NSCLC, metastatic

Dacomitinib (D) versus Erlotinib (E) in 2nd/3rd line NSCLC: Outcome for Asian patients from the ARCHER 1009 Global Phase 3 Trial

1Clinical Oncology, The Chinese University of Hong Kong, Hong Kong, CHINA
2Cancer Services, Princess Alexandra Hospital, Brisbane, ACT, AUSTRALIA
3Winship Cancer Institute, Emory University Winship Cancer Institute, Atlanta, GA, USA
4Thoracic Oncology, Dana-Farber Cancer Institute, Boston, MA, USA
5Medical Oncology, Royal Prince Alfred Hospital, Camperdown, NSW, AUSTRALIA
6Heamatoiology/oncology, Samsung Medical Centre, Seoul, KOREA
7Oncology, Pfizer (China) Research and Development Co. Ltd., Shanghai, CHINA
8Clinical Oncology, Pfizer Inc., New York, NY, USA
9Translational Oncology, Pfizer Inc, Groton, CT, USA
10Oncology Clinical Development & Medical Affairs, Pfizer Inc, Groton, CT, USA
11Medical Oncology, Hospital Universitario Virgen del Rocio, Seville, SPAIN

Aim: Dacomitinib is an irreversible pan-HER kinase inhibitor with activity in advanced NSCLC. In a Phase 2 trial in patients previously treated with chemotherapy, D showed improved PFS compared to E (median PFS 12.4 weeks vs. 8.3 weeks; HR 0.66, P = 0.0120). A Phase 3 trial has been completed (Proc ASCO 2014, Abs 8018).

Methods: The ARCHER 1009 trial randomized patients to blinded treatment with D (45 mg PO QD) or E (150 mg PO QD). The primary endpoint was progression-free survival (PFS) by independent review in the co-primary populations [all patients and those with KRAS WT]. Stratification factors were histology, smoking status, ECOG and Asian versus non-Asian/Indian race.

Results: Of 878 patients enrolled, 174 (20%) were self-designated as Asian. The PFS per investigator for Asian patients favored D with HR = 0.81 (95% CI: 0.584-1.125, p value, 1-sided = 0.105); median PFS is 3.7 vs 2.8 months in D and E arms, respectively. The Response Rate (CR + PR) was 30.3% and 21.2% in D and E arms respectively with an odds ratio of 1.62 (95% CI: 0.81-3.23). The most common adverse events for D vs E were diarrhea (79.8% vs 65.9%), rash (42.7% vs 42.4%) and dermatitis acneiform (42.7% vs 52.9%) and stomatitis (65.2% vs 41.2%) and led to discontinuation in 9 patients on D vs 7 on E.

Table: 1243P

<table>
<thead>
<tr>
<th></th>
<th>Dacomitinib (n= 89)</th>
<th>Erlotinib (n= 85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>60.4 (38.0-88.8)</td>
<td>59.1 (40.0-90.0)</td>
</tr>
<tr>
<td>ECOG 0-1/ 2 (%)</td>
<td>93/3/6.7</td>
<td>94/1/5.9</td>
</tr>
<tr>
<td>Male/ female (%)</td>
<td>67/32.6</td>
<td>61/38.8</td>
</tr>
<tr>
<td>Smoker/ non-Smoker (%)</td>
<td>66/33.7</td>
<td>64/35.3</td>
</tr>
<tr>
<td>KRAS wt/ mu/ unknown(%)</td>
<td>58/7/9/3/7</td>
<td>68/3/3/28.2</td>
</tr>
<tr>
<td>EGFR Activating mutation</td>
<td>24 (27%)</td>
<td>20 (23.5%)</td>
</tr>
</tbody>
</table>

Conclusions: The ARCHER 1009 trial suggested improvement in efficacy for D relative to E in Asian patients. The number of patients with EGFR mu was similar between arms. Treatment discontinuation for drug toxicity was uncommon. Survival data is not mature.

Disclosure: T. Mok: Ad boards: AZ, Roche, Eli Lilly, Merck Serono, Eisai, BMS, AVEO, Pfizer, Taba, Boehringer-Ingelheim, Novartis, GSK Biologics, Clovis Oncology, Amgen, Janssen, BioMarin Pharmaceutical; Board of directors: IASLC; Corporate-sponsored research: AZ; K.J. O’Byrne: Advisory boards: Pfizer; Other substantive relationships (Honoraria): Pfizer; S.S. Ramalingam: Advisory boards: Pfizer, AstraZeneca, Genentech; P.A. Janne: Advisory boards: Boehringer-Ingelheim, AstraZeneca, Genentech, Pfizer, Merrimack Pharmaceuticals, Clovis Oncology, Sanofi, Chugai; Stock ownership: Gatekeeper Pharmaceuticals; Other substantive relationships: LabCorp; M. Boyer: Advisory boards: Merck Sharpe & Dohme; Corporate-sponsored research: Pfizer, Boehringer-Ingelheim, Merck Sharpe & Dohme, Peregrine Pharmaceuticals; H. Zhang: Employment and stock ownership: Pfizer; J. O’Connell: Employment and stock ownership: Pfizer; I. Taylor: Employment and stock ownership: Pfizer; C. Mather: Employment and stock ownership: Pfizer, L. Paz-Ares: Advisory boards: Pfizer, BMS. All other authors have declared no conflicts of interest.