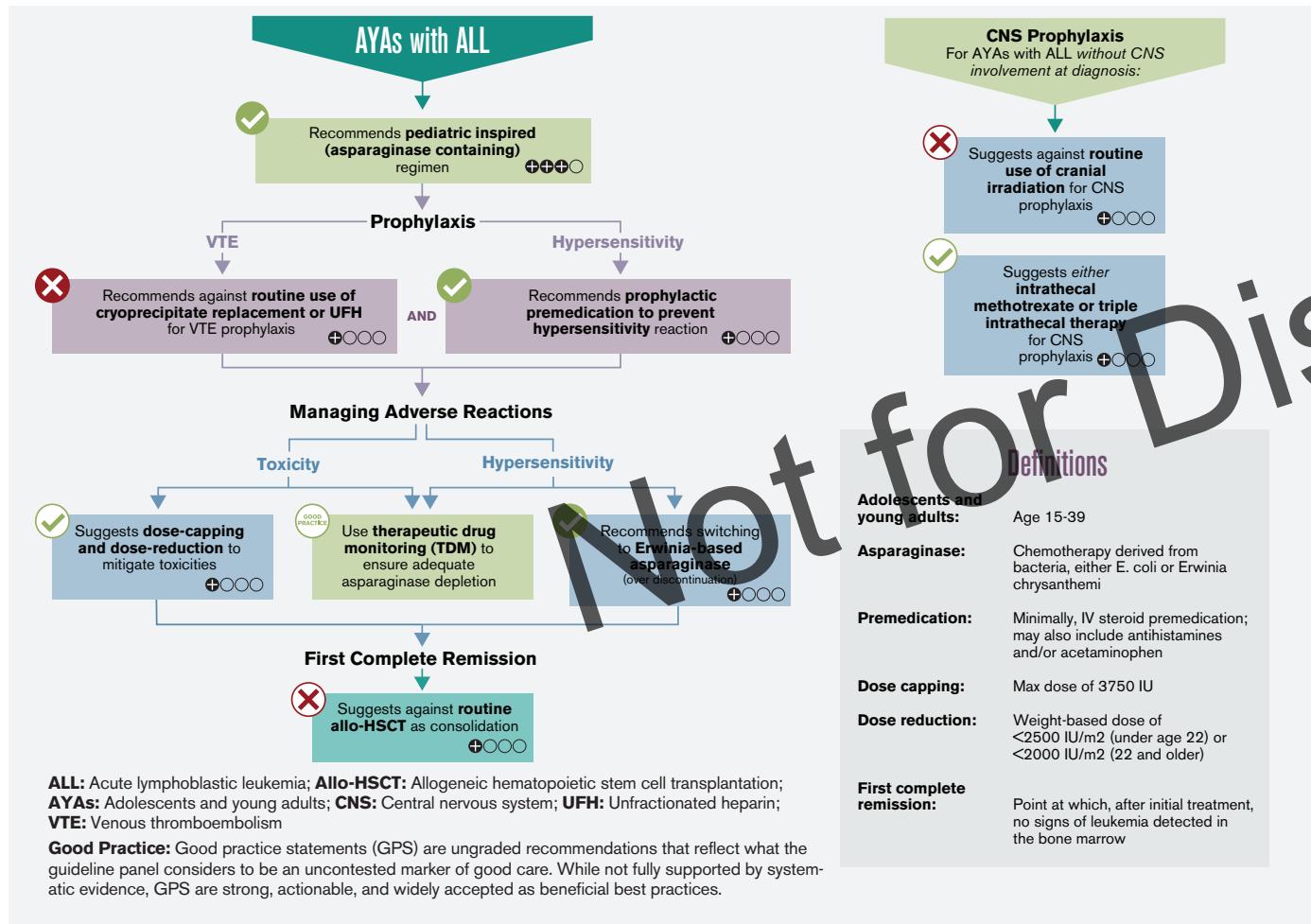


Frontline Management of ALL in AYAs



Frontline Management and CNS Prophylaxis



| Strong Recommendations | | Conditional Recommendations | |
|--|-----------------------|--|---------------------|
| Recommends... | Recommends against... | Suggests... | Suggests against... |
| ✓ | ✗ | ✓ | ✗ |
| 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. | |



ASH CLINICAL PRACTICE GUIDELINES
ACUTE LYMPHOBLASTIC LEUKEMIA

Frontline Management of Acute Lymphoblastic Leukemia in Adolescents and Young Adults (ALL in AYAs)

