# The effects of tislelizumab treatment on the health-related quality of life of non−small cell lung cancer patients who progressed on a prior platinum-containing regimen

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## Background

- The prognosis for patients with advanced non−small cell lung cancer (NSCLC) is relatively poor;[1] disease-related symptoms are also associated with poor health-related quality of life (HRQoL)[2,3]
- Inhibitors targeting the PD-1/PD-L1 axis have improved clinical outcomes, including HRQoL, in patients with advanced NSCLC[4–7]
- Tislelizumab, a monoclonal antibody against PD-1, was engineered to minimize binding to Fcγ receptor on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy[8]
- RATONALE 303 (NCT03358875), a randomized, open-label, multicenter, Phase 3 trial, examined the efficacy and safety of single-agent tislelizumab vs docetaxel in patients with NSCLC who had progressed on a prior platinum-containing regimen[9]
  - Compared with docetaxel, tislelizumab significantly prolonged OS, improved PFS, and had a higher ORR[9]
- The objective of this poster was to compare the changes from baseline in the HRQoL scores and time to deterioration in patients receiving tislelizumab vs docetaxel in RATIONALE 303

## Methods

**Study Design, Patients, and Treatment**

- Full study details have been previously described[9]
  - Briefly, adult patients with histologically confirmed Stage IIIB or IV NSCLC of either squamous or non-squamous histology, were randomized 2:1 to receive tislelizumab 200 mg IV or docetaxel 75 mg/m² IV in 21-day cycles

**HRQoL Assessments and Endpoints**

- The PROs were collected at every treatment cycle to the end of treatment
  - Descriptive analyses were performed on all the domains and single items
- Compliance (eg, proportion of patients who completed ≥1 HRQoL assessment among those who were expected to complete the questionnaire) was summarized by treatment group and visit
- HRQoL endpoints included the GHS/QoL, physical function and fatigue domains of the EORTC QLQ-C30 and the QLQ-LC13's index score and most relevant lung cancer symptoms (eg, dyspnea, coughing, peripheral neuropathy, pain in chest, pain in arms/shoulders, hemoptysis)
  - Endpoint selection criteria was based on the descriptive analysis and previous published studies
- For GHS/QoL and physical functional domain, higher scores indicate a higher (better) function; for the fatigue domain and symptom scales, higher scores indicate a higher (worse) severity of symptoms
- Changes from baseline were evaluated at cycle 4 (Week 10) and cycle 6 (Week 16)
  - Changes from baseline in the QLQ-C30 GHS/QoL, physical functioning scale and fatigue scale from EORTC QLQ-C30 are presented
  - Changes from baseline to cycle 4 and cycle 6 of QLQ-LC13 index score, dyspnea, coughing, peripheral neuropathy, pain in chest, and pain in arm or shoulder, and hemoptysis are presented
- Time to deterioration (TTD) was defined as the time from randomization to first onset of a ≥10 points increase from baseline score, confirmed by a second increase of ≥10 points increase from baseline in QLQ-LC13 index score, dyspnea, coughing, peripheral neuropathy, pain in chest, pain in arm/ shoulder, and hemoptysis

**Analysis**

- The analysis population was comprised of all randomized patients who received at least one dose of study drug and completed at least one HRQoL assessment
- Least square (LS) mean score change from baseline to cycle 4 and cycle 6 were assessed using a constrained longitudinal data analysis model with the PRO score as the response variable, and treatment by study visit interaction and stratification factors for randomization as covariates, based on the missing at random assumption
- The median TTD in each treatment was estimated using Kaplan-Meier method, and the treatment difference in TTD was assessed by the stratified log-rank test, and one-sided *P*-value from stratified log-rank test is presented
  - A stratified Cox proportional hazard model with Efron's method of tie handling was used to assess the magnitude of the treatment difference (hazard ratio [HR]) between treatment arms
- Unless otherwise specified, *P*-values were two-sided and nominal, without multiple adjustment
- Analyses were conducted using the data cutoff of 10 Aug 2020

## Results

**Patient Characteristics**

- Overall, 805 patients were randomized and included in the intent-to-treat population (ITT); demographics and baseline characteristics were well balanced across the two arms (Table 1)

