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# RATIONALE-309: Effects of Tislelizumab on Health-Related Quality of Life (HRQoL) in Patients with Recurrent or Metastatic Nasopharyngeal Cancer (R/M NPC)

Yunpeng Yang*[1], Jianji Pan[2], Nianyong Chen[3], Yanjie Wu[4], Shiangjiin Leaw[4], Fan Bai[4], Yu Wang[4], Na Zhao[4], Boxiong Tang[5], Gisoo Barnes[5]

*First and presenting author
[1]Sun Yat-sen University Cancer Center, Guangzhou, China; [2]Fujian Cancer Hospital, Fuzhou, China; [3]West China Hospital of Sichuan University, Chengdu, China; [4]BeiGene (Shanghai) Co., Ltd., Shanghai, China; [5]Beigene Ltd, Emeryville, California

# DECLARATION OF INTERESTS

Yunpeng Yang, MD

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# Background (1 of 2)

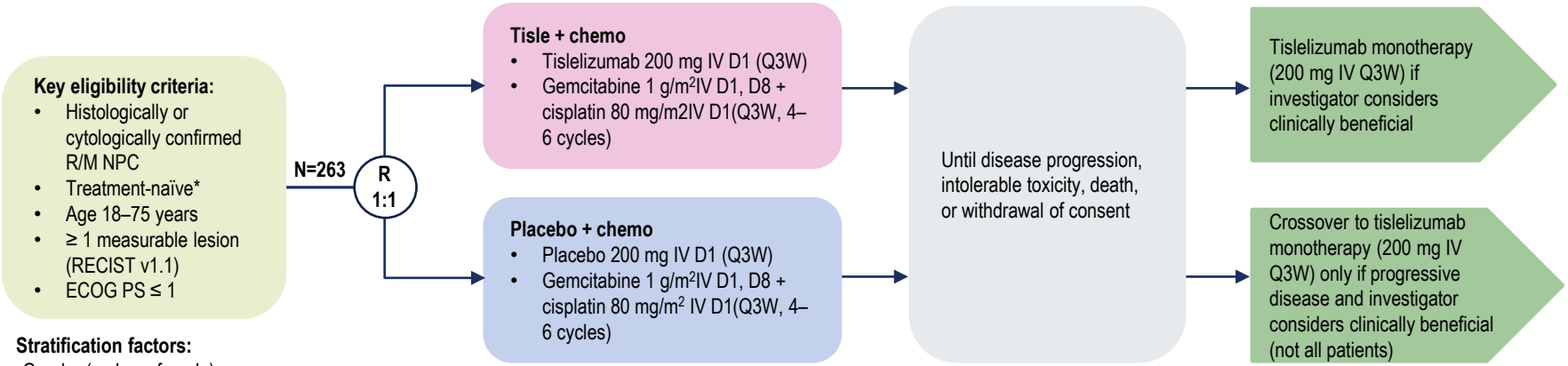
- Patients with nasopharyngeal cancer (NPC) suffer from significant declines in health-related quality of life (HRQoL)[1-6]
  - HRQoL is an important patient-reported outcome (PRO) that may impact the mortality risk for patients with NPC[7]
- Liver metastases (LM) in NPC patients is considered as a significant negative prognostic factor for overall survival and cancer-specific survival for patients with NPC[8-11]
  - The presence of liver metastasis in patients with NPC is significantly associated with poor response to chemotherapy[1,2]

# Background (2 of 2)

- RATIONALE-309 (NCT03924986) - double-blinded, randomized, phase 3 study
  - Tislelizumab + gemcitabine and cisplatin (tisle + chemo) vs placebo + gemcitabine and cisplatin (placebo + chemo) as first-line treatment for recurrent or metastatic (R/M) NPC
  - Significant improvement in progression-free survival for Tisle + chemo compared to placebo + chemo (median progression free survival (PFS): 9.6 vs 7.4 months, respectively; hazard ratio [HR]=0.50, 95% confidence interval [CI]: 0.37, 0.68)
  - mPFS2 was not reached for the tisle + chemo arm and was 13.9 months for the placebo + chemo arm (HR=0.38, 95% CI: 0.25, 0.58)
- The objective of this analysis was to evaluate the impact of tisle + chemo on patients' HRQoL and NPC-related symptoms
  - Post-hoc analysis also explored HRQoL and NPC-related symptoms in patients with LM

