

# ASH 2026 Guidelines for Relapsed/Refractory Management of Acute Lymphoblastic Leukemia in Adolescents and Young Adults (ALL in AYAs)

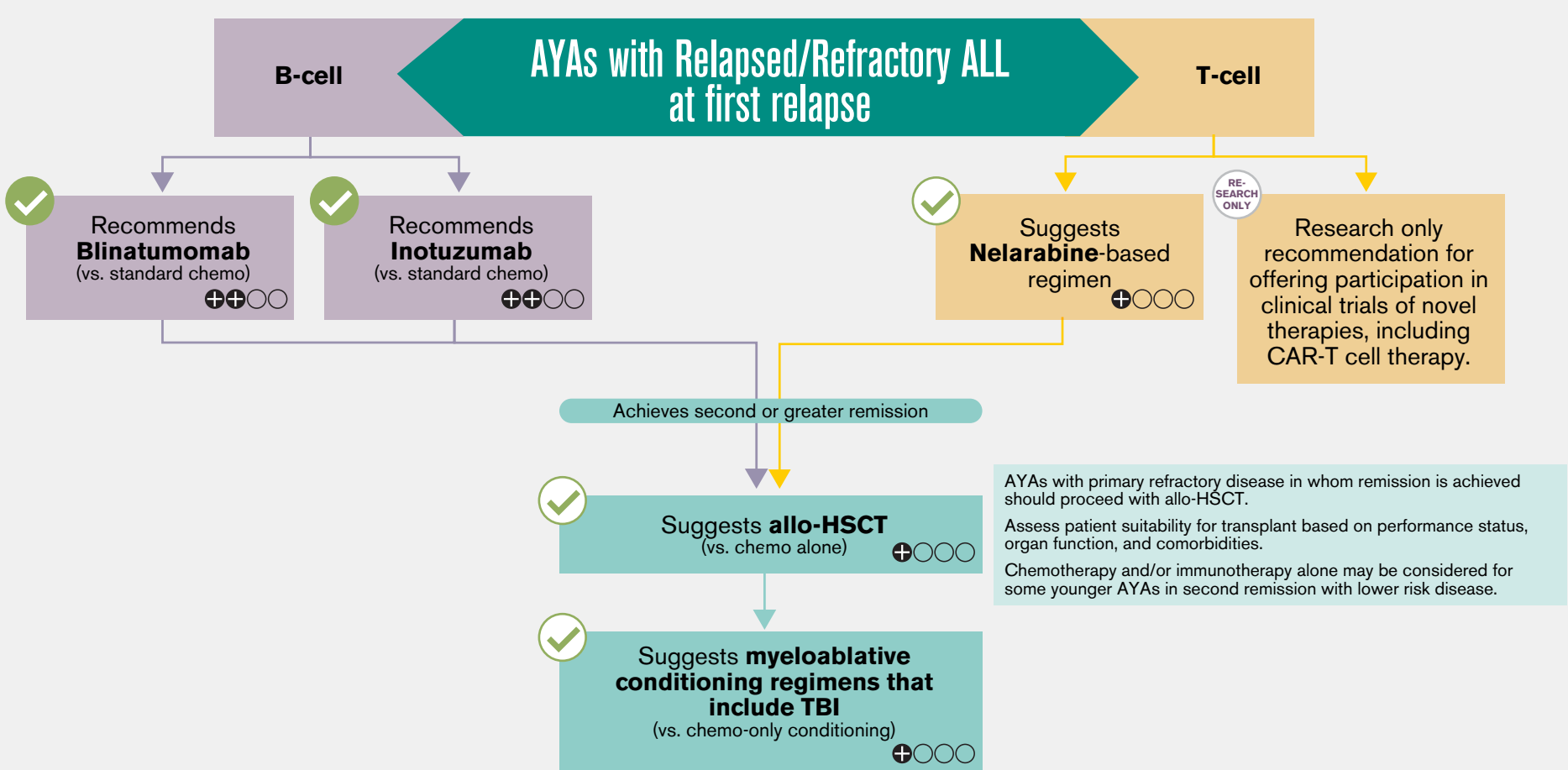
Visual Summary of Recommendations



## Relapsed or Refractory Management of ALL in AYAs



## Therapeutic Approaches



**ALL:** Acute lymphoblastic leukemia; **Allo-HSCT:** Allogeneic hematopoietic stem cell transplant; **AYAs:** Adolescents and young adults; **CAR-T:** Chimeric antigen receptor T-cell **CNS:** Central nervous system; **TBI:** Total body irradiation

**Research Only:** A research only recommendation is a recommendation that confines the use of intervention options in a specific population to a research setting.

## Isolated CNS Relapse



## Consolidation After CAR-T Therapy



Emerging evidence may aid in identifying individuals and clinical scenarios in which CAR-T therapy alone is sufficient, and in which the risks of transplant might outweigh the benefit. Individualized patient assessment and shared decision making are warranted.

\* with FDA approved autologous CD19 CAR-T products (tisagenlecleucel and brexucabtagene autoleucel)

## Minimal Residual Disease

GOOD PRACTICE

Measurement of disease response using MRD is considered standard of care in AYAs with ALL for both prognostic value and, in some cases, determination of treatment intensity.\*

**Good Practice:** Good practice statements (GPS) are ungraded recommendations that reflect what the guideline panel considers to be an uncontested marker of good care. While not fully supported by systematic evidence, GPS are strong, actionable, and widely accepted as beneficial best practices.

