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First-line nivolumab plus ipilimumab versus chemotherapy for the treatment of unresectable malignant pleural mesothelioma: patient-reported outcomes in CheckMate 743

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ABSTRACT

Objective: In CheckMate 743 (NCT02899299), nivolumab + ipilimumab significantly prolonged overall survival in patients with unresectable malignant pleural mesothelioma (MPM). We present patient-reported outcomes (PROs).

Materials and Methods: Patients (N = 605) were randomized to nivolumab + ipilimumab or chemotherapy. Changes in disease-related symptom burden and health-related quality of life (HRQoL) were evaluated descriptively using the Lung Cancer Symptom Scale (LCSS)-Mesothelioma (Meso) average symptom burden index (ASBI), LCSS-Meso 3-item global index (3-IGI), 3-level EuroQol 5-dimensional (EQ-5D-3L) visual analog score (VAS), and EQ-5D-3L utility index. PROs were assessed at baseline and every 2 (nivolumab + ipilimumab) or 3 weeks (chemotherapy) through 12 weeks, every 6 weeks through 12 months, every 12 weeks thereafter, and at

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specified follow-ups. Mixed-effect model repeated measures (MMRM) and time to deterioration analyses were conducted.

Results: Completion rates were generally >80%. LCSS-Meso ASBI mean changes from baseline trended to improve over time with nivolumab + ipilimumab and deteriorate with chemotherapy, but did not meet clinically important difference thresholds [±10 score change]. EQ-5D-3L VAS mean scores improved over time with nivolumab + ipilimumab; by week 60, patients had scores consistent with United Kingdom normal population values. MMRM analyses favored nivolumab + ipilimumab for all individual symptoms except cough. Nivolumab + ipilimumab delayed time to definitive deterioration in HRQoL (hazard ratio 0.52 [95% confidence interval 0.36–0.74]) and showed a trend in symptom delay versus chemotherapy.

Conclusions: Nivolumab + ipilimumab decreased the risk of deterioration in disease-related symptoms and HRQoL versus chemotherapy and maintained QoL in patients with unresectable MPM.

1. Introduction

Assessing health-related quality of life (HRQoL) in oncology clinical studies is important to understand benefits and risks from the patient perspective. Immunotherapy has increased survival in patients with a number of malignancies; however, long-term treatment may extend up to 2 years [1–3]. Impact of HRQoL should be considered when evaluating treatment options for malignant pleural mesothelioma (MPM), given the potential impact of treatment-related adverse effects in the elderly population. Most patients with MPM present at an advanced stage with symptoms such as dyspnea, fatigue, chest pain, and weight loss [4], which impact their HRQoL [5]. Thus, results from patient-reported outcomes (PROs) assist in selecting treatment in clinical practice as well as evaluating agents from a payer or health technology assessment perspective. Factoring in improvement based on PRO measures can impact MPM management and enhance patient care [6].

Nivolumab and ipilimumab have distinct but complementary mechanisms of action. Nivolumab is a fully human anti-programmed cell death 1 (PD)-1 immune checkpoint inhibitor antibody that restores anti-tumor T-cell function [7,8]. Ipilimumab is a fully human anti-cytotoxic T lymphocyte antigen-4 (CTLA-4) immune checkpoint inhibitor antibody that induces de novo anti-tumor T-cell responses, including an increase in memory T cells [9,10]. CheckMate 743 (ClinicalTrials.gov identifier NCT02899299) is the first phase 3 randomized trial of dual immunotherapy to demonstrate a statistically significant and clinically meaningful improvement in overall survival (OS) with nivolumab + ipilimumab versus chemotherapy in the first-line treatment of unresectable MPM (median OS 18.1 versus 14.1 months; hazard ratio [HR] 0.74 [96.6% confidence interval (CI), 0.60–0.91], $P = 0.002$) [11]. The results from CheckMate 743 have led to approval of nivolumab in combination with ipilimumab as first-line treatment for adult patients with unresectable MPM in the United States, European Union, and other countries, as well as NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) adoption as a preferred first-line treatment option (category 1) for patients with unresectable MPM of biphasic or sarcomatoid histology, and as an option for those with epithelioid histology [12–17]. The objective of this pre-specified analysis was to evaluate HRQoL for patients with unresectable MPM in CheckMate 743.

2. Materials and methods

2.1. Study design and treatment

The study design for CheckMate 743 has been described previously [11]. Briefly, eligible patients were adults, with MPM not amenable to curative therapy, no prior systemic therapy, and Eastern Cooperative Oncology Group performance status 0–1. Patients were stratified by tumor histology (epithelioid versus non-epithelioid) and sex, and randomized 1:1 to receive either nivolumab 3 mg/kg every 2 weeks + ipilimumab 1 mg/kg every 6 weeks for up to 2 years or platinum-doublet chemotherapy every 3 weeks for 6 cycles; treatment continued in either arm until disease progression or unacceptable toxicity.

This study was conducted in accordance with the ethical principles in the Declaration of Helsinki and an institutional review board at each center approved the trial protocol. All patients gave written informed consent.

2.2. Endpoints and assessments

Pre-specified PRO exploratory endpoints were disease-related symptom burden and HRQoL, assessed using the Mesothelioma Lung Cancer Symptom Scale (LCSS-Meso), and overall health status assessed using the 3-level EuroQol 5-dimensional questionnaire (EQ-5D-3L) [18–23].

