**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**

**Sonja Loges1,2, J. Michael Heuser1, Jörg Oromki2, Gerk Sutartawang2, Silke Kape-Schwoerer1, Monica Cernosel1, Nicola Di Renzo1, Roberto Lemoli1, Daniele Mattei2, Isabel Ben Batalla4,5, Jonas Waizenegger2, Lisa-Marie Rieckmann2,3, Melanie Ahning2,3, Charles Dombusch2, Niklas Beuneu1, Y. David Micklem2, Claudia Gorcea-Carson1, Cristina Oliva1, Walter Fiedler1, Yasir Alavard-Valero6, Bjarni J. Gjertsen2**

**Introduction**

The standard care (SOC) in newly-diagnosed (ND) AML patients (pts) unfit for intensive chemotherapy (IC) has changed recently with the introduction of venetoclax and hypomethylating agents, yielding a median overall survival (mOS) of 13.7 months. However, beyond first-line, the prognosis of both relapsed/refractory (R/R) AML is only 2.3 months (venetoclax). The standard of care (SOC) in newly-diagnosed (ND) AML patients (pts) unfitness for intensive chemotherapy (IC) has changed recently with the introduction of venetoclax and hypomethylating agents, yielding a median overall survival (mOS) of 13.7 months. However, beyond first-line, the prognosis of both relapsed/refractory (R/R) AML is only 2.3 months (venetoclax). Plasma and peripheral PB (plasma) samples were used for PK and phospho-Axl (p-Axl) analyses (Figure 2).

**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) (CRB=CR+CRi+PR), CRp, CRi, PR, MR or PMR, ND AML patients (pts) unfitness for intensive chemotherapy (IC) has changed recently with the introduction of venetoclax and hypomethylating agents, yielding a median overall survival (mOS) of 13.7 months. However, beyond first-line, the prognosis of both relapsed/refractory (R/R) AML is only 2.3 months (venetoclax). Plasma and peripheral PB (plasma) samples were used for PK and phospho-Axl (p-Axl) analyses (Figure 2).

**PK/PD Results**

- BEM inhibited pAxl in its downstream targets (pAxl, pERK, pS6 and pSTAT5) in longitudinal peripheral blood from patients in cohort A in a dose concentration manner generating EC50 values in a plasma concentration range of 89-162 ng/mL (Table 4).
- pAxl: EC50 of 10 ng/mL equivalent to free BEM concentration of 20 ng/mL, which is similar to concentration needed to occupy 80-90% of Axl receptors (based on Kd value for BEM).
- Mean trough values at steady state following a maintenance dose of 200 mg in BEM daily cohorts B2 and B5 were 188 ± 334 ng/mL and 214 ± 97.1 ng/mL, respectively.

**Disease Status**

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) (CRB=CR+CRi+PR), CRp, CRi, PR, MR or PMR, ND AML patients (pts) unfitness for intensive chemotherapy (IC) has changed recently with the introduction of venetoclax and hypomethylating agents, yielding a median overall survival (mOS) of 13.7 months. However, beyond first-line, the prognosis of both relapsed/refractory (R/R) AML is only 2.3 months (venetoclax). Plasma and peripheral PB (plasma) samples were used for PK and phospho-Axl (p-Axl) analyses (Figure 2).

**Conclusions**

BEM demonstrated on-target effect by inhibition of pAxl and downstream signalling in a concentration-dependent manner. BEM monotherapy and in combination was well tolerated across all cohorts. A survival benefit (mOS 16.5 months) was observed with BEM+LDAC in ND AML pts, which would warrant further validation.

**Clinical Results**

**Overall Response Rate**

Table 4: Overall Response Rate

**Overall Survival**

Table 5: Overall Survival

**PK/PD Results**

- BEM inhibited pAxl in its downstream targets (pAxl, pERK, pS6 and pSTAT5) in longitudinal peripheral blood from patients in cohort A in a dose concentration manner generating EC50 values in a plasma concentration range of 89-162 ng/mL (Table 4).
- pAxl: EC50 of 10 ng/mL equivalent to free BEM concentration of 20 ng/mL, which is similar to concentration needed to occupy 80-90% of Axl receptors (based on Kd value for BEM).
- Mean trough values at steady state following a maintenance dose of 200 mg in BEM daily cohorts B2 and B5 were 188 ± 334 ng/mL and 214 ± 97.1 ng/mL, respectively.

**Disease Status**

- BEM demonstrated on-target effect by inhibition of pAxl and downstream signalling in a concentration-dependent manner. BEM monotherapy and in combination was well tolerated across all cohorts. A survival benefit (mOS 16.5 months) was observed with BEM+LDAC in ND AML pts, which would warrant further validation.

**PK/PD Results**

- BEM inhibited pAxl in its downstream targets (pAxl, pERK, pS6 and pSTAT5) in longitudinal peripheral blood from patients in cohort A in a dose concentration manner generating EC50 values in a plasma concentration range of 89-162 ng/mL (Table 4).
- pAxl: EC50 of 10 ng/mL equivalent to free BEM concentration of 20 ng/mL, which is similar to concentration needed to occupy 80-90% of Axl receptors (based on Kd value for BEM).
- Mean trough values at steady state following a maintenance dose of 200 mg in BEM daily cohorts B2 and B5 were 188 ± 334 ng/mL and 214 ± 97.1 ng/mL, respectively.