the setting of major transient risk factors (surgery, trauma or prolonged immobility).

Thrombophilia testing is costly and can result in harm to patients if the duration of anticoagulation is inappropriately prolonged or if patients are incorrectly labeled as thrombophilic. Thrombophilia testing does not change the management of VTEs occurring in the setting of major transient VTE risk factors. When VTE occurs in the setting of pregnancy or hormonal therapy, or when there is a strong family history plus a major transient risk factor, the role of thrombophilia testing is complex and patients and clinicians are advised to seek guidance from an expert in VTE.

3 Don't use inferior vena cava (IVC) filters routinely in patients with acute VTE.

IVC filters are costly, can cause harm and do not have a strong evidentiary basis. The main indication for IVC filters is patients with acute VTE and a contraindication to anticoagulation such as active bleeding or a high risk of anticoagulant-associated bleeding. Lesser indications that may be reasonable in some cases include patients experiencing pulmonary embolism (PE) despite appropriate, therapeutic anticoagulation, or patients with massive PE and poor cardiopulmonary reserve. Retrievable filters are recommended over permanent filters with removal of the filter when the risk for PE has resolved and/or when anticoagulation can be safely resumed.

4 Don't administer plasma or prothrombin complex concentrates for non-emergent reversal of vitamin K antagonists (i.e. outside of the setting of major bleeding, intracranial hemorrhage or anticipated emergent surgery).

Blood products can cause serious harm to patients, are costly and are rarely indicated in the reversal of vitamin K antagonists. In non-emergent situations, elevations in the international normalized ratio are best addressed by holding the vitamin K antagonist and/or by administering vitamin K.

5 Limit surveillance computed tomography (CT) scans in asymptomatic patients following curative-intent treatment for aggressive lymphoma.

CT surveillance in asymptomatic patients in remission from aggressive non-Hodgkin lymphoma may be harmful through a small but cumulative risk of radiation-induced malignancy. It is also costly and has not been demonstrated to improve survival. Physicians are encouraged to carefully weigh the anticipated benefits of post-treatment CT scans against the potential harm of radiation exposure. Due to a decreasing probability of relapse with the passage of time and a lack of proven benefit, CT scans in asymptomatic patients more than 2 years beyond the completion of treatment are rarely advisable.

Released December 4, 2013

Choosing Wisely®

An initiative of the ABIM Foundation

American Society of Hematology

Ten Things Physicians and Patients Should Question

6 Don't treat with an anticoagulant for more than three months in a patient with a first venous thromboembolism (VTE) occurring in the setting of a major transient risk factor.

Anticoagulation is potentially harmful and costly. Patients with a first VTE triggered by a major, transient risk factor such as surgery, trauma or an intravascular catheter are at low risk for recurrence once the risk factor has resolved and an adequate treatment regimen with anticoagulation has been completed. Evidence-based and consensus guidelines recommend three months of anticoagulation over shorter or longer periods of anticoagulation in patients with VTE in the setting of a reversible provoking factor. By ensuring a patient receives an appropriate regimen of anticoagulation, clinicians may avoid unnecessary harm, reduce health care expenses and improve quality of life. This *Choosing Wisely*® recommendation is not intended to apply to VTE associated with non-major risk factors (e.g., hormonal therapy, pregnancy, travel-associated immobility, etc.), as the risk of recurrent VTE in these groups is either intermediate or poorly defined.

7 Don't routinely transfuse patients with sickle cell disease (SCD) for chronic anemia or uncomplicated pain crisis without an appropriate clinical indication.

Patients with SCD are especially vulnerable to potential harms from unnecessary red blood cell transfusion. In particular, they experience an increased risk of alloimmunization to minor blood group antigens and a high risk of iron overload from repeated transfusions. Patients with the most severe genotypes of SCD with baseline hemoglobin (Hb) values in the 7-10 g/dl range can usually tolerate further temporary reductions in Hb without developing symptoms of anemia. Many patients with SCD receive intravenous fluids to improve hydration when hospitalized for management of pain crisis, which may contribute to a decrease in Hb by 1-2 g/dL. Routine administration of red cells in this setting should be avoided. Moreover, there is no evidence that transfusion reduces pain due to vaso-occlusive crises. For a discussion of when transfusion is indicated in SCD, readers are referred to recent evidence-based guidelines from the National Heart, Lung, and Blood Institute (NHLBI) (see reference below).

8 Don't perform baseline or routine surveillance computed tomography (CT) scans in patients with asymptomatic, early-stage chronic lymphocytic leukemia (CLL).

In patients with asymptomatic, early-stage CLL, baseline and routine surveillance CT scans do not improve survival and are not necessary to stage or prognosticate patients. CT scans expose patients to small doses of radiation, can detect incidental findings that are not clinically relevant but lead to further investigations and are costly. For asymptomatic patients with early-stage CLL, clinical staging and blood monitoring is recommended over CT scans.

9 Don't test or treat for suspected heparin-induced thrombocytopenia (HIT) in patients with a low pre-test probability of HIT.

In patients with suspected HIT, use the "4T's" score to calculate the pre-test probability of HIT. This scoring system uses the timing and degree of thrombocytopenia, the presence or absence of thrombosis, and the existence of other causes of thrombocytopenia to assess the pre-test probability of HIT. HIT can be excluded by a low pre-test probability score (4T's score of 0-3) without the need for laboratory investigation. Do not discontinue heparin or start a non-heparin anticoagulant in these low-risk patients because presumptive treatment often involves an increased risk of bleeding, and because alternative anticoagulants are costly.

10 Don't treat patients with immune thrombocytopenic purpura (ITP) in the absence of bleeding or a very low platelet count.

Treatment for ITP should be aimed at treating and preventing bleeding episodes and improving quality of life. Unnecessary treatment exposes patients to potentially serious treatment side effects and can be costly, with little expectation of clinical benefit. The decision to treat ITP should be based on an individual patient's symptoms, bleeding risk (as determined by prior bleeding episodes and risk factors for bleeding such as use of anticoagulants, advanced age, high-risk activities, etc.), social factors (distance from the hospital/travel concerns), side effects of possible treatments, upcoming procedures, and patient preferences. In the pediatric setting, treatment is usually not indicated in the absence of mucosal bleeding regardless of platelet count. In the adult setting, treatment may be indicated in the absence of bleeding if the platelet count is very low. However, ITP treatment is rarely indicated in adult patients with platelet counts greater than 30,000/microL unless they are preparing for surgery or an invasive procedure, or have a significant additional risk factor for bleeding. In patients preparing for surgery or other invasive procedures, short-term treatment may be indicated to increase the platelet count prior to the planned intervention and during the immediate post-operative period.