**Table 1. Demographics and baseline characteristics (ITT)**

| | Tislelizumab (N=533) | Docetaxel (N=270) |
|---|---|---|
| Median age, years (range) | 61.0 (28–88) | 61.0 (32–81) |
| Patients < 65 years, n (%) | 364 (68.0) | 180 (66.7) |
| Sex, n (%) | | |
| Male | 416 (77.8) | 206 (76.3) |
| Race, n (%) | | |
| Asian | 424 (79.3) | 219 (81.1) |
| ECOG performance status, n (%) | | |
| 0 | 115 (21.5) | 50 (18.5) |
| 1 | 420 (78.5) | 220 (81.5) |
| Smoking status, n (%) | | |
| Never | 162 (30.3) | 82 (30.4) |
| Current/former | 373 (69.7) | 188 (69.6) |

## Conclusions

- The RATIONALE 303 study results show that tislelizumab monotherapy improved HRQoL in patients who previously experienced treatment failure with a platinum containing chemotherapy via reduction in lung cancer symptoms, fatigue, and improvements in their physical functioning, which also indicated improvements in their GHS
- The symptom improvements were tested via two types of analysis and both results showed similar patterns; these findings were in line with the clinical and survival benefits seen with tislelizumab[8] as well as other HRQoL results[5]
- Comparative analyses were not meaningful beyond cycle 6 due to low number of patients still on study in the docetaxel arm
- These HRQoL data, together with the efficacy and favorable safety profile, demonstrated a favorable risk-benefit ratio of tislelizumab in patients with NSCLC who had progressed on a prior platinum-containing regimen

**Compliance Rates for HRQoL Assessments**

- The analysis population included 784 patients (tislelizumab, n=530 [99.4%]; docetaxel, n=254 [99.2%])
- Compliance with the QLQ-C30 and QLQ-LC13 questionnaires were similar between arms at cycles 4 and 6 and remained high (≥ 90%) at both time points (Table 2)

**Table 2. Compliance rates for HRQoL assessments**

| Compliance | Tislelizumab (N=533) | Docetaxel (N=256) |
|---|---|---|
| QLC-C30 | | |
| Baseline | 530 (99.4) | 254 (99.2) |
| Cycle 4 | 368/381 (96.6) | 109/121 (90.1) |
| Cycle 6 | 318/322 (98.8) | 78/78 (100.0) |
| QLC-LC13 | | |
| Baseline | 530 (99.4) | 254 (99.2) |
| Cycle 4 | 368/381 (96.6) | 109/121 (90.1) |
| Cycle 6 | 318/322 (98.8) | 78/78 (100.0) |

Data presented as n (%)

**EORTC QLQ-C30 and QLQ-LC13 Baseline Scores**

- Baseline mean QLQ-C30 and QLQ-LC13 scores were similar between treatment arms (Table 3)

**Table 3. Mean baseline scores for EORTC QLQ-C30 and EORTC QLQ-LC13 domains**

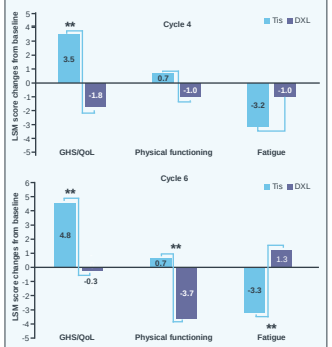
| | Tislelizumab (N=533) | Docetaxel (N=256) |
|---|---|---|
| QLC-C30 | | |
| GHS/QoL | 69.8 (18.92) | 69.1 (19.25) |
| Physical Functioning | 86.6 (13.32) | 85.9 (14.74) |
| Fatigue | 21.0 (18.53) | 21.9 (18.56) |
| QLC-LC13 | | |
| Index Score | 11.9 (8.82) | 11.9 (10.14) |
| Dyspnea | 19.1 (14.70) | 20.4 (16.97) |
| Coughing | 31.3 (24.60) | 30.3 (25.23) |
| Peripheral Neuropathy | 7.7 (18.36) | 5.8 (15.17) |
| Pain in Chest | 14.9 (20.03) | 13.5 (22.30) |
| Pain in Arm/Shoulder | 13.3 (20.76) | 15.4 (25.42) |

Data presented as mean (SD).

