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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Timing of Vaccination Impacts Serological Response to COVID-19 Myeloma Patients after BCMA-Targeted CAR T

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Whereas COVID-19 mRNA vaccines have shown remarkable efficacy in the prevention of severe disease and mortality in healthy individuals, the effectiveness in cancer patients has been more variable. Patients with multiple myeloma (MM) are at a high risk for severe infection due to disease- or treatment-related immune suppression. Our prior work demonstrated that the immune response to SARS-CoV-2 immunization in MM patients with 2 doses of mRNA vaccine was suboptimal and that a 3rd dose significantly improved neutralization of viral variants. MM patients undergoing treatment targeting BCMA were among those at a higher risk of ineffective immune responses. As BCMA-targeted (CAR T) treatment becomes more widely available, guidance on initiation of vaccination after treatment is needed.

To assess the impact of BCMA-targeted CAR T (BCMA CAR T) on the serological immune response to COVID-19, we studied 45 MM patients who received ≥1 dose of a COVID-19 mRNA vaccine after prior BCMA CAR T. We collected demographics, disease/treatment characteristics, and COVID-19 infection/vaccination data via retrospective chart review. We analyzed SARS-CoV-2 spike-binding (anti-spike) IgG level using a validated assay (FDA/EUA approved Kantaro). Cumulative incidence of COVID-19 was analyzed using Kaplan-Meier statistics. All subjects were enrolled to studies approved by the Institutional Review Board at a single US academic hospital.

Our cohort consisted of 16 women and 29 men with a median age of 61 years. The patients had received a median 6 lines of treatment and 33/45 (73%) had an ongoing response to BCMA CAR T. Patients received dose 1 at median 567 days after CAR T infusion (range 73-1,374 days). 36 patients (80%) received ≥3 doses and 17 (38%) received ≥4 doses. Across the cohort, anti-spike IgG levels increased from median 8 AU/mL after a single dose to 91, 474 and 612 AU/mL after 2, 3 or 4 mRNA vaccine doses respectively. After 2 doses, 6 patients (of 28 for which the timepoint was available, 21%) had no detectable anti-spike IgG levels, whereas all patients in the cohort had a detectable serological response after ≥3 vaccine doses. We compared the 13 patients (29%) that initiated mRNA vaccination at <12 months (mo) after CAR T infusion (i.e. "early vaccination") with those who received the first dose after >12 mo. In the early vaccination group, anti-spike IgG levels were significantly lower when measured 0-3 months after 2 vaccine doses ($p<0.01$). Serological responses were not different when measured after 3 or 4 doses respectively (Fig A). Nevertheless, after 3 vaccine doses, 30% of patients (3/10) in the early vaccination group had anti-spike IgG <100 AU/mL, a level previously shown to be associated with less effective viral neutralization, versus only 5% (1/20) of patients in the group that started vaccination > 12 mo after CAR T.

Twenty-four patients (52%) developed a documented COVID-19 infection after vaccination. Of these, 21 (88%) were characterized as mild (i.e. not requiring hospital admission); two patients required hospitalization and recovered, and 1 patient in the early vaccination group passed away from COVID-19. Of note, in the early vaccination group, there was a non-significant

trend towards earlier breakthrough infections (Fig B, p=0.16), consistent with the finding of a delayed serological response with suboptimal antibody levels after 2 doses.
In this study, all MM patients who initiated mRNA vaccination after prior BCMA CAR T therapy had detectable anti-spike IgG after ≥3 vaccine doses. However, starting vaccination against COVID-19 early (i.e. within 1 year) after CAR T therapy does not result in protective levels of antibody as quickly and to the same extent as when vaccinated >1 year post CAR T infusion. Patients starting vaccination within 12 months need ≥3 doses to achieve comparable serological efficacy to later initiation. A trend towards earlier breakthrough infections suggests that study of neutralizing titers against variants and comprehensive immune phenotyping may be needed to confirm effective immunity in these vulnerable patients. For the first year after CAR T cell therapy, adherence to preventive measures and passive immunization with IVIG with higher titers of anti-spike IgG may be warranted. Analyses comparing this cohort with MM patients receiving other modalities of BCMA-targeted therapy incl. bispecific antibodies are ongoing and will be presented at the meeting.

