

# Health-Related Quality of Life With Ivonescimab Versus Pembrolizumab for PD-L1 Positive, Non-Small Cell Lung Cancer (HARMONI-2): A Randomised, Double-Blind, Phase 3 Study in China

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## BACKGROUND

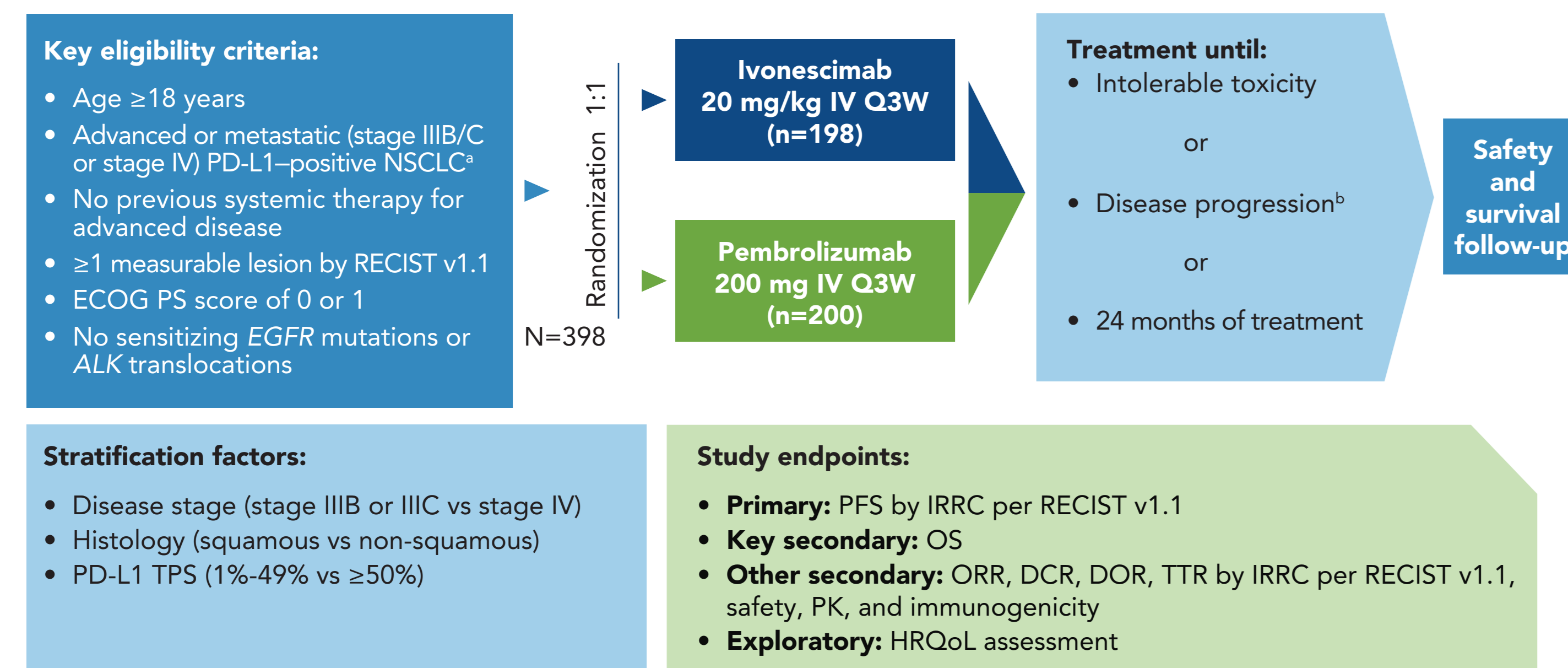
- Ivonescimab is an investigational bispecific antibody against programmed cell death protein 1 (PD-1) and vascular endothelial growth factor that is approved in China as first-line treatment for patients with programmed cell death ligand 1 (PD-L1)-positive non-small cell lung cancer (NSCLC) based on the results from the randomized phase 3 HARMONI-2 trial<sup>1,2</sup>
- The HARMONI-2 study is evaluating the safety and efficacy of ivonescimab compared with pembrolizumab in patients with PD-L1-positive advanced NSCLC<sup>2</sup>
  - In the primary analysis of HARMONI-2, ivonescimab significantly improved progression-free survival (PFS) compared with pembrolizumab in previously untreated patients with advanced NSCLC (11.1 vs 5.8 months; stratified hazard ratio [HR], 0.51; 95% CI, 0.38-0.69), and had a manageable safety profile<sup>2</sup>
  - In that analysis, the median time to deterioration for global health status (GHS) and quality of life (QoL) domain of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) was not reached in the ivonescimab arm and was 9.9 (95% CI, 8.0-not estimable) in the pembrolizumab arm (HR, 0.92; 95% CI, 0.63-1.33), with similar deterioration-free rates at 12 months in both treatment arms (ivonescimab, 51% [95% CI, 36-64]; pembrolizumab, 46% [95% CI, 24-65])<sup>2</sup>
- The objective of the current exploratory analysis was to further assess patient-reported health-related quality of life (HRQoL) in HARMONI-2

