



The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALY AVAILABLE THERAPIES

Early Predictors of Severe Cytopenia Post CAR-T for Identification of Patients for Potential Stem Cell Collection

Andre De Menezes Silva Corraes, MD¹, Radhika Bansal, MBBS², Larissa Argenau Marques Brunaldi, MD³, Sikander Ailawadhi⁴, Arushi Khurana, MBBS¹, Paul J Hampel, MD⁵, Urshila Durani, MD MPH⁵, David Dingli, MD¹, Suzanne R. Hayman, MD¹, Prashant Kapoor, MD⁶, Yucai Wang, MD PhD⁵, Moritz Binder, MD¹, Saad S. Kenderian, MD⁵, Taxiarchis Kourelis, MD⁵, Rahma M Warsame, MD⁶, N. Nora Bennani, MD¹, Morie A. Gertz, MD⁷, Patrick B Johnston, MD PhD⁵, Stephen M Ansell, MD PhD⁵, Rafael Fonseca, MD⁸, P. Leif Bergsagel, MD⁹, Shaji Kunnathu Kumar, MD⁵, Ricardo Parrondo, MD¹⁰, Saurabh Chhabra, MDMS⁸, Yi Lin, MD PhD¹¹

¹ Mayo Clinic, Rochester, MN

² Mayo Clinic Cancer Center, Bismarck, ND

³ Mayo Clinic, Ribeirao preto, Brazil

⁴ Division of Hematology-Oncology, Mayo Clinic, Jacksonville, FL

⁵ Division of Hematology, Mayo Clinic, Rochester, MN

⁶ Division of Hematology, Department of Internal Medicine, Mayo Clinic, Rochester, MN

⁷ Department of Medicine, Division of Hematology, Mayo Clinic, Rochester, MN

⁸ Mayo Clinic, Phoenix, AZ

⁹ Mayo Clinic Arizona, Phoenix, AZ

¹⁰ Mayo Clinic, Jacksonville, FL

¹¹ Mayo Clinic Cancer Center, Rochester, MN

Background: Cytopenias are a common complication of and prolonged (beyond month 3 post CAR-T infusion), severe (grade 3 or higher) cytopenias can be difficult to manage. Stem cell boosts have been reported to restore hematopoiesis; however, stem cells would need to be available prior to CAR-T therapy for potential use post CAR-T. Most lymphoma patients and limited number of myeloma patients may have pre-collected stem cells in storage. Identifying patients at high risk for prolonged and severe cytopenia post CAR-T at the time of CAR-T evaluation (baseline), before leukapheresis, can help identify the patients for coordination of stem cell collection during CAR-T manufacturing and increase the likelihood that the collected stem cells would be used. In this study, we aim to identify clinical variables at the time of CAR-T evaluation, prior to leukapheresis, that are associated with severe cytopenias at month 3 post CAR-T infusion and identify patients who could be considered for pre-emptive stem cell collection prior to CAR-T therapy.

Methods: We conducted a retrospective analysis of patients with multiple myeloma (MM) and non-Hodgkin lymphoma (NHL) who received CAR-T products at Mayo Clinic from 01/2016 to 06/2022. Patients with progressive disease in the first year post CAR-T were excluded from the analysis. Baseline (at CAR-T evaluation, prior to leukapheresis) variables were compared between those with and without severe cytopenia at month 3 post CAR-T. Severe cytopenias were defined as hemoglobin (Hg) < 8 g/dL, absolute neutrophil count (ANC) < 0.5 x 10⁹/L, and/or platelet count (PLT) < 50 x 10⁹/L. Statistically significant variables (p<0.05) by analysis were examined for statistical significance in multivariate analysis (MVA).

Results: Among the 166 patients who received CAR-T (88 NHL, 78 MM) during the study period, 31 (18.67%) had a severe cytopenia at month 3. Twenty baseline variables were examined; HGB, PLT, ANC, and c-reactive protein (CRP). We devised a cytopenia risk score using 1 point each for Hg<10 or PLT<100k at baseline, with a range of 0 to 2. Demographics and clinical outcome by cytopenia risk score is shown in Table 1B. A higher percentage of patients with a score of 1 or 2 had a severe cytopenia at month 3 (Figure 1). In particular, there was a . In addition

Conclusion: Baseline cytopenias before leukapheresis may identify patients with increased risk for severe cytopenias at month 3 post CAR-T. These patients can have continued slow hematopoietic recovery in the first year. Stem cell collection, if feasible, could be considered before CAR-T to alleviate post-CAR-T severe prolonged cytopenias.

