

Efficacy Analysis of Allogeneic Hematopoietic Stem Cell Transplantation for Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions

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Abstract

Objective

To investigate the clinical characteristics, diagnostic features, treatment strategies and prognosis of patients with myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions (MLN-TK).

Methods

Clinical data of 13 patients diagnosed with MLN-TK from January 2013 to October 2024 were retrospectively analyzed.

Results

A total of 13 patients were enrolled, including 12 males and 1 female, with a median age of 42 years (range, 6–59 years). The initial diagnoses comprised 4 cases of acute lymphoblastic leukemia (ALL), 4 cases of myeloproliferative neoplasms (MPN), 2 cases of myelodysplastic syndromes (MDS), 2 cases of acute myeloid leukemia (AML), and 1 case of mixed-phenotype acute leukemia (MPAL). Genetic detection identified FGFR1 rearrangement in 6 cases, PDGFRA rearrangement in 3 cases, PDGFRB rearrangement in 2 cases, JAK2 rearrangement in 1 case, and ETV6::ABL1 fusion in 1 case. Eight patients (61.5%) were complicated with eosinophilia, and 5 patients (38.4%) had extramedullary disease involvement. All patients were followed up until September 2025. Six patients received allogeneic hematopoietic stem cell transplantation (Allo-HSCT), among whom 5 survived and 1 died of severe acute graft-versus-host disease. The 5-year overall survival rate of transplanted patients was 83.3%. Among the 7 patients who did not undergo transplantation, 4 died of primary disease relapse and 3 were lost to follow-up.

Conclusion

MLN-TK is highly heterogeneous and easily misdiagnosed or missed. Tyrosine kinase inhibitor can be used as an effective bridging therapy. However, most subtypes except PDGFRA-rearranged neoplasms cannot achieve durable therapeutic responses. Allo-HSCT is the core curative approach for long-term survival of MLN-TK patients.

BACKGROUND

Myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase (TK) gene fusions (MLN-TK) constitute a group of highly heterogeneous clonal hematopoietic stem-cell disorders. The 5th-edition WHO classification released in 2022 has renamed and expanded this disease category, which includes rearrangement subtypes such as PDGFRA, PDGFRB, FGFR1, JAK2, FLT3 and ETV6::ABL1. Owing to its extremely low incidence, this disease frequently presents with myeloid proliferation or lymphoid-lineage involvement at blast phase in clinical settings, resulting in a high rate of misdiagnosis. By analyzing clinical data from 13 patients, this study aims to standardize the diagnostic workflow and evaluate the therapeutic efficacy of allogeneic hematopoietic stem-cell transplantation (Allo-HSCT).

PATIENTS AND METHODS

Patients

A retrospective analysis was performed on 64 consecutive patients admitted to Hebei Yanda Lu Daopei Hospital from January 2013 to October 2024, who were detected to carry rearrangements of PDGFRA, PDGFRB, FGFR1, JAK2, FLT3 and ETV6. Thirteen patients with incomplete clinical data that precluded accurate diagnosis, 22 patients with primary acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL), and 16 patients with Ph-like B-ALL were excluded. Ultimately, 13 patients with confirmed or revised diagnosis of MLN-TK were enrolled (Fig. 1 for the screening flow chart). Diagnostic criteria referred to the 5th edition WHO Classification of Haematolymphoid Tumours (2022)[1] and relevant consensus statements[2]. Chronic phase (CP) was defined as blast cell proportion < 10% in peripheral blood or bone marrow with chronic proliferative features; blast phase (BP) was diagnosed according to the diagnostic criteria for acute leukemia[3]. All patients were confirmed to harbor tyrosine kinase (TK) fusion genes by fluorescence in-situ hybridization (FISH) or quantitative PCR (qPCR). Secondary eosinophilia and other WHO-defined hematological malignancies were ruled out[4].

Baseline Observational Indicators

Complete clinical data of the patients were collected. Baseline assessments included blood cell counts, bone marrow smear, bone marrow pathological biopsy and immunohistochemical staining. Cytogenetic and molecular biological examinations consisted of chromosome karyotype analysis, FISH detection for gene rearrangements of PDGFRA, PDGFRB, FGFR1, JAK2, FLT3 and ETV6, qPCR assay for the FIP1L1::PDGFRA fusion gene, as well as targeted next-generation sequencing (NGS) for hematological malignancies.

Differential Diagnosis

Differential diagnosis from primary AML/ALL and Ph-like B-ALL: (1) MLN-TK originates from bone-marrow pluripotent hematopoietic stem cells, which is frequently accompanied by eosinophilia and capable of differentiation along both myeloid and lymphoid lineages. Tyrosine-kinase gene fusions involve myeloid and lymphoid lineages simultaneously, and components of chronic myeloid neoplasm (CMN) may emerge before, during or after ALL-directed treatment; (2) MLN-TK differs from Ph-like B-ALL in the partner genes of tyrosine-kinase fusions, and is often characterized by multi-lineage involvement; (3) The diagnosis of MLN-eo-TK applies to hematopoietic neoplasms carrying specific genetic abnormalities at initial onset, rather than cases that acquire such abnormalities in the course of disease progression or evolution[5]. Detection of the corresponding gene fusions within myeloid cell populations via fluorescence in-situ hybridization (FISH) helps distinguish MLN-TK from ALL.

Treatment Regimens for Patients After Confirmed Diagnosis

One patient with positive PDGFRA rearrangement received oral imatinib targeted therapy as bridging treatment for hematopoietic stem cell transplantation (HSCT) after diagnosis; one patient was treated with imatinib monotherapy, and the remaining one patient received chemotherapy combined with tyrosine kinase inhibitors (TKIs) including imatinib and dasatinib. One patient with PDGFRB rearrangement was administered chemotherapy plus oral imatinib, while the other patient received imatinib monotherapy. One BCR::JAK2-positive patient sequentially received chemotherapy, blinatumomab and CAR-T therapy, followed by bridging Allo-HSCT. One ETV6::ABL1-positive patient was given oral dasatinib prior to bridging Allo-HSCT. Among the six patients with positive FGFR1 rearrangement, three received TKI therapy followed by bridging Allo-HSCT, one was treated with imatinib monotherapy, and two were treated with chemotherapy combined with ponatinib and ruxolitinib. The disease course of the 13 patients can be referred to in Fig. 2.

Allogeneic Hematopoietic Stem-Cell Transplantation

HLA matching was performed for donors and recipients among patients who intended to receive Allo-HSCT. Principles for donor selection: matched-sibling donors were the first choice, followed by fully-matched unrelated donors, and haploidentical related donors were selected as the final option.

Conditioning Regimens

Busulfan combined with cyclophosphamide- or fludarabine-based regimens were used for patients receiving matched-sibling donor transplantation. For patients undergoing unrelated-donor or haploidentical transplantation, rabbit anti-human thymocyte immunoglobulin and semustine were added to the above-mentioned regimens.

