Medical Consultation Report

Patient Information

Patient Name	Eva Teterinova
Gender	Female
Date of Birth	February,9 ,2025
Diagnosis	B-cell acute lymphoblastic leukemia

Patient's condition

1.MLL-AF4–positive infant B-cell acute lymphoblastic leukemia (B-ALL) is an extremely high-risk subtype characterized by primary chemoresistance. The patient has shown no response to multiple lines of intensive chemotherapy, FLAG-IDA salvage therapy, or blinatumomab (a CD19/CD3 bispecific antibody).

2. Current disease burden (August 14, 2026):

- Bone marrow blasts: 93.8%
- Flow cytometry MRD: 78.0%
- Leukemic immunophenotype: $CD19^{+}$, $CD10^{-}$, $CD34^{+}$, $CD20^{-}$
- Peripheral blood WBC: 15.94 × 10^{9}/L, with 86% blasts
- Severe anemia and thrombocytopenia
- No evidence of leukemic involvement in the cerebrospinal fluid (CSF)
- History of Klebsiella pneumoniae and Candida glabrata infections
- Previous external hydrocephalus and cerebral cysts
- Hepatosplenomegaly
- Markedly elevated ferritin: 2,673 ng/mL
- Vitamin D deficiency

3. Previous lines of treatment:

MLL-Baby-2006 induction regimen

AIEOP-BFM-2009 HR-1

AIEOP-BFM-2009 HR-2

FLAG-IDA salvage chemotherapy

HR-block bridging chemotherapy + blinatumomab immunotherapy/targeted therapy

Despite all of the above treatments, the patient failed to achieve remission and the disease continued to progress. Following multidisciplinary team (MDT) evaluation at the local hospital, the patient was discharged with a palliative care plan.

Expert Recommendations

The leukemic cells continue to express the CD19 antigen, despite the failure of prior blinatumomab therapy. Therefore, CD19 CAR-T cell therapy remains a potential treatment option.

However, the patient has multiple high-risk factors associated with an unfavorable outcome following CAR-T therapy, including an extremely high tumor burden, the MLL-AF4 genotype, infant age, and failure of multiple prior lines of therapy. Consequently, the risks of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) are significantly increased. Even if remission is achieved, the patient will remain at high risk of subsequent relapse.

In this setting, CAR-T therapy should be considered primarily as a means of achieving remission rather than as definitive curative therapy. If MRD-negative remission can be achieved, the subsequent strategy should be to bridge the patient to allogeneic hematopoietic stem cell transplantation (allo-HSCT).

If the patient is unable to tolerate intensive therapeutic interventions, then best supportive and palliative care should be continued.

Stage Treatment Plan

Stage 0: Baseline Assessment and Preparation (1–2 Weeks)

Donor search: Perform high-resolution HLA typing (10/10) for the patient, parents, and siblings, with priority given to identifying a suitable related or matched unrelated donor.

Bone marrow assessment, flow cytometry, and target confirmation: Reassess hematologic, laboratory, flow cytometric, and genetic/molecular findings, including bone marrow morphology and confirmation of potential therapeutic targets.

Organ function and infection assessment: Perform echocardiography, liver and renal function tests, coagulation studies, ferritin and LDH testing, and correct vitamin D deficiency. Conduct a thorough evaluation for and control of any occult infections, particularly intestinal bacterial colonization and fungal colonization/infection. Complete CSF routine examination, biochemistry, flow cytometry, and CNS imaging.

Bridging/supportive therapy: While awaiting the availability of targeted therapeutic agents, use low-intensity chemotherapy as appropriate to maintain disease control, protect organ function, minimize the risk of tumor lysis syndrome (TLS), and stabilize the patient's overall clinical condition.

Stage 1: Targeted Therapy Combined with Chemotherapy for Rapid Tumor Burden Reduction

Regimen: Administer the targeted agent according to body surface area/body weight, in combination with reduced-intensity chemotherapy (such as low-dose cytarabine/cyclophosphamide or a vinca alkaloid) for 2–3 cycles. Continue intrathecal therapy for CNS prophylaxis.

Key toxicities: Myelosuppression, differentiation syndrome (DS), QTc prolongation, and elevated liver enzymes are characteristic toxicities and require close monitoring.

Assessment and monitoring:

Every 2–4 weeks: bone marrow morphology, multiparameter flow cytometry for MRD, and quantitative MLL/AF4 testing.

