PB2211 PLASMA REG3α MAY PREDICT PROGNOSIS IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED WITH CAR-T BRIDGING TRANSPLANTATION

**Topic:** Gene therapy, cellular immunotherapy and vaccination - Clinical

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**Background:** Although ST-2, Reg3α, and Elafin can serve as potential prognosis biomarkers for post-transplantation aGVHD, the relationship between serum cytokines and outcomes in chemircic antigen receptor(CAR)-T cell therapy or CAR-T bridging transplantation treatment remain uncleared.

**Aims:** To investigate the inner connection between clinical outcomes and plasma cytokines level in aGVHD.

**Methods:** 14 acute lymphoblastic leukemia (ALL) patients (2 T-ALL and 12 B-ALL, 9 males and 5 females) who received CD7 or CD19 CAR-T therapy bridging allogeneic hematopoietic stem cell transplantation(allo-HSCT) were enrolled from September 2019 to January 2022 in Beijing Lu Daopei hospital. The median last time of cytokine detection before CART therapy was +29d. The levels of cytokines were determined both after CART and one month before the transplantation. The median follow-up time was 997d(374-1239). 4 out of 14 patients died due to aGVHD(28.6% of total, 1 in intestine, 1 in lung and liver, 1 in lung and 1 in skin, intestine, and liver). The rest 10 patients were alive in the period of the research.

**Results:** cytokine levels before CAR-T related with outcomes. The levels of IL-8, IL-10, TNF-α, IFN-γ, sCD25, MIP-1α, MCP-1, Elafin, ST-2, and TNFRI in the death group were higher than those in the survival group, while the serum IL-4 level was higher in the survival group. But the difference was not statistically significant (P>0.05). The serum Reg3α level in the death group was higher than that in the survival group, and the difference was statistically significant (P<0.05). Analysis of serum Reg3α levels at different time points before transplantation showed that the average Reg3α level in the death group was higher than that in the survival group two months before allo-HSCT, indicating that the patients in the death group had a higher level of Reg3α protein pre-existing in the body before treatment. Before treatment, with the use of the induction regimen, the levels of Reg3α protein in the death group and the survival group were decreased (Figure 1).

According to the ROC curve between the concentration of Reg3α and disease outcome in the two groups about one month before transplantation, the optimal critical value was calculated as 1200.57 pg/mL, and the AUC was 0.938 (95% confidence interval was 0.792-1.000, P<0.05). The specificity was 75.0%, the sensitivity was 100%, the PPV was 60.0%, and the NPV was 100% of the 14 patients were divided into a high Reg3α group and a low Reg3α group by the optimal critical value of Reg3α in patients before transplantation (1200.57pg/mL) obtained from the ROC curve. Started on the date of the allogeneic HSCT, the survival analysis showed that the average survival period of the low Reg3α group was 472 days, and the average survival of the high Reg3α group was 94 days, and the difference between the two groups was statistically significant (P<0.05)

Image:
Summary/Conclusion: High serum Reg3α level in patients after CART treatment before hematopoietic stem cell transplantation is associated with poor prognosis, which can be used as a marker to prompt clinical selection of appropriate therapy.