Bemcentinib (Oral AXL Inhibitor) in combination with Low-dose Cytarabine Is Well Tolerated and Efficacious in Elderly Relapsed AML Patients

Updates to the Ongoing Phase II Trial (NCT02488408) and Preliminary Translational Results indicating Bemcentinib elicits anti-AML immune responses

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BACKGROUND

• Relapsed (REL) & refractory (REF) AML patients unsuitable for intensive chemotherapy (IC) due to age or comorbidities, have limited treatment options.

• The lack of a SOC and poor survival, highlight the unmet medical need for new treatments in this patient population.

• AXL is a receptor tyrosine kinase conferring poor prognosis, resistance to chemotherapy and decreased antitumor immune response in several cancers, including AML.

Bemcentinib (BEM) is a first-in-class highly selective, potently bioavailable AXL-inhibitor

• Inhibits AXL-mediated pro-tumour signalling and reverses AXL-dependent innate immune suppression

• Reduces AML cell survival, enhances efficacy of chemotherapy and overcomes resistance.

• BEM+LDAC combination showed an additive effect in AML.

RESULTS

• As of 30 Sept 2021, the B+L cohorts comprised 28/21 (21 REL, 7 REF) AML patients.

• Overview of the 21 REL patients: median age at enrolment was 76 years (range 66-88) with a male preponderance (85%), ECOG 0-1 and median prior lines of therapy 2 (range 1-4).

• 18/21 REL patients were evaluable for efficacy: 4/18 (22%) achieved CRi/CR; 12/18 (67%) achieved CR/CR-
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• CRi/CR was reported between wk 10-12 (N=17): Median T(0)-T(11) 43±9.9; mDQR 32.75±1.786 (4/7) (B+L).

• Late onset responses may reflect AXL related immunological MoA and contribute to a longer T SURVIVAL data continues to mature.

• Overall, the BEM+LDAC combination was well tolerated and safe. TRAEs of ≥iG3 observed in 31% of patients were anemia (7%/BEM) and ECOG CT unzended (7%/BEM) No G5 TRAEs reported.

AIMS

• The ongoing BGC003 Phil trial aimed to explore safety and efficacy and to pursue translational biomarker analysis in REL/REF older AML patients until IC, treated with BEM+LDAC combination.

• Here, we present initial preliminary and multiclinics (in bone marrow mononuclear cells [BMMCs]) data.

CONCLUSIONS

• BEM+LDAC is well tolerated and efficacious in older unrel AML patients.

• Survival benefit was observed, indicating BEM+LDAC warrants evaluation in a randomized clinical study in this population.

• Translational research including scRNA and multomics, identified specific activation of CD8 T cells and B cells in responders associated with response to treatment, indicating that BEM elicits activation of the two major adaptive immune cell populations responsible for anti-AML immune responses.

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MATERIALS AND METHODS

CLINICAL STUDY OVERVIEW

• Patients received combination BEM at 200mg PO x3 loading dose, 100 mg maintenance and LDAC SOC schedule.

• Efficacy endpoints were objective response (OR) and clinical benefit rate (CRR=OR+CR+PR). Stable disease [SD=unchanged disease for at least 3 BEM cycles].

• Secondary objectives looked at overall survival (OS) and exploratory biomarker analysis.

TRANSLATIONAL ANALYSIS

• Longitudinal BM/MNC samples (n=32) from 13 patients were subjected to scRNA-seq and CisDEseq (Chromosome 10x genomics, Totalises, Biologos). For scRNA-seq data analyses, Cell Ranger (v3.1.0) and the Seurat (v4.0.1) were used.

• Patients were stratified by Best Response (CR, CRi, PR for Responders; SD, UC, or No Responders).

• Cell type annotations were based on the identified clusters and were inferred from the expression of known marker features on both RNA and protein level.

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