## METHODS

### Design

- HARMONI-2 (NCT05499390) is a randomized, double-blind, phase 3 trial conducted at 55 hospitals in China<sup>2</sup>
  - Eligible patients were ≥18 years of age with locally advanced or metastatic PD-L1-positive NSCLC<sup>2</sup>
  - Patients were randomly assigned (1:1) to receive ivonescimab (20 mg/kg) or pembrolizumab (200 mg) intravenously every 3 weeks (Figure 1)<sup>2</sup>

Figure 1. Trial Design



ALK, anaplastic lymphoma kinase; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HRQoL, health-related quality of life; IRRC, independent radiology review committee; IV, intravenously; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PK, pharmacokinetics; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; TPS, tumor proportion score; TTR, time to response.

<sup>a</sup>Squamous or non-squamous NSCLC subtype confirmed histologically or cytologically.

<sup>b</sup>Confirmed by the masked IRRC.

- HRQoL was an exploratory endpoint, measured by the EORTC QLQ-C30 version 3, EORTC QLQ-Lung Cancer (LC13), and EuroQol 5-dimensional 5-level (EQ-5D-5L) questionnaires<sup>3</sup>
  - The QLQ-C30 is composed of 5 functional scales (including physical and emotional function), 9 symptom measures, and a global health status and QoL scale; all domains range in score from 0 to 100<sup>4,6</sup>
  - The QLQ-LC13 is composed of lung cancer-related symptom measures (including cough, hemoptysis, and dyspnea) and treatment-related symptom measures<sup>7</sup>
  - The EQ-5D-5L is composed of a descriptive system that measures 5 dimensions of health and the EQ visual analog scale (VAS) that measures current overall health
    - Each dimension has 5 response levels ranging from “no problems” to “unable to/extreme problems”
    - An index-based utility score is calculated using an index derived from the Chinese national-specific value set and ranges from 0 (worst health) to 1 (full health)
- VAS scores range from 0 to 100.<sup>8</sup> Assessments were performed every 2 cycles for cycles 1 to 7, every 4 cycles thereafter, and at end-of-treatment and safety follow-up visits
  - Completion rate was defined as the percentage of patients who completed ≥1 HRQoL assessment at each time point expressed relative to the total number of randomized patients in each treatment arm