Released December 3, 2014

How This List Was Created (1–5)

The American Society of Hematology (ASH) *Choosing Wisely*® Task Force utilized a modified Delphi technique to collect suggestions from committee members and recipients of its clinically focused newsletter, the *ASH Practice Update*. Respondents were asked to consider the core values of harm, cost, strength of evidence, frequency and control. Fifty-nine of 167 ASH committee members (35%) and 2 recipients of the *ASH Practice Update* submitted 81 unique suggestions. The Task Force used a nominal group technique (NGT) to identify the top 20 items, which were scored by ASH committee and practice community members, with a 46 percent participation rate. ASH's Task Force reviewed all scores to develop a 10-item list. A professional methodologist conducted a systematic literature review on each of the 10 items; the Task Force chair served as the second reviewer. Evidence reviews and source material for the 10 items were shared with ASH's Task Force, which ranked the items according to the core values. The Task Force then identified the top 5 items plus 1 alternate. ASH member content experts provided external validation for the veracity and clarity of the items.

How this List was Created (6–10)

Suggestions for the second ASH *Choosing Wisely* list were solicited from members of the ASH Committee on Practice, the ASH Committee on Quality, the ASH *Choosing Wisely* Task Force, ASH Consult-a-Colleague volunteers and members of the ASH Practice Partnership. Six principles were used to prioritize items: avoiding harm to patients, producing evidence-based recommendations, considering both the cost and frequency of tests and treatments, making recommendations in the clinical purview of the hematologist, and considering the potential impact of recommendations. Harm avoidance was established as the campaign's preeminent guiding principle. Guided by the 6 principles, the ASH *Choosing Wisely* Task Force scored all suggestions. Modified group technique was used to select 10 semi-finalist items. Systematic reviews of the literature were then completed for each of the 10 semi-finalist items. Guided by the 6 core principles outlined above, and by the systematic reviews of the evidence, the ASH *Choosing Wisely* Task Force selected 5 recommendations for inclusion in ASH's second *Choosing Wisely* Campaign.

ASH's disclosure and conflict of interest policy can be found at www.hematology.org.

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1

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About the ABIM Foundation

The mission of the ABIM Foundation is to advance medical professionalism to improve the health care system. We achieve this by collaborating with physicians and physician leaders, medical trainees, health care delivery systems, payers, policymakers, consumer organizations and patients to foster a shared understanding of professionalism and how they can adopt the tenets of professionalism in practice.

To learn more about the ABIM Foundation, visit www.abimfoundation.org.

About the American Society of Hematology

The American Society of Hematology (ASH) is the world's largest professional society of hematologists, serving more than 14,000 clinicians and scientists from around the world who are dedicated to furthering the understanding, diagnosis, treatment and prevention of disorders affecting the blood.

For more than 50 years, the Society has led the development of hematology as a discipline by promoting research, patient care, education, training and advocacy in hematology. By providing a forum for clinicians and scientists to share the latest discoveries in the field, ASH is helping to improve care and possibly lead to cures for diseases that affect millions of people, including leukemia, lymphoma, myeloma, anemias and various bleeding and clotting disorders.

For more information, visit www.hematology.org.

For more information or to see other lists of Five Things Physicians and Patients Should Question, visit www.choosingwisely.org.

Non-ASH Choosing Wisely® Recommendations of Relevance to Hematology

Choosing Wisely®

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American Society of Hematology

ACR

Don't image for suspected PE without moderate or high pre-test probability of PE.

While deep vein thrombosis (DVT) and PE are relatively common clinically, they are rare in the absence of elevated blood D-Dimer levels and certain specific risk factors. Imaging, particularly computed tomography (CT) pulmonary angiography, is a rapid, accurate, and widely available test, but has limited value in patients who are very unlikely, based on serum and clinical criteria, to have significant value. Imaging is helpful to confirm or exclude PE only for such patients, not for patients with low pre-test probability of PE. *Source: American College of Radiology (ACR). Wording reflects that of the Radiology recommendation, other societies have similar recommendations, some explicitly recommended D-Dimer testing prior to imaging.*

ASRM

Don't routinely order thrombophilia testing on patients undergoing a routine infertility evaluation.

There is no indication to order these tests, and there is no benefit to be derived in obtaining them in someone that does not have any history of bleeding or abnormal clotting and in the absence of any family history. This testing is not a part of the infertility workup. Furthermore, the testing is costly, and there are risks associated with the proposed treatments, which would also not be indicated in this routine population. *Source: American Society for Reproductive Medicine (ASRM).*

SHM

Don't perform repetitive CBC and chemistry testing in the face of clinical and lab stability.

Hospitalized patients frequently have considerable volumes of blood drawn (phlebotomy) for diagnostic testing during short periods of time. Phlebotomy is highly associated with changes in hemoglobin and hematocrit levels for patients and can contribute to anemia. This anemia, in turn, may have significant consequences, especially for patients with cardiorespiratory diseases. Additionally, reducing the frequency of daily unnecessary phlebotomy can result in significant cost savings for hospitals. *Source: Society for Hospital Medicine – Adult Hospital Medicine (SHM). Wording reflects that of the Adult Hospital Medicine recommendation; other societies have similar recommendations.*

AABB

Don't transfuse red blood cells for iron deficiency without hemodynamic instability.

Blood transfusion has become a routine medical response despite cheaper and safer alternatives in some settings. Pre-operative patients with iron deficiency and patients with chronic iron deficiency without hemodynamic instability (even with low hemoglobin levels) should be given oral and/or intravenous iron. *Source: American Association of Blood Banks (AABB).*

ASCO

Avoid using positron emission tomography (PET) or PET-CT scanning as part of routine follow-up care to monitor for a cancer recurrence in asymptomatic patients who have finished initial treatment to eliminate the cancer unless there is high-level evidence that such imaging will change the outcome.

PET and PET-CT are used to diagnose, stage and monitor how well treatment is working. Available evidence from clinical studies suggests that using these tests to monitor for recurrence does not improve outcomes and therefore generally is not recommended for this purpose. False positive tests can lead to unnecessary and invasive procedures, overtreatment, unnecessary radiation exposure and incorrect diagnoses. Until high level evidence demonstrates that routine surveillance with PET or PET-CT scans helps prolong life or promote well-being after treatment for a specific type of cancer, this practice should not be done. *Source: American Society of Clinical Oncology (ASCO).*

The Purpose of This List

Starting in early 2015, the ASH Choosing Wisely Task Force launched a review of all existing Choosing Wisely items to identify recommendations published by other professional societies that are highly relevant and important to the practice of hematology. Using a carefully administered methodology, items were scored for relevance and importance over a series of iterations, resulting in a list of items that were deemed to be especially useful to hematologists. The items in this list represent the top five highest-scoring items. The full list of items is available on the ASH website at ***www.hematology.org/choosingwisely***.

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How this List Was Created (Non-ASH Recommendations)

A two-phase process was developed to identify and rank non-ASH Choosing Wisely recommendations of relevance to hematologists. First, the ASH Choosing Wisely Task Force independently scored all published ABIM Foundation Choosing Wisely recommendations on the MORE reliability scale, a validated seven-point Likert scale used to assess medical relevance. Modified group technique was used to identify the top 50 unique non-ASH Choosing Wisely recommendations with regard to relevance. Overlapping recommendations from different societies were grouped together as one recommendation. Taking into consideration the core values of harm, cost, strength of evidence, frequency, relevance, and impact, the ASH Choosing Wisely Task Force was asked to score each of the remaining 50 Choosing Wisely recommendations between 1 and 10 for prioritization for inclusion on ASH's top 10 list of non-ASH Choosing Wisely recommendations. Harm avoidance was established as the campaign's preeminent guiding principle. Modified group technique was used to select the top 10 non-ASH Choosing Wisely recommendations of relevance and importance to hematologists and their patients, with the top five highest-ranked items presented in this list.

