EMBARGOED DRAFT IN REVIEWS

ASH 2023 TIP SHEET: Many physician-scientists and other researchers from **Sylvester Comprehensive Cancer Center** at the University of Miami Miller School of Medicine, will be making oral or poster presentations or participating in panel discussions at the American Society of Hematology's 2023 **annual meeting** in San Diego, Dec. 9-12.

Below is an **EMBARGOED** summary, highlighting several presentations involving Sylvester physicians and other staff members. For more information on any of these story ideas or to arrange an interview, please email Sandy Van, **sandy.van@miami.edu** or call/text **808.206.4576**.

Please note that all information is strictly embargoed until the date and time of each presentation. Thank you.

Lymphomas

984 **Limited Duration Loncastuximab Tesirine with Rituximab Induces High Complete Metabolic Response Rate in High-Risk Relapsed/Refractory Follicular Lymphoma -- a Phase 2 Study**
EMBARGOED UNTIL Monday, December 11, 2023: 5:45 PM, Grand Hall C
Presenting Author: **Juan Pablo Alderuccio, MD**, Sylvester Comprehensive Cancer Center
Intro: No standard-of-care exists for treatment of relapsed/refractory follicular lymphoma (FL) with worse prognosis in those demonstrating progression of disease within 24 months from frontline immunochemotherapy. Loncastuximab tesirine (loncastuximab) is an antibody-drug conjugate comprising a monoclonal antibody. The authors report results of a single-institution, investigator-initiated study evaluating this combination for the first time to treat FL.
Conclusion: A limited duration program combining loncastuximab with rituximab in patients with FL is well tolerated and highly effective for high-risk patients or those with high disease burden.

615 **Chimeric Antigen Receptor (CAR) T Cell Infusion for Large B Cell Lymphoma in Complete Remission: A Center for International Blood & Marrow Transplant Research (CIBMTR) Analysis**
EMBARGOED UNTIL Monday, December 11, 2023: 11:45 AM
Presenting Author: **Trent Wang, DO, MPH**, Sylvester Comprehensive Cancer Center
Intro: Only limited studies with small sample sizes exist for reported outcomes of patients with large B-cell lymphoma (LBCL) who are identified as being in radiographic complete remission (CR) after CAR T cell production. The authors hypothesize that these patients in complete remission before CAR T cell infusion will likely have favorable progression-free and overall survival rates with lower toxicity.
Conclusion: CAR T cell infusion in LBCL patients who are CR after receiving two or more lines of prior therapy is feasible, with a subset of patients remaining progression-free at two years. Their 9% rate of non-relapse mortality highlights the importance of continued follow-up.

1032 **Five Year Outcomes of Patients with Large B-Cell Lymphoma Treated with Standard-of-Care Axicabtagene Ciloleucel: Results from the US Lymphoma CAR-T Cell Consortium**
EMBARGOED UNTIL Monday, December 11, 2023: 5:45 PM
Presenting Author: **Jay Y. Spiegel, MD, FRCPC**, Sylvester Comprehensive Cancer Center

Intro: Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 CAR T-cell therapy that induces durable responses in patients with relapsed or refractory large B-cell lymphoma. The authors previously reported outcomes for axi-cell patients treated with standard-of-care therapy, including 42% who were ineligible for the Zuma-1 trial. Now, they update outcomes for this cohort at 58 months.
Conclusion: This multicenter, retrospective study showed similar five-year results to the Zuma-1 trial, despite including patients ineligible for that trial due to comorbidities. It supports the curative potential of axi-cel therapy but highlights the risk for non-relapse morbidity in this group.