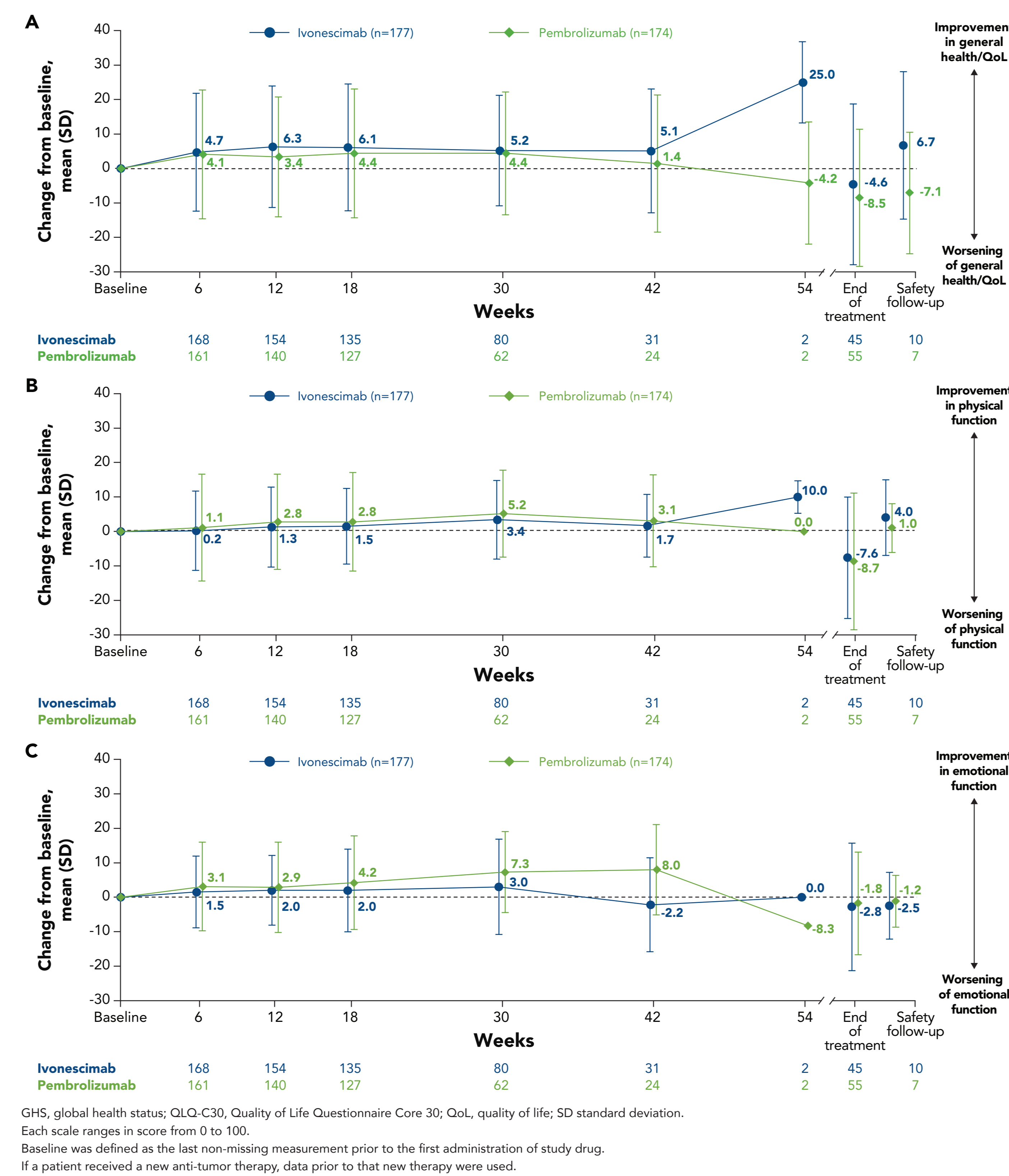
## RESULTS

- Baseline demographic and disease characteristics were generally well balanced between the ivonescimab (n=198) and pembrolizumab (n=200) treatment arms<sup>2</sup>
  - All patients were enrolled from China. The majority of patients were male (ivonescimab, 83%; pembrolizumab, 85%), and most patients were current or former smokers (80%; 81%)<sup>2</sup>
- At the data cutoff (January 29, 2024; median follow-up, 8.7 months),<sup>2</sup> completion rates for the 3 assessments at baseline were 97% (192/198) in the ivonescimab arm and 98% (196/200) in the pembrolizumab arm