ASH's disclosure and conflict of interest policy can be found at ***www.hematology.org***.

Released December 2, 2015.

For more information or to see other lists of Five Things Physicians and Patients Should Question, visit *www.choosingwisely.org*.

Choosing Wisely®

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American Society of Clinical Oncology

ASCO®

American Society of Clinical Oncology

Five Things Physicians and Patients Should Question

The American Society of Clinical Oncology (ASCO) is a medical professional oncology society committed to conquering cancer through research, education, prevention and delivery of high-quality patient care. ASCO recognizes the importance of evidence-based cancer care and making wise choices in the diagnosis and management of patients with cancer. After careful consideration by experienced oncologists, ASCO highlights ten categories of tests, procedures and/or treatments whose common use and clinical value are not supported by available evidence. These test and treatment options should not be administered unless the physician and patient have carefully considered if their use is appropriate in the individual case. As an example, when a patient is enrolled in a clinical trial, these tests, treatments and procedures may be part of the trial protocol and therefore deemed necessary for the patient's participation in the trial.

These items are provided solely for informational purposes and are not intended to replace a medical professional's independent judgment or as a substitute for consultation with a medical professional. Patients with any specific questions about the items on this list or their individual situation should consult their health care provider. New evidence may emerge following the development of these items. ASCO is not responsible for any injury or damage arising out of or related to any use of these items or to any errors or omissions.

1 Don't use cancer-directed therapy for solid tumor patients with the following characteristics: low performance status (3 or 4), no benefit from prior evidence-based interventions, not eligible for a clinical trial, and no strong evidence supporting the clinical value of further anti-cancer treatment.

- Studies show that cancer directed treatments are likely to be ineffective for solid tumor patients who meet the above stated criteria.
- Exceptions include patients with functional limitations due to other conditions resulting in a low performance status or those with disease characteristics (e.g., mutations) that suggest a high likelihood of response to therapy.
- Implementation of this approach should be accompanied with appropriate palliative and supportive care.

2 Don't perform PET, CT, and radionuclide bone scans in the staging of early prostate cancer at low risk for metastasis.

- Imaging with PET, CT, or radionuclide bone scans can be useful in the staging of specific cancer types. However, these tests are often used in the staging evaluation of low-risk cancers, despite a lack of evidence suggesting they improve detection of metastatic disease or survival.
- Evidence does not support the use of these scans for staging of newly diagnosed low grade carcinoma of the prostate (Stage T1c/T2a, prostate-specific antigen (PSA) <10 ng/ml, Gleason score less than or equal to 6) with low risk of distant metastasis.
- Unnecessary imaging can lead to harm through unnecessary invasive procedures, over-treatment, unnecessary radiation exposure, and misdiagnosis.

3 Don't perform PET, CT, and radionuclide bone scans in the staging of early breast cancer at low risk for metastasis.

- Imaging with PET, CT, or radionuclide bone scans can be useful in the staging of specific cancer types. However, these tests are often used in the staging evaluation of low-risk cancers, despite a lack of evidence suggesting they improve detection of metastatic disease or survival.
- In breast cancer, for example, there is a lack of evidence demonstrating a benefit for the use of PET, CT, or radionuclide bone scans in asymptomatic individuals with newly identified ductal carcinoma in situ (DCIS), or clinical stage I or II disease.
- Unnecessary imaging can lead to harm through unnecessary invasive procedures, over-treatment, unnecessary radiation exposure, and misdiagnosis.

4 Don't perform surveillance testing (biomarkers) or imaging (PET, CT, and radionuclide bone scans) for asymptomatic individuals who have been treated for breast cancer with curative intent.

- Surveillance testing with serum tumor markers or imaging has been shown to have clinical value for certain cancers (e.g., colorectal). However for breast cancer that has been treated with curative intent, several studies have shown there is no benefit from routine imaging or serial measurement of serum tumor markers in asymptomatic patients.
- False-positive tests can lead to harm through unnecessary invasive procedures, over-treatment, unnecessary radiation exposure, and misdiagnosis.

5 Don't use white cell stimulating factors for primary prevention of febrile neutropenia for patients with less than 20 percent risk for this complication.

- ASCO guidelines recommend using white cell stimulating factors when the risk of febrile neutropenia, secondary to a recommended chemotherapy regimen, is approximately 20 percent and equally effective treatment programs that do not require white cell stimulating factors are unavailable.
- Exceptions should be made when using regimens that have a lower chance of causing febrile neutropenia if it is determined that the patient is at high risk for this complication (due to age, medical history, or disease characteristics).

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Five More Things Physicians and Patients Should Question

6

Don't give patients starting on a chemotherapy regimen that has a low or moderate risk of causing nausea and vomiting antiemetic drugs intended for use with a regimen that has a high risk of causing nausea and vomiting.

- Over the past several years, a large number of effective drugs with fewer side effects have been developed to prevent nausea and vomiting from chemotherapy. When successful, these medications can help patients avoid spending time in the hospital, improve their quality of life and lead to fewer changes in the chemotherapy regimen.
- Oncologists customarily use different antiemetic drugs depending on the likelihood (low, moderate or high) for a particular chemotherapy program to cause nausea and vomiting. For chemotherapy programs that are likely to produce severe and persistent nausea and vomiting, there are new agents that can prevent this side effect. However, these drugs are very expensive and not devoid of side effects. For this reason, these drugs should be used only when the chemotherapy drugs that have a high likelihood of causing severe or persistent nausea and vomiting.
- When using chemotherapy that is less likely to cause nausea and vomiting, there are other effective drugs available at a lower cost.

7

Don't use combination chemotherapy (multiple drugs) instead of chemotherapy with one drug when treating an individual for metastatic breast cancer unless the patient needs a rapid response to relieve tumor-related symptoms.

- Although chemotherapy with multiple drugs, or combination chemotherapy, for metastatic breast cancer may slow tumor growth for a somewhat longer time than occurs when treating with a single agent, use of combination chemotherapy has not been shown to increase overall survival. In fact, the trade-offs of more frequent and severe side effects may have a net effect of worsening a patient's quality of life, necessitating a reduction in the dose of chemotherapy.
- Combination chemotherapy may be useful and worth the risk of more side effects in situations in which the cancer burden must be reduced quickly because it is causing significant symptoms or is life threatening. As a general rule, however, giving effective drugs one at a time lowers the risk of side effects, may improve a patient's quality of life, and does not typically compromise overall survival.

8

Avoid using PET or PET-CT scanning as part of routine follow-up care to monitor for a cancer recurrence in asymptomatic patients who have finished initial treatment to eliminate the cancer unless there is high-level evidence that such imaging will change the outcome.