Mobilization and collection: Donors received subcutaneous injection of G-CSF at a dose of $10 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ for 5 consecutive days. Peripheral-blood hematopoietic stem cells were collected on day 4 and day 5.

GVHD Prophylaxis

Prophylaxis was performed according to the Chinese expert consensus (2020 edition)[6]. Matched-sibling transplantation adopted cyclosporine A (CsA) combined with short-course methotrexate (MTX). For haploidentical and unrelated-donor transplantation, the regimen consisted of CsA, short-course MTX and mycophenolate mofetil (MMF). CsA was initiated at day - 1 or day - 9 before transplantation, with the minimal concentration of CsA maintained at 150–250 $\mu\text{g}/\text{L}$.

Supportive Care and Engraftment Assessment

G-CSF and TPO were routinely administered after transplantation to accelerate hematopoietic reconstitution. Irradiated blood products were transfused to maintain hemoglobin (Hb) $\geq 60 \text{ g}/\text{L}$ and platelet count (PLT) $\geq 20 \times 10^9/\text{L}$. Neutrophil engraftment was defined as an absolute neutrophil count (ANC) $\geq 0.5 \times 10^9/\text{L}$ for 3 consecutive days. Megakaryocyte engraftment was defined as PLT $\geq 20 \times 10^9/\text{L}$ for 7 consecutive days without platelet transfusion support[7].

Efficacy Evaluation and Follow-up

Treatment responses in the chronic phase were assessed according to criteria proposed by the MLN International Working Group[8], while responses in blast phase were evaluated using criteria for acute leukemia[9, 10]. Grading of acute GVHD (aGVHD) and chronic GVHD (cGVHD) followed the modified Glucksberg criteria and NIH consensus criteria[11]. Overall survival (OS) was defined as the interval from diagnosis to death or the date of last follow-up.

Statistical Analysis

Data analyses were performed using SPSS 26.0 and GraphPad Prism 10.0 software. Continuous variables were presented as median (range/IQR), and categorical variables were expressed as number of cases (percentage). Survival analysis was conducted via the Kaplan-Meier method, and between-group comparisons were performed using the Log-rank test.

RESULTS

1. Clinical features and laboratory tests

Among the 13 patients with MLN-TK, 12 were male and 1 was female; the median age at disease onset was 42 years (range 6–59 years).

1.1 Tyrosine kinase genetic subtypes

Six patients harbored FGFR1 rearrangement (3 cases each of BCR::FGFR1 and ZNF198::FGFR1); three patients had PDGFRA rearrangement (all FIP1L1::PDGFRA); two patients had PDGFRB rearrangement (all ETV6::PDGFRB); one patient was positive for BCR::JAK2 fusion and one for ETV6::ABL1 fusion, respectively.

1.2 Clinical diagnosis and revised diagnosis (Table 1)

Two patients were admitted with eosinophilia without prior treatment. One patient was admitted after receiving oral Chinese patent medicine, folic acid and vitamin B12 for a prior external-hospital diagnosis of myelodysplastic syndrome (MDS). One patient was admitted with untreated chronic myeloproliferative neoplasm. One patient was admitted after three cycles of ALL-directed chemotherapy for an external-hospital diagnosis of T-cell lymphoblastic lymphoma-leukemia. Eight patients (61.5%) presented with eosinophilia. Initial diagnoses included ALL/LBL (4 cases), MPN (4 cases), MDS (2 cases), AML (2 cases), and MPAL (1 case).

1.3 Extramedullary disease involvement

Four patients had extramedullary disease (EMD), among whom three had lymph node involvement (lymphoma-like morphology on pathology) and one had central nervous system involvement.

1.4 Cytogenetics and concomitant mutations

Four patients had normal karyotypes and two had complex karyotypes. Other cytogenetic abnormalities included + 21 (4 cases), + 8 (2 cases), t(8;13) (2 cases); single cases of t(1;5), t(9;22), t(5;12), inv(5), and t(8;21). Five patients had no additional detectable mutations; three carried TET2 mutations; single cases harbored U2AF1, ATM, KMT2D and RUNX1 mutations, respectively.

2. Transplant-Related Characteristics and Survival Outcomes in the Allo-HSCT Group (Table 2)

Six patients received Allo-HSCT (5 males, 1 female), with a median age at transplantation of 34 years (range, 16–60 years). Two patients with FGFR1 rearrangement and one BCR::JAK2-positive patient achieved complete remission (CR) prior to transplantation. The remaining three patients (FGFR1-rearranged, ETV6::ABL1-positive, and PDGFRA-rearranged) were in partial remission (PR) before transplant.

2.1 Conditioning regimens, donor and hematopoietic reconstitution

Modified Bu/Cy regimen was used in 2 patients, TBI/Flu in 2 patients, and TBI/Cy and Bu/Flu in 1 patient each. Five patients received haploidentical related-donor transplantation and one received matched-sibling transplantation. Five patients received combined bone-marrow plus peripheral-blood stem-cell grafts, and one received peripheral-blood stem-cell graft alone. The median infused mononuclear cell (MNC) dose was $6.225 (5.01–10.42) \times 10^8/\text{kg}$, and the median infused CD34⁺ cell dose was $4.86 (3.37–12) \times 10^6/\text{kg}$. All six transplant recipients achieved neutrophil engraftment, with a median neutrophil engraftment time of 13 days (range, 11–23 days). One patient failed to achieve platelet engraftment at day 42 post-transplant; for the other five patients, the median platelet engraftment time was 13 days (range, 12–34 days).

2.2 Transplant-related complications

Five patients (83.3%) developed acute graft-versus-host disease (aGVHD), including grade I in 3 patients (skin-only involvement) and grade II–IV in 2 patients (intestinal and hepatic involvement). One patient developed chronic GVHD (cGVHD) with bladder involvement. Other complications included CMV viremia (4 cases), EBV viremia (3 cases), HHV-6 encephalitis (1 case), and TA-TMA (1 case).

2.3 Post-transplant maintenance therapy:

One ETV6::ABL1-positive patient initiated dasatinib maintenance therapy at 3 months after Allo-HSCT and discontinued treatment due to pulmonary infection accompanied by cytopenia. One ZNF198::FGFR1-positive patient started pemigatinib maintenance at 7 months post-transplant, and another BCR::FGFR1-positive patient commenced ponatinib maintenance therapy at 2 months post-transplant.

2.4 Follow-up

The follow-up period ends on September 30, 2025, five patients were alive and one died from grade IV intestinal aGVHD. The 5-year overall survival (OS) rate of the transplant group was 83.3%. Compared with the non-transplant group, OS is shown in Fig. 3.

