Introduction

- This analysis provides additional evidence for the efficacy of afatinib in EGFR+ NSCLC patients with brain metastases (BMs).
- This is a phase IIb trial of afatinib in EGFR+ NSCLC: analysis of outcomes in patients with brain metastases or dose reductions.

Objectives:

- Primary: safety
- Secondary: TTSP, PFS

Methods

- Eligible: patients naïve to EGFR TKIs
- Exclusion: BMs treated with prior RT, immunotherapy, or PD1/PDL1 inhibitors

Baseline characteristics (N=479)

| Country     | Patients, n (%) | Metastatic Brain | EGFR
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>40 (10)</td>
<td>32 (80)</td>
<td>8 (20)</td>
</tr>
<tr>
<td>Taiwan</td>
<td>29 (6)</td>
<td>23 (82)</td>
<td>6 (28)</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>24 (5)</td>
<td>19 (80)</td>
<td>5 (20)</td>
</tr>
<tr>
<td>Singapore</td>
<td>5 (1)</td>
<td>4 (80)</td>
<td>1 (20)</td>
</tr>
</tbody>
</table>

Age at baseline, years: Median 63, Range 18-86

Methods

- Objective: to evaluate the safety of afatinib in patients with locally advanced or metastatic NSCLC harboring EGFR mutation (EGFR-m) who have never been treated with an EGFR TKI.
- Study design: open-label, randomized phase 2/3 study with a 2:1 randomization to 40 mg or 80 mg/d.

Use of dose reductions with afatinib: frequency and impact on efficacy outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Median PFS, months (95% CI)</th>
<th>Median TTSP, months (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dose reduction</td>
<td>14.1 (6.2-19.0)</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Dose reduction during 6 months</td>
<td>11.3 (8.7-19.0)</td>
<td>14.7 (9.1-19.0)</td>
</tr>
<tr>
<td>No dose reduction</td>
<td>17.7 (11.0-20.0)</td>
<td>15.4 (9.8-19.0)</td>
</tr>
</tbody>
</table>

Presence of brain metastases at baseline: frequency and impact on efficacy outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Median PFS, months (95% CI)</th>
<th>Median TTSP, months (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No brain metastases</td>
<td>14.9 (6.2-19.0)</td>
<td>15.4 (9.8-19.0)</td>
</tr>
<tr>
<td>With brain metastases</td>
<td>10.9 (6.2-14.0)</td>
<td>15.0 (9.8-15.4)</td>
</tr>
</tbody>
</table>

Medication adherence

- All patients were ≥ 18 years old, had histologically confirmed NSCLC, and uncontrolled BMs at baseline.
- Evaluable patients were naïve to EGFR TKIs and had BMs at baseline.
- Dose interruptions were allowed.

Key findings and conclusions

- The most frequently reported TRAEs were rash/dermatitis (all grades and ≥ grade 3) and diarrhea (any grade and ≥ grade 3).
- The use of dose reductions was associated with a decrease in TRAEs and an improvement in efficacy outcomes.
- The frequency of grade ≥ 2 rash/dermatitis was reduced by 30-50% with dose reductions.
- The overall response rate (ORR) was 4% without dose reductions and 5% with dose reduction (≥ grade 3).
- The median PFS was 14.1 months with dose reduction and 17.7 months without dose reduction.
- The median TTSP was 14.7 months with dose reduction and 15.4 months without dose reduction.
- The impact of dose reductions on safety and tolerability was encouraging.

Funding

- This study was funded by Boehringer Ingelheim.

References


Presented at the IASLC 18th World Conference on Lung Cancer (WCLC), Toronto, Canada, September 23–26, 2018.