



Relapsed/Refractory Management of ALL in AYAs: What You Should Know



What it covers

- Relapsed/Refractory Management of Acute Lymphoblastic Leukemia in Adolescents and Young Adults (ALL in AYAs)



Why it matters

- Relapsed or refractory ALL in AYAs presents distinct challenges, including resistance to initial therapies, higher likelihood of treatment failure, high rates of toxicity, and a need for more intensive or novel therapies.
- AYA with relapsed or refractory ALL have worse prognoses than younger children, including higher relapse rates.
- Conventional therapies have often failed to provide durable remission.
- Several new immunotherapies have recently been approved for adults with relapsed or refractory ALL.
- Approaches to relapsed or refractory ALL differ significantly between pediatric and adult oncologists, highlighting a critical need for evidence-based, AYA-specific guidelines to standardize management and help clinicians determine the most appropriate agents and treatment strategies for this population.



Who it affects

- Adult and pediatric hematologists/oncologists, transplant specialists, AYA oncology specialists, pharmacists, social workers, psychologists, palliative care specialists, and additional specialists involved in the management of relapsed/refractory ALL in AYAs.



What are the highlights

- A major shift is occurring in the treatment of relapsed/refractory ALL in AYAs, with immunotherapy (blinatumomab, inotuzomab) recommended above traditional chemotherapy approaches, despite limited direct comparisons between these approaches.
- While CAR T-cell therapy shows immense promise in the treatment of this population, direct evidence for optimal sequencing relative to other immunotherapies is still emerging.
- While pediatric approaches to relapsed/refractory ALL may sometimes avoid transplant (e.g., late relapse with strong response to re-induction or use of CAR T-cell therapy), evidence for generalizing these strategies to older AYAs is lacking, making individualized assessment and shared decision-making essential.
- CNS-directed therapy (intrathecal chemotherapy) is recommended for isolated CNS relapse, while CNS radiation alone is not advised; the role of CAR-T therapy in CNS relapse is under investigation.
- Critical research priorities include AYA-specific clinical trials or sub-analyses, direct comparisons of immunotherapies, and studies assessing whether transplant use can be reduced without compromising cure rates in select AYAs.

Total number of panel recommendations: 8 (+ 1 research-only rec)

REFERENCE

O'Dwyer, K.*†, Winestone, L.*, Cheung, M.C., Benitez, L., Buldini, B., Cole, P., Damla, M., Dholaria, B., Dias, A., Dils, A., Fritsch, M., Greer, J., Hayes-Lattin, B., Henry, M., Jaffe, A., Jamy, O., Kebriaei, P., Mehrtens, I., Shah, N., Wilde, L., Young, P., Mai, H.J., Kanaan, G., Sereida, 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.202506479>.

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For more information on the ASH Clinical Practice Guidelines on Acute Lymphoblastic Leukemia in Adolescents and Young Adults, visit www.hematology.org/allguidelines

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