Disclosures Ailawadhi: AbbVie, Amgen, Ascentage, BMS, Cellectar, GSK, Janssen, Pharmacyclics, Sanofi: Research Funding; Beigene, BMS, Cellectar, GSK, Janssen, Pfizer, Regeneron, Sanofi, Takeda: Consultancy. **Dingli:** Alexion (AstraZeneca); Apellis

Pharmaceuticals; BMS; GSK; Janssen; Novartis; Sanofi; Takeda: Consultancy; Apellis: Consultancy; BMS: Consultancy; Janssen: Consultancy; K-36 Therapeutics: Research Funding; Novartis: Consultancy; Sanofi: Consultancy; Sorrento: Membership on an entity's Board of Directors or advisory committees; Genentech: Consultancy; BioCryst: Consultancy. **Wang:** Incyte: Membership on an entity's Board of Directors or advisory committees, Research Funding; Innocare: Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; LOXO Oncology: Membership on an entity's Board of Directors or advisory committees, Research Funding; Eli Lilly: Membership on an entity's Board of Directors or advisory committees, Research Funding; Morphosys: Research Funding; Novartis: Research Funding; Genentech: Research Funding; Genmab: Research Funding; TG Therapeutics: Membership on an entity's Board of Directors or advisory committees; Kite: Honoraria, Membership on an entity's Board of Directors or advisory committees; Janssen: Membership on an entity's Board of Directors or advisory committees; BeiGene: Membership on an entity's Board of Directors or advisory committees; AbbVie: Consultancy. **Kenderian:** Torque: Consultancy; Luminary therapeutics: Other: scientific advisory board; MustangBio: Patents & Royalties; Sendero: Patents & Royalties; Mettaphore: Patents & Royalties; Lentigen: Research Funding; Tolero/Sumtomo: Research Funding; Morphosys: Research Funding; LEAHLabs: Consultancy, Current equity holder in private company, Research Funding; CapstanBio: Consultancy, Other: Scientific advisory board; Humanigen: Consultancy, Membership on an entity's Board of Directors or advisory committees, Patents & Royalties, Research Funding, Speakers Bureau; Juno/BMS: Other: Membership on an entity's board of directors or advisory committees, Research Funding; Kite/Gilead: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; Novartis: Consultancy, Honoraria, Patents & Royalties, Research Funding, Speakers Bureau. **Bennani:** Kymera: Other: Advisory board; No personal compensation; Secura Bio: Other: Advisory board; No personal compensation; Affimed: Other: Advisory board; No personal compensation; Astellas Pharma: Other: Advisory board; No personal compensation; Acrotech: Other: Advisory board; No personal compensation; Acrotech: Other: Scientific Advisory Committee, No personal compensation. **Gertz:** AbbVie: Other: Data Safety Monitoring board; Ionis/Akcea, Prothena, Sanofi, Janssen, Aptitude Healthgrants, Ashfield, Physicians Education Resource, Research to Practice, Johnson & Johnson, and Celgene: Consultancy; i3Health: Other: For development of educational material; Juno Pharmaceuticals, and Sorrento Therapeutics: Other: Meetings. **Ansell:** Seagen Inc: Other: Contracted Research; Regeneron Pharmaceuticals Inc: Other: Contracted Research; Pfizer, Inc: Other: Contracted Research; Takeda Pharmaceuticals USA Inc: Other: Contracted Research; Affirmed: Other: Contracted Research; Bristol-Myers Squibb: Other: Contracted Research; ADC Therapeutics: Other: Contracted Research. **Fonseca:** Pharmacyclics: Consultancy; Millenium: Consultancy; Takeda: Consultancy; Janssen: Consultancy; Merck: Consultancy; Sanofi: Consultancy; Pfizer: Consultancy; Adaptive Biotechnologies: Membership on an entity's Board of Directors or advisory committees; Juno: Consultancy; Regeneron: Consultancy; FISH: Patents & Royalties; FISH; BMS (Celgene): Consultancy; Kite: Consultancy; Caris Life Sciences: Membership on an entity's Board of Directors or advisory committees; Oncotracker: Membership on an entity's Board of Directors or advisory committees; AMGEN: Consultancy; AZBio: Membership on an entity's Board of Directors or advisory committees; Antegene: Membership on an entity's Board of Directors or advisory committees; Binding Site: Consultancy; Bayer: Consultancy; Aztrazenica: Consultancy; Adaptive Biotechnologies: Consultancy; AbbVie: Consultancy. **Bergsagel:** Aptitude Health: Honoraria; Novartis: Patents & Royalties: Royalty for hCRBN mice; Mayo Clinic: Patents & Royalties: Royalty for hCRBN and V κ *MYC mice; Pfizer: Research Funding; Janssen: Consultancy; Salarius: Consultancy; CellCentric: Consultancy; Omeros: Consultancy; Radmetrix: Consultancy.