Weekly: complete blood count (CBC), liver and renal function tests, electrolytes, ECG with QTc monitoring, ferritin, and LDH.

Stage 2:CD19 CAR-T Cell Therapy

Goal: Achieve Flow Cytometry MRD Negativity and MLL/AF4 Negativity

Despite the failure of blinatumomab (BiTE) therapy, CAR-T cells have a different mechanism of action. Since the leukemic cells remain CD19-positive, with no evidence of CD19 antigen loss, CD19 CAR-T cell therapy still represents a potential strategy for achieving a deep remission. Autologous CD19 CAR-T cells may be administered following lymphodepleting conditioning, with the aim of achieving MRD-negative remission before the disease progresses again.

CRS/ICANS management: The patient is only 18 months old and weighs approximately 8.7 kg. Given the high risk of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), reducing the leukemia burden as much as possible before CAR-T infusion is important for improving treatment safety.

Assessment and monitoring: Bone marrow morphology, multiparameter flow cytometry for MRD, and quantitative MLL/AF4 testing should be performed on Day +14, Day +28, and Day +90 after CAR-T infusion. CAR-T cell expansion and peak levels should also be monitored, with daily assessment for CRS and ICANS during the high-risk period.

Once MRD-negative remission is achieved, the patient may proceed to allogeneic hematopoietic stem cell transplantation (allo-HSCT) as the next treatment stage.

Stage 3: Allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT)

Timing of transplantation: The transplant should be performed during the MRD-negative "window of opportunity."

Donor selection and conditioning: If no 10/10 HLA-matched related or unrelated donor is available, a TCRαβ-depleted haploidentical transplantation approach using a related donor may be considered.

Early post-transplant management: The main priorities will include graft-versus-host disease (GVHD) prophylaxis, infection prevention and control, and dynamic MRD monitoring.

Stage 4: Post-Transplant Hypomethylating Therapy + Oral Targeted Maintenance Therapy, with Dynamic Adjustment Based on Treatment Response

For patients who achieve and maintain MRD-negative status after transplantation, oral targeted maintenance therapy may be continued for 1–2 years to suppress KMT2A fusion-driven leukemogenesis and reduce the risk of molecular relapse.

Meanwhile, MRD and quantitative MLL-AF4 monitoring should be performed regularly, with the maintenance strategy adjusted dynamically according to the patient's treatment response and molecular disease status.

Estimated Treatment Duration and Cost (Based on an exchange rate of 1 USD = 7RMB; final costs will be calculated based on the actual exchange rate upon admission. Hospitalization fees are settled in RMB)

Stage / Item	Main Components	Estimated Cost (CNY, ¥)	Estimated Cost USD	Notes

Stage 0: Baseline Assessment and Preparation	High-resolution HLA typing, bone marrow evaluation, flow cytometry, genetic testing, imaging/CNS assessment, infection screening, and other baseline evaluations	50,000-100,000	7,143-14,286	One-time cost; includes approximately 1–2 weeks of inpatient evaluation
Stage 1: Targeted Therapy Combined with Chemotherapy for Tumor Burden Reduction	Targeted Therapy Combined with reduced-intensity chemotherapy + complication management and supportive care	400,000 – 600,000	57,143-85,714	Approximately 1–2 treatment cycles; cost will be dynamically assessed depending on the degree of tumor burden reduction
Stage 2: CD19 CAR-T	Apheresis, lymphodepletion, CAR-T cell manufacturing/product, infusion, and inpatient management of CRS/ICANS	800,000 – 1,000,000	114,286 – 142,857	Commercial CAR-T product pricing
Stage 3: allo-HSCT	Donor search, conditioning regimen, transplantation hospitalization, GVHD prophylaxis, engraftment/chimerism monitoring	600,000 – 800,000	85,714 – 114,286	Costs may be higher for haploidentical/unrelated donor transplantation; excludes provisions for severe early complications
Stage 4: Post-Transplant Maintenance	Hypomethylating therapy + oral targeted maintenance therapy, with long-term MRD/organ function monitoring			
Estimated Total	Total for Stages 0–3	1,850,000 – 2,500,000	264,286 – 357,143	Does not include costs associated with unpredictable severe complications

Note: All amounts above are stated in Chinese Yuan (CNY/RMB) and are budgetary estimates only, not final quotations. Actual treatment costs may vary depending on the patient's tolerance to medications, development of complications, and length of hospitalization. As the child is a Kazakhstani national, cross-border medical treatment (e.g., at centers in China, Türkiye, or Russia) will also require additional budgeting for travel, interpretation services, visa expenses, and an emergency medical contingency fund, estimated at approximately RMB 200,000–400,000.