- PET and PET-CT are used to diagnose, stage and monitor how well treatment is working. Available evidence from clinical studies suggests that using these tests to monitor for recurrence does not improve outcomes and therefore generally is not recommended for this purpose.
- False positive tests can lead to unnecessary and invasive procedures, overtreatment, unnecessary radiation exposure and incorrect diagnoses.
- Until high level evidence demonstrates that routine surveillance with PET or PET-CT scans helps prolong life or promote well-being after treatment for a specific type of cancer, this practice should not be done.

9

Don't perform PSA testing for prostate cancer screening in men with no symptoms of the disease when they are expected to live less than 10 years.

- Since PSA levels in the blood have been linked with prostate cancer, many doctors have used repeated PSA tests in the hope of finding "early" prostate cancer in men with no symptoms of the disease. Unfortunately, PSA is not as useful for screening as many have hoped because many men with prostate cancer do not have high PSA levels, and other conditions that are not cancer (such as benign prostate hyperplasia) can also increase PSA levels.
- Research has shown that men who receive PSA testing are less likely to die specifically from prostate cancer. However when accounting for deaths from all causes, no lives are saved, meaning that men who receive PSA screening have not been shown to live longer than men who do not have PSA screening. Men with medical conditions that limit their life expectancy to less than 10 years are unlikely to benefit from PSA screening as their probability of dying from the underlying medical problem is greater than the chance of dying from asymptomatic prostate cancer.

10

Don't use a targeted therapy intended for use against a specific genetic aberration unless a patient's tumor cells have a specific biomarker that predicts an effective response to the targeted therapy.

- Unlike chemotherapy, targeted therapy can significantly benefit people with cancer because it can target specific gene products, i.e., proteins that cancer cells use to grow and spread, while causing little or no harm to healthy cells. Patients who are most likely to benefit from targeted therapy are those who have a specific biomarker in their tumor cells that indicates the presence or absence of a specific gene alteration that makes the tumor cells susceptible to the targeted agent.
- Compared to chemotherapy, the cost of targeted therapy is generally higher, as these treatments are newer, more expensive to produce and under patent protection. In addition, like all anti-cancer therapies, there are risks to using targeted agents when there is no evidence to support their use because of the potential for serious side effects or reduced efficacy compared with other treatment options.

Abbreviations

CT, computed tomography; DCIS, ductal carcinoma in situ; PET, positron emission tomography; PSA, prostate-specific antigen.

How This List Was Created (1–5)

The American Society of Clinical Oncology (ASCO) has had a standing Cost of Cancer Care Task Force since 2007. The role of the Task Force is to assess the magnitude of rising costs of cancer care and develop strategies to address these challenges. In response to the 2010 New England Journal of Medicine article by Howard Brody, MD, "Medicine's Ethical Responsibility for Health Care Reform – the Top Five List," a subcommittee of the Cost of Cancer Care Task Force began work to identify common practices in oncology that were both common as well as lacking sufficient evidence for widespread use. Upon joining the Choosing Wisely campaign, the members of the subcommittee conducted a literature search to ensure the proposed list of items were supported by available evidence in oncology; ultimately the proposed Top Five list was approved by the full Task Force. The initial draft list was then presented to the ASCO Clinical Practice Committee, a group composed of community-based oncologists as well as the presidents of the 48 state/regional oncology societies in the United States. Advocacy groups were also asked to weigh in to ensure the recommendations would achieve the dual purpose of increasing physician-patient communication and changing practice patterns. A plurality of more than 200 clinical oncologists reviewed, provided input and supported the list. The final Top Five list in oncology was then presented to, discussed and approved by the Executive Committee of the ASCO Board of Directors and published in the Journal of Clinical Oncology. ASCO's disclosure and conflict of interest policies can be found at www.asco.org.

How This List Was Created (6–10)

To guide ASCO in developing this list, suggestions were elicited from current ASCO committee members (approximately 700 individuals); 115 suggestions were received. After removing duplicates, researching the literature and discussing practice patterns, the Value in Cancer Care Task Force culled the list to 11 items, which comprised an ASCO Top Five voting slate that was sent back to the membership of all standing committees. Approximately 140 oncologists from its leadership cadre voted, providing ASCO with an adequate sample size and perspective on what oncologists find to be of little value. The list was reviewed and finalized by the Value in Cancer Care Task Force and ultimately reviewed and approved by the ASCO Board of Directors and published in the *Journal of Clinical Oncology*. ASCO's disclosure and conflict of interest policies can be found at www.asco.org.

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About the ABIM Foundation

The mission of the ABIM Foundation is to advance medical professionalism to improve the health care system. We achieve this by collaborating with physicians and physician leaders, medical trainees, health care delivery systems, payers, policymakers, consumer organizations and patients to foster a shared understanding of professionalism and how they can adopt the tenets of professionalism in practice.

To learn more about the ABIM Foundation, visit www.abimfoundation.org.

About the American Society of Clinical Oncology

The American Society of Clinical Oncology (ASCO) is the world's leading professional organization representing physicians who care for people with cancer. With more than 30,000 members, ASCO is committed to improving cancer care through scientific meetings, educational programs and peer-reviewed journals. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation, which funds ground-breaking research and programs that make a tangible difference in the lives of people with cancer. ASCO's membership is comprised of clinical oncologists from all oncology disciplines and sub-specialties including medical oncology, therapeutic radiology, surgical oncology, pediatric oncology, gynecologic oncology, urologic oncology, and hematology; physicians and health care professionals participating in approved oncology training programs; oncology nurses; and other health care practitioners with a predominant interest in oncology.

For more information, please visit www.asco.org.

For more information or to see other lists of Five Things Physicians and Patients Should Question, visit www.choosingwisely.org.

American Society of Hematology Practice-Related Resources

ASH offers a wide range of practice-related resources on its website (www.hematology.org). Below, please find a list of resources that may be of interest to you.

Resources for Clinicians (www.hematology.org/Clinicians/)

- MACRA – The ASH MACRA webpage is dedicated to keeping ASH members up-to-date on the Quality Payment Program (QPP), part of the Medicare Access and CHIP Reauthorization Act (MACRA). This page provides members with answers to frequently asked questions, links to comment letters ASH has submitted related to MACRA, and information on MIPSPRO, a 2018 Qualified MIPS Registry through which ASH members can submit MIPS data directly to the Centers for Medicare and Medicaid Services.
- ASH Practice Partnership - The ASH Practice Partnership (APP) is a group within the Society that was formed to better represent the interests of practicing hematologists. The APP is comprised of practicing hematologists from across the nation; participants must be board-certified in hematology and active members of ASH. Ideal candidates should be interested in malignant and nonmalignant hematology.
- Drug Resources - This page provides links to patient assistance programs and sample letters of appeal for high-cost drugs, links to REMS resources, an up-to-date list of hematologic drug shortages, resources for physicians dealing with shortages, and links to ASH/FDA webinars featuring an unbiased discussion of newly approved drugs and their uses.
- Pediatric to Adult Hematologic Care Transitions - This new webpage offers links to assessment and summary forms designed to facilitate discussion about patient transitions from pediatric to adult care.
- Consult a Colleague - A member service designed to help facilitate the exchange of information between hematologists and their peers.
- ASH Choosing Wisely List - Evidence-based recommendations about the necessity and potential harm of certain practices developed as part of Choosing Wisely®, an initiative of the ABIM Foundation.
- ASH Clinical Guidelines, ASH Pocket Guides, and Hematology Quality Metrics - Access guidelines on the management and treatment of Sickle Cell Disease, Acute Leukemia, Idiopathic Thrombocytopenic Purpura, Antithrombotic Drug Dosing and Management, Heparin-Induced Thrombocytopenia (HIT), Immune Thrombocytopenia (ITP), von Willebrand Disease, Red Blood Cell Transfusion, and Thrombocytopenia in Pregnancy.
- Well-Being and Resilience - Well-being is a critical factor in the strength of the workforce, and the Society is committed to helping hematologists address the myriad factors impacting well-being through interventions such as openly addressing burnout in live meetings and in publications, advocating on behalf of hematologists to streamline administrative work, and sharing approaches to building resilience among hematologists.