The LCSS-Meso consists of 5 individual symptom items associated with mesothelioma (anorexia/loss of appetite, fatigue, cough, dyspnea, and pain) and 3 global items for overall symptom burden and HRQoL

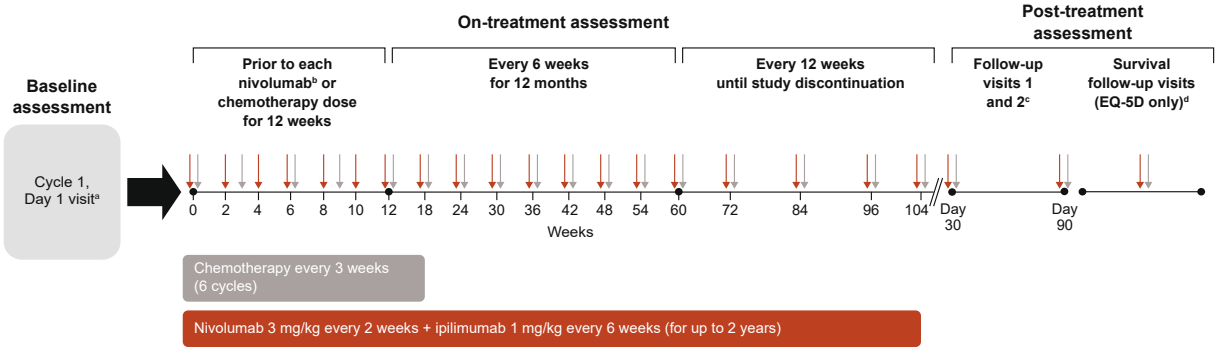

Fig. 1. Schedule of PRO assessments (LCSS-Meso and EQ-5D-3L). [a]Performed after randomization and prior to first dose. [b]Ipilimumab dosed with nivolumab every 6 weeks. [c]Follow-up visit 1 occurred 30 days (±7 days) from the last dose or coincided with the date of discontinuation (±7 days) if date of discontinuation was >35 days after last dose. Follow-up visit 2 occurred 90 days (±7 days) from follow-up visit 1. [d]Survival follow-up visits occurred approximately every 3 months (±7 days) from follow-up visit 2 for the first year, then every 6 months thereafter. LCSS-Meso, Mesothelioma Lung Cancer Symptom Scale; EQ-5D-3L, 3-level EuroQol 5-dimensional questionnaire.

