PF179 DIFFERENT IMPACT OF BCR BREAKPOINT ON THE OUTCOME OF ALLERGIC HEMATOPOIETIC CELL TRANSPLANTATION FROM DIFFERENT GRAFT SOURCE FOR PH+ALL IN THE ERA OF TKI

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Background: Prognostic significance of different BCR breakpoints in Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL) has not been established. BCR-ABL1-positive cells outside the B-lineage compartment was reported in 40% of adult patients with Ph+ALL and the frequency was different between patients with minor BCR (mi-bcr) and major BCR (Ma-bcr). This could suggest the possibility of biological differences in Ph+ALL according to BCR breakpoint. In the era of tyrosine kinase inhibitors (TKIs), allogeneic hematopoietic cell transplantation (allo-HCT) is still considered to be a choice to cure Ph+ALL. Different effect of unrelated graft source was reported on the outcome of allo-HCT with positive minimal residual disease (MRD) in a recent study.

Aims: We aimed to clarify the impact of BCR breakpoint as well as MRD status and graft source on the outcome of allo-HCT for Ph+ALL in the era of TKI.

Methods: We analyzed data from a registry database for 803 adult Ph+ALL patients who underwent unrelated allo-HCT in the first complete remission. BCR breakpoint was mi-bcr in 627 patients (78%), and Ma-bcr in 154 (19%).

Results: Overall survival (OS) rates at 4 years were 64% in mi-bcr and 61% in Ma-bcr among patients who underwent unrelated bone marrow or peripheral blood transplantation (UBMT) (P = 0.43), and 65% in mi-bcr and 67% in Ma-bcr among patients who underwent unrelated cord blood transplantation (UCBT) (P = 0.53). Similarly, the cumulative incidence of relapse or non-relapse mortality (NRM) was not significantly different between patients with mi-bcr and those with Ma-bcr in either UBMT or UCBT (Relapse: UBMT, 20% in mi-bcr and 18% in Ma-bcr at 4 years, P = 0.73; UCBT, 20% in mi-bcr and 22% in Ma-bcr at 4 years, P = 0.35; NRM: UBMT, 25% in mi-bcr and 30% in Ma-bcr at 4 years, P = 0.31; UCBT, 23% in mi-bcr and 26% in Ma-bcr at 4 years, P = 0.98).

BCR breakpoint was not a significant prognostic factor in multivariate analyses, regardless of graft source. However, in subanalyses, Ma-bcr was a significant risk factor for survival and NRM in multivariate analyses among patients with MRD(+) at UBMT [Ma-bcr (vs. mi-bcr): OS: Hazard ratio (HR) 2.29, 95%CI 1.38 to 3.80, P = 0.001; NRM: HR 3.29, 95%CI 1.72 to 6.27, P < 0.001]. NRM was higher in patients with Ma-bcr than in those with mi-bcr among patients with MRD(+) at UBMT (44% in Ma-bcr vs. 14% in mi-bcr at 4 years, P < 0.001), which led to lower survival rate in patients with Ma-bcr.

Summary/Conclusion: BCR breakpoint was a significant prognostic factor in Ph+ALL patients with MRD(+) at UBMT. This is the first study reporting the possibility of significant impact of BCR breakpoint on MRD-based transplant outcome in Ph+ALL in the era of TKI.

PF180 THE SIGNIFICANCE OF MONOSOMAL KARYOTYPE IN PHILADELPHIA CHROMOSOME NEGATIVE ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Monosomal karyotype (MK) is a prognostic factor significantly associated with poor survival in acute myeloid leukemia and myelodysplastic syndrome. However, its significance in acute lymphoblastic leukemia (ALL) remains controversial.

Aims: To explore the characteristics and outcomes of Philadelphia chromosome (Ph)-negative ALL patients with MK.

