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POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Positron Emission Tomography Evaluation in Relapsed/Refractory B-Cell Lymphoma Patients Treated with Anti-19 Chimeric Antigen Receptor (CAR) T-Cells in the CART-SIE Observational Study

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Background: CD19 direct chimeric antigen receptor (CAR) T-cell therapy is an efficacious therapy for patients (pts) affected by relapsed/refractory (R/R) large B-cell lymphomas (LBCL). The role of early evaluation by Positron emission tomography/computed tomography (PET/CT) is still undefined. The study's objective was to analyze the role of early PET/CT according to histology and CAR T-cell product administered.
Methods:CART-SIE is an ongoing prospective and retrospective observational study evaluating the outcome of lymphoma pts treated with CAR T-cells. From March 2019 to June 2023, 659 patients were enrolled. In this study, we included only pts with adequate follow-up (30 days) and an FDG-PET/CT before infusion (PET-0) and at least one month (PET-1) after CAR-T cells infusion. A landmark analysis based on PET-1 and PET-3 (3 months evaluation) results was performed for Progression-free survival (PFS) and Overall Survival (OS) estimation.
Results: Three hundred twenty-seven pts with R/R LBCL [n= 189 (58%) Diffuse large B-cell lymphomas, n= 59 (18%) High-grade B-cell lymphomas (HGBCL), n= 41 (13%) Primary Mediastinal B-cell lymphomas (PMBCL), n= 38 (11%) Mantle Cell Lymphoma (MCL)] received CAR T-cell treatment with axicabtagene-ciloleucel [n=161(49%), axicel], tisagenlecleucel [n=128 (39%), tisacel] or brexucabtagene autoleucel [n=38(12%), brexucel]. The median age of the pts was 58 years (90 pts were older than 65 years). Most pts [n=280, (85,6%)] were treated with a bridging therapy. Bulky and extranodal disease were observed

in 108 (33%) and 177 (54,1%) pts, respectively. Pts who received tisacel were significantly older (p<0.0001), had a longer time from lymphocyte apheresis to the infusion (<0.0001), and did not include PMBCL. The median follow-up time was 12 months [IQR, 6,09-22,37]. At the time of PET-1, 180 pts (55%) showed a PET with DS1-3, 82(25%) had a PET with DS4 (n=61 PR, n=21 SD), and 65(20%) with DS5 (n=13 SD, n=47 PD, n=5 PR). The results of early PET were significantly different according to the histology (p<0.0005): the percentage of DS 4 and DS 5 was 22% and 23% for DLBCL, 30% and 31% for HGBCL, 39% and 7% for PMBCL, and 16% and 0% for MCL, respectively. Overall, 1-year PFS based on PET-1 was 67%, 42%, and 8% for DS1-3, DS4, and DS5 (p<0,0001), respectively. The prognostic role of DS 4 varied with histology: 1-year PFS was 36%, 58%, and 44% for DLBCL, PMBCL, and HGBCL (<0.0001), respectively. The outcome of early PET was significantly influenced by CAR T-cell product (also excluding PMBCL): 1-year PFS for pts with DS1-3 and DS4 at PET-1 was 66% and 51% for axicel and 58,7% and 32% for those treated with tisacel (p<0.0001). The 1-year OS based on PET-1 was 88%, 82%, and 33% for DS1-3, DS4, and DS5 (p<0,0001), respectively. At 90 days, only 219 pts were evaluable; 21 of 82 (26%) DS4 and 5 of 65 (8%) DS5 at PET-1 converted in CR. Overall, 1-year PFS and OS based on PET-3 was 80% and 93% for DS1-3, 64% and 93% for DS4, and 8% and 56% for DS5, respectively. Multivariable analyses identified DS4 and DS5 values on PET-1 and CAR T-cell product Tisacel associated with increasing risk of failure [HR: 1,95 (95%CI;1,01-3,76) for DS4; HR: 9,63 for DS5 (95%CI:6,13-15,13); p< 0,0001; HR: 1,53 for Tisacel vs Axicel; (95%CI:1,06-2,22); p<0.0231]. Conclusion: Early evaluation by PET significantly influenced the prognosis. Estimating the risk of failure must be integrated with CAR T- cell product.

Disclosures Chiappella: *Jannsen-Cilag:* Other: lecture fee/educational activities, advisory board; *Incyte:* Other: lecture fee/educational activities; *AstraZeneca:* Other: lecture fee/educational activities; *Takeda:* Other: lecture fee/educational activities, advisory board; *Ideogen:* Other: advisory board; *Roche:* Other: lecture fee/educational activities, advisory board; *Gilead-Sciences:* Other: lecture fee/educational activities, advisory board; *Novartis:* Other: lecture fee/educational activities; *Celgene-BMS:* Other: lecture fee/educational activities, advisory board; *SecuraBIO:* Other: advisory board. **Zinzani:** *MSD:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *ADC THERAPEUTICS:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *BEIGENE:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; 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