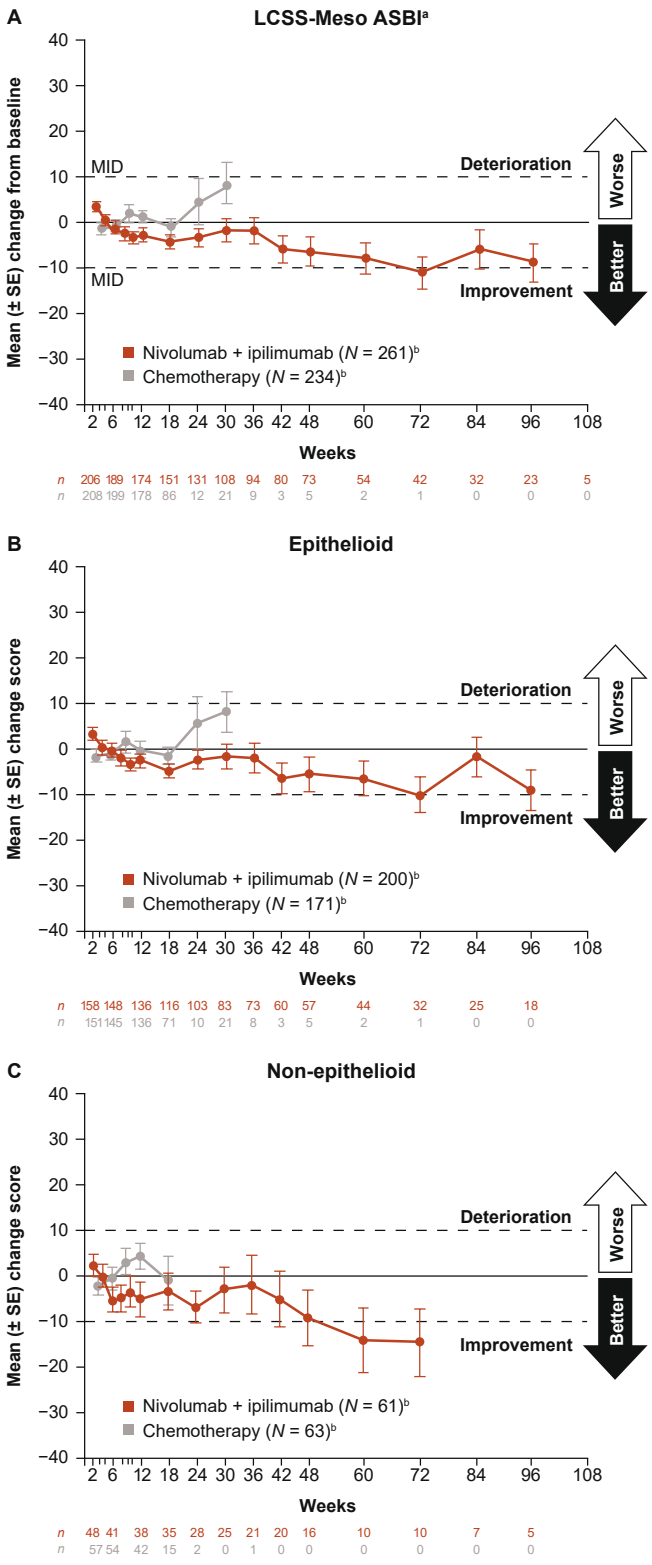

Fig. 2. Disease-related symptom burden change from baseline on treatment: LCSS-Meso ASBI in all patients (A), in patients with epithelioid histology (B), and in patients with non-epithelioid histology (C). Only time points with data for ≥10 patients in either treatment group are shown. [a]LCSS-Meso ASBI is the average of 6 disease-related symptom scores on a 100-mm VAS; range: 0 (best) to 100 (worst); MID = 10 points. [b]At baseline. ASBI, average symptom burden index; LCSS-Meso, Mesothelioma Lung Cancer Symptom Scale; MID, minimally important difference; SE, standard error; VAS, visual analog scale.

(symptom distress, interference with activity level, and global HRQoL). All individual symptom items are scored on a 0–100 visual analog scale (VAS), ranging from 0 (best) to 100 (worst, representing the highest possible symptom burden) [18] and with a difference of 10 points from baseline defined as the minimally important difference (MID), ie, the smallest change considered clinically meaningful [23]. For each global item, 100 represents the lowest possible symptom burden and best HRQoL. The average symptom burden index (ASBI) is the mean of the 5 symptom scores, whereas the LCSS-Meso 3-item global index (3-IGI) is the sum of 3 global items. LCSS-Meso 3-IGI global items were added to generate a score evaluated on a scale of 0–300, with a difference of 30 points from baseline defined as the MID.

The EQ-5D-3L is a descriptive system consisting of 5 health state dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and a VAS, for which patients rank their overall health status at each visit on a scale from 0 (worst imaginable) to 100 (best imaginable) [19,20]. The VAS MID is a difference of 7 points from baseline [19]. Patients rate each dimension as providing no, some, or severe problems; ratings for all 5 dimensions are converted into a single utility index (UI). The EQ-5D-3L UI scores range from <1 (worse than death) to 0 (death) to 1 (full health state), with the MID being a difference of 0.08 points from baseline [19]. The UK scoring algorithm was used to derive the utilities from the EQ-5D.

Symptom burden and HRQoL were assessed by the LCSS-Meso and EQ-5D-3L before each dose through 12 weeks (Fig. 1). On-treatment assessments were completed prior to each nivolumab dose of the nivolumab + ipilimumab combination (every 2 weeks) or chemotherapy dose (every 3 weeks). For weeks 12–60, patients in both arms completed the LCSS-Meso and EQ-5D-3L every 6 weeks. Subsequently, starting at week 60, patients in both arms completed the LCSS-Meso and EQ-5D-3L every 12 weeks until study discontinuation. LCSS-Meso and EQ-5D-3L assessments were completed by patients at follow-up visit 1, which occurred 30 days (±7 days) from the last dose, and follow-up visit 2, which occurred 90 days (±7 days) after follow-up visit 1. EQ-5D-3L was also completed by patients at survival follow-up visits (every 3 months for the first year of follow-up, then every 6 months thereafter).

2.3. Statistical analyses

Analyses were performed on the PRO population, defined as all randomized patients who had a baseline assessment and ≥1 matched on-treatment post-baseline assessment. Descriptive statistics were used to report mean change from baseline for each PRO assessment for subgroup analysis (histology and age) and were unadjusted. Statistical testing was not performed for subgroup analyses.

Analysis of longitudinal overall change from baseline in PRO score was performed using mixed-model repeated measures (MMRM) analyses, which adjusted for baseline scores and multiple observations per patient. No imputation for missing PRO score data was performed. These analyses were conducted using PRO data from on-treatment visits common to both arms (up to week 30 based on having sufficient patient numbers for analyses) with follow-up visits not included. Histology, sex, and baseline PRO score were included as covariates in the model, change from baseline score was the dependent variable, and models contained treatment group, study visit (as a categorical variable), and interaction of treatment group by study visit as fixed effects. For all endpoints, differences in LS mean between treatment arms and associated 95% CIs were assessed and *P*-values (2-sided) were presented to aid interpretation (no adjustment for multiple testing).

Time to first deterioration was defined as the time between date of randomization and the first date of a worsening change from baseline meeting or exceeding the MID, provided a sufficient number of events (≥20% of the all-randomized population) had been observed. Death was not considered an event; patients were censored at last PRO assessment. Time to definitive deterioration was defined as the time between date of randomization and the first deterioration from baseline meeting or

exceeding the MID, with deterioration at all subsequent assessments on treatment or during follow-up. Both time to deterioration endpoints used data from on-treatment time points common to both arms in the all-randomized population as well as follow-up visits, and were analyzed by the Kaplan-Meier method. The HR, and 95% CI of HR, were calculated using a stratified Cox proportional hazards model (stratified for the randomization stratification factors). All analyses were conducted using SAS (version 9.4, SAS Institute, Cary, NC).

3. Data availability

Data are available upon reasonable request. Bristol Myers Squibb policy on data sharing may be found at https://www.bms.com/researchers-and-partners/independent-research/data-sharing-request-process.html.