383 **Risk of Transformation by Frontline Management in Follicular Lymphoma and Marginal Zone Lymphoma: A US Population-Based Analysis**
EMBARGOED UNTIL Saturday, December 9, 2023: 5 PM
Presenting Author: Jorge A. Florindez, MD, University of North Carolina School of Medicine
Sylvester Authors: Izidore S. Lossos, MD, and **Juan Pablo Alderuccio, MD**
Intro: Some patients with follicular or marginal zone lymphoma experience high-grade transformation (HGT) into diffuse large B-cell lymphoma. This study used population-based data to assess incidence and risk factors for HGT, post-HGT overall survival and lymphoma-specific survival across subtypes with treatment or surveillance as initial strategies.
Conclusion: Frontline treatment was associated with lower risk for HGT in follicular lymphoma, with advanced stage and female gender identified as risk factors. For other lymphomas, initial treatment neither diminished HGT risk nor improved survival afterward.

Hematologic Malignancies

750 **Bromodomain and Extra-Terminal Inhibitor INCB057643 (LIMBER-103) in Patients with Relapsed or Refractory Myelofibrosis and Other Advanced Myeloid Neoplasms: A Phase 1 Study**
EMBARGOED UNTIL Monday, December 11, 2023: 11:45 AM
Presenting Author: Justin Watts, MD, Sylvester Comprehensive Cancer Center
Intro: Bromodomain and extra-terminal (BET) proteins regulate expression of critical oncoproteins associated with myelofibrosis (MF) and other blood-cancer malignancies, including B-lymphoma-2. This ongoing phase I, dose-escalation study is evaluating the safety and tolerability of a BET inhibitor as monotherapy and in combination with ruxolitinib.
Conclusion: Monotherapy and combination therapy with ruxolitinib were generally well-tolerated, except for the largest monotherapy amount that caused two dose-limiting toxicities. Dose-finding for both therapies is ongoing to determine the recommended expansion dose.

Myelodysplastic Syndromes/Neoplasms

998 **Data-Driven Harmonization of 2022 Who and ICC Classifications of Myelodysplastic Syndromes/Neoplasms (MDS): A Study By the International Consortium for MDS (icMDS)**
EMBARGOED UNTIL Monday, December 11, 2023: 4:45 PM
Presenting Author: Luca Lanino, MD, Humanitas Clinical and Research Center, Milano, Italy
Sylvester Authors: Mikkael A. Sekeres, MD, **Justin W. Taylor, MD** and **Stephen D. Nimer, MD**
Intro: Significant discrepancies still exist between WHO and ICC classifications of myelodysplastic syndromes/neoplasms, despite their recent inclusion of gene mutations and chromosomal abnormalities to enhance diagnosis and clinical decision-making. These differences potentially cause inconsistent practices within the clinical setting. This study for the International Consortium for MDS adopted a data-driven model to develop a harmonization roadmap for these classifications.
Conclusion: The study demonstrated the value of this approach based on advanced statistical methods to generate harmonized MDS classifications.

1872 **Olutasidenib Alone or in Combination with Azacitidine Induces Durable Complete Remissions in Patients with mIDH1 Myelodysplastic Syndromes/Neoplasms (MDS)**
EMBARGOED UNTIL Saturday, December 9, 2023: 5:30-7:30 PM, Halls G-H (San Diego Convention Center)
Last Author: Justin M. Watts, MD, Sylvester Comprehensive Cancer Center (Presenting author is Jorge Cortes, MD, Georgia Cancer Center, Augusta)
Intro: Olutasidenib, a small molecule drug that targets a mutation involved in certain cancers and approved for relapsed and refractory acute myeloid leukemia (AML), was studied in 22 patients with a specific type of myelodysplastic syndromes/neoplasms (MDS).
Conclusion: In this subgroup of patients in a Phase 1/2 study, the drug – used both alone and in combination with another drug – induced durable remissions in patients with intermediate-, high-, or very high-risk MDS, and the treatment had a tolerable and manageable safety profile.