Advocacy Resources (www.hematology.org/advocacy/)

ASH's Advocacy Center houses all of the Society's policy positions, advocacy efforts, and campaigns. Hematologists and their patients can follow the latest national policy news and directly influence their representatives through ASH Action Alerts. The Center also displays ASH's official policy statements along with testimony and correspondence related to federal regulation and private insurance developments.

- In August 2017, ASH launched a new online advocacy toolkit to provide members with the information and guidance necessary to communicate with elected officials in support of hematology. The new toolkit clearly and concisely explains how members can undertake a number of actions to support ASH's advocacy efforts.
- ASH recently launched a survey of all U.S. members to learn about what advocacy topics matter most to the Society's membership and the ways in which members would like to engage with their elected officials. If

you have not yet taken the survey but would like the opportunity to help shape the future of ASH's advocacy and policy efforts in Washington, please click here.

- Action Alerts
  - Contact Congress in Support of Sustained and Predictable Funding for NIH - Reach out to your legislators to protect funding for non-defense discretionary (NDD) programs including the National Institutes of Health (NIH).
  - Contact your Elected Officials to Support the Sickle Cell Disease Legislation - Your elected officials need to hear from you to improve the life of patients living with Sickle Cell Disease.
  - Urge your Representative to Support the Cancer Drug Parity Act – Legislation has been introduced in the U.S. House of Representatives that would ensure that patients enrolled in certain federally regulated health plans have access and insurance coverage for all anti-cancer regimens. Your Representative needs to cosponsor this bill in order for it to be considered by the full Congress.

Sickle Cell Disease

ASH is undertaking a multifaceted initiative to address the global burden of sickle cell disease (SCD). In September 2016, the Society issued *the State of Sickle Cell Disease: 2016 Report*, which can be found on the ASH SCD Initiative page along with other ASH SCD priorities. This report outlines the most pressing areas of need and provides a blueprint to advance these actions. To address issues related to access to care, ASH is (1) implementing a strategy to educate hematologists and other health care providers in all settings to recognize and properly respond to SCD complications; and (2) pursuing payment reforms to encourage appropriate care for individuals with SCD. ASH also continues to expand the Society's clinical SCD resources and plans to release new SCD-related educational tools and guidelines over the next few years.

ASH Publications

- Practice Update - The *Practice Update* is the society's bimonthly e-newsletter reporting on breaking news and activities of interest to the practice community.
- ASH Clinical News - *ASH Clinical News* is a magazine for ASH members and non-members alike – offering news and views for the broader hematology/oncology community.
- The Hematologist: ASH News and Reports - An award-winning, bimonthly publication that updates readers about important developments in the field of hematology and highlights what ASH is doing for its members.
- Blood – *Blood* is a weekly medical journal published by the American Society of Hematology. With an impact factor of 15.132 (2017), *Blood* is the most cited peer-reviewed publication in the field of hematology.
- Blood Advances – *Blood Advances* is a semimonthly medical journal published by the American Society of Hematology. It is the first journal to join the *Blood* family in 70 years and is a peer-reviewed, online only, open access journal.
- ASH-SAP - *American Society of Hematology Self-Assessment Program, Sixth Edition*. This is the most comprehensive ASH Self-Assessment Program edition to date, with 7 multimedia components and 23 updated chapters that cover the latest advancements in benign and malignant disorders, laboratory hematology, transfusion medicine, and other areas of hematology.

Meeting Information (www.hematology.org/meetings/)

- ASH Meeting on Hematologic Malignancies – September 7-8, 2018, Chicago, IL. This event will allow you to hear top experts in hematologic malignancies discuss the latest developments in clinical care and to find answers to your most challenging patient care questions.
- ASH Annual Meeting and Exposition – December 1-4, 2018, San Diego, CA. The Society's Annual Meeting and Exposition is designed to provide hematologists from around the world a forum for discussing critical issues in the field. Abstracts presented at the meeting also contain the latest and most exciting developments in hematology research.
- Consultative Hematology Course – Thursday, September 6, 2018 in conjunction with the ASH Meeting on Hematologic Malignancies, or Monday, December 3, 2018 in conjunction with the ASH Annual Meeting.

This intensive half-day program focuses on updates in non-malignant hematology designed for practitioners who are trained as hematologists or hematologist-oncologists, but now see patents with non- malignant hematologic conditions on a less frequent basis.

- Highlights of ASH - This meeting is designed to provide the highlights of the top presentations from ASH's annual meeting.
- Annual Meeting of the Hematology / Oncology Carrier Advisory Committee (CAC) Network– July 26 – 27, 2018, Washington, DC. This annual event brings together the hematologists and oncologists who serve as representatives to regional Medicare Contractors, Medicare Contractor Medical Directors, leaders from hematology and oncology state societies, and members of ASH and ASCO practice committees. The meeting is intended to provide attendees with a better understanding of the CAC process; discuss issues of common concern and develop solutions; and improve the overall CAC process throughout the year.

Other ASH Activities and Resources

- The ASH Academy – The ASH Academy provides hematologists with easy-to-use options for knowledge testing (for both MOC and CME purposes), completing practice improvement modules, as well as evaluating ASH meetings you attend and claiming CME credit for participating. The sixth edition of the ASH Self- Assessment Program (ASH-SAP) is also available on the ASH Academy.
- FDA – ASH partners with the Food and Drug Administration to alert members on new approved hematologic therapies.
- AMA – ASH is an involved member in the American Medical Association's (AMA) activities such as the AMA House of Delegates (HOD), AMA Current Procedural Terminology (CPT) Committee, and RVS Update Committee (RUC).
- Committee on Practice - The Committee on Practice is concerned with all issues affecting the practice of hematology. The Committee communicates with other organizations that have programs and policies that affect hematology practice. With appropriate review and approval by the Executive Committee, the Committee on Practice responds to practice-related issues by formulating positions on pending federal legislation, regulatory issues, and private insurance developments. The Committee also responds to matters of importance at the regional, state, and local levels, and to Society member requests.

If you have any questions on this list or any of the programs, please contact Katherine Stark, Policy and Practice Coordinator at kstark@hematology.org.