4. Results

4.1. Patients

Patients were randomized to receive nivolumab + ipilimumab (n = 303) or chemotherapy (n = 302) in CheckMate 743. This PRO analysis (database lock, April 3, 2020; median follow-up of 29.7 months) included 526 patients with data at baseline and at one or more post-baseline visits for either the LCSS-Meso or EQ-5D-3L. Baseline characteristics for these patients were generally similar between treatment arms (**Supplementary** Table 1). At baseline, 89.1% and 81.1% of patients in the nivolumab + ipilimumab and chemotherapy arms, respectively, completed LCSS-Meso questionnaires. Completion rates were >80% for almost all on-treatment assessments in which ≥10 patients had evaluable PRO assessments (**Supplementary** Table 2), with slightly higher completion rates for the ED-5D-3L. There was no clear pattern of decline in missing PRO data over all assessment time points while patients were on treatment.

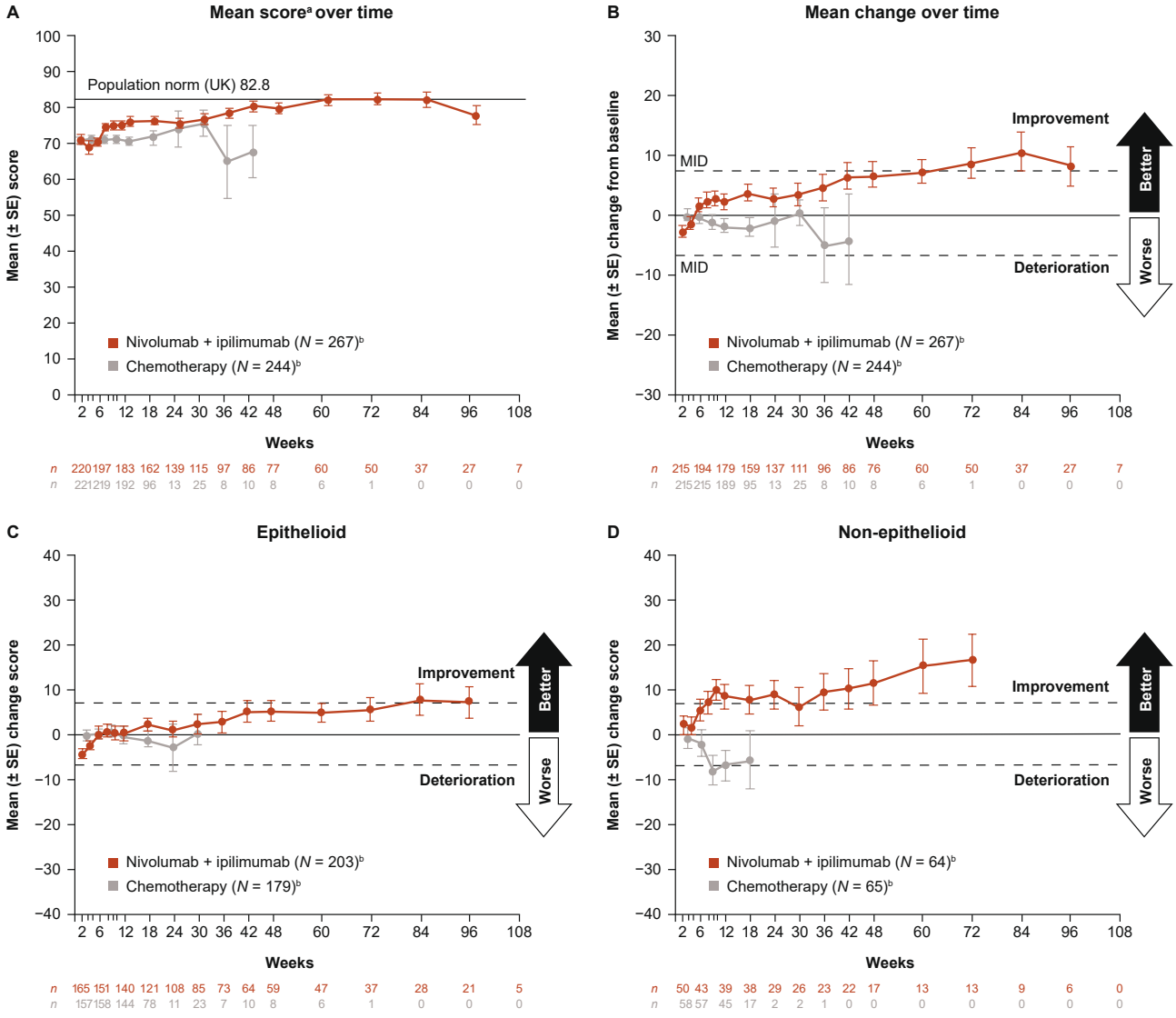

Fig. 3. Overall health status on treatment: EQ-5D-3L VAS mean score over time (A), mean change over time (B), and mean change from baseline on treatment for patients with epithelioid (C) and non-epithelioid (D) histology. Only time points with data for ≥10 patients in either treatment group are shown. [a]EQ-5D-3L 100-point VAS; range: 0 (worst) to 100 (best); MID = 7 points. [b]At baseline. EQ-5D-3L, 3-level EuroQol 5-dimensional questionnaire; SE, standard error; UK, United Kingdom; VAS, visual analog scale.