1860 **Correlation between Peripheral Blood and Bone Marrow Somatic Mutations Among Patients with Suspected or Established Myelodysplastic Syndromes from the National MDS Study**
EMBARGOED UNTIL Saturday, December 9, 2023: 5:30-7:30 PM, Halls G-H (San Diego Convention Center)
Last Author: Mikkael A. Sekeres, MD, Sylvester Comprehensive Cancer Center (Presenter: Amy E. DeZern, MD, Johns Hopkins University)
Intro: Myelodysplastic syndromes (MDS) – disorders of blood cells in the bone marrow – may result from mutations in stem cells responsible for blood cell creation. Screening and monitoring of some diseases can be accomplished by assessing mutations in peripheral blood, from a basic blood draw, but because the ability to detect and monitor mutations involved with MDS and related conditions is less certain, guidelines often require invasive bone marrow evaluations instead.
Conclusion: This study, which included 36 patients, compared results from peripheral blood and bone marrow studies and found that peripheral blood can be used to reliably identify somatic (non-hereditary) mutations in patients with suspected or established MDS and related conditions.

4613 **Impact of Type of Hypomethylating Agent (HMA) Used on Outcomes of Patients (Pts) with Higher-Risk Myelodysplastic Syndromes/Neoplasms (HR-MDS) – A Large, Multicenter, Retrospective Analysis**
EMBARGOED UNTIL Monday, December 11, 2023: 6-8 PM, Halls G-H (San Diego Convention Center)
Sylvester Co-Authors: Mikkael A. Sekeres, MD, and **Namrata Sonia Chandhok, MD**, Sylvester Comprehensive Cancer Center (Presenting Author: Jan Philipp Bewersdorf, MD, Memorial Sloan Kettering Cancer Center)
Intro: This multicenter analysis aimed to provide a better understanding of treatment options for patients with cancers of blood cells in the bone marrow – higher-risk myelodysplastic syndromes/neoplasms (HR-MDS). Two drugs, azacitidine and decitabine, both hypomethylating agents, or HMA, provide the foundation of mainstay, frontline treatments for HR-MDS, but they have not been compared directly in randomized trials.
Conclusion: This study, involving 1,223 patients, with 919 patients included in the survival analysis, found no significant difference in overall survival or overall responses between the two groups of patients treated with the drugs.

Leukemias

The Future Paradigm of HMA + ven or Targeted Inhibitor Approaches: Sequencing or Triplet Combinations in AML Therapy

EMBARGOED UNTIL Sunday, December 10, 2023: 4:30-5:45 PM, Room 6CF (San Diego Convention Center

Presenting Author: Justin M. Watts, MD, Sylvester Comprehensive Cancer Center

Description: This Education Session will review the transformation in AML therapy from traditional 7+3 for fit patients and hypomethylating agents for unfit patients to new standards of care and ongoing questions in the field. We will discuss the data regarding the development of hypomethylating agents plus venetoclax as the new standard of care for older patients and those not eligible for induction chemotherapy. There is growing interest in the use of HMA/Ven combinations for younger and fit patients and in specific subsets of AML - limited data in these patient populations and ongoing clinical trials will be reviewed. Resistance to HMA/Ven therapy remains a significant concern and recent data regarding mechanisms of resistance and potential strategies to overcome ven resistance will be addressed. Given the FDA approval of several targeted agents in AML since 2017, there is a need to understand and optimize the use of these medications in combinations with traditional AML therapy. Questions regarding combinations, sequencing and management of toxicities will be discussed. Optimization of 7+3 chemotherapy in specific subsets of AML will be reviewed, including 7+3 based combinations with FLT3 inhibitors or gemtuzumab, as well as the use of CPX-351 in older patients with secondary AML and recent data in other AML patient populations.

2888 **Olutasidenib for the Treatment of mIDH1 Acute Myeloid Leukemia in Patients Relapsed or Refractory to Hematopoietic Stem Cell Transplant, Prior mIDH1 Inhibitor, or Venetoclax**

EMBARGOED UNTIL Sunday, December 10, 2023: 6-8 PM, Halls G-H (San Diego Convention Center)

Last Author: Justin M. Watts, MD, Sylvester Comprehensive Cancer Center (Presenter: Jorge Cortes, MD, Georgia Cancer Center, Augusta)

Intro: Olutasidenib, a small molecule drug approved for treatment of relapsed and refractory acute myeloid leukemia, targets a specific mutation that exists in these cancers. It is being studied in subsets of patients whose disease returned after treatment with stem cell transplant or the drugs ivosidenib (IVO) or venetoclax (VEN). The research team is conducting post-study analyses to better understand the response to olutasidenib in these poor-prognosis subgroups.