POCKET GUIDE
2026

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

Access additional tools and resources at hematology.org/ALLguidelines:

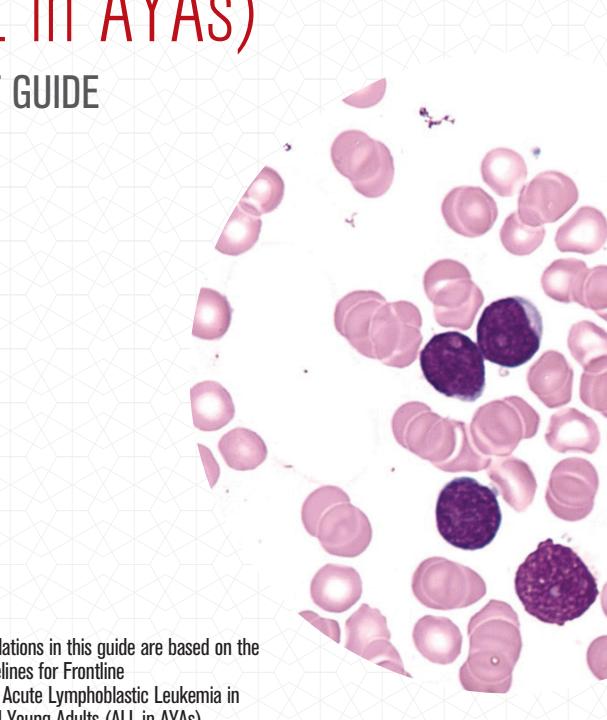
- Visual Summaries
- Teaching slides
- Infographics
- Snapshots
- Patient resources
- Additional pocket guides

Reference: DuVall, A.*, McNeer, J.*, Cheung, M.C., Adrianzen-Herrera, D., Advani, A., Aljurf, M., Audino, A., Benitez, L., Deeter, A., Dworkin, E., Hiltbrand, O., Isenlumhe, L., Jain, H., Li, L., Miller-Chism, C., Mozesohn, L., Ng, A., Pu, J., Shafer, D., Vargas-Madueno, F., Viny, A., Wadhwa, A., Yang, J., Zarnegar-Lumley, S., Mai, H.J., Kanaan, G., Sereda, Y., Saldanha, I., Balk, E., Stock, W.‡, Wolfson, J.‡. American Society of Hematology. 2026 guidelines for Frontline Management of Acute Lymphoblastic Leukemia in Adolescents and Young Adults (ALL in AYAs). *Blood Advances*. doi: <https://doi.org/10.1182/bloodadvances.2025006469>.

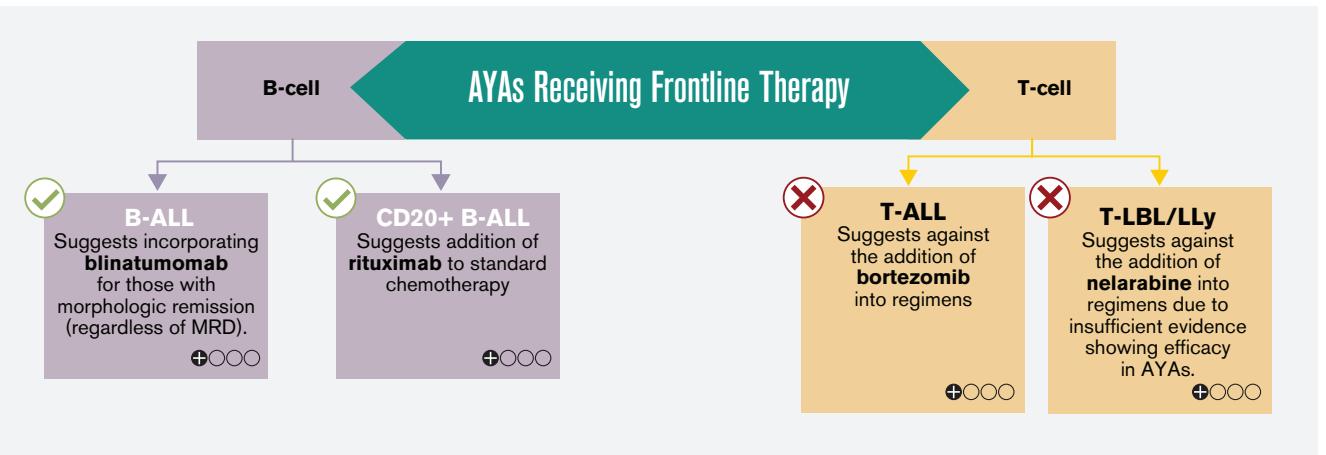
* DuVall, A. and McNeer, J. contributed equally to this work and share co-first authorship as co-writers of the guideline panel.