ASCO® Clinical Affairs

YOUR PRACTICE IS OUR FOCUS

ASCO CLINICAL AFFAIRS

Our Focus

The American Society of Clinical Oncology (ASCO) is working—through research, education, and promotion of the highest quality patient care—toward a world where cancer is prevented or cured, and every survivor is healthy. With the goal of ensuring that all patients receive the high-quality care that they expect and deserve, ASCO is committed to helping your oncology practice thrive in the ever-changing, ever-demanding healthcare delivery system.

ASCO Clinical Affairs is your one-stop shop for the operations side of cancer care, from educational resources and practical tools to transition your practice to a value-based reimbursement system, to data and information to enhance your business operations and quality of care.

Established in 2014 and staffed by national leaders in clinical oncology care and practice management, ASCO Clinical Affairs supports practicing oncologists, oncology administrators, and oncology practices in all settings—large and small community practices, hospital-based oncology departments and practices, and those in academic and research institutions.

How We Can Help

ASCO's Clinical Affairs team is here to provide the educational tools, training programs, services, and resources you need to deliver high-quality, high-value care to your patients. We can help your practice with practice management, quality, and performance improvement. Our team can help you collaborate with practices across the United States, innovate your practice's delivery of cancer care, and respond to the growing economic and administrative challenges that all oncology practices face today.

PRACTICE MANAGEMENT SUPPORT

ASCO Clinical Affairs offers the insight, tools, and support to help you deliver the highest quality cancer care and thrive in the ever-changing business of health care.

ASCO PracticeNET

PracticeNET is a rapid learning network where oncology practices of all sizes and in all settings share and receive insights to make improvements to the patient experience while enhancing business operations. PracticeNET analyzes your practice data to tell you how your practice performance is trending, the effectiveness of your business practices, and how your practice compares to others. PracticeNET participation helps practices bolster practice operations and productivity; better allocate resources; identify billing and coding opportunities; and discuss best practices in oncology practice management. For more information, contact **PracticeNET@asco.org**.

Coding & Reimbursement Assistance

Do you have questions about oncology-related coding, billing, and reimbursement? ASCO has answers. ASCO members have access to ASCO's electronic coding and reimbursement service at **asco.org/billingcoding**.

MACRA & the Quality Payment Program

The Medicare Access and CHIP Reauthorization Act of 2015 (MACRA) established the Quality Payment Program (QPP), which is transforming the way physicians are reimbursed for services provided under Medicare Part B. As your partner in preparing for these changes, ASCO has assembled a library of tools and information to help you implement the Quality Payment Program in your practice. Visit **asco.org/macra**.

Physician Payment Reform

ASCO has developed the Patient-Centered Oncology Payment (PCOP) model, an alternative payment model designed for oncology. PCOP fundamentally restructures the way oncologists are paid for cancer care in the United States and addresses one of the major problems in today's fee-for-service system: inadequate payment for the wide range of services critical to supporting patients with cancer and managing complex illnesses. PCOP also includes a much more streamlined quality reporting requirement than the Oncology Care Model. ASCO is proposing to Centers for Medicare & Medicaid Services (CMS) that PCOP be approved as an Advanced Alternative Payment Model and has developed tools to help practices achieve success under PCOP or any other alternative payment model.

FDA Alerts

ASCO partners with the U.S. Food and Drug Administration (FDA) to alert members on newly approved therapies for cancer patients to ensure you are current with the most effective, safest treatments available.

Influencing the Cancer Care Delivery System

ASCO Clinical Affairs brings together ASCO members and key stakeholders to influence policies that affect practice management. Join us and make your voice heard!

- **ASCO's Clinical Practice Committee:** ASCO Clinical Affairs supports ASCO's Clinical Practice Committee (CPC), a diverse group of community oncologists who provide leadership across a wide range of current practice issues, including physician reimbursement, clinical pathways in oncology, chemotherapy safe handling, and coding and billing concerns.
- **ASCO's Oncology Administrator Workgroup:** The Oncology Administrator Workgroup, supported by ASCO Clinical Affairs and guided by the CPC, is tasked with identifying issues facing oncology practices and providing a forum for discussion and evaluation of solutions. This group has addressed a wide range of practice issues, including insurance pre-authorization, outreach to administrators, practice needs assessment, and more.
- **AMA Activities:** ASCO participates in American Medical Association (AMA) activities such as the AMA House of Delegates, AMA CPT Advisory Committee, and AMA Relative Value Update Committee Advisory Committee to provide oncology-specific leadership in these influential decision-making entities.

Survey of Oncology Practice Operations

ASCO conducts an annual Survey of Oncology Practice Operations (SOPO) to capture the current state of business and operational issues in oncology to help practices navigate the evolving cancer delivery system. Participation in this survey allows practices to compare their operations to national benchmarks. For more information contact **clinicalaffairs@asco.org**.

ASCO® Survey of Oncology Practice Operations

ASCO® Practice Consulting Services & Support

ASCO Clinical Affairs provides cross-cutting consulting services by nationally recognized oncology experts, offering comprehensive, personalized support to oncology practices across the United States.

Services include:

- **Readiness assessment**, preparing practices for value-based care, new payment models and success in the Quality Payment Program
- **Practice operational assessment**, focused on the highest standards of care with review of patient flow, practice services, personnel, and physical space – resulting in actionable recommendations for practice success
- **Practice transformation implementation support**, personalized consulting services designed to meet your practice's specific needs
- **Analytical services**, providing support with practical data analytics - clinical, financial and operational
- **Triage pathways**, a decision support tool to help your patients get the right care at the right time in the right place. ASCO Consulting Services can help you prepare for effective implementation of triage pathways.

Practice Engagement Program

ASCO's new Practice Engagement Program provides a single point of contact for practices to help them identify and connect with the ASCO tools, programs, and resources that can best support their needs. After understanding the needs of each specific practice, the Practice Engagement Team can identify the ASCO resources to help resolve outstanding challenges, prepare for pending changes, and succeed in an ever-changing practice environment. Contact **clinicalaffairs@asco.org** for more information or assistance.

Data Analysis

ASCO Clinical Affairs Data Warehouse

Unlock valuable data to help your practice provide high-quality cancer care with ASCO's Clinical Affairs Data Warehouse. The data warehouse includes publicly available Medicare data, as well as previously unavailable survey and practice data, that the ASCO team uses to assist practices and support policy positions.

ASCO Practice Central

ASCO® Practice Central

ASCO Practice Central is the first ASCO website dedicated to the business of oncology. The new website provides one centralized, convenient place for oncology professionals to easily find resources on business services, quality improvement, hiring and recruitment, staff burnout, reimbursement, and other topics to help their practice succeed. Visit **practice.asco.org**.

QUALITY AND PERFORMANCE IMPROVEMENT

We know your practice is constantly striving to deliver the highest quality care possible to your patients.

Cancer programs and practices need to focus their quality strategies on high-impact metrics that will reflect quality, costs, health care utilization, and patient outcomes. ASCO Clinical Affairs offers unique opportunities to help enhance your quality assessment activities, understand quality and value, and provide you with information and tools to focus your resources to improve your practice performance.