3. Survival Outcomes in the Non-Transplant Group

Among the seven non-transplanted patients: one PDGFRA-rearranged patient received imatinib monotherapy; another PDGFRA-rearranged patient was treated with chemotherapy combined with TKIs including imatinib and dasatinib. One PDGFRB-rearranged patient received chemotherapy plus oral imatinib, and the other PDGFRB-rearranged patient received imatinib monotherapy. Of the three FGFR1-rearranged patients, one received imatinib monotherapy, and two were treated with chemotherapy combined with ponatinib or ruxolitinib. Three patients were lost to follow-up and four died of primary-disease relapse or progression. The 1-year overall survival (OS) rate was 75.0%.

DISCUSSION

MLN-TK is a highly heterogeneous clonal hematopoietic stem-cell disorder, whose clinical manifestations and prognosis are markedly influenced by driver-gene subtypes and concomitant mutations. The 5th-edition WHO classification and International Consensus Classification (ICC) criteria in 2022 further refined the scope of this disease entity and formally added novel subtypes including ETV6::ABL1 and FLT3 rearrangements[1, 5]. In this retrospective study of 13 patients with MLN-TK, we aimed to explore precise diagnostic approaches and stratified therapeutic strategies based on real-world clinical practice.

The clinical manifestations of MLN-TK exhibit prominent subtype-specific features. In our cohort, PDGFRA/B rearrangements mostly presented in the chronic phase, whereas FGFR1, JAK2 and ETV6::ABL1 subtypes were more aggressive and frequently manifested as acute leukemia or accompanied by extramedullary disease at onset. Among the four patients diagnosed in blast phase, three harbored FGFR1 rearrangement and one carried JAK2 rearrangement; two out of four patients who progressed to blast-phase transformation had FGFR1 rearrangement. A registry-based cohort study by Metzgeroth et al[12] involving 135 patients demonstrated that over 90% of PDGFRA/B-positive patients achieved favorable responses to imatinib (IM) with rare disease progression, while other subtypes were frequently complicated by extramedullary involvement or acute leukemia (AL). In our series, two patients with PDGFRB rearrangement progressed from chronic phase (CP) to blast phase (BP), which was considered attributable to poor treatment adherence and clonal evolution induced by irregular drug administration.

Although eosinophilia represents a characteristic feature of MLN-TK, and marked eosinophilia is predominantly reported in PDGFRA-rearranged and ETV6::ABL1-fused subtypes[12, 13], eosinophilia is not universally present. Approximately 10% of patients with FIP1L1::PDGFRA rearrangement present without eosinophilia at initial diagnosis[12, 13]. The incidence of eosinophilia in our cohort was 57.7% (8/13). This finding indicates that routine screening for tyrosine-kinase-related gene fusions should be performed for patients with suspected MPN, MDS, or biphenotypic/mixed-phenotype acute leukemia (MPAL), even in the absence of prominent eosinophilia.

Accurate diagnosis of MLN-TK relies on genetic testing. Since this neoplasm originates from multipotential stem cells, it may exhibit dual myeloid and lymphoid (especially T-cell-lineage) involvement[5]. Conventional karyotyping alone carries a high risk of missed diagnosis for MPAL or Ph-like ALL without eosinophilia. Advanced molecular techniques such as next-generation sequencing (NGS) and RNA-seq play an irreplaceable role in identifying cryptic translocations (e.g. FIP1L1::PDGFRA resulting from t(4;12) deletion) and rare fusion partner genes. Our study highlights that transcriptome sequencing should be implemented early for special leukemia subtypes with suboptimal chemotherapy responses to identify potential TK gene fusions and avoid delayed initiation of targeted therapy.

For PDGFRA/B rearrangements, imatinib remains the cornerstone of first-line therapy. PDGFRA-rearranged neoplasms achieve nearly 100% response rates to imatinib (100–400 mg daily), and molecular complete remission (CMR) can be sustained even at low drug doses[14]. Grzegorz Helbig et al. reported a median time to hematologic remission of 13 days, while the median time to molecular remission reached 10 months; molecular remission could be maintained at a minimal dose of 100 mg per week for a median duration of 41 months, with a maximum follow-up of 71 months[14]. Julien Rohmer et al. published data on 151 FIP1L1::PDGFRA-positive MLN-TK patients in 2020[13], of whom 143 were male with a median age of 49 years at diagnosis. Common symptoms included fatigue, weight loss and persistent fever. The most frequently involved organs were the spleen (44%) and skin (32%), followed by the lungs (30%) and heart (19%). All 148 patients treated with imatinib achieved molecular remission. Among 46 patients who discontinued imatinib, 20 experienced subsequent relapse; 17 rapidly regained molecular remission after imatinib re-initiation. Multivariate analysis demonstrated that the initiation time and duration of imatinib treatment were independent risk factors for post-discontinuation relapse. To date, only two secondary imatinib-resistant point mutations (PDGFRA T674I and D842V) have been documented[15–18]; switching to nilotinib or dasatinib yields limited therapeutic efficacy. The novel targeted agent avapritinib shows promising activity against imatinib-resistant PDGFRA D842V mutation[19]. Therapy for PDGFRB-rearranged neoplasms resembles that for PDGFRA-rearranged disease; most patients are sensitive to imatinib, and primary resistance-associated point mutations have rarely been reported[20]. Nevertheless, Lucia Cavellier described one imatinib-resistant ETV6::PDGFRB-positive MLN-TK case in 2025[21], which harbored high-risk co-occurring mutations including ASXL1, KRAS, NRAS, SETBP1 and SRSF2, together with one variant of uncertain significance (VUS) in IDH2. This suggests that comprehensive molecular profiling and prompt evaluation for transplantation should be performed for PDGFRB-rearranged patients with unsatisfactory imatinib responses. One PDGFRA-positive patient in our cohort exhibited a poor response to imatinib, which was considered related to concurrent high-risk alterations such as MLL::PTD, indicating that concomitant gene mutations constitute an important factor influencing TKI efficacy.

FGFR1 rearrangement is relatively rare among MLN-TK, formerly termed 8p11 myeloproliferative syndrome, accounting for approximately 6% of cases. The most frequent fusion partner gene is ZMYM2 (also known as ZNF198), located at chromosome 13q12, followed by BCR. Previous studies have demonstrated that ZMYM2::FGFR1 is frequently associated with T-cell-origin lymphoma/leukemia or mixed-phenotype leukemia, mostly accompanied by elevated eosinophil counts, whereas BCR::FGFR1 usually presents as an MPN or CML-like phenotype with less frequent eosinophilia[22–45]. Patients with FGFR1/JAK2/FLT3 rearrangements or ETV6::ABL1 fusion harbor relatively abundant types and frequencies of concomitant mutations[46]. It has been well-established that FGFR1 rearrangement combined with RUNX1 mutation correlates with disease progression and adverse prognosis. RUNX1 mutations are detected in approximately 70–80% of FGFR1-rearranged patients[47]. In a cohort of seven FGFR1-rearranged patients reported by Paolo Strati in 2017, five carried RUNX1 mutations with distinct variant sites, and all presented with acute leukemia. Dasatinib, midostaurin and ponatinib cannot achieve durable remissions for FGFR1-rearranged disease. The FGFR1-3 inhibitor pemigatinib can be administered for relapsed/refractory disease at a dose of 13.5 mg daily for both treatment and maintenance, achieving a complete remission (CR) rate of 88.9% in chronic phase and 61.5% in blast phase; however, it is mostly applied as bridging therapy prior to Allo-HSCT[48]. Kento Umino summarized 45 FGFR1-rearranged patients in 2018; 14 patients ultimately received allogeneic hematopoietic stem-cell transplantation, including 3 transplanted in chronic phase and 11 in blast phase. The 1-year post-transplant overall survival (OS) rates were 66.7% and 61.5%, respectively[49]. This finding suggests that transplantation performed before blast-phase transformation may improve outcomes for patients in the chronic phase.