**EORTC QLQ-C30: Change from Baseline**

- Patients in the tislelizumab arm experienced improvements in GHS/QoL and fatigue in both cycles 4 and 6 compared with those in the docetaxel arm (Figure 1)
- The physical function domain decreased/worsened in the docetaxel arm in both cycle 4 and 6; in the tislelizumab arm, physical functioning domain score remained stable and the difference between treatments became significant at cycle 6

**Figure 1. Changes from baseline in EORTC QLQ-C30 domain scores**

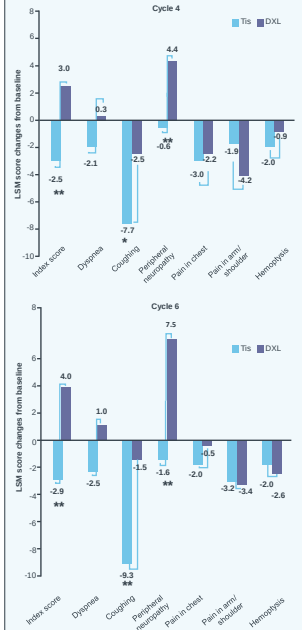



**P<.01.
DXL, docetaxel; LSM, least-square means; TIS, tislelizumab.

**EORTC QLQ-LC13: Change from Baseline**

- Compared with the docetaxel arm, the EORTC QLQ-LC13 index score (overall symptomatology), coughing, and peripheral neuropathy improved significantly in the tislelizumab arm at both cycles 4 and 6 (Figure 2)
  - By cycle 6, dyspnea was trending toward significant improvement with tislelizumab
- The difference in pain measures (chest; arms or shoulders) and hemoptysis were not significant between the two arms as patients in both treatment arms experienced similar decreases in scores

**Figure 2. Changes from baseline in EORTC QLQ-LC13 scores**




*P<.05; **P<.01
DXL, docetaxel; LSM, least-square means; TIS, tislelizumab.

**Time to Deterioration**

- Compared with the docetaxel arm, the tislelizumab arm experienced a lower risk of deterioration in overall symptoms (as indicated by the QLQ-LC13 index score), dyspnea, coughing, and peripheral neuropathy (Table 4)
  - TTD was not achieved for either arm in either pain scales or hemoptysis; both arms were at similar risk for deterioration

**Table 4. Time to deterioration (EORTC QLQ-LC13)**

| | | TIS (N=533) | DXL (N=256) |
|---|---|---|---|
| Index score | Patients with event, n (%) | 50 (9.4) | 60 (23.4) |
| | Median TTD, months (95% CI) | NE (NE, NE) | NE (6.93, NE) |
| | Stratified[1] HR, 95% CI | 0.23 (0.153, 0.342) | |
| | Stratified[1] log-rank test p value | <.0001 | |
| Dyspnea | Patients with event, n (%) | 169 (31.7) | 87 (34.0) |
| | Median TTD, months (95% CI) | NE (NE, NE) | 4.9 (2.79, NE) |
| | Stratified[1] HR, 95% CI | 0.73 (0.559, 0.945) | |
| | Stratified[1] log-rank test p value | 0.0083 | |
| Coughing | Patients with event, n (%) | 114 (21.4) | 58 (22.7) |
| | Median TTD, months (95% CI) | NE (NE, NE) | 9.9 (5.65, NE) |
| | Stratified[1] HR, 95% CI | 0.72 (0.519, 0.994) | |
| | Stratified[1] log-rank test p value | 0.0217 | |
| Peripheral neuropathy | Patients with event, n (%) | 74 (13.9) | 40 (15.6) |
| | Median TTD, months (95% CI) | NE (NE, NE) | NE (6.93, NE) |
| | Stratified[1] HR, 95% CI | 0.58 (0.391, 0.866) | |
| | Stratified[1] log-rank test p value | 0.0035 | |
| Pain in chest | Patients with event, n (%) | 90 (16.9) | 38 (14.8) |
| | Median TTD, months (95% CI) | NE (NE, NE) | NE (10.58, NE) |
| | Stratified[1] HR, 95% CI | 0.78 (0.530, 1.155) | |
| | Stratified[1] log-rank test p value | 0.1065 | |
| Pain in arm or shoulder | Patients with event, n (%) | 111 (20.8) | 31 (12.1) |
| | Median TTD, months (95% CI) | NE (24.54, NE) | NE (NE, NE) |
| | Stratified[1] HR, 95% CI | 1.26 (0.837, 1.888) | |
| | Stratified[1] log-rank test p value | 0.1369 | |
| Hemoptysis | Patients with event, n (%) | 38 (7.1) | 16 (6.3) |
| | Median TTD, months (95% CI) | NE (NE, NE) | NE (NE, NE) |
| | Stratified[1] HR, 95% CI | 0.74 (0.405, 1.336) | |
| | Stratified[1] log-rank test p value | 0.1536 | |

[1]Stratified histology (squamous vs non-squamous), lines of therapy (second vs third), and TC PD-L1 expression (≥25% vs <25%).
NE, not estimable.

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Questions/comments about this presentation please contact Gisoo Barnes at: gisoo.barnes@beigene.com