# Method (1 of 2)

## Study Design: Randomized, Double-Blind, Phase 3 Trial




**Stratification factors:**
•Gender (male vs female)
•Liver metastases (yes vs no)

**PRO endpoints:**
- The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 items (QLQ-C30): global health status/quality of life (GHS/QoL), physical functioning, and fatigue
- EORTC Head and Neck Module (QLQ-H&N35): symptom index, pain, senses, and speech problems scales

# Method (2 of 2)

- The key clinical cycles were cycle 4 and cycle 8 and were selected to measure change in PRO endpoints representing during chemotherapy (cycle 4) as well as after chemotherapy (cycle 8)
- Two sets of analyses were conducted for the PRO endpoints: intent-to-treat (or, ITT) population and intent-to-treat (or, ITT) population with liver metastasis (or the LM subgroup) were conducted
- Change from baseline in each key PRO endpoint to cycle 4 and cycle 8 was analyzed using the linear mixed effect model for repeated measures
- Time to deterioration (TTD) for each key PRO endpoint was assessed in both the full ITT population and the LM subgroup
    - TTD was defined as the time from randomization to first onset time at which deterioration is as defined by ≥10-point change from baseline in the direction of worsening for two consecutive assessments or 1 assessment followed by death from any cause within 3 weeks

# Results

## Patients Demographics

| | Tisle + chemo (N = 131) | Placebo + chemo (N = 132) |
|---|---|---|
| Age (years) | | |
| Median | 50.0 | 50.0 |
| Min, Max | 26, 74 | 23, 73 |
| Age Group, n (%) | | |
| < 65 years | 121 (92.4) | 120 (90.9) |
| ≥ 65 years | 10 (7.6) | 12 (9.1) |
| Sex, n (%) | | |
| Male | 103 (78.6) | 103 (78.0) |
| Female | 28 (21.4) | 29 (22.0) |
| Ethnicity, n (%) | | |
| Not Hispanic or Latino | 131 (100.0) | 132 (100.0) |
| Race, n (%) | | |
| Asian | 131 (100.0) | 132 (100.0) |
| Region, n (%) | | |
| China | 122 (93.1) | 126 (95.5) |
| Thailand | 5 (3.8) | 1 (0.8) |
| Taiwan, China | 4 (3.1) | 5 (3.8) |
| Liver Metastases,n (%) | 56 (42.7) | 57 (43.2) |
| ECOG Performance Status, n (%) | | |
| 0 | 51 (38.9) | 46 (34.8) |
| 1 | 80 (61.1) | 86 (65.2) |

- All 263 randomized patients (tisle + chemo n=131; placebo + chemo n=132) comprised the ITT population
- 43% of the 263 patients (n=113; tisle + chemo n=56; placebo + chemo n=57) were diagnosed with liver metastases
- Demographics and clinical characteristics of the ITT population were generally balanced across the two treatment arms and were representative of the target patient population

# Results

## Completion Rates

| | Tisle + chemo (n=131) | Placebo + chemo (n=132) |
|---|---|---|
| **Baseline** | | |
| **Completion rate[a] (%)** | 100/100 (100.0) | 100/100 (100.0) |
| **Adjusted completion rate[b] (%)** | 100/100 (100.0) | 100/100 (100.0) |
| **Cycle 4** | | |
| **Completion rate[a] (%)** | 109/131 (83.2) | 117/132 (88.6) |
| **Adjusted completion rate[b]** | 109/110 (99.1) | 117/117 (100.0) |
| **Cycle 8** | | |
| **Completion rate[a] (%)** | 98/131 (74.8) | 88/132 (66.7) |
| **Adjusted completion rate[b]** | 98/98 (100.0) | 88/88 (100.0) |

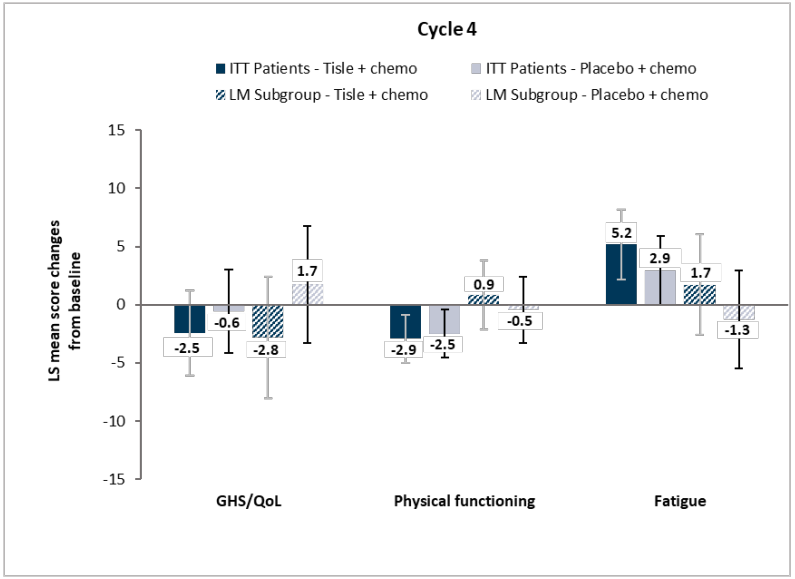
[a] Completion rate = number of patients completed questionnaire / total number of patients in relevant treatment arm. [b] Adjusted completion rate = number of patients completed questionnaire / total number of patients in study at relevant visits in relevant treatment arm.