ASCO Quality programs are expanding internationally. QOPI® is available to ASCO member practices in a number of countries outside the United States, and practices have achieved international QOPI® Certification and participated in the Quality Training Program.

QOPI®

The Quality Oncology Practice Initiative (QOPI®) is an oncologist-led, practice-based quality assessment program designed to promote excellence in cancer care by helping practices create a culture of self-examination and improvement. QOPI® provides a comprehensive library of measures, developed and adapted by oncologists and the oncology community, that allows your practice to reliably assess your care and demonstrate your quality to your patients and external stakeholders. QOPI® participants are also well-positioned to meet external reporting requirements for payers and the government and to participate in new payment models focused on quality. Please contact **qopi@asco.org** for more information or assistance.

QOPI® Certification Program

QOPI® Certification recognizes medical oncology and hematology practices that are committed to delivering the highest quality of cancer care. QOPI® Certification provides a three-year certification to outpatient oncology practices of all sizes and types by evaluating performance in clinical areas that affect patient care and safety. For more information or assistance, please contact: **qopicertification@asco.org**.

QOPI® Reporting Registry

The QOPI® Reporting Registry, a Qualified Clinical Data Registry (QCDR), brought to you by ASCO and the American Society for Radiation Oncology (ASTRO) is the one stop shop for 2018 MIPS reporting. Practices can use either the System Integrated Approach to report electronically via their EHR or the Web Interface Tool to enter data manually to satisfy 2018 MIPS reporting requirements in the Quality, Improvement Activities, and Advancing Care Information categories.

Quality Training Program

The ASCO Quality Training Program empowers practice teams to improve clinical care and operational performance and teaches teams how to balance Quality improvement projects with demanding schedules and competing priorities. The training employs proven experiential learning techniques with a quality issue selected by the oncology team. It will enhance practical team skill-building, help teams prepare for a changing reimbursement environment, and includes support when the team returns to the primary institution. The course is five days over six months and offers CME and MOC Part IV credits.

1-Day Quality Improvement Workshop

ASCO's 1-day Introduction to Quality Improvement Workshop focuses on defining a problem, mapping the process for improvement, identifying the cause, implementing the solution and sustaining the gain. Members of the Quality Training Program faculty will present basics on-site at practices who want to educate more staff in clinics.

For more information or assistance on the Quality Training Program or 1-day Workshop, email: **qualitytraining@asco.org**.

ASCO CLINICAL AFFAIRS TEAM

Stephen Grubbs, MD

ASCO Clinical Affairs is led by Vice President of Clinical Affairs Stephen Grubbs, MD, who joined ASCO in 2015 after 31 years as a medical oncologist and managing partner of an independent practice in Newark, Delaware, at the Helen F. Graham Cancer Center.

Walter Birch, MBA, CMPE

Walter Birch leads the Practice Management, Resources, Performance Improvement, and Quality Certification Team. Prior to joining ASCO, he worked in all aspects of physician practice management and consulting, including running national divisions of private and public companies employing physicians, managing hospital-owned physician practices, and leading physician-owned private practices.

Elaine L. Towle, CMPE

Elaine Towle joined the Clinical Affairs Team as Director of Analysis and Consulting Services after working as Director of Consulting Services for Oncology Metrics where she developed programs and services focused on clinical, financial, and operational excellence for community oncology providers. She is a former oncology administrator and past consultant editor for ASCO's *Journal of Oncology Practice.*

About ASCO

Founded in 1964, the American Society of Clinical Oncology (ASCO) is committed to making a world of difference in cancer care. As the world's leading organization of its kind, ASCO represents nearly 45,000 oncology professionals who care for people living with cancer. Through research, education, and promotion of the highest-quality patient care, ASCO works to conquer cancer and create a world where cancer is prevented or cured, and every survivor is healthy. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation. Learn more at **www.asco.org**, explore patient education resources at www.Cancer.Net, and follow us on Facebook, Twitter, LinkedIn, and YouTube. For policy-related developments, visit **ascoaction.asco.org**.

Contact Us

For more information about ASCO Clinical Affairs, please visit ASCO Practice Central at **practice.asco.org** or email **clinicalaffairs@asco.org**.

For information about all ASCO programs and resources visit **asco.org**.

ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY
MAKING A WORLD OF DIFFERENCE IN CANCER CARE

Meeting Evaluation Form

ASH and ASCO are committed to providing the highest quality for the CAC Network Meeting. To assist in meeting that goal, we ask that you please complete the following confidential survey and provide any comments or suggestions you may have.

DEMOGRAPHIC INFORMATION

I am (please check all that apply)

- ☐ The oncology CAC representative/alternate for my state.
- ☐ The hematology CAC representative/alternate for my state.
- ☐ The president (or another physician representative) of my state oncology society.
- ☐ The executive director/administrator of my state oncology society.
- ☐ A member of ASCO's Clinical Practice Committee.
- ☐ A member of ASH's Committee on Practice or ASH's Subcommittee on Reimbursement.
- ☐ A Medicare contractor medical director.
- ☐ An invited meeting speaker.

Evaluation Key

5	4	3	2	1
Strongly Agree	Agree	Neutral	Disagree	**Strongly Disagree**

Please indicate the degree to which you agree with the statements in each section below by placing a check mark on **5 (strongly AGREE) to 1 (strongly disagree) for each statement.**

1. **Welcome Reception**

WELCOME RECEPTION	1	2	3	4	5
The Welcome Reception provided an opportunity to network with other CAC representatives, state society representatives, contractor medical directors and committee members.					
The format of the Welcome Reception was a valuable addition to the meeting.					

2. **Group Dinners**

GROUP DINNERS	1	2	3	4	5
The group dinners provided the additional opportunity to network with other CAC representatives, state society representatives, committee members, and contractor medical directors.					
The size of the dinner group was appropriate for networking.					
I enjoyed the additional opportunity to network with other CAC meeting attendees.					

3. **General Meeting**

GENERAL MEETING	1	2	3	4	5
I learned new information or obtained a better understanding of a particular issue or topic.					
The topics discussed are important to my role as a CAC representative, state society representative or committee member.					
There were adequate opportunities for questions and answers or discussions of topics.					
The contractor medical director participation in the meeting was helpful in obtaining feedback on important issues.					
The written materials and resources provided in the binder were a helpful supplement to the discussions.					
The length of the meeting was appropriate.					
The meeting facility was conducive for the meeting format/structure.					

