**INTRODUCTION**

- Outcomes remain poor in patients with high-risk RRMM receiving conventional treatments, including IMiD® agents, Pi, and anti-CD38 antibodies.

- Ide-cel, a BCMA-directed CAR T cell therapy, showed deep and durable responses in the pivotal phase II KarMMa study of patients with triple-class-exposed RRMM.

- Objective: To report safety and efficacy of ide-cel in historically difficult-to-treat patient subgroups from the KarMMa study.

**RESULTS**

**Median PFS** was ≥ 7.5 months in patients who had high tumor burden, bridging therapy, and > 1 prior regimen per year.

- **Median DOR** was ≥ 9.2 months in all high-risk subgroups examined, except patients with R-ISS stage III.

- Among patients treated with the target dose of 450 × 10^6 CAR+ T cells, median PFS was ≥ 8.0 months and median DOR was ≥ 10.3 months in all high-risk subgroups except R-ISS stage III.

**Table 2. Summary of adverse events in high-risk subgroups**

- More than one third of patients had high-risk cytogenetics and extramedullary disease (35% and 39%, respectively), and approximately half (51%) had high tumor burden.

- Most patients (88%) received bridging therapy during CAR T cell manufacturing.

- Most patients (70%) had R-ISS disease stage II, with 16% having stage III.

- Patients were heavily pretreated, with 47% having received > 1 prior antimyeloma regimen per year.

**Table 1. Baseline demographics and clinical characteristics**

**Figure 2. Response rate by subgroup**

- ORR was ≥ 65% and CR rate was ≥ 20% across all high-risk subgroups except R-ISS disease stage III.

- Presence of extramedullary disease and baseline tumor burden did not substantially affect ORR.

- Among high-risk subgroups treated with the highest target dose of 450 × 10^6 CAR+ T cells, ORR and CR rate were ≥ 75% and ≥ 19%, respectively, across all subgroups except R-ISS disease stage III.

**CONCLUSIONS**

- In the KarMMa study, ide-cel demonstrated deep and durable responses in most subgroups examined, including those with the highest risk, such as extramedul- lary disease, high-risk cytogenetics, and high tumor burden.

- No new safety signals were observed in evaluated high-risk subgroups.

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**Figure 3. PFS and DOR in high-risk subgroups**