### Health-Related Quality of Life as Assessed by QLQ-C30

- QoL as assessed by the GHS/QoL, physical function, and emotional function scales in the QLQ-C30 improved relative to baseline in both treatment arms (Figure 2)
  - For GHS/QoL, mean (standard deviation [SD]) scores at baseline and Weeks 12 and 30 were 71.8 (17.6), 78.5 (15.9), and 78.5 (16.0) in the ivonescimab arm and 73.6 (17.5), 76.7 (16.6), and 76.5 (16.9) in the pembrolizumab arm
  - For the physical function scale, mean (SD) scores at baseline and Weeks 12 and 30 were 88.5 (12.2), 90.1 (11.3), and 91.6 (9.5) in the ivonescimab arm and 88.5 (14.7), 91.2 (11.1), and 91.8 (8.0) in the pembrolizumab arm
  - For the emotional function scale, mean (SD) scores at baseline and Weeks 12 and 30 were 92.2 (10.7), 94.3 (10.3), and 94.4 (9.4) in the ivonescimab arm and 89.9 (13.0), 92.7 (12.3), and 94.9 (9.2) in the pembrolizumab arm

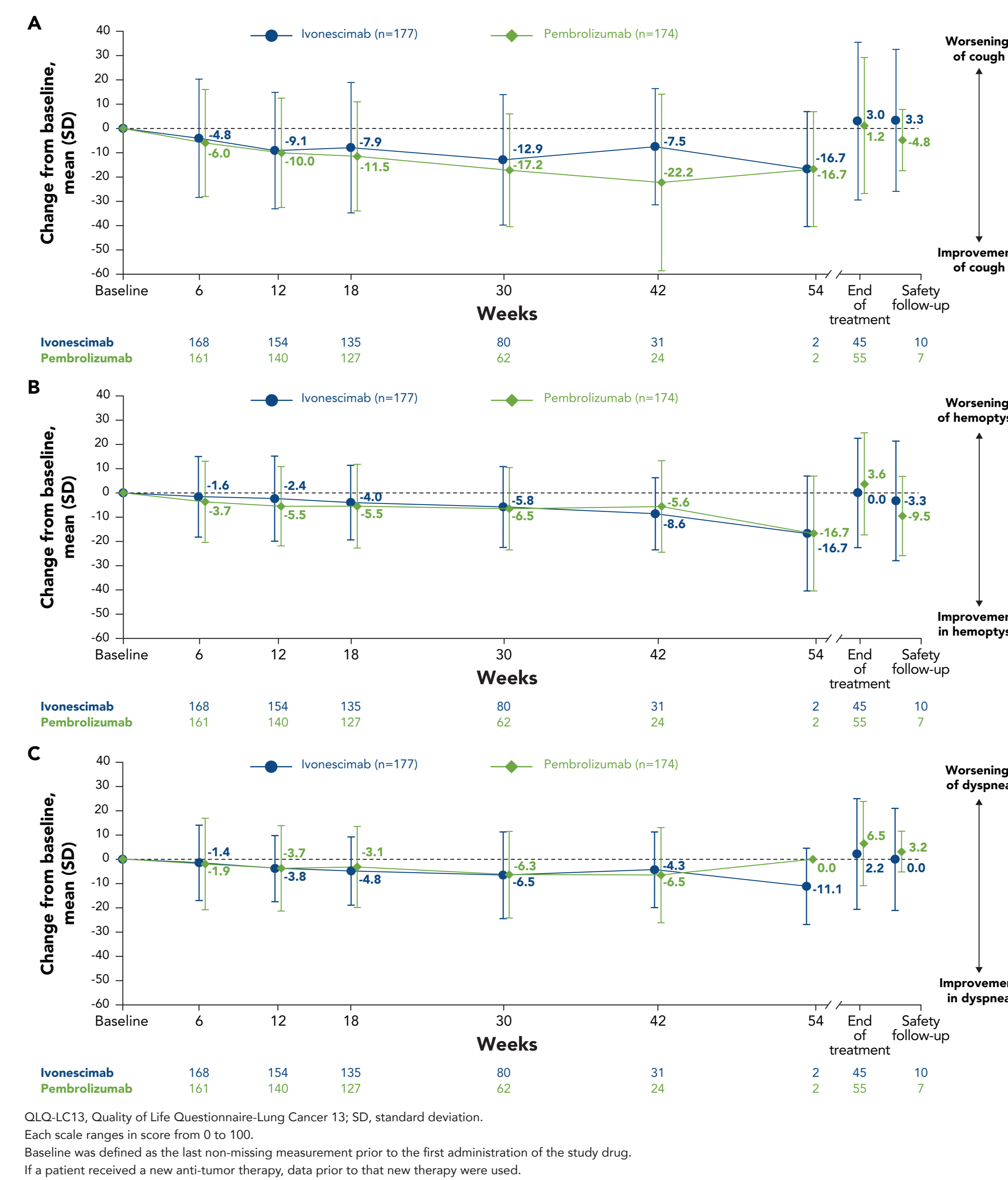
Figure 2. Mean Change From Baseline in (A) GHS/QoL, (B) Physical Function, and (C) Emotional Function Scores as Assessed Using the QLQ-C30