4. **Presentations/Speakers**

Please rate the usefulness of the following presentations as they relate to coverage/reimbursement:

PRESENTATION/SPEAKERS	1	2	3	4	5
Biosimilars by Dr. Jeffrey Crawford					
Next Generation Sequencing by Dr. Katherine Szarama					
Evidence Based Medicine by Dr. Arthur Lurvey					
CAR-T Cellular Therapy by Gary Goldstein					
Financial Implications of CAR-T Cell Therapies by Dr. Samuel Silver					

Additional Questions:

1. **If you participated in the CAC101 session this morning, what did you find most helpful?**

2. **What aspect(s) of the CAC Network Meeting do you find most valuable?**

3. **What aspect(s) of the CAC Network Meeting are most in need of improvement? (Please be specific.)**

4. **What topics or themes would you like to see addressed at future meetings?**

5. **Overall, how would you rate the CAC Network Meeting? (Please choose one.)**

   A) Excellent B) Good C) Fair D) Poor

6. **Is the current format of the CAC Network Meeting effective? (Please circle one): YES or NO**
   - **If you circled NO, please provide additional/alternative ways ASH and ASCO can make the meeting more effective.**

7. **Are there any additional resources ASH and ASCO can provide to assist you with the local coverage process?**

**** Thank you for your input! Please leave the evaluation form on your table. If you are unable to complete the form onsite, please e-mail the form directly after the meeting to ASH staff, Katherine Stark at kstark@hematology.org****

American Society of Hematology
www.hematology.org

American Society of Clinical Oncology
www.asco.org

AMERICAN SOCIETY OF HEMATOLOGY and
AMERICAN SOCIETY OF CLINICAL ONCOLOGY
2018 CAC Network Meeting
Travel Reimbursement Policy

The ASH-ASCO CAC Network Meeting Travel Reimbursement Policy is provided to travelers to provide guidance on the reimbursement for costs incurred in order to participate in the CAC Network Meeting. It is expected that the policy will be adhered to explicitly.

ASCO and ASH will reimburse the following groups for their attendance:

- CAC representatives and alternate representatives for hematology and oncology;
- Members of the ASCO Clinical Practice Committee and ASH Committee on Practice;
- Two representatives from the Hematology/ Oncology State Society*
- Medicare Contractor Medical Directors (CMDs) for all A/B MAC jurisdictions.

**Only two representatives from the state society (excluding CAC representatives) will be reimbursed for attending the ASH/ASCO CAC Network Meeting. State hematology/oncology society presidents and administrators/executive directors should determine who will attend the meeting. If more than two individuals from the state society (excluding CAC representatives) attend the meeting, reimbursement will be the responsibility of the state society or individual.*

Coverage begins at the actual start of a trip, whether it is from the traveler's regular place of employment, home, or other location, and terminates when the traveler reaches his/her original destination. Expenses for spouses and/or dependents are personal expenses and are not reimbursable.

Original receipts for all expenditures (including E-ticket passenger receipts, taxis, and parking) of **$25.01 or more** must be included with the CAC Network Meeting Expense Reimbursement Form. Requests for reimbursement must be submitted within **thirty (30)** days of the meeting for which reimbursable expenses were incurred. The approved reimbursement will be issued by check.

Air/Train Travel

ASH and ASCO will pay for coach class airline tickets (not business or first class), purchased through the ASH travel agency EWA Travel. Airline or train reservations should be made using ASH's travel agent, EWA Travel. Tickets are to be booked at least 30 days in advance of the meeting dates for domestic attendees (no later than June 22). Please contact Marika Delgado at EWA via email at ASH@ewatravel.com or by phone at 1(800) 705-8580.

ASH and ASCO will reimburse the most economical non-refundable coach fares available on a major airline carrier (American, Delta, Southwest, United, U.S. Airways, etc.). When a significantly less

expensive option is available, reservations made with a particular carrier to benefit the traveler will not be reimbursed in full; rather, the amount reimbursed will equal the amount of the equivalent ticket on the most economical carrier.

If an approved traveler wants to bring a guest, they must provide the ASH travel agent with a personal credit card for the guest's travel.

Ground Transportation

ASH and ASCO encourage the use of the most economical ground transportation to and from the airport or train station and will reimburse such expenses.

Use of a personal or university vehicle will be reimbursed at the mileage rate consistent with IRS rules and regulations (**$0.54 cents per mile as of 1/1/16, including gasoline**) plus toll and parking charges. (ASH and ASCO will reimburse parking charges and mileage as long as this amount is not greater than the cost of roundtrip taxi or shuttle service.)

If ASH and ASCO approve the use of a rental car, limits will be set and communicated to the traveler by the appropriate ASH or ASCO representative. The maximum rates set by ASH and ASCO take into account the cost of the rental, mileage, gasoline, parking, tolls, and any other expenses related to the use of the rental in order to attend the meeting.

Hotel

One night hotel stay will be provided for by ASH and ASCO. Additional nights can be reserved but the attendee will be responsible for the extra stay. (Individuals that would require two nights based on flight options and/or destinations must contact ASH or ASCO staff prior to making the reservation.)

The traveler is responsible for promptly submitting the RSVP Survey as requested by the ASH representative handling hotel room block arrangements. **Surveys are due June 22.**

Meals

Meals that are not provided during the meeting will be covered with the following limits including tax and tip:

Dinner	$75.00
Lunch	$40.00
Breakfast	$25.00

ASCO and ASH provide breakfast and lunch for Friday, July 27. Expenses incurred by attendees for either of these meals will not be reimbursed.

Cancellations and Changes

When a traveler needs to change or cancel an airline reservation, he/she must contact the issuing agent and notify the appropriate ASH or ASCO representatives **immediately**. Unless the change or cancellation is approved by ASH or ASCO, the traveler is responsible for all penalty fees and any other charges incurred due to such changes or cancellations. If the traveler does not inform the travel agency or airline of the cancellation prior to the scheduled departure time, and the ticket is thereby rendered unusable for future travel, then the traveler will be held responsible for the cost of the original ticket.

If a traveler needs to change or cancel a hotel reservation, he or she must contact the appropriate ASH or ASCO representative at least 72 hours prior to his/her originally scheduled arrival. The traveler is responsible for reimbursing ASH and ASCO for expenses incurred due to last-minute changes, cancellations, no-shows, and early departures.

Miscellaneous Expenses

- Baggage service, up to a maximum of one checked bag per flight and similar expenses are reimbursable.
- Internet service, up to $14 per day is reimbursable while attending the CAC Network Meeting.
- Tips not included with meals or cab fare should be listed separately on the CAC Network Meeting Expense Reimbursement Form.
- When a trip involves traveling for both the CAC Network Meeting and other purposes, the traveler must reasonably allocate the costs between CAC Network Meeting and the other activity.

If a traveler has any questions concerning any other reimbursable expenses, he/she should contact the appropriate ASH or ASCO representative.

American Society of Hematology
www.hematology.org

American Society of Clinical Oncology
www.asco.org

2018 ASH/ASCO CAC Network Meeting
Expense Reimbursement Form

Please fill out the information below and attach original receipts.
All forms must be submitted by August 27, 2018

Make check payable to: _____

Mail check to: _____

Meeting Attended: 2018 ASH/ASCO CAC Network Meeting

Signature: _____ **Date:** _____

Itemized Expenses:

Date	Description of Expense	Account (*internal use only*)	Amount
_____	_____	_____	$_____
_____	_____	_____	$_____
_____	_____	_____	$_____
_____	_____	_____	$_____
_____	_____	_____	$_____
_____	_____	_____	$_____

For ASH Use Only:
Approval: _____ Date Submitted to Accounting: _____

Please return completed form and original receipts by August 27, 2018 to:

Katherine Stark
American Society of Hematology
2021 L Street NW, Suite 900,
Washington, DC 20036
202-292-0252
kstark@hematology.org