Characteristics and survival outcomes of patients with RET fusion-positive (RET-fp) solid tumours receiving non-RET inhibitor therapy in a real-world setting

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BACKGROUND
• RET gene fusions are oncogenic drivers in multiple tumour types.
• Current standards of care for patients with RET-fp solid tumours have limited efficacy and/or significant target toxicity.1,4,7,13 There is a need for efficacious precision therapies that specifically target RET alterations.
• The genomic landscape and natural history of patients with RET-fp solid tumours are unknown.

METHODS
• Using real-world data, we described the clinical characteristics and survival outcomes of patients with RET-fp metastatic solid tumours who received non-selective RET inhibitor therapy, and assessed the prognostic value of RET fusions in solid tumours.

RESULTS

Patient characteristics

Overall, there were 7,220 eligible patients with RET-fp solid tumours.

The RET-fp cohort comprised 26 patients and the matched RET-WT cohort comprised 102 patients (Table 1).

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RET-fp (n=26)</th>
<th>RET-WT (n=102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (SD)</td>
<td>63.3(13.0)</td>
<td>61.9(12.0)</td>
</tr>
<tr>
<td>Sex (%)</td>
<td>Female 42.3%</td>
<td>Female 57.7%</td>
</tr>
<tr>
<td>Race (%)</td>
<td>Asian 13.0%</td>
<td>White 86.7%</td>
</tr>
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<td>TMB status (%)</td>
<td>High 13.0%</td>
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The primary objective was to evaluate overall survival (OS) in the RET-fp and matched RET-WT cohorts (Figure 1).

Objectives

• One objective was to identify the presence of a fusion with a predicted RET transcription factor (fp) status.
• A second objective was to confirm the presence of a fusion with a predicted RET transcription factor (fp) status.

Survival outcomes

When the CGP report date was used as the index date (model 1: Figure 1A),

- Median OS was 6 months (95% CI 1.6–9.3) in the RET-fp cohort and 9.7 months (95% CI 6.3–11.7) in the matched RET-WT cohort.
- The hazard ratio (HR) was 1.1 (95% CI 1.1–3.1).

When the initial diagnosis date was used as the index date (Figure 2B),

- Median OS was 6 months (95% CI 1.6–9.6) in the RET-fp cohort and 11.2 months (95% CI 7.7–16.9) in the matched RET-WT cohort.
- The HR was 2.2 (95% CI 1.3–3.3).

CONCLUSIONS

- Despite the small sample size, patients with RET-fp solid tumours had a shorter median OS than matched patients with RET-fp tumours and may have an increased risk of death.
- Oncogenic co-alterations were prevalent in patients with RET-fp tumours, which suggests that RET fusions are the primary oncogenic drivers in these tumours.
- Our data highlight the need for effective RET inhibitors that could improve the survival of patients with solid tumours harbouring RET fusions.

SUMMARY

- Median OS: RET-fp vs matched RET-WT
  - Model 1: 6.0 vs 9.7 months
  - Model 2: 6.3 vs 11.2 months
- Low TMB and MSI in RET-fp and matched RET-WT cohorts
- Low frequency of genetic co-alterations in patients with RET-fp solid tumours

References

Study design

• Clinical characteristics and survival outcomes for RET inhibitor-naïve patients with metastatic solid tumours were collected from the national (US-based) de-identified Flatiron Health Foundation Medicine/clinico-genetic database (FH FMD CGDB; version April 2022).
• The de-identified data originated from ~280 cancer clinics in the US (~800 care sites).

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