S183 UPDATED INTERIM ANALYSIS OF THE GMMG-CONCEPT TRIAL INVESTIGATING ISATUXIMAB, CARFILZOMIB, LENALIDOMIDE, AND DEXAMETHASONE (ISA-KRD) IN FRONT-LINE TREATMENT OF HIGH-RISK MULTIPLE MYELOMA

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Background: As high-risk (HR) multiple myeloma (MM) patients (pts) still have a significantly impaired prognostic outcome, there is an unmet clinical need for potent therapeutic strategies already in front-line therapy for newly diagnosed (ND) MM, leading to improvement of long-term survival. Ultra-high-risk patients with ≥ 3 HR cytogenetic aberrations (CA) have a median overall survival (OS) of less than 2 years.

Recent data indicate that achievement of deep remissions, including negativity for minimal residual disease (MRD) may translate into prolonged progression-free (PFS) and OS.

Aims: The GMMG-CONCEPT trial (NCT03104842) investigates the quadruplet regimen isatuximab plus carfilzomib, lenalidomide, and dexamethasone (Isa-KRd) in HR NDMM pts including primary high-dose melphalan for patients being transplant-eligible. First results showed an overall response rate (ORR) of 100% for induction treatment in the prespecified interim analysis (IA) of the first 50 patients included. Here, we report an update for PFS of the IA population.

Methods: 153 pts with HR NDMM were included into the trial, an extension cohort of another 93 patients is planned to start recruitment in 2021. HR MM is defined by the presence of del17p or t(4;14) or t(14;16) or > 3 copies 1q21 in combination with ISS II or III stage disease. Transplant-eligible (TE) patients undergo high-dose therapy after induction (Arm A) while transplant-ineligible (TI) patients receive 2 additional Isa-KRd cycles (Arm B). Afterwards, both arms receive another 4 Isa-KRd cycles as consolidation, followed by Isa-KR maintenance. Primary endpoint is MRD negativity measured by next-generation flow after consolidation. This IA reports on PFS data of the IA population with PFS defined as combined endpoint of progressive disease (PD) or death, whichever occurs first.

Results: 50 pts (46 arm A, 4 arm B) were included in the IA population. CA defining high-risk were del17p in 52%, t(4;14) in 38%, t(14;16) in 12% and > 3 copies 1q21 in 42%. 20% of pts showed increased LDH, 26% had 2 CA, 4% showed ≥ 3 CA. Overall (ORR) and best response rates were presented previously. ORR defined as best response achieved during induction was 100% with 90% of pts achieving a very good partial response or better. Early data on MRD negativity showed MRD negative remissions in 20/33 evaluated pts during induction. The updated IA analysis was performed with a median follow-up of 24.9 months. For the overall population analysed, 12- and 24-month PFS (95%>confidence level) was 79.6% (68.3%; 90.9%) and 75.5% (63.5%; 87.6%). In Arm A, PFS-rates were 80.0% (68.3%; 91.7%) and 75.6% (63.0%; 88.1%) for 12 and 24 months, respectively. For the 4 TI pts in Arm B, a 12-months-PFS of 75.0% (32.6%; 100%) was reported. With longer follow-up, no new safety signals occurred. End of treatment (EoT) occurred in 20 pts in Arm A and was due to PD in 8 pts, death in 4 pts or other reasons (8 pts). Reason for EoT (1 pt) in Arm B was death.

Conclusion: With a best ORR of 100% during quadruplet induction treatment, we here report an update of the IA for PFS of the first 50 pts in the CONCEPT trial. In these solely HR NDMM pts an encouraging PFS rate of 79.6% and 75.5% after 12- and 24-months is reported. Our data underline the high potency of quadruplet treatment with Isa-KRd especially in patients with HR disease. The study completed recruitment, further results will be reported.