Six fusion partner genes have been reported for JAK2 rearrangements, among which PCM1 is the most common; the PCM1::JAK2 fusion can be detected by conventional cytogenetic methods. First-line therapeutic options include the JAK-inhibitor ruxolitinib or Allo-HSCT. Among nine patients receiving ruxolitinib

in Juliana Schwaab's report, five achieved hematologic remission, while only two attained molecular and cytogenetic remission, respectively[50]. Henry G. Kaplan systematically reviewed 66 PCM1::JAK2-positive patients in 2022; 40 patients were in chronic phase and 24 subsequently underwent transplantation, yielding a 5-year OS rate of 80.2%, which was significantly superior to that of non-transplanted patients[51]. Ruxolitinib can serve as pre-transplant bridging therapy. The most frequent fusion partner for FLT3 rearrangement is ETV6, accounting for over 50% of cases. ETV6::FLT3 usually manifests as a myeloproliferative neoplasm or CML-like phenotype and is prone to extramedullary lesions. Guilin Tang summarized 28 FLT3-rearranged patients; among 12 ETV6::FLT3-positive patients, nine mainly exhibited chronic proliferative features and ten had extramedullary involvement presenting as T-cell lymphoma or myeloid sarcoma[52]. FLT3 inhibitors including sorafenib, gilteritinib and midostaurin have proven effective for treatment; nevertheless, responses are transient and complete remissions are difficult to achieve. Early bridging to Allo-HSCT is therefore recommended. Alexander K. Chao reported one patient with CCDC88C::FLT3-positive disease refractory to intensive chemotherapy, who achieved cytogenetic remission after two-week sorafenib monotherapy and successfully proceeded to transplantation. Sorafenib was continued as post-transplant maintenance, and sustained molecular remission of primary disease was maintained[53].

The formation of ETV6::ABL1 fusion involves translocations and inversions affecting the ETV6 gene at 12p13.2 and the ABL1 gene at 9q34. Marketa Zaliouva reported 44 ETV6::ABL1-positive patients in 2016, including 22 with ALL, 18 with MPN and four with AML[54]. Eosinophilia was predominantly observed in patients with MPN and AML but was uncommon in ALL cases. ETV6::ABL1-positive disease confers poor clinical prognosis; imatinib, dasatinib and even nilotinib achieve limited and non-sustained therapeutic effects against this fusion[50]. Hence, Allo-HSCT remains required for curative intent in selected patients.

Allo-HSCT represents the core curative modality for long-term survival of MLN-TK patients, with the exception of the PDGFRA-rearranged subtype. Umino et al.[49]demonstrated that patients receiving transplantation in chronic phase achieved significantly better outcomes than those transplanted in blast phase. In our cohort, five out of six transplanted patients remained alive, with a 5-year OS rate of 83.3%, which was markedly superior to the non-transplant group. Of note, one FGFR1-rearranged patient developed testicular relapse three years after transplantation. This observation highlights that prophylactic post-transplant targeted maintenance therapy (e.g., ponatinib or pemigatinib) combined with minimal residual disease (MRD) monitoring is critical for relapse prevention for such high-risk subtypes.

MLN-TK is characterized by insidious onset and substantial molecular heterogeneity. Clinicians should raise awareness for identifying cases without eosinophilia and implement multi-omics technologies to achieve early diagnosis. The comprehensive therapeutic strategy should follow the integrated model: targeted-inhibitor-induced remission followed by timely allogeneic transplantation plus post-transplant targeted maintenance. Although limited by small sample size, our real-world cohort confirms the pivotal role of transplantation in improving prognosis for high-risk MLN-TK subtypes. Further multicenter studies are warranted to explore optimal post-transplant maintenance regimens for individual molecular subtypes and clarify the precise prognostic impact of concomitant mutations.

DECLARATIONS

Ethics approval and consent to participates

This study was approved by the Lu Daopei Medical Ethics Committee and complied with the requirements of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment in this study.

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Author Contribution

LZM and LY were responsible for the study concept and design. LZM and LY collected and analyzed the data and wrote the first draft of the manuscript. ZJR, HD, CXY, ZL, SYJ, SC, ZX, YJF, ZYL and LY treated the patients and assisted in the data collection. LZM and LY provided input for the figures and table. LZM and LY wrote the final draft of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. KHOURY JD, SOLARY E, ABLA O et al (2022) The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms [J]. *Leukemia* 36(7):1703–1719

