Long-term clinical outcomes of Lenvatinib in patients with differentiated thyroid cancer: Results from the real-world practice of a single institution.

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Background

- Lenvatinib is the preferred drug for locally recurrent or metastatic progressive radiolodine-refractory differentiated thyroid cancer (RR-DTC) based on the results of the SELECT trial (NCT01321554)1,2.
- However, there are few reports on long-term outcomes - the median duration of follow-up in the Lenvatinib group in the SELECT trial was 17.1 months (interquartile range[IQR], 14.4 to 20.4).
- The current study aimed to evaluate the long-term clinical outcomes of Lenvatinib in RR-DTC.

Methods

Patients:
- We retrospectively reviewed the medical records of 91 patients with RR-DTC who received Lenvatinib from September 2011 to November 2022 at National Cancer Center Hospital East, Japan.
- Treatment:
  - All patients started Lenvatinib at a dose of 24mg/day.
  - Planned drug holidays were allowed to avoid severe or intolerable toxicities.
  - Dose escalations were allowed after disease progression.

Data Collection:
- Age, gender, ECOG PS, histologic subtypes, Disease distribution, Planned drug holidays, Dose escalations

Outcomes:
- Progression-free survival (PFS) and overall survival (OS)
- Antitumor efficacy
- The treatment status at the cut-off date of December 31, 2022.

Results

- The median follow-up time was 2.3 years (IQR, 1.1 to 3.7).
- The treatment status at the cut-off date

<table>
<thead>
<tr>
<th>The current study</th>
<th>The SELECT study†</th>
</tr>
</thead>
<tbody>
<tr>
<td>[n=91], n (%)</td>
<td>[n=261], n (%)</td>
</tr>
<tr>
<td>Median age, years (range)</td>
<td>70 (42-84)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>55 (60.4)</td>
</tr>
<tr>
<td>Female</td>
<td>36 (39.6)</td>
</tr>
<tr>
<td>ECOG PS 0 or 1</td>
<td>91 (100)</td>
</tr>
<tr>
<td>Histologic subtypes</td>
<td></td>
</tr>
<tr>
<td>Papillary ca.</td>
<td>59 (64.8)</td>
</tr>
<tr>
<td>Follicular ca.</td>
<td>22 (24.2)</td>
</tr>
<tr>
<td>Poorly differentiated ca.</td>
<td>10 (11.0)</td>
</tr>
<tr>
<td>Disease distribution†</td>
<td></td>
</tr>
<tr>
<td>Primary lesion recurrence</td>
<td>6 (6.6)</td>
</tr>
<tr>
<td>Pulmonary metastases</td>
<td>69 (75.8)</td>
</tr>
<tr>
<td>Lymph node metastases</td>
<td>57 (62.6)</td>
</tr>
<tr>
<td>Bony metastases</td>
<td>32 (35.1)</td>
</tr>
<tr>
<td>Liver metastases</td>
<td>3 (3.2)</td>
</tr>
<tr>
<td>Brain metastases</td>
<td>2 (2.2)</td>
</tr>
</tbody>
</table>

Kaplan-Meier curves for PFS and OS

PFS

- mPFS: 3.1 years (95%CI, 1.70-4.00)
- 2y-PFS: 55.0% (95%CI, 43.0-65.5)
- 6y-PFS: 31.1% (95%CI, 17.7-45.5)

OS

- mOS: 5.1 years (95%CI, 3.21-6.66)
- 2y-OS: 79.9% (95%CI, 69.1-87.2)
- 6y-OS: 43.9% (95%CI, 29.3-57.6)

AEs leading to treatment termination

- Evaluated by CTCAE ver. 4.0

<table>
<thead>
<tr>
<th></th>
<th>[n=91], n (%)</th>
<th>[n=261], n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of follow up†</td>
<td>16 (18)</td>
<td></td>
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</table>

1 The most common reason for the loss of follow-up was a change of treatment institution (referring to other hospitals) due to relocation.

Contact / Declaration of Interest

Disclosure: RD has no conflicts of interest to declare.
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Discussion

- The current study, for the first time, demonstrated a favorable long-term prognosis of RR-DTC patients treated with Lenvatinib, with mPFS of 3.1 years and mOS of 5.1 years.
- AEs were generally manageable, and the treatment discontinuation due to AEs was acceptable (11%).
- When we compared their prognosis with those from the SELECT trial, the former provided numerically better prognosis (2y-PFS was 55.0% vs. 44.3%, 2y-OS was 79.9% vs. 58.2%).
- As its background, there might be several factors in the management of Lenvatinib treatment, including planned drug holidays in (68.1% in the current study) and dose-escalation (22.0%, same as above) as an option at the disease progression, which was not allowed in the SELECT study.
- We believe they worked on the prolonged prognosis by avoiding unacceptably long treatment interruption or other treatment discontinuation due to intolerable AEs.

Conclusion

Long-term follow-up data in the real world showed that Lenvatinib could provide a reliable clinical outcome, represented by long-lasting disease stabilization with a manageable safety profile in RR-DTC. The optimization of its practical management should be increasingly important.

References

1. NCCN clinical practice guidelines in oncology, Thyroid Carcinoma, version 2.2023.

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