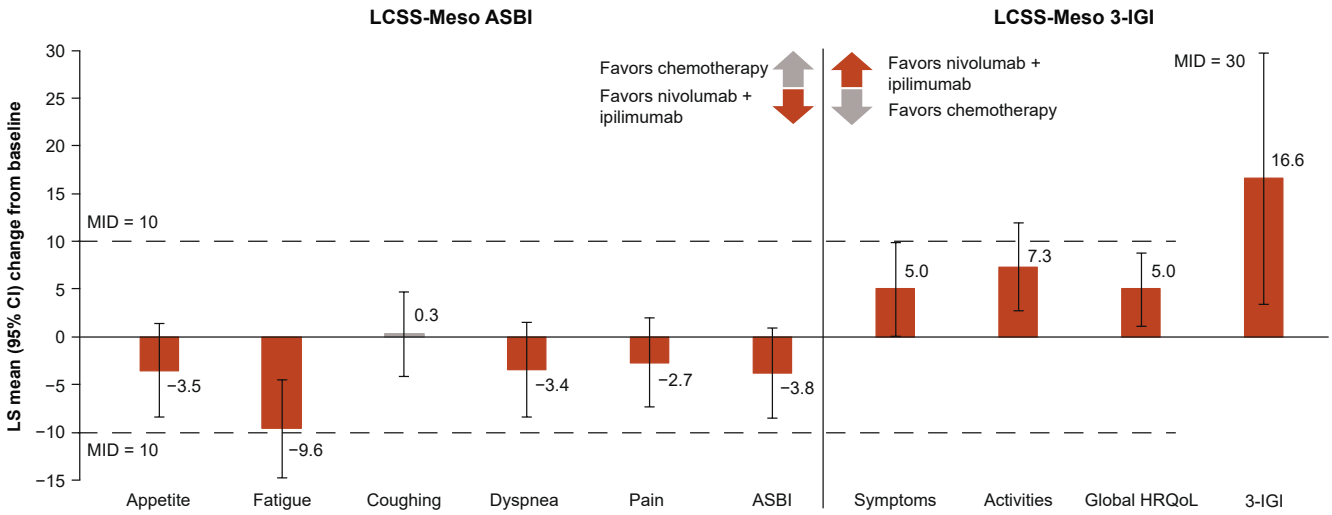

Fig. 4. MMRM analysis[a] of scores for the LCSS-Meso ASBI and 3-IGI: difference in overall change from baseline between treatment arms (on treatment). [a]MMRM included data from common time points up to week 30 where both treatment arms had ≥10 patients. 3-IGI, 3-item global index; ASBI, average symptom burden index; CI, confidence interval; HRQoL, health-related quality of life; LCSS-Meso, Mesothelioma Lung Cancer Symptom Scale; LS, least squares; MID, minimally important difference; MMRM, mixed-effect model repeated measures.

4.2. Descriptive analyses of on-treatment PROs

4.2.1. Disease-related symptom burden and HRQoL using the LCSS-Meso instrument

Mean change from baseline in LCSS-Meso ASBI symptom burden scores generally exhibited improvement in symptom burden over time in patients who received nivolumab + ipilimumab, with increases approaching the MID. Mean change from baseline symptom burden scores in patients who received chemotherapy generally exhibited worsening in level of symptoms over time, approaching the MID (Fig. 2**A**).

Among patients treated with nivolumab + ipilimumab, the LCSS-Meso ASBI scores generally improved in both epithelioid (Fig. 2**B**) and non-epithelioid histologies (Fig. 2**C**) as in the overall population. The same pattern of improvement was seen for all age groups, with change from baseline meeting MID at later timepoints for patients between ≥65 and <75 years, and those ≥75 years of age (**Supplementary** Fig. 1**A–C**).

Changes from baseline in HRQoL, normal activity, and disease symptom burden as measured by LCSS-Meso 3-IGI showed an improvement for patients in the nivolumab + ipilimumab arm, which exceeded the MID at week 72 (**Supplementary** Fig. 2**A**); patients in the chemotherapy arm showed a trend of deterioration. A similar trend in the improvement of LCSS-Meso 3-IGI scores was observed with nivolumab + ipilimumab for both histology subgroups; mean scores reached the MID for the epithelioid histology subgroup (**Supplementary** Fig. 2**B**) and exceeded the MID for the non-epithelioid histology subgroup (**Supplementary** Fig. 2**C**). Scores were maintained before improvement was seen across age subgroups (**Supplementary** Fig. 2**D–F**). While there was a trend for improvement with nivolumab + ipilimumab for the LCSS-Meso assessments, the differences were not clinically meaningful versus chemotherapy.

4.2.2. Overall health status using the EQ-5D-3L instrument

EQ-5D-3L VAS mean scores for patients in the nivolumab + ipilimumab arm improved over time and approached the general United Kingdom population norm [24] of 82.8 by week 60 (n = 60) (Fig. 3**A**). Similarly, mean score changes over time improved and reached the MID for patients in the nivolumab + ipilimumab arm, whereas mean score change was maintained until week 30, but then declined from week 36 for patients in the chemotherapy arm (Fig. 3**B**).

EQ-5D-3L VAS mean score changes improved and reached the MID at week 84 (n = 28) for patients with epithelioid histology (Fig. 3**C**) and exceeded the MID after week 36 (n = 23) for those with non-epithelioid histology in patients treated with nivolumab + ipilimumab (Fig. 3**D**). EQ-5D-3L VAS scores by age group are shown in **Supplementary** Fig. 3**A–C**; scores trended toward improvement with nivolumab + ipilimumab for patients <65 years of age and improved beyond the MID by week 42 for those between ≥65 and <75 years of age.

