

**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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**ABSTRACT**

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

**Methods:** Advanced or metastatic ESCC patients (pts) were randomly assigned (1:1) to receive 1L 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. Time to response (TTR), depth of response (DpR) and time to maximum response (TTMR) were assessed in responders (pts who achieved CR or PR). TTR was defined as the time from randomization to the first occurrence of a CR or PR, DpR as the percentage of maximal tumor reduction from the baseline of target lesion sum of diameters, and TTMR as the time from randomization to the maximum tumor shrinkage.

**Results:** As of 24 November 2023, 207 pts (68.3% of the ITT population) in the TIS + chemo arm achieved responses, with a median TTR of 6.1 weeks (range: 3.3 - 101.3). First response was detected in 64.7% of responders within 8 weeks, 22.2% between . 8 and # 14 weeks, and 13.0% after 14 weeks; the median OS was 21.8, 23.1 and 29.0 mos, respectively in pts within the three TTR categories, and the median OS post first response was 21.3, 21.3 and 23.2 mos (Table). DpR . 30% to # 50%, . 50% to # 80%, and . 80% to # 100% was observed in 29.8%, 50.2% and 20.0% of responders, respectively, and the median OS was 16.1, 23.7, and 34.5 mos. The median TTMR was 19 weeks (range: 3.3 - 201.0), with 32.7% of responders achieved maximum response within 14 weeks, 34.6% between . 14 and # 28 weeks, and 32.7% after 28 weeks, respectively. Median OS of pts with the three TTMR categories was 14.3, 17.4, and 39.9 mos, respectively, and median OS post-maximum response was 12.6, 14.3, and 24.8 mos.

**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.

|      | Cutoff          | Patients, n (%) | OS, median (95% CI), mos | OS from response*, median (95% CI), mos |
|------|-----------------|-----------------|--------------------------|---|
| TTR  | > 0 to ≤ 8w     | 134 (64.7)      | 21.8 (16.3, 25.0)        | 21.3 (16.0, 24.5)                       |
|      | > 8 to ≤ 14 w   | 46 (22.2)       | 23.1 (16.3, 26.0)        | 21.3 (14.4, 24.3)                       |
|      | > 14w           | 27 (13.0)       | 29.0 (20.4, NA)          | 23.2 (15.9, NA)                         |
| DpR  | > 30% to ≤ 50%  | 61 (29.8)       | 16.1 (13.2, 20.8)        | \                                       |
|      | > 50% to ≤ 80%  | 103 (50.2)      | 23.7 (19.6, 25.6)        | \                                       |
|      | > 80% to ≤ 100% | 41 (20.0)       | 34.5 (23.7, NA)          | \                                       |
| TTMR | > 0 to ≤ 14w    | 67 (32.7)       | 14.3 (8.7, 17.6)         | 12.6 (8.1, 15.4)                        |
|      | > 14 to ≤ 28w   | 71 (34.6)       | 17.4 (15.8, 24.1)        | 14.3 (11.8, 20.1)                       |
|      | > 28w           | 67 (32.7)       | 39.9 (28.6, NA)          | 24.8 (17.5, 39.4)                       |

\*From first response for TTR, and from maximum response for TTMR.