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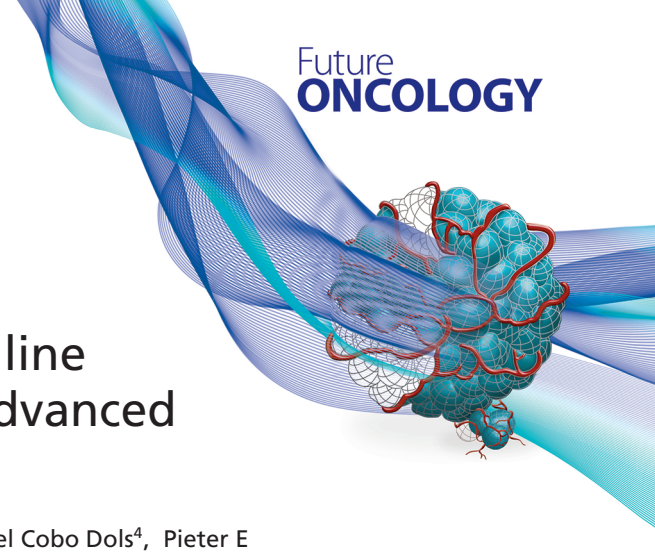

Quality of life with second or third line *nab*-paclitaxel-based regimens in advanced non-small-cell lung cancer

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Aim: Evaluate quality of life (QoL) in patients with advanced non-small cell lung cancer treated with second or third line *nab*-paclitaxel ± durvalumab. **Patients & methods:** Longitudinal QoL was assessed using Lung Cancer Symptom Scale, EuroQoL Five-Dimensions Five-Levels and European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-item core. **Results:** QoL was generally stable through eight treatment cycles (both arms). Clinically meaningful improvement from baseline was noted in Lung Cancer Symptom Scale (overall constitutional score and three-item index [*nab*-paclitaxel + durvalumab]) and European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-item core (global health status/QoL and emotional functioning [both arms] and pain [*nab*-paclitaxel + durvalumab]) analyses. EuroQoL Five-Dimensions Five-Levels domains were stable/improved or completely resolved at least once in 19–56% and 9–51% of patients, respectively. **Conclusion:** While QoL trends were promising, additional data are required to support these regimens in this setting.

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Keywords: durvalumab • EORTC QLQ-C30 • EQ-5D-5L • lung cancer symptom scale • *nab*-paclitaxel • non-small cell lung cancer • quality of life

Patients with advanced non-small cell lung cancer (NSCLC) have a high symptom burden that adversely affects their quality of life (QoL), which predictably worsens with the greater symptom burden associated with advanced disease [1,2]. In addition, QoL has been shown to significantly worsen with disease progression in patients with advanced NSCLC [3,4]. Therefore, QoL maintenance during second-line therapy for NSCLC is a valuable consideration for treatment decisions.

nab-Paclitaxel is currently approved in combination with carboplatin for frontline treatment of advanced NSCLC [5]. In the first-line setting, *nab*-paclitaxel + carboplatin has demonstrated clinically meaningful improvement in QoL from baseline [6]. Immune checkpoint inhibitors (ICIs) can improve outcomes with chemother-

apy [7–12], including *nab*-paclitaxel [10–12], in first-line treatment of advanced NSCLC. Nivolumab, pembrolizumab and atezolizumab are currently approved for second-line treatment of NSCLC [13]. Additionally, durvalumab as monotherapy has been shown to improve patient outcomes [14] and according to National Comprehensive Cancer Network guidelines, is a category 1 recommendation as consolidation treatment for patients with unresectable stage III disease that responded to platinum-based chemoradiation [15]. Additionally, targeted therapies have shown favorable QoL profiles [16–18]. However, to our knowledge, few studies have evaluated QoL, especially longitudinal QoL, in patients receiving second or third-line treatment.

The Phase II ABOUND.2L+ trial (NCT02250326) investigated treatment with second or third line *nab*-paclitaxel either alone or in combination with CC-486 (oral azacitidine) or durvalumab in patients with advanced NSCLC. The primary outcome of ABOUND.2L+ demonstrated no benefit of combining CC-486 with *nab*-paclitaxel; the median progression-free survival (PFS) was 3.2 months with *nab*-paclitaxel + CC-486 versus 4.2 months with *nab*-paclitaxel alone (hazard ratio: 1.3; 95% CI: 0.9–1.9) [19]. In the third arm of the study, the combination of *nab*-paclitaxel with durvalumab demonstrated a median PFS of 4.5 months [20]. The objective of this analysis was to evaluate QoL data collected from the *nab*-paclitaxel alone and *nab*-paclitaxel + durvalumab arms, which demonstrated promising efficacy outcomes [19,20]. QoL outcomes with *nab*-paclitaxel + CC-486 were not reported because the regimen was found to be ineffective in this setting.

