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## 705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

### Sequential Administration of Selinexor and CAR-T Therapy in Relapsed/ Refractory Multiple Myeloma

*Sarvarinder Kaur Gill*[1], *Noa Biran, MD*[2], *Pooja Phull, MD*[3], *David H. Vesole, MD PhD*[4,3], *David S. Siegel, MDPhD*[5,6], *Harsh Parmar, MBBS*[7]

[1] John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ
[2] Multiple Myeloma Division, John Theurer Cancer Center, Hackensack Meridian Health, Hackensack, NJ
[3] Multiple Myeloma Division, John Theurer Cancer Center, Hackensack Meridian Health, Hackensack, NJ
[4] Lombardi Comprehensive Cancer Center, Medstar Georgetown Medical Center, Washington, DC, DC
[5] Multiple Myeloma Division, Hackensack Univ. Med. Ctr., Hackensack, NJ
[6] Center for Discovery & Innovation, Hackensack Meridian Health, Nutley, NJ
[7] Multiple Myeloma Division, John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ

*Introduction:*
Selinexor is a novel, oral selective inhibitor of nuclear export (SINE) that binds to exportin 1 and exhibits anti-tumor activity by impairing nuclear export of proteins including oncogenes and tumor suppressor proteins and is approved for use in patients with relapsed refractory multiple myeloma(RRMM). Anti-BCMA directed CAR-T therapy for patients with relapsed/refractory multiple myeloma (RRMM) is a promising new class of therapy, which has shown a high level of efficacy. Sequential administration of selinexor followed by CD19 CAR-T has shown enhanced efficacy in human phase II trials and animal models of human non-hodgkin lymphoma(Stadel et al., 2022). In this retrospective single institutional study, we report outcomes of patients with RRMM who were treated with Selinexor based regimen prior to apheresis for CAR-T therapy.
*Methods:* We conducted a retrospective study on an IRB-approved protocol for all patients who were treated with Selinexor based regimen immediately **prior to apheresis** as a prior line of therapy at Hackensack University Medical Center between June 2015 and July 2022. Demographic characteristics, molecular studies, treatment and response information were recorded and included in the study. Response to CAR-T was assessed by the treating physician per International Myeloma Working Group (IMWG) criteria. Survival analysis was performed using the Kaplan-Meier method including PFS and Overall survival (OS).
*Results:* Between September 9, 2021, and April 3, 2023, 7 patients received CAR-T who were treated with Selinexor immediately prior to apheresis. The median age was 65.7 years (range: 55.1-77.1 years). Patients had a median of 6 (range: 4-10) lines of therapy (LOT) prior to CAR-T. 5 out of the 7 patients had double hit myeloma (all 5 with 17p and one other high risk). Four patients were treated with selinexor, carfilzomib and dexamethasone; two patients were treated with selinexor, daratumumab and dexamethasone and one patient was treated with selinexor, pomalidomide and dexamethasone. Four patients received Idecabtagene vicleucel (ide-cel) and three patients received ciltacabtagene autoleucel (cilta-cel). ORR was 100% with all 7 pts achieving very good partial response or better (>=VGPR). 2 patients had bone marrow biopsies that confirmed MRD -ve sCR in both patients. None of the patients have progressed so far, although median follow-up is short at 5.6 months. All patients had hematologic toxicities, 4/7 with grade III anemia (57.1%), 3/7 (42.8%) with grade or higher thrombocytopenia and 4/7 (57.1%) had grade 3 neutropenia. 2 of 7 patients had prolonged cytopenia for >6 months because of pre-existing underlying diagnoses of CCUS and MDS. 5 out of 7 patients had grade 1 Cytokine release syndrome (CRS). The other two patients did not experience CRS. Time of CRS onset was variable 2-10 days. No ICANS or infectious complications were observed.
*Conclusions:* These results suggest that sequential use of Selinexor and CART in high risk RRMM may be an effective treatment strategy to provide deep and durable responses. The findings of our study are promising although it is limited by a small sample size and short follow-up. Further investigation in a larger study and longer follow up would be important to confirm our findings.

**Disclosures Biran:** *Karyopharm:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Merck:* Research Funding; *Sanofi:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria, Mem-

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| Variable | N |
|---|---|
| No of patients, N | 7 |
| Gender: Male | 5 (71.4%) |
| Median age (years) (range) | 65.7 (55.1-77.1) |
| Median prior lines of therapies (range) | 6 (4-10) |
| Median time from diagnosis to therapy in years (range) | 10.5 (2.7-16.1) |
| High risk FISH (%) | 5 (71.4%) |
| ISS stage 2 or 3 (%) | 4 (66.7%) (data not available for 1 pt) |
| Triple class refractory (%) | 5 (71.4%) |
| Prior ASCT (%) | 7 (100%) |
| CRS (any grade) | 5 (71.4%) |
| CRS (Grade III or higher) | 0 (0%) |
| ICANS (any grade) | 1(14.3%) |
| ICANS (Grade III or higher) | 0 (0%) |
| Hematologic toxicity (any grade) | 7 (100%) |
| Anemia (grade III or higher) | 4 (57.1%) |
| Thrombocytopenia (GIII or higher) | 3 (42.8%) |
| Neutropenia (grade III or higher) | 4 (57.1%) |
| ORR (%) | 7 (100%) |
| VGPR or better (%) | 7 (100%). 2 had bone marrow biopsies to confirm MRD-ve sCR |
| Median PFS in months (Interquartile range) | NR (NR-NR) |

Table 1. Baseline characteristics, safety and efficacy data for our patient cohort

**Figure 1**