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POSTER ABSTRACTS

616.ACUTE MYELOID LEUKEMIAS: INVESTIGATIONAL THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Phase Ib/II Study (NCT02488408 / BGBC003) of Bemcentinib Monotherapy or in Combination with Cytarabine or Decitabine in Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS): FINAL Results

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Background: The standard of care (SOC) in newly-diagnosed (ND) AML patients (pts) unfit for intensive chemotherapy (IC) yields median overall survival (mOS) of 14.7 months. However, beyond 1 st line (1L), pts have limited treatment options and dismal mOS of 2.3 months (4.7 months in pre-venetoclax era), highlighting the need for more effective treatments in 2 nd line (2L) and beyond. Activation of AXL, a receptor tyrosine kinase, is associated with poor prognosis, resistance to chemotherapy and decreased antitumor immune response in AML. Bemcentinib (BEM) is a first-in-class, oral, highly selective AXL inhibitor.
Aims: The BGBC003 PhIb/II trial studied the safety and efficacy of BEM as monotherapy in AML (cohort B1) and MDS (cohort B4) and in combination with decitabine (cohort B3) or low-dose cytarabine (LDAC) (cohorts B2 and B5) in ND and relapsed/refractory (R/R) AML pts unfit for IC. Pharmacokinetic/pharmacodynamic (PK/PD) analysis was conducted in pts treated with BEM monotherapy in the safety run-in phase (part A). Here, we present final efficacy and safety data, as well as PK/PD analysis from part A.
Methods: In part A, 36 pts received BEM monotherapy in a dose escalation manner. In part B (cohorts B1-B5), pts received 3 loading doses at daily 400 mg BEM followed by 200 mg BEM daily. Study endpoints included OS, objective response rate (ORR), clinical benefit rate (CBR) (ORR+unchanged [UC]). Plasma and peripheral blood (PB) samples were used for PK and phospho-AXL (pAXL) analyses.
Results: From Oct-14 to Jul-21, 86 pts were enrolled in part B (72 efficacy evaluable), with a median age of 76 years (range 50-86), 77% being R/R at study entry. BEM monotherapy and in combination was well tolerated, with a safety profile com-

parable to the known safety profile of the combination agents. The ORR was 18% (B1), 0% (B3), 25% (B2+B5), and 19% (B4). The CBR was 45% (B1), 31% (B3), 31% (B2+B5) and 56% (B4). The mOS (months) was 18 (B1), 6.4 (B3), 8.0 (B2+B5) and 9.2 (B4). BEM+LDAC (B2+B5) showed promising survival benefit in ND (mOS 16.5 months, n=5) and R/R pts (mOS 7.8 months, n=27). The PK/PD analysis showed inhibition of the biological target pAXL in PB following monotherapy. BEM showed dose-dependent inhibition of pAXL and downstream targets of pAXL (pAKT, pERK and pNFkB) with EC_{50} values of 89-162 ng/mL. *Summary/Conclusions:* BEM demonstrated on-target effect by inhibition of pAXL and downstream signalling in a concentration-dependant manner. BEM monotherapy and in combination was well tolerated across all cohorts. The overall efficacy observed is comparable with historical data in 2L AML and MDS. Although the shift in 1L SOC in AML during the study limits adequate comparisons, a survival benefit was observed both in ND and R/R AML, warranting further investigation. *Keywords:* Acute myeloid leukemia, Clinical trial, Receptor tyrosine kinase

Disclosures Loges: *Merck:* Consultancy, Honoraria, Other: Travel support, Speakers Bureau; *Janssen:* Consultancy, Honoraria, Other: Travel support; *Takeda:* Consultancy, Honoraria, Other: Travel support, Speakers Bureau; *Novartis:* Consultancy, Honoraria, Other: Travel support, Speakers Bureau; *Sanofi Aventis:* Consultancy, Honoraria, Other: Travel support, Speakers Bureau; *Boehringer Ingelheim:* Consultancy, Honoraria, Other: Travel support, Speakers Bureau; *Medac:* Consultancy, Honoraria, Other: Travel support, Speakers Bureau; *AstraZeneca:* Consultancy, Honoraria, Other: Travel support, Speakers Bureau; *Amgen:* Consultancy, Honoraria, Other: Travel support, Speakers Bureau; *Bayer:* Consultancy, Honoraria, Other: Travel support, Speakers Bureau; *Pfizer:* Consultancy, Honoraria, Other: Travel support, Speakers Bureau; *ADC Therapeutics:* Research Funding; *Roche Pharma:* Consultancy, Honoraria, Other: Travel support, Research Funding, Speakers Bureau; *Eli Lilly:* Consultancy, Honoraria, Other: Travel support, Research Funding, Speakers Bureau; *BMS:* Consultancy, Honoraria, Other: Travel support, Research Funding, Speakers Bureau; *BerGenBio:* Consultancy, Honoraria, Other: Travel support, Research Funding, Speakers Bureau. **Heuser:** *Abbvie:* Consultancy, Honoraria, Research Funding; *Jazz:* Consultancy, Honoraria, Research Funding; *Janssen:* Honoraria; *Novartis:* Consultancy, Honoraria, Research Funding; *BerGenbio:* Research Funding; *Takeda:* Honoraria; *Roche:* Consultancy, Research Funding; *Bayer Pharma AG:* Research Funding; *Astellas:* Research Funding; *Loco Oncology:* Research Funding. **Janning:** *Novartis:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *AstraZeneca:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel support; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Roche:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Micklam:** *BerGenBio ASA:* Current Employment. **Gorcea-Carson:** *BerGenBio ASA:* Current Employment. **Oliva:** *BerGenBio ASA:* Current Employment. **Fiedler:** *Apis:* Research Funding; *Amgen:* Consultancy, Other: Support for meeting attendance, Patents & Royalties; *Pfizer:* Consultancy; *AbbVie:* Consultancy, Honoraria, Other: Support in medical writing; *Servier:* Consultancy, Other: Support for meeting attendance; *Morphosis:* Consultancy; *Stemline:* Consultancy; *Clinigen:* Consultancy; *Jazz Pharmaceuticals:* Consultancy, Other: Support for meeting attendance. **McCracken:** *BerGenBio ASA:* Current Employment. **Gjertsen:** *BerGenBio:* Consultancy; *Coegin:* Consultancy; *GreinDX:* Consultancy; *Immedica:* Consultancy; *InCyte:* Consultancy; *Mendus AB:* Consultancy, Research Funding; *Novartis:* Consultancy, Research Funding; *Otsuka:* Consultancy; *Pfizer:* Consultancy, Research Funding; *Sanofi:* Consultancy; *in Alden Cancer Therapy AS:* Current holder of *stock options* in a privately-held company; *KinN Therapeutics AS:* Current holder of *stock options* in a privately-held company.

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