Patients & methods

Study design

The study was approved by the institutional review board or independent ethics committee at participating sites and conducted in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki. All patients provided written informed consent prior to treatment initiation.

Inclusion and exclusion criteria as well as sample size determination for the randomized part of this open-label study were described previously [19]. Briefly, patients with advanced nonsquamous NSCLC, one prior platinum-based chemotherapy and no activating *EGFR* mutations or *ALK* translocations were randomized 1:1 to receive *nab*-paclitaxel 100 mg/m^2 on days 8 and 15 + CC-486 200 mg on days 1–14 or *nab*-paclitaxel 100 mg/m^2 on days 1 and 8 of each 21-day cycle. Randomization, when conducted, was performed centrally using a permuted-block randomization method. After enrollment for the *nab*-paclitaxel alone and *nab*-paclitaxel + CC-486 arms was completed, the ABOUND.2L+ protocol was amended to include a third arm, in which patients with advanced nonsquamous or squamous NSCLC and one prior platinum-based chemotherapy were enrolled. Patients were assigned to this third arm and received *nab*-paclitaxel 100 mg/m^2 on days 1 and 8 + durvalumab 1125 mg on day 15 of a 21-day cycle. Hence, randomization did not occur between the *nab*-paclitaxel + durvalumab and *nab*-paclitaxel alone arms. The primary end point was PFS. Key secondary end points were overall survival, response rates and safety. QoL was an exploratory end point.

QoL assessments

QoL questionnaires were completed by patients on day 1 of each cycle. Assessments were conducted using the Lung Cancer Symptom Scale (LCSS), EuroQoL Five-Dimensions Five-Levels (EQ-5D-5L) and European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-item core (EORTC QLQ-C30), which have been previously validated [21–23].

The LCSS has nine components: appetite, fatigue, cough, dyspnea, hemoptysis, pain, lung cancer symptoms, normal activity and global QoL. Each item is measured on a 100-mm visual analog scale (VAS). The LCSS composite scores include total score (average of all component scores), symptom burden index (average of appetite, fatigue, cough, dyspnea, hemoptysis and pain scores), pulmonary symptom scale (average of cough, dyspnea and hemoptysis scores), overall constitutional score (average of appetite and fatigue scores) and three-item index (sum of lung cancer symptoms, normal activity and global QoL scores; this index is measured on a 300-mm VAS). The LCSS total scores (0–100) were transformed by subtracting from 100 such that in the final outcome, a higher LCSS total score represents better health status and QoL.

The EQ-5D-5L measures five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Readouts include utility and VAS scores (a higher score represents better health status).

The EORTC QLQ-C30 is a 30-item assessment with readouts including global health status/QoL, physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning, fatigue, nausea

Table 1. Baseline patient characteristics for patients who received *nab*-paclitaxel alone.

Characteristic	*nab*-P (n = 80)
Age (years)	
Median (range)	63.0 (37–82)
≥ 65 years	39 (48.8)
≥ 70 years	19 (23.8)
≥ 75 years	10 (12.5)
Sex	
Male	50 (62.5)
Female	30 (37.5)
Race	
White	63 (78.8)
Black or African American	2 (2.5)
Asian	2 (2.5)
Other	1 (1.3)
Not reported	12 (15.0)
ECOG PS	
0	26 (32.5)
1	54 (67.5)
Histology	
Squamous	0
Nonsquamous	80 (100)
Not specified	0

Data are n (%) unless otherwise noted.
ECOG PS: Eastern Cooperative Oncology Group performance status; *nab*-P: *nab*-paclitaxel; *nab*-P + D: *nab*-paclitaxel + durvalumab.

and vomiting and pain. For global health status/QoL and functioning scales, a higher score represents better health status. For symptom scales, a lower score represents better health status.

For items measured on a VAS, improvement ≥10 mm was considered clinically meaningful [24]. For the LCSS three-item index, improvement ≥30 mm was considered clinically meaningful [25].

Patients with QoL data at baseline and ≥1 postbaseline assessment were included. Data cutoffs were 30 August 2017 for the *nab*-paclitaxel alone arm and 23 December 2017 for the *nab*-paclitaxel + durvalumab arm.

Results

Baseline patient characteristics

The ABOUND.2L+ trial included 80 patients randomized to the *nab*-paclitaxel alone arm and 79 patients assigned to the *nab*-paclitaxel + durvalumab arm. The baseline demographics by treatment arm are reported in Table 1 and 2. Notable differences were that the *nab*-paclitaxel + durvalumab arm included patients with both squamous and nonsquamous histology (the *nab*-paclitaxel alone arm included only patients with nonsquamous NSCLC) and had a higher frequency of patients with an Eastern Cooperative Oncology Group performance status (ECOG PS) of 1 (77.2 vs 67.5% for *nab*-paclitaxel + durvalumab vs *nab*-paclitaxel alone).

