EVALUATION OF CERITINIB-TREATED PATIENTS (PTS) WITH ANAPLASTIC LYMPHOMA KINASE REARRANGED (ALK+) NON-SMALL CELL LUNG CANCER (NSCLC) AND BRAIN METASTASES IN THE ASCEND-1 STUDY

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Aim: Brain metastases, seen in ~30–50% of NSCLC pts, are associated with poor prognosis. ALK+ NSCLC is sensitive to the ALK inhibitor (ALKi) crizotinib, but resistance invariably occurs, often with progression in new or existing brain metastases. Ceritinib (LDK378), a novel ALKi, is highly active in pts with ALK+ NSCLC and has demonstrated central nervous system activity. Here we report efficacy and safety of ceritinib therapy in the subset of ALK+ NSCLC pts with brain metastases treated in the phase I ASCEND-1 study.

Methods: Safety and efficacy of ceritinib 750 mg/day was analyzed based on investigator assessment of brain metastases at study entry. Patients with brain metastases had a median age of 51.0 years; 85.5% had an ECOG performance status of ≤1. Most pts were either Caucasian (58.1%) or Asian (39.5%); median time from initial NSCLC diagnosis to first ceritinib dose was 20.5 months. Median duration of exposure to ceritinib was 27 weeks. Efficacy is shown below.

<table>
<thead>
<tr>
<th>Endpointa</th>
<th>ALKi-pretreated patients with brain metastases</th>
<th>ALKi-naive patients with brain metastases</th>
<th>All NSCLC patients with brain metastases</th>
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</thead>
<tbody>
<tr>
<td>n = 98</td>
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<tr>
<td>ORR, n (%) [95% CI]</td>
<td>49 (50.0) [39.7, 60.3]</td>
<td>18 (69.2) [48.2, 85.7]</td>
<td>67 (54.0) [44.9, 63.0]</td>
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<tr>
<td>DOR, median (months)</td>
<td>6.9 [4.8, 8.5]</td>
<td>7.0 [5.5, NE]</td>
<td>6.9 [5.5, 9.7]</td>
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<tr>
<td>PFS, median (months)</td>
<td>6.7 [4.9, 8.5]</td>
<td>8.3 [4.6, NE]</td>
<td>6.9 [5.4, 8.4]</td>
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</table>

NE = Not estimable
aOverall antitumor activity, bDOR rate at 6 months 65.9% [95% CI: 35.4, 84.5]

Brain metastases were identified by investigator assessment as target lesions in 14 pts at baseline using RECIST 1.0 criteria (10 ALKipretreated, 4 ALKi naïve). Of these, 7 achieved complete or partial responses in the brain (4 ALKi pretreated; 3 ALKi naïve) while 3 had stable disease (all ALKi pretreated). Most common adverse events (all grades; grade 3) in the 124 pts with brain metastases were nausea (82.3%; 4.0%), diarrea (79.0%; 4.8%), and vomiting (62.9%; 6.5%); no grade 4 observations for these adverse events.

Conclusions: Ceritinib 750 mg/day was efficacious in pts with brain metastases, whether ALKi pretreated or ALKi naïve.

Disclosure: A.T. Shaw: Advisory boards for Novartis, Pfizer, Ariad, Chugui, Genentech; R. Mehra: Spouse is employee of GlaxoSmithKline, Consultancy for Bristol-Myers Squibb and Novartis; E. Felip: Advisory boards for Boehringer Ingelheim, Novartis, Roche, Bristol-Myers Squibb, Lilly; L.Q. Chow: Employment by University of Washington; Research grants from Novartis (to institution); Consultancy, travel expenses and advisory board for Novartis; D.R. Camidge: Advisory boards/consultancy/honoraria for Servier, Eli Lilly, Genentech/Roche, Astex, Ariad, Immunogen, Clarient, ExcelGenix, indiPharm, Astellas, Boehringer Ingelheim, Chugui, Clovis, Array Biopharma, AstraZeneca, Areo, Novartis, Syny, Pfizer; J.F. Vantsemkite: Speaker for Novartis; S. Sharma: Research grant and consultancy for Novartis; Stock in Saturas Pharmaceuticals, Beta Cat Pharmaceuticals, ConverGene; Board member of TheraTarget and member, VBL Therapeutics IDMC; G.J. Rols: Advisory role for Chugui, Ariad, Daiichi, Tragra, Foundation Medicine, Boehringer Ingelheim, Novartis; Research funding from Pfizer, BMS, Chugui, GSK, Novartis, Infinity; B. Solomon: Honoraria for Novartis, Pfizer, Clovis, AstraZeneca, Roche; Advisory boards for Novartis, Pfizer, Clovis Oncology, AstraZeneca, Roche; J. Wolf: Advisory boards, speakers bureau and research funding, all compensated, by Novartis; M. Thomas: Honoraria for Lilly, BMS, Roche Consultancy for Lilly; BMS, Roche, Novartis; M. Schuler: Consultant (Compensated): AstraZeneca, Boehringer Ingelheim, Novartis, Pfizer Research grants to institution; Boehringer Ingelheim, Novartis Honorary for CME lectures: Boehringer Ingelheim, Celgene, GlaxoSmithKline, Lilly, Novartis, Pfizer; G. Liu: Consultancy for Astra Zeneica, Pfizer, Novartis; M. Geraudies: Employment with Novartis; Stock options with Novartis A.L. Boro; Employee of Novartis; A. Yovine: Employment with Novartis; D. Kim: Consultation for Novartis, Pfizer, Lilly; Honorarium from Pfizer, Lilly. All other authors have declared no conflicts of interest.