**RESULTS**

**Baseline Demographics and Characteristics**

- A total of 118 patients were enrolled as of 20 April 2018.
- Eighty-three patients were in the dose escalation cohort and 35 patients were in the dose expansion cohort (Table 1).
- Median age was 62.5 years (28, 84) and 60% of patients were female. 81% of patients were T790M-NSCLC.

**Pharmacokinetics**

- Median Telectin® in the 83 patients treated in each cohort was 64.7 hours following single dose of 240 mg.
- Steady state was achieved by T7-12 days after first dosing, and mean AUC of 118 patients (major metabolite) was 2.4 times that of Tlectin®.
- Tlectin® of 25448 increased dose-dependently at steady state (Figure 2).

**Safety and Tolerability**

- No dose-limiting toxicities (DLTs) were observed up to Tlectin® 320 mg in the dose escalation cohorts.
- A total of 89% of treatment-emergent adverse events (TEAEs) were mild (CTCAE grade 1) or 2 across all dose levels (Table 5).
- The most common TEAEs were pruritus (40%), rash (29%), diarrhea (20%), and fatigue (8%).
- The TEAEs leading to dose-reduction, interruption and discontinuation of treatment was observed in 4%, 9% and 3% of patients, respectively.
- In all TEAEs, CTCAE grade 2 was observed in 12% of patients. The most frequent TEAEs of CTCAE grade 3 were pulmonary embolism (3%), hypoglycemia (2%), nausea (3%) and pneumonia (3%).
- There were no dose-dependently increased TEAEs.

**Anti-tumor Efficacy**

- Of the evaluable patients (n=118) with the confirmed response at the date of data cutoff (DOCC), the objective response rate (ORR) was 61% (95% confidence interval [CI], 53.1 to 70.0) across all dose levels by investigator assessment (Table 2, Figure 3).
- The ORR for the Tlectin®-patients: patients was 66% (95% CI, 56.7 to 76.0) and 76% (95% CI, 66.7 to 86.0) for the 18 Tlectin® patients was 78% (95% CI, 62.9 to 88.3).
- The disease control rate (DCR) was 89% across all dose levels (95% CI, 81.3 to 94.0).
- In patients with BM (n=11), the intracranial ORR was 59% (95% CI, 23.0 to 84.0) (Figure 4).
- The longest duration of response was 9.7 months and the median duration of response has not reached yet at the date of DOCC.

**Table 2. Summary of Anti-tumor Efficacy (Confirmed Response)**

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>N</th>
<th>CR (%)</th>
<th>PR (%)</th>
<th>SD (%)</th>
<th>DCR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 mg</td>
<td>80</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>40 mg</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>80 mg</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

**Figure 3. Best Percent Change in Target- Lesion Size**

- (A) Overall patients (n=118)
- (B) Patients treated with Tlectin® (n=35)
- (C) Intracranial lesions in patients with BM (n=11)

**COnclusions**

- Tlectin® (lazertinib) demonstrated the promising anti-tumor efficacy.
- The confirmed ORR was 61% across all dose levels in patients with locally advanced or metastatic NSCLC with acquired resistance to prior EGFR-TKI treatments.
- In patients with BM, the intracranial ORR was 59% across all dose levels.
- Lazzertinib demonstrated a good safety profile and tolerability.
- No DLT was observed up to lazertinib 230 mg.
- A total of 89% of TEAEs were mild.
- There were no dose-dependently increased TEAEs.
- In conclusion, lazertinib was safe, well-tolerated and efficacious promising systemic and intracranial antitumor activities at multiple dose levels in EGFRm-NSCLC patients.
- The dose extension cohort as the first-line setting has been initiated in April 2018.

**Acknowledgements**

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**References**


- **Poster** presented at 2018 ASO annual meeting, June 5-8, 2018, Chicago, USA, Abstract #053

**INTRODUCTION**

- The majority of patients who had treated with epidermal growth factor receptor (EGFR) inhibitor treatment eventually relapse with disease progression within 1 to 2 years. The 790M mutation in exon 20 of EGFR was present up to 60% of resistant cases.
- Brain metastasis (BM) is present in one-quarter of patients at diagnosis, and about half of patients with EGFR-mutated lung cancer develop brain metastases within 5 years.
- YH25448 (lazertinib) is a potent, highly mutant-selective and irreversible 3rd generation EGFR-TKI that is able to cross the blood-brain barrier, and targets both the 790M mutation and activating EGFR mutations (EGFRm) while sparing wild-type.