‡ Stock, W. and Wolfson, J. contributed equally to this work and share co-senior authorship as co-chairs of the guideline panel.

The recommendations in this guide are based on the ASH 2026 Guidelines for Frontline Management of Acute Lymphoblastic Leukemia in Adolescents and Young Adults (ALL in AYAs).



Therapies for Specific Subsets

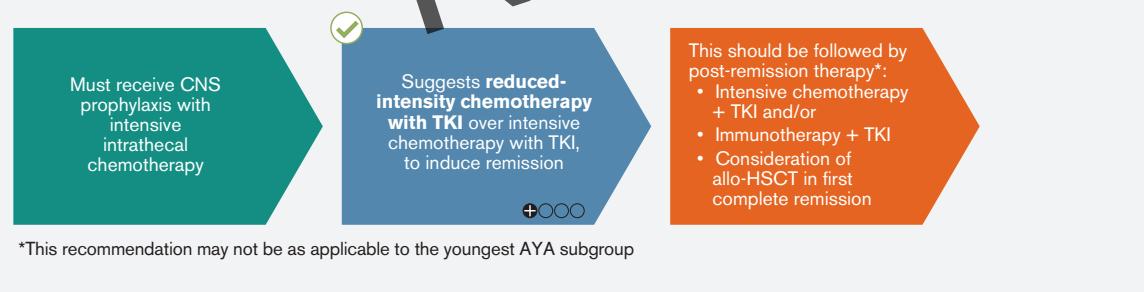


Minimal Residual Disease

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.



Treatment for Ph+ ALL



Evidence Gaps

VTE Prophylaxis

There is insufficient evidence to issue a recommendation for or against routine VTE prophylaxis with LMWH, DOACs or AT replacement. There is also uncertainty in timing or duration of VTE prophylaxis (induction, consolidation, intensification), LMWH dosing, and AT replacement targets; risk models are needed to identify high-risk patients.

Asparaginase

The evidence is insufficient to issue a recommendation on resuming asparaginase therapy after a non-hypersensitivity asparaginase-related toxicity. There is also a lack of evidence comparing effects of desensitization versus alternative asparaginase products.

Additional Therapies

Current evidence is insufficient to issue a recommendation for or against the addition of the following therapies for specific subsets:

- Inotuzumab ozogamicin for AYAs with B-ALL receiving frontline therapy.
- Nelarabine for AYAs with T-ALL receiving frontline therapy.*
- Bortezomib for AYAs with T-LBL.**

* may provide benefit among non-ETP subtype, CNS3 disease, and/or others who receive a high-dose methotrexate-based interim maintenance regimen

** may provide benefit among youngest adolescents

Psychosocial Care for AYAs

GOOD PRACTICE STATEMENTS

Specialized Care

AYAs with ALL require person-centered and specialized healthcare.

Psychological Needs

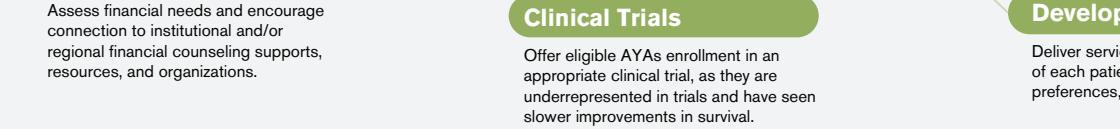
Routinely assess psychosocial functioning and implement multidisciplinary psychosocial support from diagnosis and into survivorship.

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.



ALL: Acute lymphoblastic leukemia; **allo-HSCT:** Allogeneic hematopoietic stem cell transplantation; **AT replacement:** Antithrombin replacement; **AYAs:** Adolescents and young adults; **B-ALL:** B-cell acute lymphoblastic leukemia; **CNS:** Central nervous system; **LMWH:** Low molecular weight heparin; **MRD:** Minimal residual disease; **T-ALL:** T-cell acute lymphoblastic leukemia; **TKI:** Tyrosine kinase inhibitor; **T-LBL/LLy:** T-cell lymphoblastic lymphoma; **VTE:** Venous thromboembolism