\*For more information on the MRD approach, refer to the ALL in AYAs Frontline Management Manuscript Recommendation 15.

**MRD:** Minimal residual disease

## Evidence Gaps

**CNS Relapse**

There is promising emerging data for the use of CAR-T cell therapy in the management of isolated CNS relapse; however, the data are insufficient to support a recommendation at this time. There are insufficient data to support a recommendation regarding the additional benefit of radiation when combined with other CNS-directed therapy.

**Blinatumomab vs. Inotuzumab vs. CAR-T**

There are nearly no head- to-head comparisons of these three therapies and the best sequence of their use is not yet understood. Therefore, the ASH guideline panel was unable to make a recommendation for one agent over the other. The choice should be made based on individual patient assessment, burden of disease, and candidacy for future consolidative therapy including allo-HSCT.

**CAR-T vs. Other Therapies**

With minimal comparative data to review,the panel was unable to make a recommendation between CAR-T therapy and chemotherapy or other immune-based therapies. However, the panel recognizes the notable utility of CAR-T therapy following relapse based on existing single arm studies.

## Psychosocial Care for AYAs

### Good Practice Statements

**Specialized care**

AYAs with ALL require person-centered and specialized healthcare.

**Psychological Needs**

Routinely assess psychosocial functioning and implement multidisciplinary psychosocial support from diagnosis and into survivorship.

**Social Support**

Assess existing social supports and encourage connection to supportive communities and resources as needed.

**Financial Needs**

Assess financial needs and encourage connection to institutional and/or regional financial counseling supports, resources, and organizations.

**Goals of Care**

Goals of care and end-of-life concepts should be addressed early in treatment and readdressed throughout treatment, particularly at transitional points during care (e.g., relapse).

**Clinical Trials**

Offer eligible AYAs enrollment in an appropriate clinical trial, as they are underrepresented in trials and have seen slower improvements in survival.

**Palliative care**

Interdisciplinary and/or primary palliative care should be provided throughout treatment starting at the time of diagnosis.

**Fertility**

Multidisciplinary and comprehensive fertility consultation and care should be provided prior to diagnosis and throughout treatment and into survivorship.

**Sexual Health**

Sexual health and relevant identities should be discussed with each individual patient at diagnosis and through treatment and survivorship.

**Developmental Needs**

Deliver service flexibly in consideration of each patient's developmental needs, preferences, and goals for treatment.

Learn more about the ASH 2026 Clinical Practice Guidelines on ALL in AYAs at [hematology.org/ALLguidelines](https://hematology.org/ALLguidelines)

	Recommendation Strength			
	Recommends... ✓	Recommends against... ✗	Suggests... ✓	Suggests against... ✗
	INTERPRETATION OF STRONG RECOMMENDATIONS		INTERPRETATION OF CONDITIONAL RECOMMENDATIONS	
Patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.		Most individuals in this situation would want the suggested course of action, but many would not. Decision aids may be useful in helping patients to make decisions consistent with their individual risks, values, and preferences.	
Clinicians	Most individuals should follow the recommended course of action. Formal decision aids are not likely to be needed to help individual patients make decisions consistent with their values and preferences.		Different choices will be appropriate for individual patients; clinicians must help each patient arrive at a management decision consistent with the patient's values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their individual risks, values, and preferences.	
Policymakers	The recommendation can be adopted as policy in most situations. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.		Policymaking will require substantial debate and involvement of various stakeholders. Performance measures should assess if decision making is appropriate.	
Researchers	The recommendation is supported by credible research or other convincing judgments that make additional research unlikely to alter the recommendation. On occasion, a strong recommendation is based on low or very low certainty in the evidence. In such instances, further research may provide important information that alters the recommendations.		The recommendation is likely to be strengthened (for future updates or adaptation) by additional research. An evaluation of the conditions and criteria (and the related judgments, research evidence, and additional considerations) that determined the conditional (rather than strong) recommendation will help identify possible research gaps.	

Evidence Certainty	
<b>High Certainty</b>	
++++	We are very confident that the true effect lies close to that of the estimate of the effect.
<b>Moderate Certainty</b>	
+++○	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.
<b>Low Certainty</b>	
++○○	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
<b>Very Low Certainty</b>	
+○○○	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

O'Dwyer, K.\*†, Winestone, L.\*, Cheung, M.C., Benitez, L., Buldini, B., Cole, P., Damaj, M., Dholaria, B., Dias, A., Dils, A., Fritsch, M., Greer, J., Hayes-Lattin, B., Henry, M., Jaffe, A., Jamy, O., Kebriaei, P., Mehrkens, I., Shah, N., Wilde, L., Young, P., Mai, H.J., Kanaan, G., Sereda, Y., Saldanha, I., Balk, E., Gupta, S†. American Society of Hematology 2026 guidelines for Relapsed/Refractory Management of Acute Lymphoblastic Leukemia in Adolescents and Young Adults (ALL in AYAs). *Blood Advances*. doi: <https://doi.org/10.1182/bloodadvances.2025006479>.

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