Methods: Data of consecutive patients with newly diagnosed Ph-negative ALL were retrospectively analyzed. COIPI regimen and revised Hyper-CVAD regimen were used as the induction and consolidation chemotherapy, respectively. Maintenance therapy consisted of monthly vindesine, prednisone, mercaptopurine and methotrexate for 2 years. Allogeneic hematopoietic stem-cell transplantation (allo-HSCT) was performed after at least 2 cycles of consolidation based on patients’ indication. Patients’ characteristics, treatment response and outcomes were compared between those with MK or not. COX regression model was used to identify factors associated with disease-free survival (DFS) and overall survival (OS).

Results: From January 1st 2008 to June 30th 2018, 313 patients with Ph-negative ALL were included in this study. 184 (56%) were male. Median age was 30 years (range, 13–63 years). Compared with those without MK, patients with MK had lower platelet count (p = 0.021), higher blast percentage in peripheral blood (p = 0.010), and more complex karyotype (p < 0.001) at diagnosis. There was no difference on the probabilities of complete remission (CR, 82% vs 87%, p = 0.356) and minimal residual disease (MRD) negativity after induction chemotherapy (51% vs 52%, p = 0.911) and the first cycle of consolidation (60% vs 70%, p = 0.253) between those with MK or not. In the 270 CR patients, 99 (37%) received continuous chemotherapy; 171 (63%), allo-HSCT in CR1. With a median follow-up of 33 months (range, 1.5–125.3 months) for living patients and OS at 5 years were 45.4% (95%CI, 47.5%–56.1%) and 57.8% (95%CI, 50.5%–65.1%), respectively. Variables including patients’ characteristics at diagnosis and early responses associated with outcomes were assessed in univariate analysis. In multivariate analyses, MK was not a factor associated the outcomes, however, age ≥45 year, plate count < 8×10^9/L, and achieving CR within 4 weeks, and receiving chemotherapy rather than allo-HSCT were adverse factors associated with DFS and/or OS. In further analyses by transplantation source, it was seen that allo-HSCT was associated with lower probabilities of DFS (HR 2.1, 95%CI 1.0–4.4, p = 0.030) and OS (HR 5.3, 95%CI 2.5–11.2, p = 0.001) in the chemotherapy group; in addition, age ≥45 year and MRD positivity after cycle 1 of consolidation were associated with shorter DFS. However, no variable was found to affect the outcomes in the allo-HSCT group.

Summary/Conclusion: Ph-negative ALL patients with MK had lower platelet count, higher blast percentage in peripheral blood, and more complex karyotype at diagnosis. MK was an independent poor predictor of outcome in the patients with Ph-negative ALL receiving continuous chemotherapy, but it had no significance in those receiving allo-HSCT. Our study suggested that Ph-negative ALL patients with MK might benefit from allo-HSCT.

PF181 PEDIATRIC-INSPIRED REGIMEN PLUS HDACI CHIDAMIDE YIELDED PROMISING RESPONSE IN PH-LIKE AND ETP ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Ph-like ALL is a B-cell neoplasm which lack BCR-ABL1 translocation but similar expression-pattern of the BCR-ABL1-positive ALL. Early T-cell precursor ALL is a neoplasm with a unique T-cell immunophenotype indicating limited early T differentiation. The optimal therapeutic approaches for ET-ALL and Ph-like ALL are poorly characterized. Chidamide is a novel and orally active benzamide class of histone deacetlyase inhibitor (HDACi) and approved for peripheral T-cell lymphoma (PTCL) in CHINA.

Aims: We designed two pediatric-inspired, PEG-L-asparaginase-intensified PDT-ETP-ALL and PDT-Ph-Like trials to evaluate the safety and effect of HDACi chidamide for adult ET-ALL and Ph-Like-ALL group. Methods: Based on the pediatric-inspired, PEG-L-asparaginase-intensified and MRD-directed PDT-ALL-2016 protocol, we designed two open-label, one-arm trials, PDT-ETP-ALL (NCT03353328) and PDT-Ph-Like (NCT03564470). The protocols were approved by Institutional Review Board (IRB). Chidamide at a dose of 10 mg/day will be added to ETP-ALL group from induction therapy to consolidation therapy according to PDT-ETP-ALL protocol. Chidamide will be added to HDACi...