EQ-5D-3L UI scores improved over time in patients who received nivolumab + ipilimumab, reaching the MID by week 36 (**Supplementary** Fig. 4**A**). Mean score changes remained near baseline for patients with epithelioid histology (**Supplementary** Fig. 4**B**) and exceeded the MID after week 10 for patients with non-epithelioid histology (**Supplementary** Fig. 4**C**). Scores improved and reached or exceeded the MID among all age subgroups (**Supplementary** Fig. 4**D–F**).

4.2.3. Longitudinal MMRM analysis

The overall longitudinal change from baseline in each PRO scale were assessed using an MMRM analysis; mean differences in overall change from baseline between treatment arms showed that all individual symptoms were reduced (exception cough) and symptom burden/QoL improved (3-IGI) for the nivolumab + ipilimumab arm versus chemotherapy (Fig. 4). As shown in Fig. 4, LS mean difference in the scores of average symptoms (LCSS-Meso ASBI) was −3.8 (95% CI, −7.7 to 0.0; P = 0.051) and difference in symptom burden/QoL was 16.6 (95% CI, 3.5–29.8; P = 0.013) favoring treatment with nivolumab + ipilimumab versus chemotherapy. LS mean differences from all four PRO assessments favored treatment with nivolumab + ipilimumab among patients with non-epithelioid histology. Among patients with epithelioid histology, LS mean differences favored nivolumab + ipilimumab in the LCSS-Meso ASBI, 3-IGI, and the EQ-5D-3L VAS; LS mean difference in the EQ-5D-3L UI was similar in both arms (data not shown). The results from the unadjusted and adjusted (MMRM) analyses were similar.

4.2.4. Disease-related symptom deterioration

Time to first deterioration was similar between treatment arms for LCSS-Meso ASBI for the first 6 months before a trend of worsening for the chemotherapy arm (Fig. 5**A**) and 3-IGI assessments (data not shown); however, HRs were not statistically significant. Time to first deterioration favored nivolumab + ipilimumab over chemotherapy for the EQ-5D-3L VAS (HR 0.71; 95% CI, 0.57–0.88; P < 0.01) and UI (HR 0.76; 95% CI, 0.60–0.95; P = 0.01). Deterioration occurred following completion of chemotherapy.