QoL assessment completion

A total of 55 (68.8%) and 69 (87.3%) patients completed a baseline QoL assessment in the *nab*-paclitaxel alone and *nab*-paclitaxel + durvalumab arms, respectively. However, a total of 50 (62.5%) and 58 (73.4%) patients, respectively, completed a baseline and ≥1 postbaseline QoL assessment.

LCSS results

The LCSS total score (represented as mean change from baseline) was stable through eight cycles of treatment in both arms, with no clinically meaningful changes during the first eight cycles (Figure 1A & B). The mean maximum change from baseline showed stable QoL in all five LCSS composite scores in the *nab*-paclitaxel alone arm (Figure 2A), and in three of the five composite scores (total score, symptom burden index and pulmonary

Table 2. Baseline patient characteristics for patients who received *nab*-paclitaxel + durvalumab.

Characteristic	*nab*-P + D (n = 79)
Age (years)	
Median (range)	63.0 (29–84)
≥ 65 years	36 (45.6)
≥ 70 years	25 (31.6)
≥ 75 years	9 (11.4)
Sex	
Male	54 (68.4)
Female	25 (31.6)
Race	
White	77 (97.5)
Black or African American	1 (1.3)
Asian	0
Other	0
Not reported	1 (1.3)
ECOG PS	
0	18 (22.8)
1	61 (77.2)
Histology	
Squamous	23 (29.1)
Nonsquamous	55 (69.6)
Not specified	1 (1.3)

Data are n (%) unless otherwise noted.
ECOG PS: Eastern Cooperative Oncology Group performance status; *nab*-P: *nab*-paclitaxel; *nab*-P + D: *nab*-paclitaxel + durvalumab.

symptoms) in the *nab*-paclitaxel + durvalumab arm (Figure 2B). In addition, clinically meaningful improvement was noted in the three-item index and overall constitutional score in the *nab*-paclitaxel + durvalumab arm.

LCSS component and composite scores were stable through the first eight cycles of treatment in both arms (Table 3 & 4), with a few exceptions observed primarily in the *nab*-paclitaxel alone arm. Among patients who received *nab*-paclitaxel alone, clinically meaningful improvement occurred in the cough item in several cycles, and in dyspnea, global QoL and pulmonary symptoms at cycle 7; clinically meaningful deterioration occurred in fatigue, hemoptysis, lung cancer symptoms, normal activity and overall constitutional score at cycle 8 (Table 3). Interestingly, the mean maximum scores showed clinically meaningful improvement in seven of the nine items in the *nab*-paclitaxel alone arm, and in eight of the nine items in the *nab*-paclitaxel + durvalumab arm; the scores for hemoptysis in both arms and lung cancer symptoms in the *nab*-paclitaxel alone arm were stable.

EQ-5D-5L results

EQ-5D-5L VAS score (represented as mean change from baseline) was stable through eight cycles of treatment in both arms (Figure 3A & B), with the exception of a clinically meaningful deterioration noted in the *nab*-paclitaxel alone arm at cycle 8. The domains of mobility, self-care, usual activities, pain/discomfort and anxiety/depression were stable or improved from baseline in 29–56% (Figure 4A) and 19–48% (Figure 4B) of patients in the *nab*-paclitaxel alone and *nab*-paclitaxel + durvalumab arms, respectively. The domains were completely resolved at least once during treatment in 9–39% (Figure 4C) and 31–51% (Figure 4D) of patients in the *nab*-paclitaxel alone and *nab*-paclitaxel + durvalumab arms, respectively.

EORTC QLQ-C30 results

EORTC QLQ-C30 scores were generally stable through the first eight cycles of treatment in both arms, with the exception of clinically meaningful deterioration in role functioning at cycles 6 and 8 with *nab*-paclitaxel alone (Table 5) and at cycle 8 with *nab*-paclitaxel + durvalumab (Table 6), and improvement in emotional and cognitive functioning beginning with cycles 4 and 5, respectively, as well as social functioning at cycle 7 in the *nab*-paclitaxel alone arm. Mean maximum EORTC QLQ-C30 scores showed clinically meaningful improvement in emotional

Table 3. Mean change from baseline over time and mean maximum improvement from baseline in patients treated with *nab*-paclitaxel alone (Lung Cancer Symptom Scale component and composite).