2. 中华医学会血液学分会 (2017) 原发性骨髓增殖性肿瘤(2017版) [J]. 中华血液学 38(7):561–565
3. ARBER D A, ORAZI A, HASSERJIAN R et al (2016) The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia [J]. Blood 127(20):2391–2405
4. VALENT P, KLION A D, ROUFOSSE F et al (2023) Proposed refined diagnostic criteria and classification of eosinophil disorders and related syndromes [J]. Allergy 78(1):47–59
5. ARBER D A, ORAZI A, HASSERJIAN R P et al (2022) International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: integrating morphologic, clinical, and genomic data [J]. Blood 140(11):1200–1228
6. 中华医学会血液学分会 (2024) 原发性骨髓增殖性肿瘤(2024版) [J]. 中华血液学 45(6):525–533
7. DAVIES SM, KOLLMAN C, ANASETTI C et al (2000) Engraftment and survival after unrelated-donor bone marrow transplantation: a report from the national marrow donor program [J]. Blood 96(13):4096–4102
8. SHOMALI W, COLUCCI P, GEORGE T I et al (2023) Comprehensive response criteria for myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions: a proposal from the MLN International Working Group [J]. Leukemia 37(5):981–987
9. 中华医学会血液学分会 (2024) 原发性骨髓增殖性肿瘤(2024版) [J]. 中华血液学, 45(5): 417 – 29
10. 中华医学会血液学分会 (2023) 原发性骨髓增殖性肿瘤(2023版) [J]. 中华血液学 44(9):705–712
11. SCHOEMANS H M, LEE S J FERRARAJL et al (2018) EBMT-NIH-CIBMTR Task Force position statement on standardized terminology & guidance for graft-versus-host disease assessment [J]. Bone Marrow Transpl 53(11):1401–1415
12. METZGEROTH G, STEINER L, NAUMANN N et al (2023) Myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions: reevaluation of the defining characteristics in a registry-based cohort [J]. Leukemia 37(9):1860–1867
13. ROHMER J, COUTEAU-CHARDON A, TRICHEREAU J et al (2020) Epidemiology, clinical picture and long-term outcomes of FIP1L1-PDGFRα-positive myeloid neoplasm with eosinophilia: Data from 151 patients [J]. Am J Hematol 95(11):1314–1323
14. HELBIG G, MOSKWA A, HUS M et al (2011) Durable remission after treatment with very low doses of imatinib for FIP1L1-PDGFRα-positive chronic eosinophilic leukaemia [J]. Cancer Chemother Pharmacol 67(4):967–969
15. LIERMAN E, SMITS S, APPLEBY N et al (2019) FIP1L1-PDGFRα p.T674I-D842L: A Novel and Ponatinib Resistant Compound Mutation in FIP1L1-PDGFRα Positive Leukemia [J]. HemaSphere 3(2):e182
16. LIERMAN E, MICHAUX L (2009) FIP1L1-PDGFRα D842V, a novel panresistant mutant, emerging after treatment of FIP1L1-PDGFRα T674I eosinophilic leukemia with single agent sorafenib [J]. Leukemia 23(5):845–851
17. LIERMAN E, FOLENS C, STOVER E H et al (2006) Sorafenib is a potent inhibitor of FIP1L1-PDGFRα and the imatinib-resistant FIP1L1-PDGFRα T674I mutant [J]. Blood 108(4):1374–1376
18. COOLS J, DEANGELO D J, GOTLIB J et al (2003) A tyrosine kinase created by fusion of the PDGFRA and FIP1L1 genes as a therapeutic target of imatinib in idiopathic hypereosinophilic syndrome [J]. N Engl J Med 348(13):1201–1214
19. JONES R L HEINRICHC, VON MEHREN M et al (2020) Avapritinib in advanced PDGFRA D842V-mutant gastrointestinal stromal tumour (NAVIGATOR): a multicentre, open-label, phase 1 trial [J]. Lancet Oncol 21(7):935–946
20. REITER A, METZGEROTH G, CROSS N C P (2025) How I diagnose and treat myeloid/lymphoid neoplasms with tyrosine kinase gene fusions [J]. Blood 145(16):1758–1768
21. CAVELIER L, SAFT L, SANDER B et al (2025) Resistance to imatinib in a ETV6::PDGFRB rearranged myeloid/lymphoid neoplasm with high-risk mutations: a case report [J]. Front Oncol 15:1611747
22. KONISHI Y, KONDO T, NAKAO K et al (2019) Allogeneic hematopoietic stem cell transplantation for 8p11 myeloproliferative syndrome with BCR-FGFR1 gene rearrangement: a case report and literature review [J]. Bone Marrow Transpl 54(2):326–329
23. VILLAFUERTE-GUTIÉRREZ P, LÓPEZ RUBIOM, HERRERA P et al (2018) A Case of Myeloproliferative Neoplasm with BCR-FGFR1 Rearrangement: Favorable Outcome after Haploidentical Allogeneic Transplantation [J]. Case reports in hematology, 2018: 5724960
24. LIU JJ, MENG L (2018) 8p11 Myeloproliferative syndrome with t(8;22)(p11;q11): A case report [J]. Experimental therapeutic Med 16(2):1449–1453
25. MONTENEGRO-GARREAU X, MIRANDA R N, REYNOLDS A et al (2017) Myeloproliferative neoplasms with t(8;22)(p11.2;q11.2)/BCR-FGFR1: a meta-analysis of 20 cases shows cytogenetic progression with B-lymphoid blast phase [J]. Hum Pathol 65:147–156
26. LANDBERG N, DREIMANE A, RISSLER M et al (2017) Primary cells in BCR/FGFR1-positive 8p11 myeloproliferative syndrome are sensitive to dovitinib, ponatinib, and dasatinib [J]. Eur J Haematol 99(5):442–448
27. KHODADOUST MS, MEDEIROS B C LUOB et al (2016) Clinical activity of ponatinib in a patient with FGFR1-rearranged mixed-phenotype acute leukemia [J]. Leukemia 30(4):947–950
28. WANG W, TANG G, KADIA T et al (2016) Cytogenetic Evolution Associated With Disease Progression in Hematopoietic Neoplasms With t(8;22)(p11;q11)/BCR-FGFR1 Rearrangement [J]. J Natl Compr Cancer Network: JNCCN 14(6):708–711
29. MATIKAS A, TZANNOU I et al (2013) OIKONOMOPOULOU D. A case of acute myelogenous leukaemia characterised by the BCR-FGFR1 translocation [J]. BMJ case reports, 2013
30. SHIMANUKI M, SONOKI T, HOSOI H et al (2013) Acute leukemia showing t(8;22)(p11;q11), myelodysplasia, CD13/CD33/CD19 expression and immunoglobulin heavy chain gene rearrangement [J]. Acta Haematol 129(4):238–242
31. MORISHIGE S, OKU E, TAKATA Y et al (2013) A case of 8p11 myeloproliferative syndrome with BCR-FGFR1 gene fusion presenting with trilineage acute leukemia/lymphoma, successfully treated by cord blood transplantation [J]. Acta Haematol 129(2):83–89