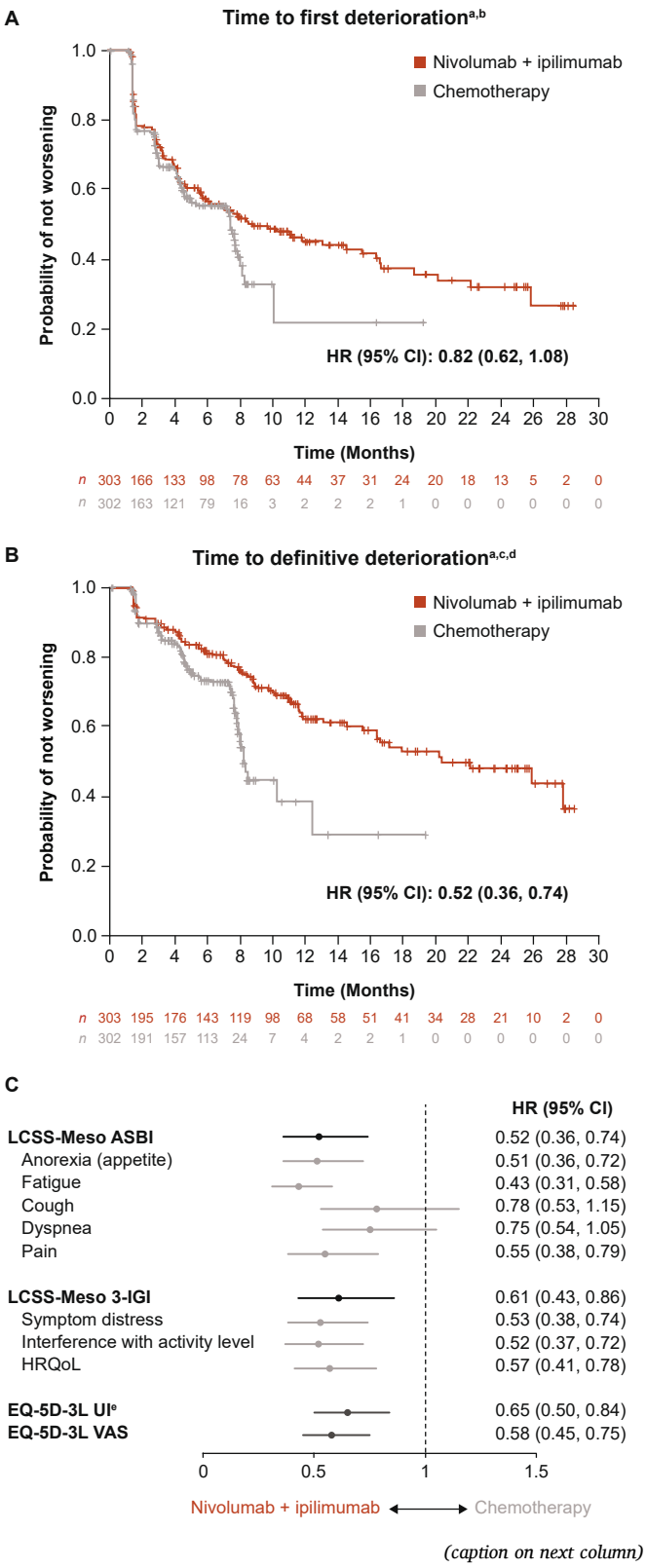

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Fig. 5. Kaplan-Meier curve of time to first deterioration (A), Kaplan-Meier curve of time to definitive deterioration (B) on treatment and follow-up in LCSS-Meso ASBI, and forest plot of time to definitive deterioration (C). [a]Data interpretation after 6 months is difficult due to drop off in data for the chemotherapy arm. [b]There were 117 (39%) patients with an event among those who received nivolumab + ipilimumab (186 [61%] patients censored) and 106 (35%) patients with an event among those who received chemotherapy (196 [65%] patients censored). [c]Defined as time from randomization to the first deterioration that met or exceeded the MID, provided that all subsequent assessments also met or exceeded the MID; MID = 10 points (LCSS-Meso ASBI), 30 points (LCSS-Meso 3-IGI), 0.08 points (EQ-5D-3L UI), and 7 points (EQ-5D-3L VAS). [d]There were 79 (26%) patients with an event among those who received nivolumab + ipilimumab (224 [74%] patients censored) and 74 (24%) patients with an event among those who received chemotherapy (228 [76%] patients censored). [e]Scoring derived from United Kingdom weights. 3-IGI, 3-item global index; ASBI, average symptom burden index; CI, confidence interval; EQ-5D-3L, 3-level EuroQol 5-dimensional questionnaire; HR, hazard ratio; HRQoL, health-related quality of life; LCSS-Meso, Mesothelioma Lung Cancer Symptom Scale; MID, minimally important difference; UI, utility index; VAS, visual analog score.

Despite the low proportion of patients with events, the pattern of delay in definitive symptom burden deterioration measured by the LCSS-Meso ASBI was longer for the nivolumab + ipilimumab arm compared with the chemotherapy arm (HR 0.52; 95% CI, 0.36–0.74; $P < 0.001$; Fig. 5**B**). Similar delays were seen for all individual symptoms and LCSS-Meso 3-IGI measures, except for dyspnea and cough (Fig. 5**C**). Delays in time to definitive deterioration with nivolumab + ipilimumab were also observed in overall health status as measured by EQ-5D-3L UI and VAS (Fig. 5**C**).

5. Discussion

In CheckMate 743, nivolumab + ipilimumab improved symptom burden and maintained overall health status with a median follow-up time of 29.7 months. Patients in the chemotherapy arm worsened more rapidly compared with those in the nivolumab + ipilimumab arm, as seen in the time to definitive deterioration with the LCSS-Meso ASBI and 3-IGI, and the EQ-5D-3L VAS and UI. Health status with nivolumab + ipilimumab, as measured by EQ-5D-3L VAS scores, improved from baseline, reaching the United Kingdom normal population value [24] in those patients continuing on treatment over a year; in contrast, deterioration was noted in the chemotherapy arm, following cessation of chemotherapy treatment. Although direct comparison was limited by non-availability of health status data after week 42 for patients in the chemotherapy arm, HRQoL was maintained with nivolumab + ipilimumab throughout the study despite longer duration of therapy. These data are complementary to clinical findings in the primary analysis of CheckMate 743, in which nivolumab + ipilimumab significantly prolonged OS compared with chemotherapy (HR 0.74; 95% CI, 0.60–0.91; $P = 0.0020$), with median durations of response of 11.0 versus 6.7 months, respectively, and estimated rates of patients with ongoing response at 2 years of 32% versus 8%, respectively [11]. This longer duration of response with nivolumab + ipilimumab may correlate with improved symptom control and HRQoL as well as delayed symptom deterioration compared with chemotherapy, although notably symptom deterioration occurred following the planned cessation of chemotherapy.

As histologic subtype is a significant prognostic factor in MPM [25], histology was a stratification factor for the study and the PRO-adjusted analyses included histology as a covariate. Results in the histology subgroups (epithelioid and non-epithelioid) were consistent with those in the overall PRO population with improvement observed with nivolumab + ipilimumab. Although sample sizes for the non-epithelioid subgroup were small, patients who received nivolumab + ipilimumab showed clinically meaningful improvements at various timepoints across PRO measures, which reflect clinical efficacy evaluations.

Similarly, clinically meaningful improvements in PRO measures in patients receiving nivolumab + ipilimumab were also seen in the epithelioid subgroup, despite the larger magnitude of clinical benefit in the non-epithelioid subgroup due to the inferior effect of chemotherapy. These PRO results support the consistent clinical benefit observed with nivolumab + ipilimumab across histologies.

Overall, these PRO results continue to complement the clinical benefit observed in those <75 years of age, while clinical improvement was minimal for those ≥75 years of age. This incongruence of results in patients ≥75 years of age may be a result of the small patient numbers and lack of statistical power. Taken together, these descriptive PRO analyses indicate no clinically meaningful or large difference in patterns between histology and age subgroups compared with the overall PRO population.

