Olmutinib (BI 1482694; HM61713), an EGFR mutant-specific inhibitor, in T790M+ NSCLC: efficacy and safety at the RP2D

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INTRODUCTION

- T790M mutation within exon 20 of the EGFR gene is the most common (~50%) acquired resistance mechanism to first- and second-generation EGFR tyrosine kinase inhibitors (TKIs)1–3 across different subtypes of non-small cell lung cancer (NSCLC).2
- Another important resistance mechanism to EGFR TKIs is the emergence of secondary EGFR T790M mutation in wild-type EGFR4
- In the majority of patients (36/43 [84%]), onset of tumor response occurred by the median PFS in patients with one prior systemic treatment (n=19) and 6.8 months (95% CI: 4.21, 8.35) in patients with two or more prior regimens (n=57)

METHODS

- Phase 1 trial enrolments were confirmed by a local test (n=76; ongoing)
- Four (5%) patients discontinued due to drug-related AEs (upper abdominal pain and diarrhea (59%/0%), pruritus (41%/5%), and nausea (39%/0%)) (Table 3)

RESULTS

- Median PFS was 8.8 months (95% CI: 3.98, 11.07) in patients with one prior regimens and approved the final version
- Evidence of the anti-tumor activity of olmutinib on CNS metastases was observed in a 62-year-old male patient enrolled in April 2015. The patient achieved complete response (CR) in the brain by August 2015 (Cycle 6), which was sustained until

ENDPOINTS AND ASSESSMENTS IN PHASE 2

- Patients were required to undergo a baseline and at least one post-baseline tumor assessment to be evaluable for independent response assessment

Efficacy

- Patients were evaluable for treatment duration by independent review. Table 2 summarizes the land response as of February 28, 2016. Figure 3 and 4 show duration of response and individual tumor change (Figure 3) and duration of treatment (Figure 4)
- In the majority of patients (36/43 [84%]), onset of tumor response occurred by the median PFS among all treated patients (n=76) by independent review was 6.9 months (95% confidence interval [CI]: 5.36, 9.49)
- Across all patients (n=76), median treatment duration was 7.3 months and approved the final version
- Evidence of the anti-tumor activity of olmutinib on CNS metastases was observed in a 62-year-old male patient enrolled in April 2015. The patient achieved complete response (CR) in the brain by August 2015 (Cycle 6), which was sustained until

CONCLUSIONS

- In the RP2D of 800 mg QD, olmutinib showed meaningful clinical activity with a safety profile suitable in Korean patients with T790M+ NSCLC progressing on initial EGFR TKI therapy
- Confirmed ORs by independent review were observed in 38 (51%) patients, with a median duration of response of 6.3 months (5–14.0)
- The most common drug-related AEs were rash (41%/5%), palmar-plantar erythrodysesthesia syndrome 23 (30%) 3 (4)
- Delayed nausea 23 (30) 3 (4)
- Liver function tests abnormalities were rarely reported 23 (30) 3 (4)

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