32. HASLAM K, LANGABEER S E, KELLY J et al (2012) Allogeneic Hematopoietic Stem Cell Transplantation for a BCR-FGFR1 Myeloproliferative Neoplasm Presenting as Acute Lymphoblastic Leukemia [J]. *Case reports in hematology*, 2012: 620967
33. DOLAN M, CIOC A, CROSS N C et al (2012) Favorable outcome of allogeneic hematopoietic cell transplantation for 8p11 myeloproliferative syndrome associated with BCR-FGFR1 gene fusion [J], vol 59. *Pediatric blood & cancer*, pp 194–196. 1
34. WAKIM JJ, TIRADO C A, CHEN W et al (2011) t(8;22)/BCR-FGFR1 myeloproliferative disorder presenting as B-acute lymphoblastic leukemia: report of a case treated with sorafenib and review of the literature [J]. *Leuk Res* 35(9):e151–e153
35. KIM S Y, OH B, SHE C J et al (2011) 8p11 Myeloproliferative syndrome with BCR-FGFR1 rearrangement presenting with T-lymphoblastic lymphoma and bone marrow stromal cell proliferation: a case report and review of the literature [J]. *Leuk Res* 35(5):e30–e34
36. BALDAZZI C, IACOBUCCI I (2010) B-cell acute lymphoblastic leukemia as evolution of a 8p11 myeloproliferative syndrome with t(8;22)(p11;q11) and BCR-FGFR1 fusion gene [J]. *Leuk Res* 34(10):e282–e285
37. PATNAIK MM, GANGAT N (2010) Chromosome 8p11.2 translocations: prevalence, FISH analysis for FGFR1 and MYST3, and clinicopathologic correlates in a consecutive cohort of 13 cases from a single institution [J]. *Am J Hematol* 85(4):238–242
38. RICHEBOURG S, THEISEN O, PLANTIER I et al (2008) Chronic myeloproliferative disorder with t(8;22)(p11;q11) can mime clonal cytogenetic evolution of authentic chronic myelogenous leukemia [J], vol 47. *Genes, chromosomes & cancer*, pp 915–918. 10
39. LEE S G, PARK T S, LEE S T et al (2008) Rare translocations involving chromosome band 8p11 in myeloid neoplasms [J]. *Cancer Genet Cytogenet* 186(2):127–129
40. PINI M, SCARAVAGLIO GOTTARDIE (2002) A fourth case of BCR-FGFR1 positive CML-like disease with t(8;22) translocation showing an extensive deletion on the derivative chromosome 8p [J]. *Hematol journal: official J Eur Haematol Association* 3(6):315–316
41. DEMIROGLU A, STEER E J, HEATH C et al (2001) The t(8;22) in chronic myeloid leukemia fuses BCR to FGFR1: transforming activity and specific inhibition of FGFR1 fusion proteins [J]. *Blood* 98(13):3778–3783
42. KASBEKAR M, NARDI V, DAL CIN P et al (2020) Targeted FGFR inhibition results in a durable remission in an FGFR1-driven myeloid neoplasm with eosinophilia [J]. *Blood Adv* 4(13):3136–3140
43. VEGA F, MEDEIROS L J, BUESO-RAMOS C, E et al (2015) Hematolymphoid neoplasms associated with rearrangements of PDGFRA, PDGFRB, and FGFR1 [J]. *Am J Clin Pathol* 144(3):377–392
44. BARNES E J, LEONARD J, MEDEIROS B C et al (2020) Functional characterization of two rare BCR-FGFR1(+) leukemias [J], vol 6. *Cold Spring Harbor molecular case studies*, 2
45. VERSTOVSEK S, SUBBIAH V (2018) Treatment of the myeloid/lymphoid neoplasm with FGFR1 rearrangement with FGFR1 inhibitor [J]. *Annals oncology: official J Eur Soc Med Oncol* 29(8):1880–1882
46. WANG SA, ORAZI A, GOTLIB J et al (2023) The international consensus classification of eosinophilic disorders and systemic mastocytosis [J]. *Am J Hematol* 98(8):1286–1306
47. STRATI P, TANG G, DUOSE D Y et al (2018) Myeloid/lymphoid neoplasms with FGFR1 rearrangement [J]. *Leuk Lymphoma* 59(7):1672–1676
48. GOTLIB J. Available and emerging therapies for bona fide advanced systemic mastocytosis and primary eosinophilic neoplasms [J]. *Hematology American Society of Hematology Education Program*, (2022) 2022(1): 34–46
49. UMINO K, FUJIWARA S I, IKEDA T et al (2018) Clinical outcomes of myeloid/lymphoid neoplasms with fibroblast growth factor receptor-1 (FGFR1) rearrangement [J]. *Hematology* 23(8):470–477
50. SCHWAAB J, NAUMANN N, LUEBKE J et al (2020) Response to tyrosine kinase inhibitors in myeloid neoplasms associated with PCM1-JAK2, BCR-JAK2 and ETV6-ABL1 fusion genes [J]. *Am J Hematol* 95(7):824–833
51. KAPLAN H G, JIN R, BIFULCO C B et al (2022) PCM1-JAK2 Fusion Tyrosine Kinase Gene-Related Neoplasia: A Systematic Review of the Clinical Literature [J]. *Oncologist* 27(8):e661–e70
52. TANG G, TAM W SHORTNJ et al (2021) Myeloid/lymphoid neoplasms with FLT3 rearrangement [J]. *Modern pathology: an official journal of the United States and Canadian Academy of Pathology, Inc.* 34(9):1673–1685
53. CHAO A K, MEYER J A, LEE A G et al (2020) Fusion driven JMML: a novel CCDC88C-FLT3 fusion responsive to sorafenib identified by RNA sequencing [J]. *Leukemia* 34(2):662–666
54. ZALIOVA M, MOORMAN A V, CAZZANIGA G et al (2016) Characterization of leukemias with ETV6-ABL1 fusion [J]. *Haematologica* 101(9):1082–1093

TABLES

Table 1

No.	Sex	Age	Blood count at onset WBC/HB/PLT/NE (10 ⁹ /L)	EO (10 ⁹ /L)	Splenomegaly	Extramedullary involvement	Initial diagnosis	Treatment before admission	Bone marrow a
									Morphology
1	Male	59	32.1/86/100/N	0.485	N	N	MDS	Oral traditional Chinese medicine, folate, and vitamin B12	Hypercellularity grade IV–V; 6% blasts, 46.12% eosinophils
2	Male	23	26.36/143/315/19.66	2.08	Y	N	MPN	No treatment	Active proliferation; 11% eosinophils, 5% blasts
3	Male	26	18.88/N/N/N	2.4	Y	Lymph node(s)	T-LBL	VDLP + MTX chemotherapy	Grade II hypercellularity, 0.5% blasts
4	Male	47	80.6/148/217/58.1	0.2	N	N	MPN-ALL	Imatinib + VP chemotherapy	Grade IV hypercellularity, 3.5% blasts
5	Male	42	26.8/104/11/N	N	N	N	B-LBL	Chemotherapy + HLA-matched sibling HSCT	91% blasts
6	Female	16	75.11/133/163/5.28	N	N	N	B-ALL	Chemotherapy + venetoclax + blinatumomab	Extremely active proliferation; 58% blasts
7	Male	50	17.18/139/158.6/3.59	9.41	N	N	Hypereosinophilia	No treatment	Grade II hypercellularity, 20.8% eosinophils
8	Male	26	8.47/109/117/N	0.37	N	N	Myelodysplastic syndrome (MDS)	No treatment	Grade IV hypercellularity, 2.5% blasts
9	Male	44	50.62/137/156/N	N	N	N	Atypical chronic myeloid leukemia (aCML)	3 courses of chemotherapy + oral imatinib	Grade I hypercellularity, granulocytic series 81.5%
10	Male	52	59.35/101/88/N	N	Y	CNS	Abnormal blood count, pending workup	No treatment	Grade III hypercellularity, 12% eosinophils
11	Male	47	27/109/60/123	N	Y	N	Chronic myeloid leukemia (CML)	No treatment	Active proliferation; 11% eosinophils, 5% blasts
12	Male	6	32/146/446/22.6	4.54	Y	Lymph node(s)	Hypereosinophilia	Glucocorticoids + imatinib	Active proliferation; 10.5% eosinophils
13	Male	37	30/210/85/N	N	N	Lymph node(s)	Polycythemia vera (PV)	5 courses of chemotherapy	Grade I–II hypercellularity, 96.6% blasts

Table 1 (cont.)

