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Blood 142 (2023) 2123–2125

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Dynamics of Radiomic Features Following Bridging Therapy Determine CD19 Chimeric Antigen Receptor (CAR) T-Cell Therapy Outcome

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Introduction: Greater burden of disease is associated with poorer outcomes after CAR T therapies. Bridging therapy (BT) is widely used to debulk or palliate between apheresis and CAR T infusion. We studied whether the degree and dynamics of radiomic cytoreduction during the bridging period are prognostic.
Methods: Patients with large B-cell lymphoma (LBCL) treated with CD19 CAR T from 2016-2022 were stratified into 3 BT cohorts: 1) no BT 2) radiotherapy (RT) or 3) systemic therapy (ST) including combined ST+RT. All patients had a pre-apheresis PET. Patients in the RT or ST cohorts also had a repeat PET post-BT but pre-CAR T infusion. Radiomic parameters of interest including max SUV and metabolic tumor volume (MTV) were calculated for all scans. MTV was determined using a semi-automated method and SUV4 threshold. Max SUV and MTV pre- and post-BT were compared using Wilcoxon signed-rank tests. Kaplan Meier was used to calculate progression free survival (PFS) and overall survival (OS) from CAR T infusion; univariable and multivariable analysis were performed by Cox proportional hazards.
Patients were stratified by disease burden using an absolute MTV cutpoint established based on pre-BT PET with a maximally selected log-rank statistic for PFS via the maxstat package in R. "High" and "low" MTV were defined as MTV above or below this cutpoint, respectively. To quantify the impact of effective cytoreduction during BT, we created 4 BT MTV risk groups: a) "Low" with low MTV pre and post BT, b) "High" with high MTV pre and post BT, c) "Rising" with baseline low MTV which increased to high post BT and d) "Improved" with baseline high MTV which decreased to low post BT.
Results: 158 patients with LBCL (79%), high grade BCL (17%) or primary mediastinal BCL (4%) received CAR T (51% axicabtagene, 28% tisagenlecleucel, 21% lisocabtagene). 42 (27%) received no BT, 93 (59%) had ST, 23 (15%) had RT. With median follow-up of 28.6 months, 12- and 24-month PFS were 43% and 36% and OS were 68% and 54%, respectively.
Median pre-BT SUV max was 19 (range: 0-47) which reduced significantly to 13 post-BT ($p<0.001$). Median baseline MTV was 55cc (0-2,278) which reduced 40% to 33cc post-BT ($p=0.001$). Of the 116 patients who received BT, 67% had any degree of quantitative cytoreduction post-BT and only 35% achieved at least 50% MTV reduction [Fig A]. In the RT bridged 2yr PFS was 52% (95% CI: 32-83) vs. No BT (37%, 95% CI: 24-56) or ST bridged (33%, 95% CI: 24-45).
Our established MTV cutoff was 35.5cc and was significantly associated with PFS both pre-BT and post-BT. The MTV dynamics during BT were further prognostic [Fig B] with best PFS seen in the Low risk group (1yr PFS: 73%) and worst in the High risk (1yr

PFS: 21%) and Rising risk groups. In contrast, despite high baseline MTV, the Improved risk group had comparatively better outcomes with 1yr PFS of 52%.

In a multivariable model of the 116 patients who had BT, several factors were associated with poorer PFS including higher pre-BT LDH (HR 2.2, p=0.004) and BT MTV risk grouping (p<0.001). Of note, while the High risk group had significantly worse PFS vs. Low risk (HR 4.7, 95% CI: 2.1-10.5) outcomes for the Improved risk group did not differ significantly from Low risk (HR 2.1, 95% CI: 0.8-5.3).

Conclusions: In our real-world experience, while most patients required BT, many did not achieve successful disease cytoreduction prior to CAR T cells. While disease extent both pre-apheresis and post-BT are prognostic, the quantitative dynamics of BT cytoreduction may further refine prognostic ability. BT responders have better outcomes while stably high or rising MTV through BT is associated with poor prognosis.

