Response characteristics of tislelizumab (TIS) plus chemotherapy (chemo) in first-line (1L) treatment of locally advanced or metastatic esophageal squamous cell carcinoma (ESCC): a post hoc analysis of RATIONALE-306

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Conclusions

In the TIS + chemo arm, 64.7% of responders achieved response within 8 weeks, while still 35.2% of responders achieved response at later tumor assessments, and the OS benefits were comparable between early responders and late responders. Responders with deeper tumor response and/or longer TTMR tended to have longer OS.

Background

- The global phase 3 RATIONALE-306 study (NCT03783442) demonstrated superior OS, PFS, ORR and manageable safety profile of tislelizumab (TIS) + chemotherapy (chemo) as first line treatment of ESCC, which was well maintained at 3 years[1,2].
- This post-hoc analysis aims to explore the response characteristics of responders in TIS + chemo arm from RATIONALE-306.

Methods

- In RATIONALE-306 study, advanced or metastatic ESCC patients (pts) were randomly assigned (1:1) to receive first line TIS + chemo or placebo + chemo. Assessments of tumor response were done every 6 weeks for the first 48 weeks, then every 9 weeks thereafter per RECIST v1.1.
- In this post hoc analysis, time to response (TTR), depth of response (DpR) and time to maximum response (TTMR) were assessed in responders (pts who achieved CR or PR) of TIS + chemo group. Overall survival (OS), OS post first response and OS post-maximum response of pts with different response characteristics were also analyzed using the Kaplan-Meier method.
- TTR was defined as the time from randomization to the first occurrence of a CR or PR. DpR was defined as the percentage of maximal tumor reduction from the baseline of target lesion sum of diameters. TTMR was defined as the time from randomization to the maximum tumor shrinkage.
- OS post first response was defined as the time from the first response (CR or PR) to the death due to any cause. OS post-maximum response was defined as the time from the maximum tumor shrinkage to the death due to any cause.

Results

OS in pts with different TTR

- As of 24 November 2023, 207 pts (68.3% of the ITT population) in the TIS + chemo arm achieved response with the median TTR of 6.1 (range: 3.3 - 101.3) weeks.
- For responders, most pts (64.7%) achieved first response within 8 weeks, 22.2% between > 8 and ≤ 14 weeks, and 13.0% after 14 weeks (Fig 1).
- For pts within the three TTR categories, the median OS was 21.8, 23.1 and 29.0 months, respectively, and the median OS post first response was 21.3, 21.3 and 23.2 months, respectively (Fig 2).

OS in pts with different DpR

- The median DpR was 62.1% (range: 30%-100%) in responders of TIS + chemo group. DpR > 30% to ≤ 50%, > 50% to ≤ 80%, and > 80% to ≤ 100% was observed in 29.8%, 50.2% and 20.0% of responders, respectively (Fig 3).
- The median OS of pts within the three DpR categories was 16.1, 23.7, and 34.5 months, respectively (Fig 4).

OS in pts with different TTMR

- The median TTMR was 19 (range: 3.3-201) weeks of responders in TIS + chemo group. 32.7% of responders achieved maximum response within 14 weeks, 34.6% between > 14 and ≤ 28 weeks, and 32.7% after 28 weeks, respectively (Fig 5).
- For pts within the three TTMR categories, the median OS was 14.3, 17.4, and 39.9 months, respectively, and the median OS post-maximum response was 12.6, 14.3, and 24.8 months, respectively (Fig 6).

