





Blood 142 (2023) 4757-4758

The 65th ASH Annual Meeting Abstracts

## POSTER ABSTRACTS

## 653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

## GEN3014 (HexaBody ®-CD38) in Anti-CD38 Mab-Naive Patients with Relapsed/Refractory Multiple Myeloma: Preliminary Results from a Dose-Expansion Cohort of a Phase 1/2 Trial

Sebastian Grosicki, MD PhD<sup>1</sup>, Torben Plesner, MD<sup>2</sup>, Wojciech Jurczak, MDPhD<sup>3</sup>, Jakub Radocha, MD PhD<sup>4</sup>, Ehsan Malek, MD<sup>5</sup>, Ida Hiemstra, PhD<sup>6</sup>, Lauren K. Brady, PhD<sup>7</sup>, Jenny Chen, MD PhD<sup>7</sup>, Nian Gong, PhD<sup>7</sup>, Charlotte Hindsberger, MS<sup>8</sup>, Andrew Spencer, MBBS, MD FRACP, FRCPA<sup>9</sup>

<sup>1</sup>Department of Hematology and Cancer Prevention, Faculty of Health Sciences, Medical University of Silesia, Katowice, Poland

<sup>2</sup>Vejle Hospital, Vejle, Denmark

<sup>3</sup>MSC National Research Institute of Oncology, Kraków, Poland

<sup>4</sup>4th Department of Internal Medicine - Hematology, University Hospital and Faculty of Medicine, Hradec Králov, Czech Republic

<sup>5</sup>University Hospitals Seidman Cancer Center, Cleveland, OH

<sup>6</sup>Genmab, Utrecht, NLD

<sup>7</sup>Genmab, Plainsboro, NJ

<sup>8</sup>Genmab, Copenhagen, Denmark

<sup>9</sup>Department of Malignant Haematology & Stem Cell Transplantation, The Alfred Hospital, Melbourne, Australia

**Background:** The treatment landscape for relapsed/refractory multiple myeloma (RRMM) has changed dramatically with the approval of CD38-targeted antibodies such as daratumumab. Despite this advancement in therapy, some patients still experience progression following daratumumab regimens. Clinical outcomes may be improved by more potent CD38-targeted treatment options. GEN3014 (HexaBody ®-CD38) is a next-generation human IgG1 anti-CD38 monoclonal antibody (mAb) that contains a hexamerization-enhancing mutation, E430G, that facilitates highly efficient complement-dependent cytotoxicity (CDC). In preclinical studies, GEN3014 showed robust tumor-cell killing through highly potent CDC, with increased efficiency compared with daratumumab, as well as potent antibody-dependent cellular cytotoxicity and antibody-dependent cellular phagocytosis (Hiemstra et al, *eBioMedicine* 2023). Preliminary dose-escalation data from the first-in-human phase 1/2 trial of GEN3014 in RRMM patients showed clinical activity and a tolerable safety profile, and the recommended phase 2 dose was 16 mg/kg (NCT04824794). Based on these findings, expansion was initiated. Herein we describe the preliminary results of an expansion cohort in anti-CD38 mAb-naive RRMM patients.

**Methods:** Adult RRMM patients were eligible if they had  $\geq$ 3 prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory imide drug (IMiD), were double refractory to a PI and an IMiD, or had  $\geq$ 2 prior lines of therapy with 1 combining a PI and an IMiD. Patients received GEN3014 16 mg/kg intravenously in 28-day cycles (QW, cycles 1-2; Q2W, cycles 3-6; Q4W, cycles  $\geq$ 7). The primary objective was to assess the preliminary antitumor activity of GEN3014. Secondary objectives included assessment of safety, tolerability, and pharmacokinetics/pharmacodynamics.

**Results:** As of May 5, 2023, 11 anti-CD38 mAb-naive RRMM patients were treated in this expansion cohort (median age, 66 years; range, 56-75). With a median duration of exposure of 2.4 months (range, 0.2-8.3), 4 patients (36.4%) remained on treatment. Primary reasons for discontinuation included disease progression (n=3), AEs (n=3), and death (n=1). The most common treatment-emergent AEs (TEAEs) were neutropenia (36.4%), headache (27.3%), infusion-related reactions (IRRs; 27.3%), and thrombocytopenia (27.3%). IRRs were all grade 2 and did not lead to treatment discontinuation. There were 2 grade 5 TEAEs (respiratory tract infection, n=1; cardiac arrest, n=1). Of the 11 patients treated, 7 received  $\geq$ 1 cycle of GEN3014, and among them, the best overall responses were 1 complete response, 2 very good partial responses, 2 partial responses, 1 minimal response, and 1 stable disease. GEN3014 treatment was associated with a transient reduction in either complement component C2 or total complement lytic activity in all patients, suggesting CDC activity. T cells transiently decreased after administration of the first dose in all patients, and T-cell expansion ( $\geq$ 50% increase from baseline for  $\geq$ 2 visits) was observed in 2 of 4 evaluable patients who reached cycle 3 day 1 at the time of analysis. Updated data will be presented.

## POSTER ABSTRACTS

**Conclusions:** GEN3014 showed a manageable safety profile and clinical activity in anti-CD38 mAb-naive RRMM patients in this expansion cohort. The preliminary pharmacodynamic observations were in line with observations from the dose-escalation part of the study. The study is ongoing and open for enrollment.

Disclosures Plesner: Genmab: Consultancy, Research Funding, Speakers Bureau; Celgene/BMS: Consultancy. Jurczak: BeiGene: Consultancy; AstraZeneca: Consultancy; AbbVie: Consultancy; Eli Lilly: Consultancy; Pfizer: Consultancy; Roche: Consultancy; SOBI: Consultancy; Takeda: Consultancy; AbbVie: Research Funding; AstraZeneca: Research Funding; Bayer: Research Funding; BeiGene: Research Funding; Celgene: Research Funding; Janssen: Research Funding; Eli Lilly: Research Funding; Merck: Research Funding; Pfizer: Research Funding; Roche: Research Funding; SOBI: Research Funding; Takeda: Research Funding. Radocha: Amgen: Honoraria, Membership on an entity's Board of Directors or advisory committees; BMS: Honoraria, Membership on an entity's Board of Directors or advisory committees; GSK: Honoraria, Membership on an entity's Board of Directors or advisory committees; Janssen: Honoraria, Membership on an entity's Board of Directors or advisory committees; Sanofi: Honoraria, Membership on an entity's Board of Directors or advisory committees. Malek: Karyopharm: Speakers Bureau; Medpacto Inc.: Research Funding; BMS: Consultancy; Sanofi: Consultancy; Amgen: Speakers Bureau; Cumberland Inc.: Research Funding. Hiemstra: Genmab: Current Employment. Brady: Genmab: Current Employment, Current equity holder in publicly-traded company. Chen: Genmab: Current Employment. Gong: Genmab: Current Employment. Hindsberger: Genmab: Current Employment. Spencer: Haemalogix: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; Janssen: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; Pfizer: Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; Amgen: Consultancy, Honoraria; Sanofi: Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; IDP Pharma: Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; Abbvie: Consultancy, Honoraria, Research Funding, Speakers Bureau; Roche: Honoraria, Membership on an entity's Board of Directors or advisory committees; Antengene: Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; BMS: Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau.

https://doi.org/10.1182/blood-2023-179504