Disclosures Shah: *ArcellX:* Other: DSMB; *Beyond Spring:* Research Funding; *Amgen:* Research Funding; *Janssen:* Research Funding; *BMS:* Research Funding. **Giralt:** *Amgen, Actinuum, Celgene/BMS, Kite Pharma, Janssen, Jazz Pharmaceuticals, Johnson & Johnson, Novartis, Spectrum Pharma, Takeda:* Membership on an entity's Board of Directors or advisory committees; *Amgen, Actinuum, Celgene/BMS, Omeros, Johnson & Johnson, Miltenyi, Takeda:* Research Funding. **Scordo:** *Omeros Corporation:* Consultancy, Research Funding; *CancertNetwork (Intellisphere LLC):* Honoraria; *Medscape, LLC:* Honoraria; *Amgen, Inc.:* Research Funding; *Angiocrine Bioscience, Inc.:* Research Funding. **Salles:** *Debiopharm:* Consultancy; *Ipsen:* Consultancy, Research Funding; *Loxo/Lilly:* Consultancy; *Genentech, Inc./F. Hoffmann-La Roche Ltd:* Consultancy, Research Funding; *Merck:* Consultancy, Honoraria; *Genmab:* Consultancy; *Incyte:* Consultancy; *BeiGene:* Consultancy; *Janssen:* Consultancy, Research Funding; *Owkin:* Current holder of *stock options* in a privately-held company; *BMS/Celgene:* Consultancy; *Kite/Gilead:* Consultancy; *Novartis:* Consultancy; *ATB Therapeutics:* Consultancy; *Orna:* Consultancy; *Nordic Nanovector:* Consultancy; *Nurix:* Consultancy; *Molecular Partners:* Consultancy; *EPIZYME:* Consultancy; *AbbVie:* Consultancy, Honoraria. **Yahalom:** *Convergent R.N.R Ltd.:* Other: Provision of Services (uncompensated). **Palomba:** *Thymofox:* Honoraria; *Smart Immune:* Honoraria; *Seres Therapeutics:* Honoraria, Patents & Royalties; *Rheos:* Honoraria; *Pluto Immunotherapeutics:* Honoraria; *Novartis:* Honoraria; *GarudaTherapeutics:* Honoraria; *MustangBio:* Honoraria; *Kite:* Honoraria; *Juno:* Honoraria, Patents & Royalties; *Ceramedix:* Honoraria; *Cellectar:* Honoraria; *Synthekine:* Honoraria; *BMS:* Honoraria. **Schoder:** *Aileron Therapeutics:* Honoraria. **Perales:** *Allovir:* Consultancy; *Astellas:* Consultancy, Honoraria; *AbbVie:* Consultancy, Honoraria; *Orcabio:* Consultancy, Current equity holder in publicly-traded company, Honoraria; *Kite:* Consultancy, Honoraria, Research Funding; *Novartis:* Consultancy, Honoraria, Research Funding; *Nektar Therapeutics:* Consultancy, Honoraria, Research Funding; *Omeros:* Consultancy, Current equity holder in publicly-traded company, Honoraria; *BMS:* Consultancy, Honoraria; *Caribou:* Consultancy, Honoraria; *Equillium:* Consultancy, Honoraria; *Exevir:* Consultancy, Honoraria; *Karyopharm:* Consultancy, Honoraria; *Merck:* Consultancy, Honoraria; *Miltenyi Biotec:* Consultancy, Honoraria, Research Funding; *MorphoSys:* Consultancy, Honoraria; *Takeda:* Consultancy, Honoraria; *VectivBio AG:* Consultancy, Honoraria; *Vor Biopharma:* Consultancy, Honoraria; *Adicet:* Honoraria; *Celgene:* Honoraria; *Syncopation:* Honoraria; *Cidara Therapeutics:* Consultancy, Other; *Medigene:* Consultancy, Other; *Sellas Life Sciences:* Consultancy; *NexImmune:* Consultancy, Current equity holder in publicly-traded company; *Servier:* Other; *Miltenyi Biotec:* Honoraria; *DSMB:* Other; *Allogene:* Research Funding; *Incyte:* Consultancy, Honoraria, Research Funding. **Imber:** *GT Medical Technologies:* Honoraria.

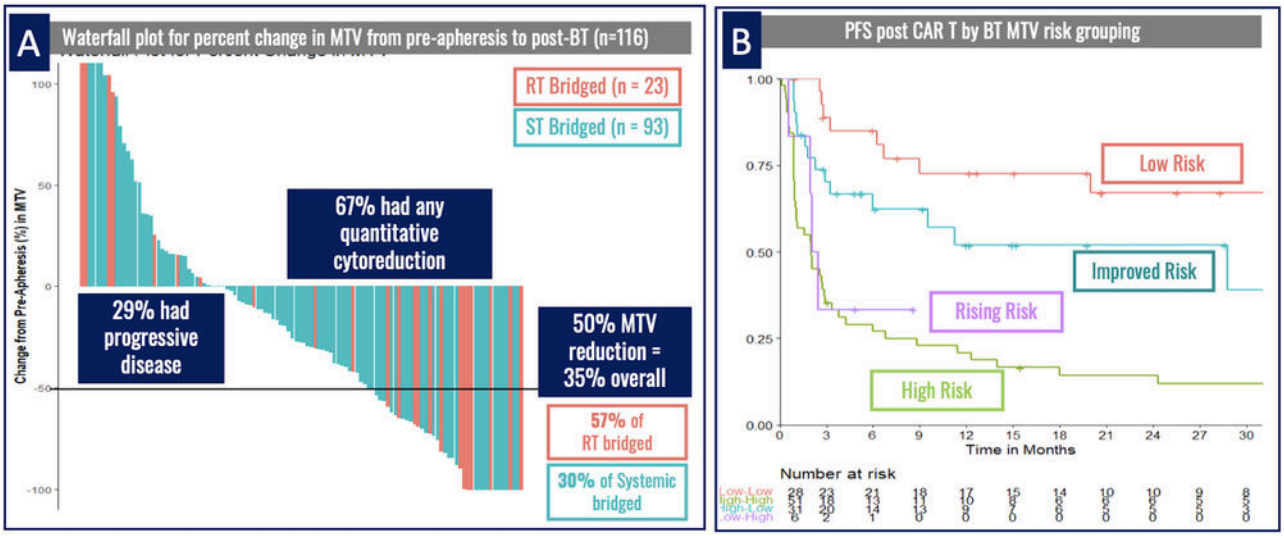

Figure 1

https://doi.org/10.1182/blood-2023-187763