No.	Revised diagnosis & stage	Treatment after diagnosis	HSCT	Outcome	Cause of death	Survival after diagnosis	Survival after HSCT
1	MLN-TK / CP	Imatinib + HSCT	Yes	Alive		64m	61m10d
2	MLN-TK / CP	Dasatinib + HSCT	Yes	Alive		10m	8m16d
3	MLN-TK / BP	Venetoclax + pemigatinib + HSCT	Yes	Alive		23m	21m9d
4	MLN-TK / BP	VDP + ponatinib + HSCT	Yes	Alive		130m	128m7d
5	MLN-TK / BP	(After relapse) ponatinib + CAR-T + second HSCT	Yes	Deceased	Acute GVHD	20m	54d
6	MLN-TK / BP	CAR-T + HSCT	Yes	Alive		44m	15m3d
7	MLN-TK / CP	Oral imatinib only, not evaluated	No	Lost to follow-up		1m	
8	MLN-TK / CP	DEC + AA chemotherapy + imatinib–dasatinib	No	Lost to follow-up		3m	
9	MLN-TK / CP-BP	Imatinib + chemotherapy	No	Deceased	CNS relapse	1m	
10	MLN-TK / CP-BP	Oral imatinib only	No	Lost to follow-up		1m	
11	MLN-TK / CP	Oral imatinib only	No	Deceased	Relapse	20m	
12	MLN-TK / CP-BP	Ponatinib + chemotherapy	No	Deceased	Relapse	22m	
13	MLN-TK / CP-BP	Chemotherapy + ruxolitinib	No	Deceased	Relapse	12m	

Table 2

No.	Gender	Age (years)	Fusion gene	Time from diagnosis to HSCT	Disease status before HSCT	HCT-CI score	Extramedullary disease	Transplant type
1	Male	59	FIP1L1::PDGFRA	4 months	PR	3 (coronary heart disease + diabetes)	No	Related haploidentical
2	Male	23	ETV6::ABL1	2 months	PR	0	No	Related haploidentical
3	Male	26	ZNF198::FGFR1	2 months	PR	0	Lymph node involvement	Unrelated haploidentical
4	Male	47	BCR::FGFR1	2 months	CR	1	No	Related fully matched
5	Male	42	BCR::FGFR1	First HSCT: 3 months; Second HSCT: 20 months	CR	1	No	Related haploidentical
6	Female	16	BCR::JAK2	29 months	CR	0	No	Related haploidentical

Table 2 (continued)

No.	Conditioning regimen	Graft source	Hematopoietic recovery	aGVHD	cGVHD	Viral infection	Post-HSCT maintenance therapy	Outcome
1	Ara-C + decitabine + BuCy + ATG (Fresenius) + semustine	BM + PB	WBC engraftment: day 22; PLT engraftment: day 34	Grade III; grade 2 liver, involving the intestine; bladder	—	CMV viremia	No	Alive
2	Thiotepa/Ara-C/Bu/Flu/ATG (immediate) / semustine	PB	WBC engraftment: day 12; PLT engraftment: day 12	Grade I; grade 2 skin	No	EBV and CMV viremia	Dasatinib (discontinued due to febrile neutropenia)	Alive
3	Thiotepa/Ara-C/TBI/Flu/ATG (Fresenius) / semustine	PB	WBC engraftment: day 11; PLT engraftment: day 13	Grade I; grade 1 intestine	No	EBV and CMV viremia	Pemigatinib	Alive
4	FLAG + BuCy + ATG (immediate) + semustine	BM + PB	WBC engraftment: day 12; PLT engraftment: day 12	No	No	EBV viremia	Ponatinib	Alive
5	Ara-C + TBI + Flu + ATG (porcine) + semustine	BM + PB	WBC engraftment: day 23; PLT not engrafted	Grade IV; skin, liver, and intestine	No	CMV viremia	No	Died of aGVHD
6	Ara-C/TBI/Cy/ATG (Fresenius)/semustine	BM + PB	WBC engraftment: day 15; PLT engraftment: day 16	Grade I; grade 1 skin	No	No	No	Alive

