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Poster Session

Cell Processing: Poster II

BKT140 Is a Novel CXCR4 Antagonist with Stem Cell Mobilization and Antimyeloma Effects: An Open-Label First Human Trial In Patients with Multiple Myeloma Undergoing Stem Cell Mobilization for Autologous Transplantation

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Background: **BKT140** is a high affinity CXCR4 inhibitor with an extended K off-rate. Pre-clinical studies in animal models with **BKT140** showed a robust mobilization of white blood cells (WBC) and hematopoietic stem cells (HSC). Furthermore, **BKT140** also showed a direct anti-tumor effect against human-derived multiple myeloma (MM), lymphoma and primary leukemia cells and cell lines in vitro and in vivo, causing significant apoptosis.

Aims: To assess **BKT140** toxicity (primary endpoints), the mobilization capacity of CD34+ hematopoietic progenitors and CD138 MM cells, and pharmacokinetic (PK) and pharmacodynamic (PD) (secondary endpoints).

Methods: 16 MM patients in first CR/PR were included in a phase I/IIa study, in which escalating doses of **BKT140** (30, 100,300,900 µg/kg) were administered together with a high-dose cyclophosphamide (Cy) (2 g/m^2) and G-CSF (5 µg/Kg) for stem cell mobilization. G-CSF was started on day 5 post Cy and **BKT140** was injected subcutaneously (SC) once on day 10. Toxicity, PK, and mobilization capacity (assessed by serial measurements of number of WBC and CD34+ and CD138+ cells) were measured pre- and post **BKT140** administration.

Results: **BKT140** was well tolerated at all doses and none of the patients developed grade II-IV toxicity. **BKT140** was rapidly absorbed with no observed lag time, with peak plasma concentrations occurring 0.5h after administration. Clearance was rapid, with a median terminal half-life of 0.69h. **BKT140** administration resulted in a significant dose-dependent increase in the number of peripheral blood neutrophils, monocytes, lymphocytes, and CD34+ cells compared to the G-CSF/Cy individual patient baseline. The maximum increase in the number of WBC from baseline was observed within 8h following **BKT140** injection, 2.5-, and 3.0-, 4.1- and 4.8-fold, for the 4 **BKT140** doses, respectively. Furthermore, **BKT140** administration resulted in a significant increase in the mean absolute PB CD34+ cells mobilized (6.6, 7.5, 11.2 and 20.6 x10^6/kg) for the 4 **BKT140** administered doses, respectively. Moreover, the number of aphaeresis was reduced from 2.25 procedures at the first two **BKT140** doses to 1.25 and 1 aphaeresis at the highest **BKT140** doses, respectively. An increase in the number of CD138+ cells was observed in 6 out of 6 pts that had CD138+ cells in their blood and were treated with lower doses of **BKT140** (30 and 100 µg/kg). Interestingly, in pts that were treated with the highest doses of **BKT140** (300 and 900 µg/kg) a reduced number of CD138+ cells was observed in 3 out of 7 pts that had CD138+ cells in their blood, whereas in 4 pts, an increase in the number of CD138+ cells was shown. Three pts who did not have CD138+ cells in their blood were not affected by **BKT140**. The **BKT140** mobilized grafts were used for AutoSCT following 200 mg/m^2 melphalan conditioning. Pts received an average of 5.3x10^6 CD34+ cells/kg. All transplanted pts rapidly

engrafted (n=15). The median day for neutrophil (>500/mm^3) and platelet (>20,000/mm^3, >50,000/mm^3,) was on day 11 (range, 0–13), day 11 (range, 0–14), and day 14 (range, 0–23), respectively.

Conclusions: The current data suggests that **BKT140** can safely be added to G-CSF-based harvesting regimens, can increase CD34+ cell mobilization and reduce the number of collection days. Furthermore, due to its ability to release MM cells from the bone marrow and stimulate their cell death, additional studies are warranted to further evaluate the effect of **BKT140** as an anti-MM agent.

Disclosures: Nagler: *Biokine Therapeutics Ltd:* Consultancy. Abraham: *Biokine Therapeutics Ltd:* Employment, Equity Ownership, Patents & Royalties. Wald: *Biokine Therapeutics Ltd:* Employment. Shaw: *Biokine Therapeutics Ltd:* Consultancy, Equity Ownership, Membership on an entity's Board of Directors or advisory committees. Eizenberg: *Biokine Therapeutics Ltd:* Employment, Equity Ownership, Patents & Royalties. Peled: *Biokine Therapeutics Ltd:* Consultancy, Equity Ownership, Membership on an entity's Board of Directors or advisory committees, Patents & Royalties, Research Funding.

Footnotes

* Asterisk with author names denotes non-ASH members.

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