BI 1482694 (HM61713) is an oral, third-generation EGFR mutant-specific TKI active against EGFR isoforms, including T790M, while sparing wild-type EGFR. The most common mechanism of acquired resistance (~50% of cases) is a T790M mutation within exon 20 of the EGFR kinase domain (E746-V795). While these agents are effective, resistance to first-line treatment eventually develops in most patients. Korean patients or the second-generation ErbB family blocker, afatinib1

First-line therapy for patients with TKI-resistant NSCLC harboring a T790M mutation

- ORR was similar whether or not the last treatment prior to study entry was an EGFR TKI
- Safety of BI 1482694 (HM61713) at 800 mg QD
- Abdominal pain upper and vomiting (n=1), diarrhea (n=1) and interstitial lung disease (n=1)
- There were no treatment-related deaths
- No AEs of QT prolongation or hyperglycemia were reported at 800 mg QD

Preliminary signs of activity in metastatic brain disease were observed in a single patient with a T790M-positive NSCLC patient who had previously received a first-line EGFR TKI. Imaging of the target brain lesion in March 2015 (baseline; A), July 2015 (confirmed PR; B), October 2015 (stable disease; C)

The patient continues on treatment, maintaining the CR of the brain lesion as of July 2015. BI 1482694 (HM61713) 800 mg QD since April 2015 and achieved CR in the target brain lesion as of December 2015.

- Clinical activity and safety of the EGFR mutant-specific inhibitor, BI 1482694 (HM61713), in patients with T790M-positive NSCLC
- BI 1482694 (HM61713) showed meaningful clinical activity in EGFR T790M patients is ongoing (see Poster #476TiP);9 the broader ELUXA trial (N=76) is in expansion Part 2 (N=76; ongoing)
- No AEs of QT prolongation or hyperglycemia were reported at 800 mg QD

Safety of BI 1482694 (HM61713) at 800 mg QD

- Treatment exposure ranged from 0.3 to 9.0 months
- Treatment-related adverse events (AEs) reported in >10% of patients are shown in Table 3
- There were no treatment-related deaths
- No AEs of QT prolongation or hyperglycemia were reported at 800 mg QD

Table 3. Treatment-related AEs in ≥10% of patients

Table 2. Tumor response (independent assessment)

Table 1. Patient demographics

Table 3. Treatment-related AEs in ≥10% of patients

Figure 4. Imaging of the target brain lesion in March 2015 (baseline; A), July 2015 (confirmed PR; B), October 2015 (stable disease; C)

CONCLUSIONS

- ORR was similar whether or not the last treatment prior to study entry was an EGFR TKI
- The most common treatment-related AEs included fatigue, nausea, anorexia, abdominal pain, and vomiting
- There was no adverse effect on QoL measured on nausea metastatic disease (N=10) and interstitial lung disease (n=1)
- No AEs of QT prolongation or hyperglycemia were reported at 800 mg QD

REFERENCES


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Clinical activity and safety of the EGFR mutant-specific inhibitor, BI 1482694 (HM61713), in patients with T790M-positive NSCLC #425PD

INTRODUCTION

Patients and treatment

- Between August 2014 and April 2015, 76 patients with T790M-positive NSCLC were enrolled, patient demographics are shown in Table 1

Efficacy

- ORR by independent assessment was 62%, including 32 (41%) patients whose tumor response had been confirmed by the time of data cut-off (Table 2)

RESULTS

Table 3. Treatment-related AEs in ≥10% of patients

Figure 3. Individual treatment duration

- Dose escalation phase

NE, n (%) 3 (4)

Safety of BI 1482694 (HM61713) at 800 mg QD

- Treatment response ranged from 0.3 to 9.0 months

Table 2. Tumor response (independent assessment)

Figure 2. Individual tumor change in target lesions (independent assessment)

Figure 1. Imaging of the target brain lesion in March 2015 (baseline; A), July 2015 (confirmed PR; B), October 2015 (stable disease; C)

- There were no treatment-related deaths
- No AEs of QT prolongation or hyperglycemia were reported at 800 mg QD

Table 1. Patient demographics

- Patients and treatment

- Biopsy test for T790M mutation status required

- Findings at 300 mg (below maximum tolerated dose [MTD]) were presented

Table 1. Patient demographics

- Tumor volume change (%)

Figure 1. Study design and Phase II expansion cohort

METHODS

- Study design and patients

- ECOG PS, Eastern Cooperative Oncology Group performance status

Table 1. Patient demographics

- Median age, years (range) 60 (32–85)

Table 2. Tumor response (independent assessment)

- Findings at 300 mg (below maximum tolerated dose [MTD]) were presented

Table 1. Patient demographics

- Smoking history, n (%) Former

Table 1. Patient demographics

- Gender, n (%) Male

Table 1. Patient demographics

- T790M mutation, n (%) T790M positive or negative*

Table 1. Patient demographics

- ECOG PS, Eastern Cooperative Oncology Group performance status

Table 1. Patient demographics

- Median age, years (range) 60 (32–85)

Table 1. Patient demographics

- Smoking history, n (%) Former

Table 1. Patient demographics

- Gender, n (%) Female

Table 1. Patient demographics

- T790M mutation, n (%) T790M positive or negative*