PB2209 HIGH RISK MYELODYSPLASTIC SYNDROME DEVELOPING IN A PATIENT AFTER CHIMERIC ANTIGEN RECEPTOR (CAR) T- CELL THERAPY FOR RELAPSED DIFFUSE LARGE B CELL LYMPHOMA

Topic: 25. Gene therapy, cellular immunotherapy and vaccination - Clinical

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Background:
Chimeric antigen receptor (CAR)-T cell therapy showed exciting results in relapsed/refractory DLBCL, PML and B-ALL. Cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), transient cytopenias and hypogammaglobulinemia are the main toxicities. We report here a case of high risk myelodysplastic syndrome (HR-MDS) after CAR-T cell treatment for relapsed diffuse large B cell lymphoma (DLBCL).

Aims: To describe a case of HR-MDS occurred after CAR T-Therapy.

Methods: NA

Results:
A 57 year-old woman was diagnosed in August 2019 with germinal-center type DLBCL, IVs-A, IPI score 3, CSN-IPI 4, BCL6 and cMYC negative was treated with 4 cycles of R-CHOP and one more cycle of R-MAD, achieving clinical and PET scan complete remission (CR). At this time, bone marrow (BM) biopsy revealed hyperplastic erythropoiesis with hypoplastic megakaryo-granulopoiesis, without lymphoma infiltration. A second course of intensification with HD-AraC and autologous stem cell transplantation (ASCT) was performed on April 2020.

Unfortunately, on December 2020 the patient relapsed. She was evaluated for CAR-T cell therapy and the leukapheresis (T-Ly) was performed on January 2021. After two courses of R-ESHAP no response was achieved and Tisagenlecleucel was administrated on April 2021.

The abdominal ultrasound 30 days after CAR-T cell therapy and TC scan on day 90 showed a partial remission (PR); neither CRS nor ICANS were observed but a progressive pancytopenia (grade II anemia, grade IV thrombocytopenia, grade II leukopenia according to CTCAE). Six month later CAR T-cell infusion, the patient was in clinical and CT-PET scan CR but, the pancytopenia worsened, requiring recombinant human G-CSF, erythrocyte and platelet support. On January 2022, a bone marrow biopsy ruled out lymphoma infiltration but revealed a multilineage dysplasia without excess of blasts and the karyotype showed a chromosome 7 deletion. A diagnosis of Intermediate-2 IPSS risk or high revised-IPSS risk myelodysplastic syndrome (MDS) was made and the patient started azacitidine as bridge allogeneic hematopoietic stem cell transplantation (alloHSCT). Bone marrow NGS analysis before ASCT and after CAR-T cell therapy is ongoing in order to evaluate clonal hematopoiesis and mutational profile.

Summary/Conclusion:
Prolonged cytopenias after CAR-T cell treatment for DLBCL have been reported both in the Juliet and ZUMA-1 trial. Outside clinical trials, sustained myelosuppression after BCMA-CAR-T therapy for relapsed myeloma was...
successfully treated with back up of autologous stem cells and a case of bone marrow failure after axicabtagene-
ciloleucel for DLBCL was submitted to allo-HSCT. This first case of HR-MDS developed after CAR-T cell infusion in
day with DLBCL raises several questions: should the candidates to CAR T-cell be evaluated for the presence of a clonal hematopoiesis before the procedure? Is there a rationale for performing BM NGS mutational profile in all patients receiving CAR T-therapy especially in those previously submitted to ASCT? When should myelodysplastic or myeloproliferative disease be suspected after CAR T-cell therapy? May CAR T therapy itself play a role in developing a clonal hematopoiesis or myeloid diseases? Further informations are needed to give us conclusive answers to these questions.