Background

- Selcetinib, a first-in-class highly selective and potent RET kinase inhibitor with CNS activity, is approved in multiple countries for the treatment of RET-fusion-positive thyroid and lung cancers and RET-mutant MTC (including pediatric patients ≥12 years of age).
- Selcetinib has demonstrated clinically meaningful and durable antitumor activity with a favourable safety profile in patients with advanced or metastatic RET-activated thyroid cancer (TC) in the ongoing phase 1/2 LIBRETTO-001 (NCT03157128) trial.

At the time of the previous report, most patients were alive and remained progression-free, thus duration of response (DoR) and progression-free survival (PFS) estimates were immature.

Study Design

Phase 1 Dose Escalation - Expansion (N=65) including: n=837

- All patients enrolled with RET-altered cancers, including thyroid cancer, MTC, NSCLC, and other cancers N=837
- Safety population -_thyroid cancer n=65
- Safety profile for patients with RET-fusion positive TC was similar to the overall safety population

- Two patients (3.0%) discontinued treatment due to treatment-emergent adverse events (TEAEs) (1.5%) related

Study Naive Patients with RET-Fusion Positive TC

Best overall response

Treatment-Related adverse events

- RET-fusion positive TC safety population n=65
- Overall safety population n=837

N (%) Any grade Grd 2 Grd 3

Diabetes 36 (54.5) 5 (7.6) 41 (60.9) 49 (5.9)
Dysphagia 30 (45.5) 0 (0.0) 36 (53.0)
Fatigue 31 (47.0) 10 (15.2) 35 (53.2) 165 (19.7)
Fever 19 (29.3) 1 (1.5) 33 (57.9) 22 (2.7)
Constitutional 27 (42.0) 0 (0.0) 25 (37.5) 17 (2.1)
Abdominal pain 24 (36.4) 3 (4.5) 23 (37.3) 25 (3.0)
Vomiting 24 (36.4) 2 (3.0) 26 (37.8) 20 (2.4)
Nausea 30 (45.5) 3 (4.5) 29 (43.5) 17 (2.1)
Anorexia 19 (29.3) 1 (1.5) 19 (29.3) 3 (4.0)
Decreased appetite 19 (29.3) 1 (1.5) 18 (27.2) 7 (0.8)
Rash 18 (27.3) 0 (0.0) 13 (19.7) 3 (0.4)
Back pain 17 (25.8) 2 (3.0) 17 (27.3)

Safety in Patients with RET-Fusion Positive TC

- The safety profile for patients with RET-fusion positive TC was similar to the overall safety population
- Two patients (3.0%) discontinued treatment due to treatment-emergent adverse events (1.5%) related

Treatment Naomi Patients with RET-Fusion Positive TC

Best overall response

Baseline Characteristics in Patients with RET-Activated Thyroid Cancer

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Timepoint</th>
<th>Treatment (N=24)</th>
<th>Prior treatment (N=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – Median (range) in years</td>
<td>60.5 (20-84)</td>
<td>58.0 (25-86)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>14 (58.3)</td>
<td>18 (43.9)</td>
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<tr>
<td></td>
<td>Female</td>
<td>10 (41.7)</td>
<td>23 (56.1)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>White</td>
<td>18 (75.0)</td>
<td>28 (68.3)</td>
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<tr>
<td></td>
<td>Asian</td>
<td>1 (4.2)</td>
<td>12 (29.3)</td>
</tr>
<tr>
<td></td>
<td>Black or African American</td>
<td>0 (0.0)</td>
<td>3 (7.3)</td>
</tr>
<tr>
<td>ECOG performance-status score, n (%)</td>
<td>0</td>
<td>14 (58.3)</td>
<td>11 (27.8)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>9 (37.5)</td>
<td>27 (66.0)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1 (4.2)</td>
<td>3 (7.3)</td>
</tr>
<tr>
<td>RET fusion partner, n (%)</td>
<td>CCO44</td>
<td>15 (62.5)</td>
<td>25 (61.0)</td>
</tr>
<tr>
<td></td>
<td>NCC44</td>
<td>7 (29.2)</td>
<td>8 (19.5)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>3 (12.5)</td>
<td>4 (9.8)</td>
</tr>
<tr>
<td>Prior systemic regimens included</td>
<td>Median (range)</td>
<td>1.0 (0.0)</td>
<td>3.0 (1.7)</td>
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<tr>
<td></td>
<td>Retropertinib</td>
<td>2 (8.3)</td>
<td>8 (19.5)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>0 (0.0)</td>
<td>3 (7.3)</td>
</tr>
</tbody>
</table>

Efficacy in Patients with RET-Fusion Positive TC

- With longer follow-up and additional patients, selcetinib continues to demonstrate robust and durable responses in patients with RET-fusion-positive thyroid cancer
- ORR was 95.5% in treatment-naive population at a median follow-up of 17.8 months, 73.0% of responses ongoing
- PFS was 85.4% in previously treated patients at a median follow-up of 33.9 months, 40% of responses ongoing
- The safety profile was consistent and remained tolerable despite longer duration on treatment
- Furthermore, a separate study evaluating patient-reported outcomes from LIBRETTO-001 demonstrated favorable health-related quality of life during treatment with selcetinib (Poster 169P)

Conclusions

- We would like to thank the Clinical Trial participants and their caregivers, without whom this work would not have been possible.

Acknowledgements

References

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