Disclosures Mouhieddine: *Legend Biotech:* Consultancy. **Sanchez:** *Janssen Pharmaceuticals:* Consultancy, Honoraria. **Rodriguez:** *Janssen, Takeda, Bristol Myers Squibb, Amgen, Karyopharm Therapeutics:* Membership on an entity's Board of Directors or advisory committees. **Richter:** *Astra Zeneca:* Membership on an entity's Board of Directors or advisory committees; *Takeda:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Genentech:* Consultancy; *Bristol-Meyers-Squibb:* Membership on an entity's Board of Directors or advisory committees; *Janssen:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Sanofi:* Membership on an entity's Board of Directors or advisory committees; *Celgene:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Adaptive Biotechnologies:* Membership on an entity's Board of Directors or advisory committees; *Karyopharm:* Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Consultancy; *Abbvie:* Consultancy. **Cho:** *Takeda, Inc.:* Research Funding; *Bristol Myers-Squibb:* Research Funding. **Rossi:** *JNJ:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Membership on an entity's Board of Directors or advisory committees; *Adaptive:* Membership on an entity's Board of Directors or advisory committees. **Richard:** *C4 Therapeutics:* Research Funding; *Bristol Myers Squibb:* Honoraria; *Janssen:* Honoraria; *Heidelberg Pharma:* Research Funding. **Cordon-Cardo:** *Kantaro:* Patents & Royalties. **Krammer:** *Kantaro:* Patents & Royalties. **Jagannath:** *Regeneron:* Consultancy; *Takeda:* Consultancy; *Karyopharma:* Consultancy; *Genmab:* Other: DMC chairman; *Sanofi:* Consultancy, Other: DMC Chariman; *IMS:* Membership on an entity's Board of Directors or advisory committees; *Caribou:* Consultancy; *Legend Biotech:* Consultancy; *SOHO:* Membership on an entity's Board of Directors or advisory committees; *ASH:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Consultancy, Honoraria; *Janssen Pharmaceuticals:* Consultancy, Honoraria. **Simon:** *Kantaro:* Patents & Royalties: Serological Tests. **Parekh:** *Caribou Biosciences:* Research Funding; *Karyopharm Therapeutics:* Research Funding; *Amgen:* Research Funding; *Celgene/BMS Corporation:* Research Funding; *Grail, LLC:* Membership on an entity's Board of Directors or advisory committees.

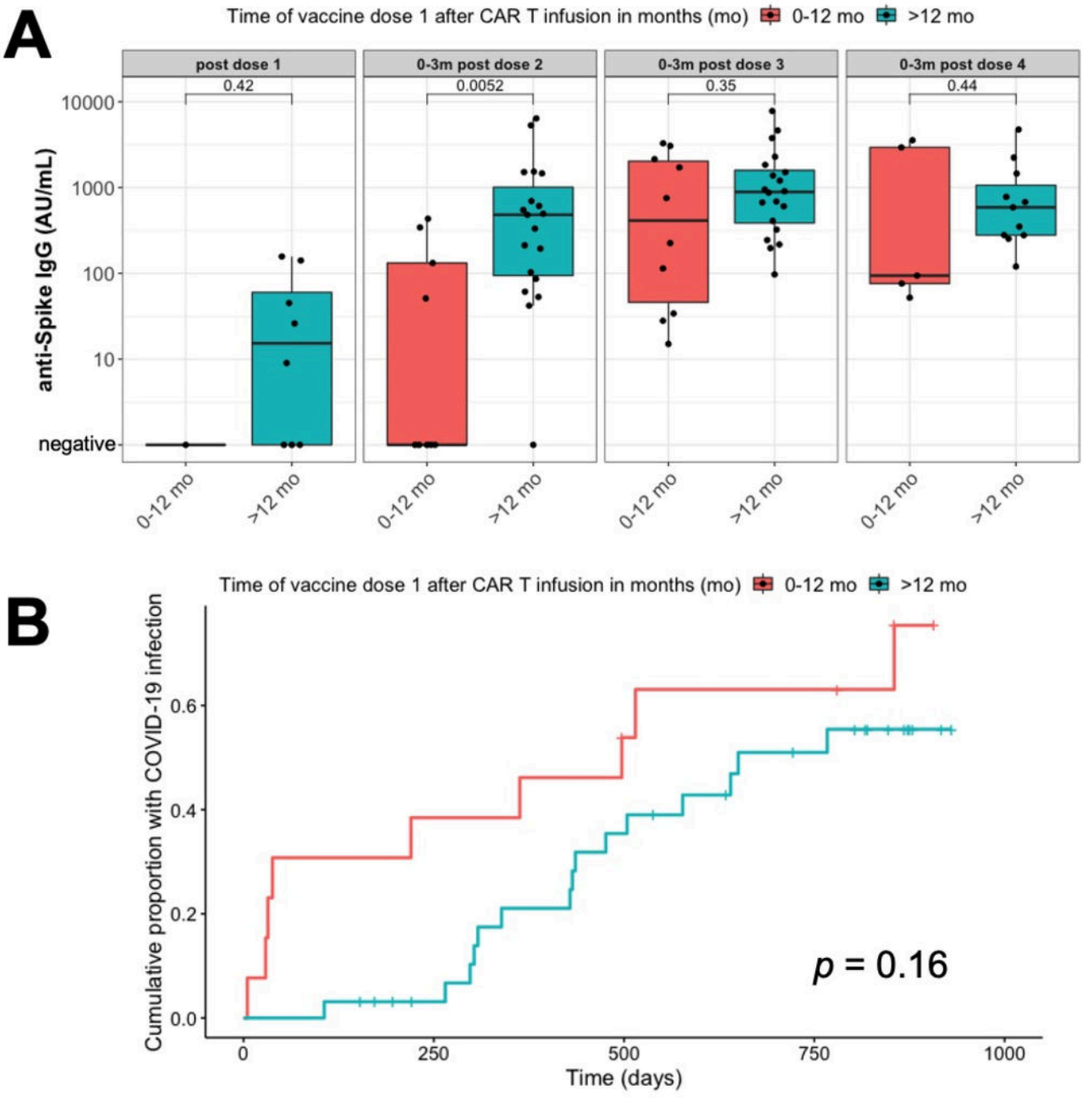

Figure 1

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