### Health-Related Quality of Life as Assessed by QLQ-LC13

- QoL as assessed by cough, hemoptysis, and the dyspnea scale in the QLQ-LC13 improved relative to baseline in both treatment arms (Figure 3A)
  - For cough, mean (SD) scores at baseline and Weeks 12 and 30 were 29.9 (23.3), 19.0 (18.2), and 19.6 (21.7) in the ivonescimab arm and 30.3 (19.7), 20.0 (19.1), and 19.4 (18.7) in the pembrolizumab arm
  - The median time to deterioration of the QLQ-LC13 cough symptom was not reached in either group (HR, 1.49; 95% CI, 0.97-2.29; P=0.067)
  - For hemoptysis, mean (SD) scores at baseline and Weeks 12 and 30 were 7.2 (14.6), 4.5 (12.7), and 2.9 (9.5) in the ivonescimab arm and 7.9 (16.7), 2.6 (9.8), and 2.2 (8.3) in the pembrolizumab arm
  - For the dyspnea scale, mean (SD) scores at baseline and Weeks 12 and 30 were 17.5 (16.0), 13.3 (13.7), and 12.1 (14.6) in the ivonescimab arm and 16.5 (16.2), 13.3 (13.3), and 14.5 (13.1) in the pembrolizumab arm

