Table 3. Time to CNS outcomes for patients with NTRK-fp NSCLC

<table>
<thead>
<tr>
<th>Event</th>
<th>All patients (n=22)</th>
<th>Baseline CNS metastases* (n=13)</th>
<th>No baseline CNS metastases (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS progression</td>
<td>19.9 (18.0–21.8)</td>
<td>19.5 (17.8–21.5)</td>
<td>20.4 (18.3–22.4)</td>
</tr>
<tr>
<td>CNS failure</td>
<td>20.4 (18.3–22.4)</td>
<td>19.5 (17.8–21.5)</td>
<td>20.7 (18.5–22.9)</td>
</tr>
<tr>
<td>Death</td>
<td>15.9 (13.9–18.2)</td>
<td>15.0 (12.7–17.5)</td>
<td>18.4 (16.4–20.4)</td>
</tr>
<tr>
<td>CNS failure (death censored)</td>
<td>19.9 (18.0–21.8)</td>
<td>19.5 (17.8–21.5)</td>
<td>20.7 (18.5–22.9)</td>
</tr>
</tbody>
</table>

Table 2. Overall efficacy

- **Objective response rate (ORR)**: 53.8% (95% CI: 31.9–73.6%)
- **Complete response**: 2 (9.1%)
- **Partial response**: 12 (53.8%)
- **Stable disease**: 5 (22.2%)
- **Progressive disease**: 2 (9.1%)
- **Non CR/PD**: 1 (4.5%)

Overall survival

- **Median duration of survival follow-up**: 19.9 months (95% CI: 17.8–21.8 months).
- **Confirmed ORR** in all patients was 53.8% (95% CI: 31.9–73.6%)
- **Early responses were seen in the majority of patients**: the median time to response was 9.9 months (95% CI: 9.3–10.5 months).
- **Median treatment duration**: 11.1 months (IQR: 4.6–20.1).

RESULTS

- **Adult patients (18 years old) with locally advanced/metastatic, measurable NTRK-fp NSCLC were enrolled in STARTRK-1 and STARTRK-2**
- **Patients with CNS metastases (asymptomatic or previously treated and controlled) were eligible**
- **Patients received entrectinib 600 mg once daily**
- **All patients who had received ≥1 dose of entrectinib were evaluable for safety**
- **The efficacy-evaluable population comprised all patients who had received ≥1 dose of entrectinib and had ≥3 months follow-up since start of treatment**
- **Tumour response was assessed at Week 4 and then every 8 weeks by blinded independent central review (BICR) per RECIST v1.1**
- **Primary end points were ORR and DoR by BICR**
- **Secondary end points included PFS, OS, intracranial efficacy, time to CNS progression and safety**

**PATIENT POPULATION**

- **At data cut-off, the efficacy-evaluable population comprised 22 patients with NTRK-fp NSCLC (NTRK1, n=13; NTRK2, n=9)**
- **59.1% of patients had investigator-assessed CNS metastases at baseline (Table 1)**

**METHODS**

- **Neurotrophic tyrosine receptor kinase (NTRK) gene fusions are oncogenic drivers in many solid tumours, including non-small cell lung cancer (NSCLC).**
- **Entrectinib is a potent inhibitor of tropomyosin receptor kinase (TRK) proteins with central nervous system (CNS) activity.**
- **Entrectinib has shown strong efficacy in patients with NTRK-fp NSCLC from the phase I/II ALKA-372-001 (NCT03199918) study and STARTRK-1 (NCT02387161) and STARTRK-2 (NCT02585667) clinical trials.**
- **In a prior integrated analysis of the NTRK-fp NSCLC cohort (n=13; 31 October 2018 data cut-off):**
  - Objective response rate (ORR) was 62.5% (95% CI: 36.6–83.0%)
  - Duration of response was not reached (NE)
  - Median progression-free survival (PFS) was 14.0 months (95% CI: 4.7–NE);
  - Median overall survival (OS) was 14.9 months (95% CI: 5.9–NE).
- **We present updated data for this cohort (enrolment cut-off: 28 February 2020, data cut-off: 31 July 2019; data cut-off: 31 August 2020).**

**CONCLUSIONS**

In this updated analysis with longer follow-up and a larger patient population, entrectinib was associated with deep and durable responses in patients with NTRK-fp NSCLC, including those with baseline CNS metastases. Entrectinib demonstrated robust intracranial activity in patients with NTRK-fp NSCLC with baseline CNS metastases. Entrectinib continues to show a manageable safety profile in patients with NTRK-fp NSCLC.