Immunotherapies have been shown to maintain or improve HRQoL, as reported in previous studies in patients with advanced lung cancers and MPM [26–30]. While cross-study comparisons should be made with caution due to differences in patient populations, study design, and other key elements such as HRQoL assessments, the PRO results of CheckMate 743 are consistent with those reported with first-line nivolumab + ipilimumab treatment showing maintained or improved HRQoL in patients with advanced non-small cell lung cancer [26,31], melanoma [32], and renal cell carcinoma [33]. Additionally, while other treatment modalities such as bevacizumab (MAPS study) [34] or nintedanib (LUME-Meso study) [35] combined with chemotherapy, have also been evaluated in MPM with HRQoL assessments, the LCSS-Meso tool either was not used or data not reported in these studies, thus precluding direct comparisons with the PRO results from CheckMate 743.

Most patients with MPM are >65 years of age, and HRQoL is a key factor in determining treatment options in this population. However, data evaluating symptom burden and health status among elderly patients with MPM are limited. Immune-related side effects associated with immunotherapy are of particular concern among elderly patients. However, regardless of age, adequate management of such side effects can help patients maintain their QoL with the improvement in clinical benefits obtained from combination immunotherapy. Our findings demonstrate that HRQoL was improved or maintained with immunotherapy among patients of all ages, including those ≥75 years of age.

Strengths of the study include high PRO completion rates while patients were on treatment (**Supplementary** Table 2) and the use of comprehensive and disease-specific instruments [6]. Limitations to conducting robust PRO assessment comparisons include study design (eg, different PRO assessment schedules, LCSS-Meso assessments only completed on treatment [and 2 post-treatment assessments], and the open-label nature of the trial), different times on treatment in both arms, and the low number of events in the time to definitive deterioration analysis. Additionally, small sample size may limit comparison between treatment arms for the subgroup analyses. While baseline characteristics were balanced between treatment arms, there may be differences in clinical factors that were not captured, such as comorbidities or concomitant medication use.

In conclusion, the significant OS benefit experienced by patients who received nivolumab + ipilimumab versus chemotherapy was accompanied by maintenance of HRQoL and decreased risk of definitive deterioration in disease-related symptoms during treatment. These PRO results further support the use of nivolumab + ipilimumab as first-line treatment for patients with unresectable MPM.

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Previous presentations

Data from this study was previously presented at the European Society for Medical Oncology Immuno-Oncology virtual congress, December 12, 2020 (presentation number LBA1) and the International Mesothelioma Interest Group virtual congress, May 7, 2021 (presentation number MS02:08).

CRediT authorship contribution statement

Arnaud Scherpereel: Validation, Investigation, Resources, Data curation, Writing – review & editing. **Scott Antonia:** Validation, Investigation, Resources, Data curation, Writing – review & editing. **Yolanda Bautista:** Validation, Investigation, Resources, Data curation, Writing – review & editing. **Francesco Grossi:** Validation, Investigation, Resources, Data curation, Writing – review & editing. **Dariusz Kowalski:** Validation, Investigation, Resources, Data curation, Writing – review & editing. **Gérard Zalcman:** Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing – review & editing, Supervision. **Anna K. Nowak:** Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing – review & editing, Supervision. **Nobukazu Fujimoto:** Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing – review & editing, Supervision. **Solange Peters:** Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing – review & editing, Supervision. **Anne S. Tsao:** Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing – review & editing, Supervision. **Aaron S. Mansfield:** Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing – review & editing, Supervision. **Sanjay Popat:** Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing – review & editing, Supervision. **Xiaowu Sun:** Software, Validation, Formal analysis, Writing – review & editing, Visualization. **Rachael Lawrance:** Software, Validation, Formal analysis, Writing – review & editing, Visualization. **Xiaoqing Zhang:** Validation, Resources, Data curation, Writing – review & editing, Visualization, Supervision, Project administration, Funding acquisition. **Melinda J. Daumont:** Methodology, Validation, Resources, Data curation, Writing – review & editing, Visualization, Supervision, Funding acquisition. **Bryan Bennett:** Methodology, Validation, Resources, Data curation, Writing – review & editing, Visualization, Supervision, Funding acquisition. **Mike McKenna:** Methodology, Resources, Data curation, Writing – review & editing, Visualization, Supervision, Funding acquisition. **Paul Baas:** Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing – review & editing, Supervision.

Declaration of Competing Interest

Arnaud Scherpereel reports receiving grants/research support for the institution from AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Epizyme, MSD, Roche; other fees (honoraria) from AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, MSD, and Roche; and other (presenter) from AstraZeneca, Bristol Myers Squibb, MSD, and Roche. **Scott Antonia** reports receiving personal fees from Bristol Myers Squibb for the submitted work; personal fees from Achilles Therapeutics, Amgen, AstraZeneca, Caris Life Sciences, Celsius Therapeutics, EMD Serono, G1 Therapeutics, GlaxoSmithKline, Glympse, Memgen, Merck & Co Inc, Nektar, RAPT Therapeutics, Samyang, and Venn Therapeutics outside of the submitted work; grants from Cellular Biomedicine Group outside of the submitted work; and non-financial support from Amgen outside of the submitted work. **Yolanda Bautista** declares no conflicts of interest. **Francesco Grossi** reports receiving grants from Bristol Myers Squibb; honoraria/personal fees from Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, MSD, Pierre Fabre, Pfizer, Roche, and Takeda. **Dariusz Kowalski** reports receiving other fees (consultant/advisor) from Amgen, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, MSD, Roche/Genentech, and Pfizer. **Gerald Zalcman** reports receiving grants from Inventiva, Roche-France, and Takeda outside of the submitted work; personal fees from AstraZeneca, Bristol Myers Squibb, Da

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Appendix A. Supplementary data

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