**Phase II/III trial of ensartinib** (X-396), a novel anaplastic lymphoma kinase (ALK) inhibitor, in patients with ALK+ non-small cell lung cancer (NSCLC)

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**BACKGROUND**
- The anaplastic lymphoma kinase (ALK) is a receptor tyrosine kinase that is genetically altered in a variety of malignancies.
- Ensartinib is a novel, potent ALK small molecule tyrosine kinase inhibitor (TKI)
- Ensartinib has additional activity against MET, AXL, EPHAX, LTK, ROS1, and SLK.
- It has demonstrated significant pre-clinical anti-tumor activity in both ALK TKI-naive and crizotinib-resistant models of ALK re-arranged NSCLC.

**METHODS**

**Expansion Cohort Major Inclusion Criteria:**
- Advanced or recurrent NSCLC with a documented activating ALK rearrangement.
- May have received prior crizotinib and/or second generation ALK TKIs or have been ALK TKI naive.
- ECOG performance status of 0 or 1.
- Asymptomatic treated and untreated brain metastases permitted.

**Dose Schema:**

**RESULTS**

**Common Drug-Related Adverse Events**

<table>
<thead>
<tr>
<th>Event</th>
<th>All</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>All Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>All at All Levels</td>
<td>83</td>
<td>50%</td>
<td>20%</td>
<td>17%</td>
<td>3%</td>
<td>70%</td>
</tr>
<tr>
<td>Rash (all)</td>
<td>25</td>
<td>31%</td>
<td>9%</td>
<td>2%</td>
<td>1%</td>
<td>33%</td>
</tr>
<tr>
<td>Nausea</td>
<td>22</td>
<td>26%</td>
<td>4%</td>
<td>1%</td>
<td>1%</td>
<td>28%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>17</td>
<td>21%</td>
<td>4%</td>
<td>1%</td>
<td>1%</td>
<td>22%</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>10</td>
<td>12%</td>
<td>5%</td>
<td>2%</td>
<td>0%</td>
<td>16%</td>
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<tr>
<td>Fatigue</td>
<td>9</td>
<td>11%</td>
<td>5%</td>
<td>2%</td>
<td>0%</td>
<td>13%</td>
</tr>
<tr>
<td>Rash (grade ≥2)</td>
<td>6</td>
<td>7%</td>
<td>2%</td>
<td>0%</td>
<td>0%</td>
<td>9%</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>5</td>
<td>6%</td>
<td>1%</td>
<td>0%</td>
<td>0%</td>
<td>6%</td>
</tr>
<tr>
<td>Pruritus</td>
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<td>1%</td>
<td>1%</td>
<td>0%</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td>Rash</td>
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<td>0%</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td>Alopecia</td>
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<td>2%</td>
</tr>
<tr>
<td>Anorexia</td>
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<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>1%</td>
</tr>
</tbody>
</table>

**Common drug-related adverse events (AEs)**, mostly Grade 1-2, include rash, nausea, vomiting, pruritus, and fatigue.

- In patients taking X-396 with food, few patients had nausea or vomiting.
- Few drug-related AEs of diarrhea (7%, Grade 1), constipation (2%, Grade 1), abdominal pain (4%, Grade 1-2), myalgia/ muscle/skeletal pain (5%, Grade 1), transaminase elevations (2%, Grade 1), or QT prolongation (2%, Grade 2).

**Best Change from Baseline in Target Lesions (%)**

- For the 42 evaluable ALK+ patients at 200 mg or above:
  - 24 patients had a PR (57%) and 9 had SD (21%) as best response.
  - Duration of treatment has been from 1 to 34+ months.
  - In a previous study (NCCT/01278504), 23% of patients achieved lasting tumor control.

**CONCLUSIONS**

- Ensartinib has shown promising activity in both crizotinib-naive and crizotinib-resistant ALK+ NSCLC patients.
- Responses are seen in patients with CNS disease and patients with prior 2nd generation ALK TKI.
- Ensartinib is generally well tolerated with most common toxicities being rash and nausea/vomiting, the latter often resolved with food.
- A phase II trial is ongoing comparing ensartinib to crizotinib in TKI naive ALK-positive NSCLC patients.

**REFERENCES**

**ACKNOWLEDGEMENTS**
- The patients and families for participation in the study.
- Participating sites.
- Our colleagues at XcyteX Holding Company.
- Ensartinib = proposed International Nonproprietary Name (INN); formerly referred to as X-396.