Fig 1. The distribution of pts with different TTR

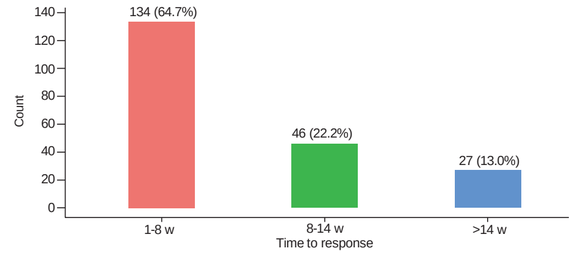


Fig 2. The OS (A) and OS post first response (B) of pts with different TTR

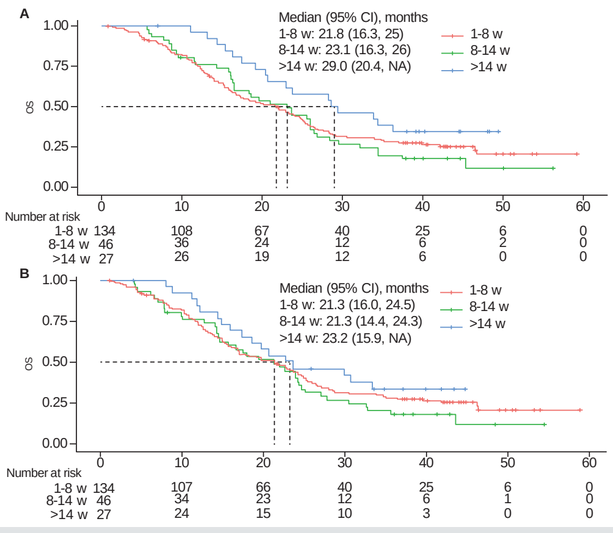


Fig 3. The distribution of pts with different DpR

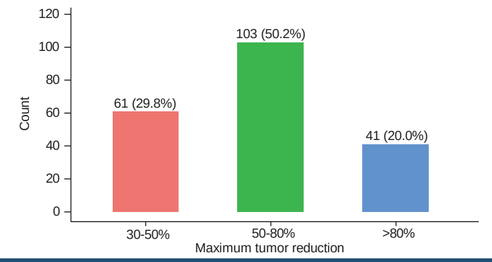


Fig 4. The OS of pts with different DpR

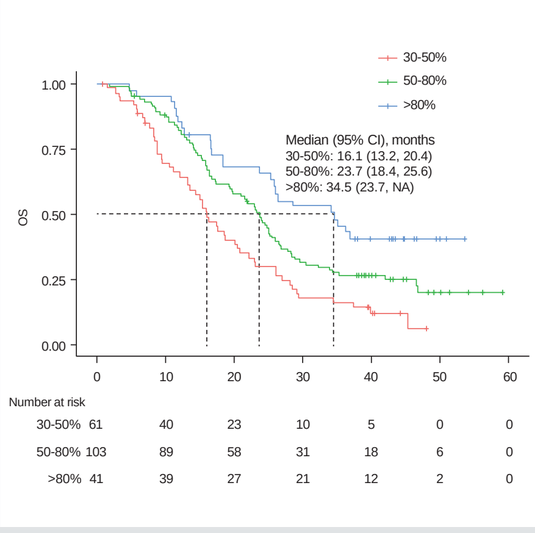


Fig 5. The distribution of pts with different TTMR

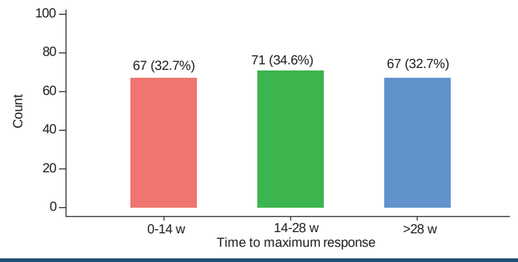
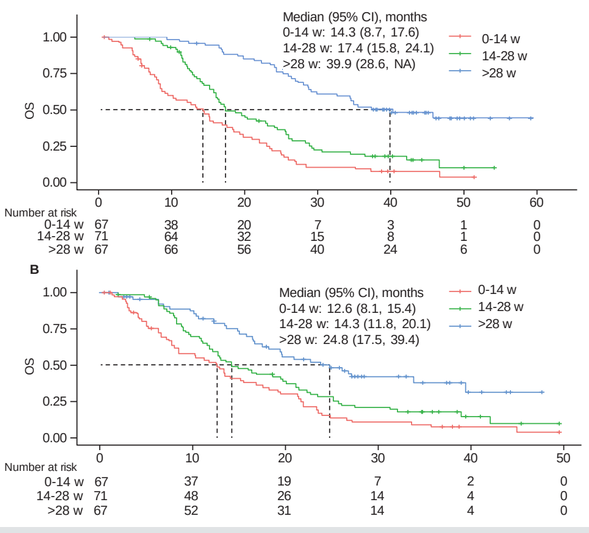


Fig 6. The OS (A) and OS post-maximum response (B) of pts with different TTMR



References 1. Xu J, et al. Lancet Oncol. 2023 May;24(5):483-495. 2. Harry H. Yoon et al. JCO 42, 4032-4032(2024).

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