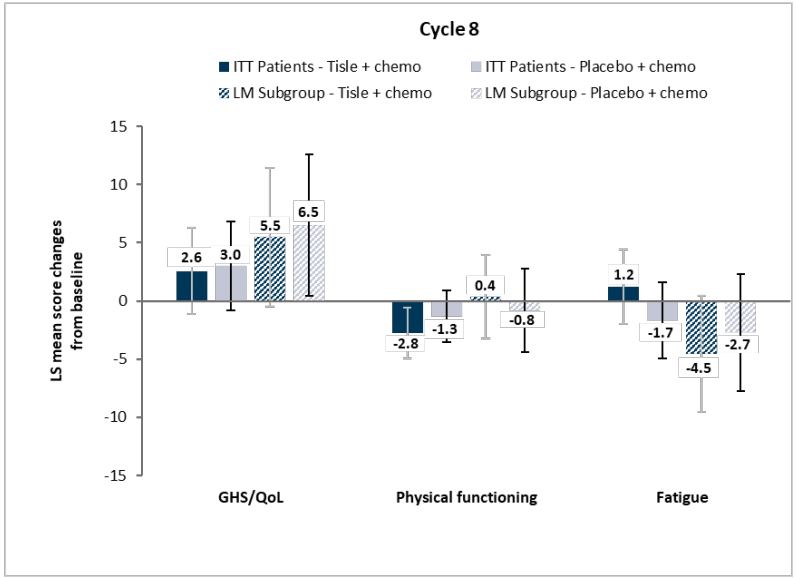
- For the two PRO questionnaires QLQ-C30 and QLQ-H&N35, the completion rate was 100% at baseline
- At cycle 4, the completion rate was 83% or higher
- At cycle 8, the completion rate decreased to 74.8% in the tisle + chemo arm and 66.7% in the placebo + chemo arm
- The adjusted completion rates remained over 99% for both arms at cycle 4 and cycle 8

# Results

## EORTC QLQ-C30 Change from Baseline

- No differences in change from baseline to cycles 4 or 8 between the arms were observed for the ITT population or LM subgroup for the QLQ-C30 scales