Table 1. Baseline cytopenia risk score

| (A) Baseline variables associated with month 3 severe cytopenia | | | | |
|---|-----------------------------|----------------------|-------------------------------|------------------------|
| Variable | OR (95% CI) (univariate) | P value (univariate) | OR (95% CI) (multivariate) | P value (multivariate) |
| Hg | 0.75 (0.57, 0.95) | .0055 | 0.74 (0.6, 0.91) | 0.0052 |
| Plt | 0.99 (0.98, 0.99) | <.001 | 0.99 (0.98, 0.99) | 0.0003 |

(B) Demographics and clinical outcome based on baseline cytopenia risk score

| EVAL SCORE | 0 (N=119) | 1 (N=31) | 2 (N=16) | Total (N=166) |
|---|-------------------|-------------------|------------------|-------------------|
| Age, Median (Range) | 62 (29-81) | 61 (29-77) | 62 (26-76) | 62 (26-81) |
| Gender, Male, n (%) | 70 (58.8%) | 19 (61.3%) | 6 (37.5%) | 95 (57.2%) |
| Diagnoses, n (%) | | | | |
| - Aggressive NHL | 56 (47.1%) | 15 (48.4%) | 9 (56.2%) | 80 (48.2%) |
| - Indolent NHL | 8 (6.7%) | 0 (0.0%) | 0 (0.0%) | 8 (4.8%) |
| - MM | 55 (46.2%) | 16 (51.6%) | 7 (43.8%) | 78 (47.0%) |
| Hg g/L at baseline, Median (Range) | 12.3 (10.0-16.2) | 9.5 (7.4-13.4) | 8.5 (6.9-9.6) | 11.7 (8.0-16.2) |
| Plt $\times 10^9/L$ at baseline, Median (Range) | 190 (102-644) | 144 (42-723) | 63 (14-94) | 173 (14-723) |
| ANC $\times 10^9/L$ at baseline, Median (Range) | 2.83 (0.32-13.13) | 2.68 (0.02-10.73) | 2.30 (0.21-7.56) | 2.82 (0.02-13.13) |
| CRP mg/L at baseline, Median (Range) | 4.3 (2.9-158.1) | 6.9 (2.9-189.3) | 17.1 (2.9-566.0) | 5.3 (2.9-566.0) |
| Ferritin mcg/L at baseline, Median (Range) | 124 (8-1852) | 211 (23-1470) | 652 (57-2732) | 174 (8-2732) |
| LDH U/L at baseline, Median (Range) | 201 (99-588) | 220 (99-521) | 221 (132-823) | 207 (99-823) |
| ICANS | | | | |
| - Any grade, n (%) | 71 (59.7%) | 17 (54.8%) | 13 (81.2%) | 101 (60.8%) |
| - \geq Gr3, n (%) | 12 (10.1%) | 5 (16.1%) | 1 (6.2%) | 18 (10.8%) |
| CRS | | | | |
| - Any grade, n (%) | 95 (79.8%) | 28 (90.3%) | 14 (87.5%) | 137 (82.5%) |
| - \geq Gr3, n (%) | 2 (1.7%) | 1 (3.2%) | 0 (0.0%) | 3 (1.8%) |
| Toxicumab use, n (%) | 35 (46.2%) | 16 (51.6%) | 5 (31.2%) | 76 (45.8%) |
| Steroid use, n (%) | 62 (52.1%) | 19 (61.3%) | 5 (31.2%) | 86 (51.8%) |

Figure 1: Cytopenia pattern post CAR-T based on baseline cytopenia risk score

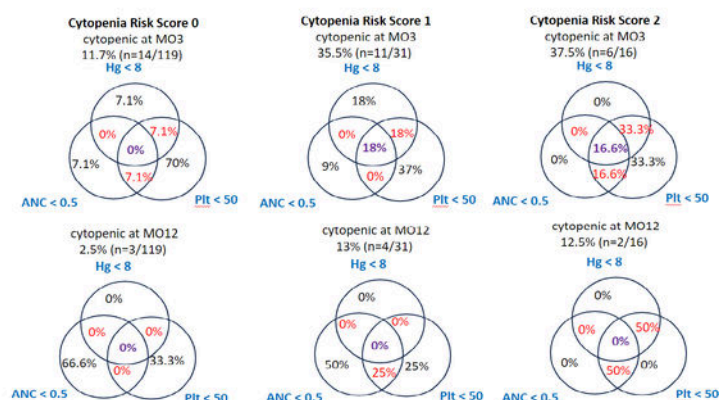


Figure 1

<https://doi.org/10.1182/blood-2023-189683>