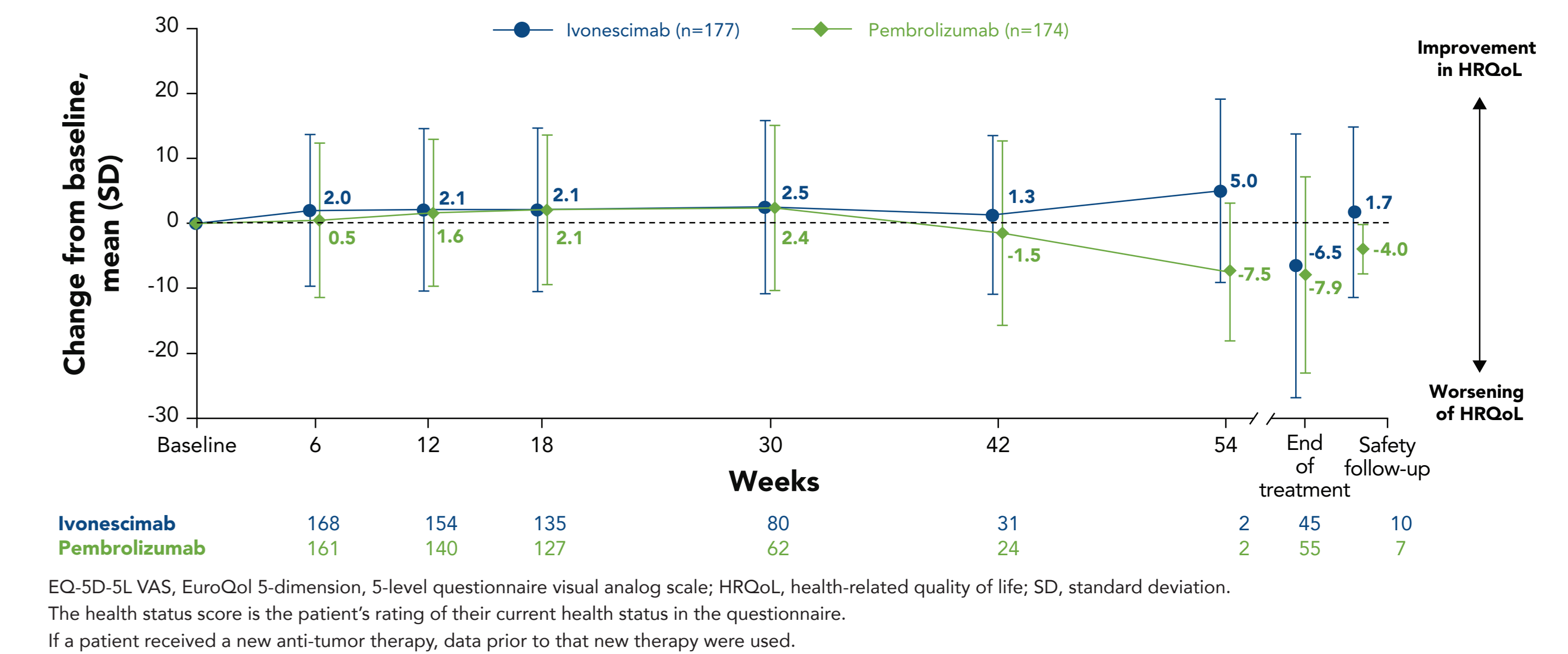
Figure 3. Mean Change From Baseline in (A) Cough, (B) Hemoptysis, and (C) Dyspnea Scale Scores as Assessed Using the QLQ-LC13



### Health-Related Quality of Life as Assessed by EQ-5D-5L

- QoL as assessed by the EQ-5D-5L VAS improved in both treatment arms, as indicated by an increase in mean health status scores relative to baseline (Figure 4)
  - Mean (SD) health status scores at baseline and Weeks 12 and 30 were 81.9 (13.5), 84.3 (10.6), and 83.7 (11.4) in the ivonescimab arm and 82.3 (13.0), 83.6 (11.9), and 83.5 (12.8) in the pembrolizumab arm

Figure 4. Mean Change From Baseline in Health Status Score Using the EQ-5D-5L VAS



- The mean EQ-5D-5L utility value remained stable in both groups; mean (SD) utility values at baseline and Weeks 12 and 30 were 0.9 (0.1), 0.9 (0.1), and 0.9 (0.1) in the ivonescimab arm and 0.9 (0.1), 0.9 (0.1), and 1.0 (0.1) in the pembrolizumab arm

## CONCLUSIONS

- Treatment with ivonescimab was associated with improvement in QoL relative to baseline as measured across multiple instruments, and the improvement was comparable to that observed in the pembrolizumab arm
- These results support the PFS benefit of ivonescimab seen in patients with advanced PD-L1-positive NSCLC in HARMONI-2

### ACKNOWLEDGMENTS

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### DISCLOSURES

Dr Chen is an employee of Akeso Biopharma. Ivonescimab is an investigational therapy not approved by any regulatory authority other than China's National Medical Products Administration (NMPA).

### CONTACT INFORMATION

Please contact the presenting author, Jianhua Chen, at [xinyi.chen@akesobio.com](mailto:xinyi.chen@akesobio.com) for questions or comments.



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