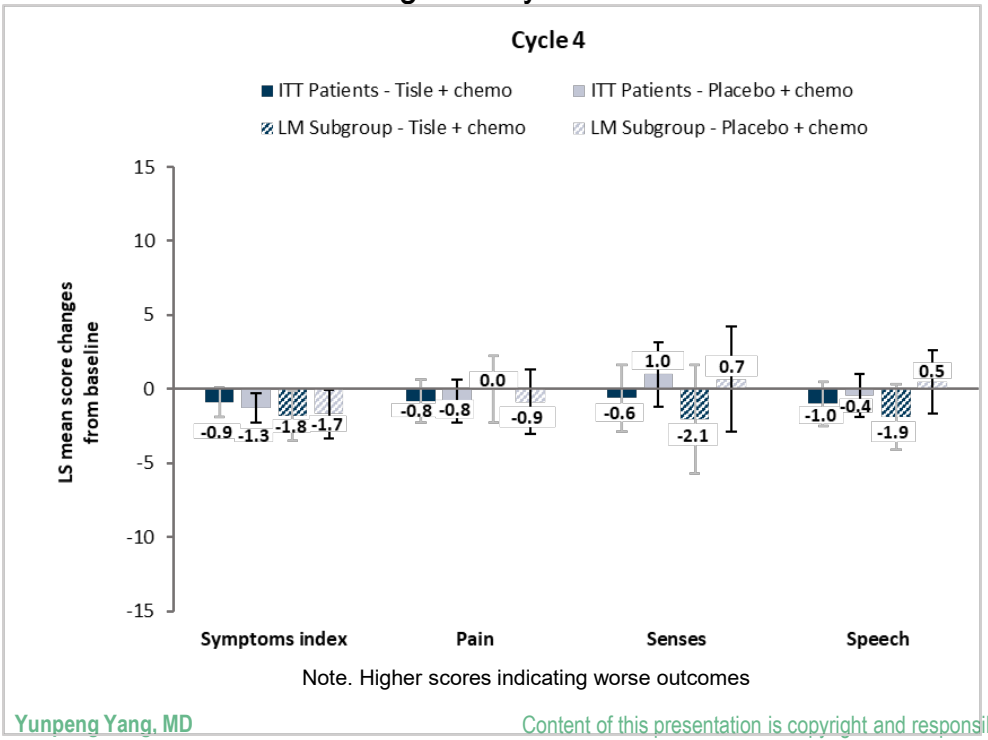




Note: Higher scores represent better outcomes on the GHS/QoL scale and physical functioning scale but worse outcome on the fatigue scale

# Results

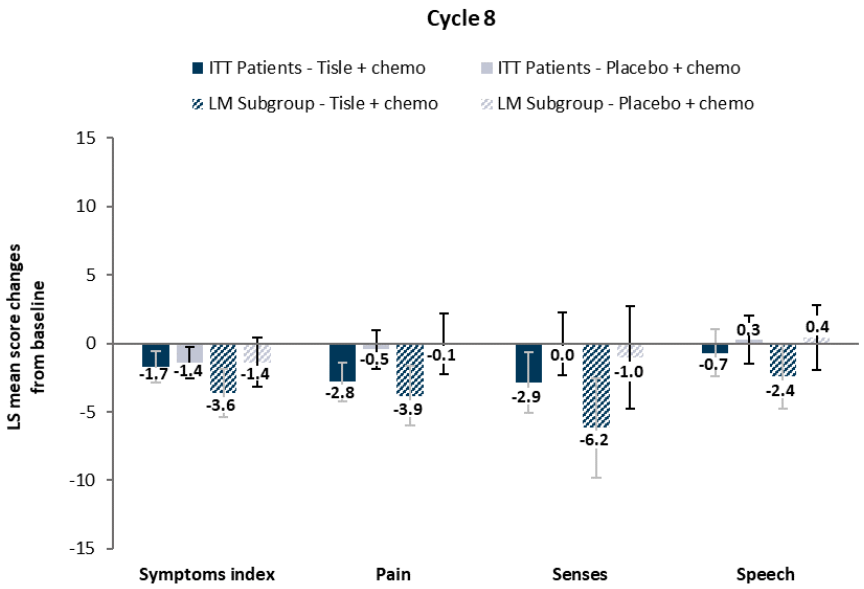
## EORTC QLQ-H&N35 Change from Baseline to Cycle 4

- No differences between the arms emerged at cycle 4



# Results

## EORTC QLQ-H&N35 Change from Baseline to Cycle 8




- There was a greater reduction from baseline in the tisle + chemo arm vs the placebo + chemo for the **pain score** (**ITT**: -2.37 [95% CI: -4.21, -0.53], P=0.0117; **LM**: -3.79 [95% CI: -6.62, -0.97], *P*=0.0092)
- In the LM subgroup, there was a greater improvement from baseline in the tisle + chemo arm vs the placebo + chemo arm for **senses problems** (**LM** -5.13 [95% CI: -9.86, -0.40], *P*=0.0338)
- In the LM subgroup, improvements from baseline in the tisle + chemo arm vs the placebo + chemo were observed for
  - Symptoms index (-2.22 [95% CI: -4.51, 0.08], P=0.0580).
  - Speech problems (-2.85 [95% CI: -5.92, 0.23], P=0.0694)

# Results

## Time to deterioration

- There were no significant differences between the two arms in the risk of deterioration for all the key PRO endpoints in either the ITT population or LM subgroup

# Discussion

- The findings of current investigation suggest that HRQoL and NPC associated symptoms remained relatively stable in NPC patients treated with tislelizumab + chemo in the ITT population through cycle 8
- In addition, the subgroup patients clinically diagnosed with LM experienced reductions in overall NPC symptoms as well as reductions in individual symptoms
- These results, along with improved survival and favorable safety profile, suggest tislelizumab + chemo represents a potential first line treatment option for patients with R/M NPC

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**European Society for Medical Oncology (ESMO)**
Via Ginevra 4, CH-6900 Lugano
T. +41 (0)91 973 19 00
esmo@esmo.org

**esmo.org**

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