The cost includes:

1.Single-room accommodation

1.All necessary tests as per the treatment plan

3.Medications, cell immunotherapy, and other treatment costs in accordance with the treatment plan

4.Routine medical services, doctor consultations, examinations, laboratory tests, etc.

The payment doesn't include:

1. Food;
2. Discharge medicine;
3. Unexpected treatment and examination such as life-threatening infection, serious CRS, CRES or ICU fees.
4. Treatment for unrelated disease;
5. Unexpected emergency management;
6. Personal expenses such as phone calls, flight tickets.

Payment Terms:

Initial Deposit: A minimum initial deposit of 100,000 USD equivalent to 700,000 RMB is required upon admission to the hospital. This deposit will be applied towards the estimated total cost of treatment.

Final Payment: The remaining balance will be due upon completion of the treatment. Any additional costs incurred during the treatment process will be added to the final payment, and any unused funds from the initial deposit will be refunded.

Important Notes

1. The above preliminary treatment plan is based on the information provided by the patient and/or their representative. Upon hospital admission, a comprehensive re-evaluation will be conducted. If there are significant discrepancies between actual condition and previously submitted history or test results, the treatment plan and costs may be adjusted accordingly after discussion with the patient and/or legal guardian.

2. This child has primary refractory MLL-AF4–positive infant acute lymphoblastic leukemia (ALL) with an extremely poor prognosis, and has failed multiple lines of standard therapy. Even with CD19 CAR-T cell therapy, there remains a substantial possibility that remission may not be achieved. Even if remission is achieved, the subsequent risk of relapse remains high. No treatment can guarantee a cure.

3. For the side effects of CAR-T therapy, particularly cytokine release syndrome (CRS) and neurotoxicity, close monitoring and timely intervention are recommended. The occurrence of CRS varies depending on individual differences, and the hospital has a comprehensive response system in place. After treatment, the hospital will provide detailed treatment records and follow-up plans to ensure that the patient receives support and monitoring upon returning home, focusing on disease recovery and potential side effects, with necessary adjustments to the treatment plan.

4. Based on currently available evidence, the treatment pathway described above represents a reasonable strategy aimed at maximizing the possibility of long-term disease-free survival. CD19 CAR-T therapy should be regarded as a means of achieving remission rather than definitive curative therapy. If remission is achieved, subsequent allogeneic hematopoietic stem cell transplantation (allo-HSCT) would still be required to provide a realistic possibility of long-term survival.

   However, the entire treatment course may involve substantial toxicity and considerable financial burden. Treatment should therefore proceed step by step only after the family has been fully informed of the potential benefits, limitations, and risks. The child's expected prognosis, quality of life, and the family's financial capacity should all be carefully considered. In this extremely high-risk situation, both active salvage treatment and palliative/supportive care are medically reasonable options, depending on the patient's clinical condition and the family's informed preferences.

5. One week prior to admission, it is necessary to provide recent external laboratory test reports and the patient's general condition, such as:

   A recent week's complete blood count (CBC) report to assess for bone marrow suppression or infection risk.

   Liver and kidney function reports, as well as cardiac function reports, to ensure the patient can tolerate chemotherapy.

   Infection control status, to confirm whether the patient has a severe infection.

   Physical condition assessment, especially to check for symptoms of GVHD (graft-versus-host disease).

   Blood type and RH blood type reports, in preparation for using donor cells during treatment.

We understand that seeking medical treatment abroad is a physical and emotional challenge for both patients and their families. Our hospital provides multilingual support, cultural sensitivity,

personalized meals, assistance with accommodation and transportation, and family companion services to create a safe and welcoming environment. From airport pickup and admission to recovery and follow-up, our international patient service team will accompany you throughout the entire process. Rest assured, we are committed to offering professional guidance and compassionate care to ensure your treatment journey is clear, reassuring, and well-managed.

Director of the Department of Hematology: Liuhuaying

Date: August,19, 2026