Figures

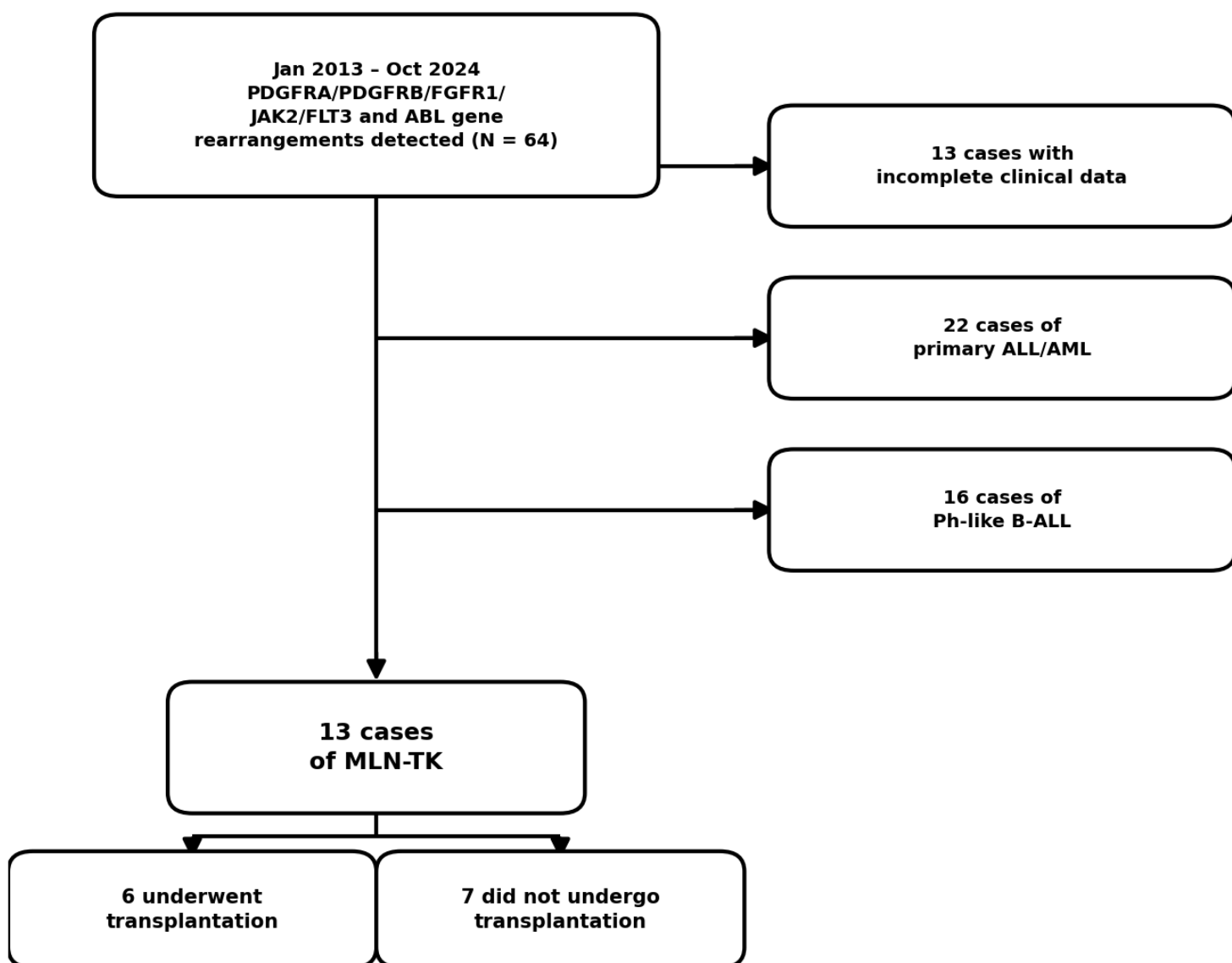


Figure 1

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Swimmer Plot of HSCT Treatment in CML Patients
N=13 | Treatment Timeline: Chronic Phase (CP) vs Blast Phase (BP)

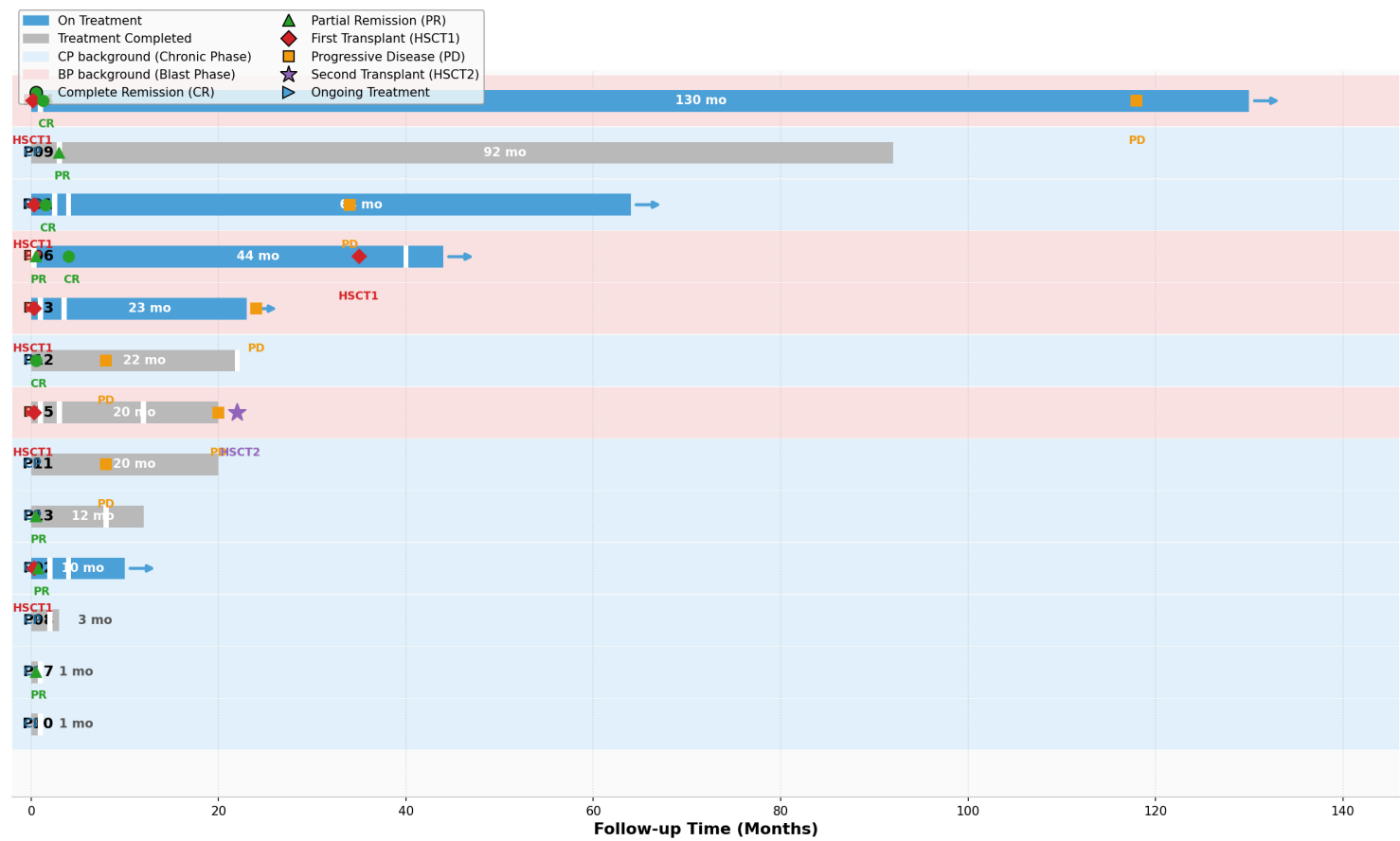


Figure 2
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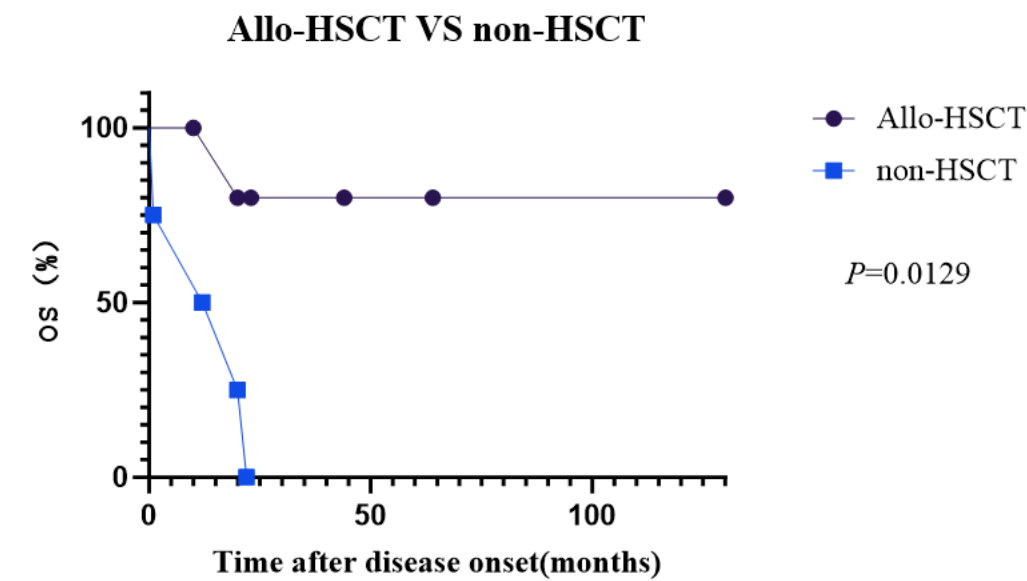


Figure 3
Legend not included with this version.