Results of a Global Phase II Study with Crizotinib in Advanced ALK-positive Non-small Cell Lung Cancer (NSCLC)

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Lung Adenocarcinomas

- KRAS mutation
- EGFR mutation
- 35% Unknown
- BRAF mutation
- ALK rearrangement
- MEK mutation
- PIK3CA mutation
- HER2 mutation
- ROS1 fusion
- RET translocation
- MET amplification
Background

- Anaplastic lymphoma kinase (ALK) gene rearrangements have been identified in approximately 3–5% of non-small cell lung cancers, most frequently occurring in adenocarcinomas.\(^1\–^3\)

- Crizotinib (PF-02341066) is an oral ALK inhibitor

- In a phase 1 study of crizotinib, patients with ALK-positive lung cancer treated with 250 mg twice daily had a response rate of 61% and median PFS of 10 months.\(^4\)

- Here we present updated data from the subsequent phase 2 study of crizotinib in patients with previously treated, advanced ALK-positive NSCLC (NCT00932451)
Phase 2 Study of Crizotinib in ALK+ NSCLC

Study Design

- Phase II, single-arm, multicenter study; ~1100 patients (enrollment ongoing)

Key eligibility criteria:
- ALK+ NSCLC by central laboratory
- ECOG PS: 0–3
- ≥1 prior line of chemotherapy
- Stable/controlled brain metastases allowed

Treatment

- Crizotinib 250 mg po BID continuous daily dosing

Primary endpoints:
- ORR
- safety/tolerability
Phase 2 Study of Crizotinib in ALK+ NSCLC

Best Response of Indicator Lesions

Response-evaluable patients  
\( n = 259 \)

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<table>
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<tbody>
<tr>
<td>Complete Response</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>Partial Response</td>
<td>151 (58%)</td>
</tr>
<tr>
<td>Stable Disease</td>
<td>69 (27%)</td>
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<tr>
<td>Progressive Disease</td>
<td>19 (7%)</td>
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</table>

Decrease or increase from baseline (%)
Phase 2 Study of Crizotinib in ALK+ NSCLC

Progression-free Survival

Median PFS 8 months (95% CI: 7–10)
28% of patients in follow-up for progression

Probability of survival without progression

Time (months)

95% Hall-Wellner Band
Phase 2 Study of Crizotinib in ALK+ NSCLC

Response of Brain Metastases to Crizotinib

• There were 18 patients with asymptomatic, non-irradiated brain metastases in the mature response-evaluable population who were evaluable for both brain and systemic disease

<table>
<thead>
<tr>
<th>Brain Response</th>
<th>N=18</th>
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<tbody>
<tr>
<td>Complete Response</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Partial Response</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Stable Disease</td>
<td>12 (67%)</td>
</tr>
<tr>
<td>Progressive Disease</td>
<td>2 (11%)</td>
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Conclusions

• Crizotinib treatment led to a response rate of 60% and median PFS of 8 months

• Crizotinib continued to show a good safety profile in patients with previously treated ALK-positive advanced NSCLC

• Clinically meaningful improvement was observed global QOL and in lung cancer symptoms such as fatigue, cough, dyspnea, chest pain

• These data are consistent with the efficacy and safety findings previously reported and further support the use of crizotinib in patients with ALK-positive lung cancer