Conclusion: Olutasidenib alone or in combination with a drug called azacitidine may induce complete remissions in patients with this type of AMD or myelodysplastic syndromes/neoplasms (MDS) that was relapsing or refractory to VEN, IVO or even hematopoietic stem cell transplant. This supports further study in larger groups of difficult-to-treat patients.

918 **Patient-Reported Outcomes in Acute Myeloid Leukemia Patients with FLT3-ITD Mutation Receiving Quizartinib Vs. Standard Chemotherapy: Results from the Quantum-First Trial - Clinically Relevant Abstract**

EMBARGOED UNTIL Monday, December 11, 2023: 4 PM

Presenting Author: Esther Natalie Oliva, MD, U.O.C. Ematologia, Grande Ospedale Metropolitano Bianchi Melacrino Morelli, Reggio Calabria, Italy

Last Author: Mikkael A. Sekeres, MD

Intro: QuANTUM-First, a global, phase 3 clinical trial evaluated the safety and effectiveness of the novel oral inhibitor quizartinib in combination with standard first-line and consolidation chemotherapy, and as a maintenance monotherapy for adults with acute myeloid leukemia (AML). While quizartinib showed clinically meaningful improvements in overall survival, an exploratory endpoint assessed its impact on patient-reported outcomes. The authors report the first longitudinal results of these outcomes.

Conclusion: Quizartinib showed improvement in overall survival without any detrimental impact on quality of life and symptoms when added to standard chemotherapy, followed by maintenance monotherapy in newly diagnosed AML patients.

Lung Cancer

2649 **Predictors and Timing of Venous Thromboembolism in Lung Cancer**
EMBARGOED UNTIL Sunday, December 10, 2023: 6-8 PM, Halls G-H (San Diego Convention Center)
Presenter: Thomas Plate IV, MD, Sylvester Comprehensive Cancer Center (all authors affiliated with Sylvester and/or University of Miami)
Intro: Venous thromboembolism (VTE), the blockage of a blood vessel by a clot, is a common complication in lung cancer, and physicians often prescribe blood thinners for prevention, but there's uncertainty about true incidence, risk factors and effects of treatments with various subtypes of lung cancer. Sylvester researchers analyzed data from their tumor registry to identify patients diagnosed with lung cancer between 2018 and 2022 and assess venous thromboembolism events and related factors.
Conclusion: The retrospective study found an increased risk of VTE among patients treated for lung cancer and determined that the development of thrombosis was associated with a significantly decreased overall survival. Every subgroup of patients was at high risk of developing VTE. Statistical analyses showed that VTE and other factors including age, gender, cancer stage, and blood counts were significant predictors of death.

Myeloid Malignancies

1547 **E7820, an Anti-Cancer Sulfonamide, in Combination with Venetoclax in Patients with Splicing Factor Mutant Myeloid Malignancies: A Phase II Clinical Trial**
EMBARGOED UNTIL Saturday, December 9, 2023: 5:30-7:30 PM, Halls G-H (San Diego Convention Center)
Last Author: Justin Taylor, MD, Sylvester Comprehensive Cancer Center (Additional Sylvester co-authors: Namrata Sonia Chandhok, MD, [co-first author] and Justin M. Watts, MD) (Presenting author: Jan Philipp Bewersdorf, MD, Memorial Sloan Kettering Cancer Center)
Intro: Researchers at Sylvester and Memorial Sloan Kettering have studied the effects of an experimental drug, E7820, in patients with relapsing or refractory acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) that result from mutations in certain genes. Preclinical data from their work shows a synergy between E7820 and a drug called venetoclax.
Conclusion: Based on preclinical data, the researchers plan to amend their current Phase II study to include a separate arm of E7820 in combination with venetoclax – a combination that has never been studied in human AML and MDS patients.

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