Updated data from Beamion LUNG-1, a Phase Ia/b trial of the HER2-specific tyrosine kinase inhibitor, zongertinib (BI 1810631), in patients with HER2 mutation-positive NSCLC

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Introduction

- HER2 mutations are present in 3–4% of patients with NSCLC of these, approximately 80% are in the tyrosine kinase domain (TKD) and most of them are truncation mutations
- Tyrosine kinase inhibitors (TKIs) that inhibit both HER2 and EGFR are associated with baseline. Thus, there is an rational to develop TKIs that target patients with HER2 mutation positive variants such as E59K

- Here, we present updated Phase Ia and results from a planned Phase Ib trial of the HER2-specific tyrosine kinase inhibitor, zongertinib (BI 1810631), in patients with HER2 mutation-positive NSCLC of whom most of these are ex20ins mutations

- We evaluated objective response rates and safety in previously untreated TKI-naive patients with HER2 mutation-positive NSCLC

Methods

- One oral dose, QD, 3-week cycles
- Cohort 1: Preclinical NSCLC with a HER2 TKD mutation
- Cohort 2: Treatment-naive NSCLC with a HER2 TKR mutation
- Cohort 3: NSCLC with a wild type HER2 mutation or NSCLC, pretreated with previous chemotherapy
- Cohort 4: TKR-mutation positive patients with HER2, pretreated with previous chemotherapy
- Cohort 5: TKR-mutation positive NSCLC, pre-treated with prior treatment with HER2-directed antibody-drug conjugates

Key findings and conclusions

- In Cohort 1, the MTD of zongertinib was not reached
- Doses taken in Phase Ib for dose escalation were 240 mg and 132 mg QD
- Baseline characteristics of patients included in NSCLC with a non-TKD mutation-positive NSCLC

- The median duration of response was over a year
- Two patients had TRAEs that led to dose reductions
- The toxicity analysis was performed, and the trial is continuing, with recruitment into all cohorts ongoing

Phase Ia: dose escalation and safety

- No dose escalation was performed
- No DLT was observed
- The maximum tolerated dose (MTD) period was 132 mg QD

Phase Ia: efficacy

- The overall response rates (range) of treatment with zongertinib were 4/11 (36.4%) patients, with 5 patients ongoing

Phase Ib: baseline characteristics

- Cohort 1: Preclinical NSCLC with a HER2 TKD mutation
- Cohort 2: Treatment-naive NSCLC with a HER2 TKR mutation
- Cohort 3: NSCLC with a wild type HER2 mutation or NSCLC, pretreated with previous chemotherapy
- Cohort 4: TKR-mutation positive patients with HER2, pretreated with previous chemotherapy
- Cohort 5: TKR-mutation positive NSCLC, pre-treated with prior treatment with HER2-directed antibody-drug conjugates

Phase Ib: safety

- Phase Ib: efficacy (pooled doses)

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References


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