Assessment	C2,D1 (n = 42)	C3,D1 (n = 33)	C4,D1 (n = 29)	C5,D1 (n = 23)	C6,D1 (n = 19)	C7,D1 (n = 12)	C8,D1 (n = 12)	C9,D1 (n = 10)	Max (n = 50)
LCSS component									
Appetite	-2.3	2.0	6.9	2.5	0.7	8.8	-9.8	-1.7	11.5
Fatigue	-3.7	-1.8	3.2	1.1	-8.6	7.8	-13.2	-13.2	10.9
Cough	1.9	8.1	15.0	11.0	6.2	20.8	5.1	10.2	16.8
Dyspnea	-1.6	2.6	7.9	6.8	3.6	13.2	-7.0	6.9	11.8
Hemoptysis	2.6	1.9	0.4	-3.8	-6.1	-1.8	-15.4	-7.4	5.5
Pain	-1.3	-4.5	4.9	5.2	-1.7	8.4	-6.9	-6.0	11.5
Lung cancer symptoms	-0.1	3.5	-0.3	3.3	-7.4	5.5	-14.3	-3.7	9.7
Normal activity	1.0	-5.2	1.1	-4.7	-7.5	4.5	-12.2	-17.0	12.1
Global QoL	-0.3	6.1	5.6	7.4	5.2	14.8	5.4	-3.7	12.2
LCSS composite									
Pulmonary symptoms†	1.0	4.2	7.8	4.7	1.2	10.7	-5.8	3.2	9.6
Three-item index‡	0.6	4.5	6.4	6.0	-9.7	24.8	-21.1	-24.4	25.0
Symptom burden index§	-0.7	1.4	6.4	3.8	-1.0	9.5	-7.9	-1.9	7.9
Overall constitutional score¶	-3.0	0.1	5.1	1.8	-3.9	8.3	-11.5	-7.5	9.5

A higher score represents a better health status.
†Average of cough, dyspnea and hemoptysis scores.
‡Sum of lung cancer symptoms, normal activity and global QoL scores. This index is measured on a 300-mm scale, with clinically meaningful improvement defined as ≥30 mm.
§Average of appetite, fatigue, cough, dyspnea, hemoptysis and pain scores.
¶Average of appetite and fatigue scores.
C: Cycle; D: Day; LCSS: Lung Cancer Symptom Scale; *nab*-P: *nab*-paclitaxel; *nab*-P + D: *nab*-paclitaxel + durvalumab; QoL: Quality of life.

Table 4. Mean change from baseline over time and mean maximum improvement from baseline in patients treated with *nab*-paclitaxel + durvalumab (Lung Cancer Symptom Scale component and composite).

Assessment	C2,D1 (n = 52)	C3,D1 (n = 49)	C4,D1 (n = 43)	C5,D1 (n = 43)	C6,D1 (n = 37)	C7,D1 (n = 35)	C8,D1 (n = 31)	C9,D1 (n = 23)	Max (n = 58)
LCSS component									
Appetite	1.4	-1.0	2.9	6.3	5.2	-3.5	2.8	4.7	16.0
Fatigue	-3.0	-2.0	1.8	7.6	-1.8	0.1	0.1	-4.2	15.2
Cough	-5.1	-3.1	4.2	5.0	6.2	2.9	3.0	6.7	14.7
Dyspnea	-4.1	-1.3	-1.3	2.8	0.7	-4.3	2.0	-2.2	11.5
Hemoptysis	2.2	0.6	2.8	4.0	1.5	0.8	4.7	-0.3	5.5
Pain	5.3	2.4	-1.6	5.6	8.0	7.3	2.4	9.0	15.1
Lung cancer symptoms	2.9	2.0	0.1	5.3	12.5	7.6	6.1	5.9	16.4
Normal activity	-4.5	-1.7	1.3	2.7	0.8	-4.1	-4.8	-2.2	11.3
Global QoL	-1.5	-4.7	-1.3	0.4	-3.5	-6.1	-9.2	-5.2	10.9
LCSS composite									
Pulmonary symptoms†	-2.3	-1.3	1.9	3.9	2.8	-0.2	3.2	1.4	9.2
Three-item index‡	-3.1	-4.4	0.1	8.5	9.7	-2.7	-7.9	-1.6	30.4
Symptom burden index§	-0.5	-0.7	1.5	5.2	3.3	0.5	2.5	2.3	9.3
Overall constitutional score¶	-0.8	-1.5	2.3	7.0	1.7	-1.7	1.5	0.3	13.0

A higher score represents a better health status.
†Average of cough, dyspnea and hemoptysis scores.
‡Sum of lung cancer symptoms, normal activity and global QoL scores. This index is measured on a 300-mm scale, with clinically meaningful improvement defined as ≥30 mm.
§Average of appetite, fatigue, cough, dyspnea, hemoptysis and pain scores.
¶Average of appetite and fatigue scores.
C: Cycle; D: Day; LCSS: Lung Cancer Symptom Scale; *nab*-P: *nab*-paclitaxel; *nab*-P + D: *nab*-paclitaxel + durvalumab; QoL: Quality of life.

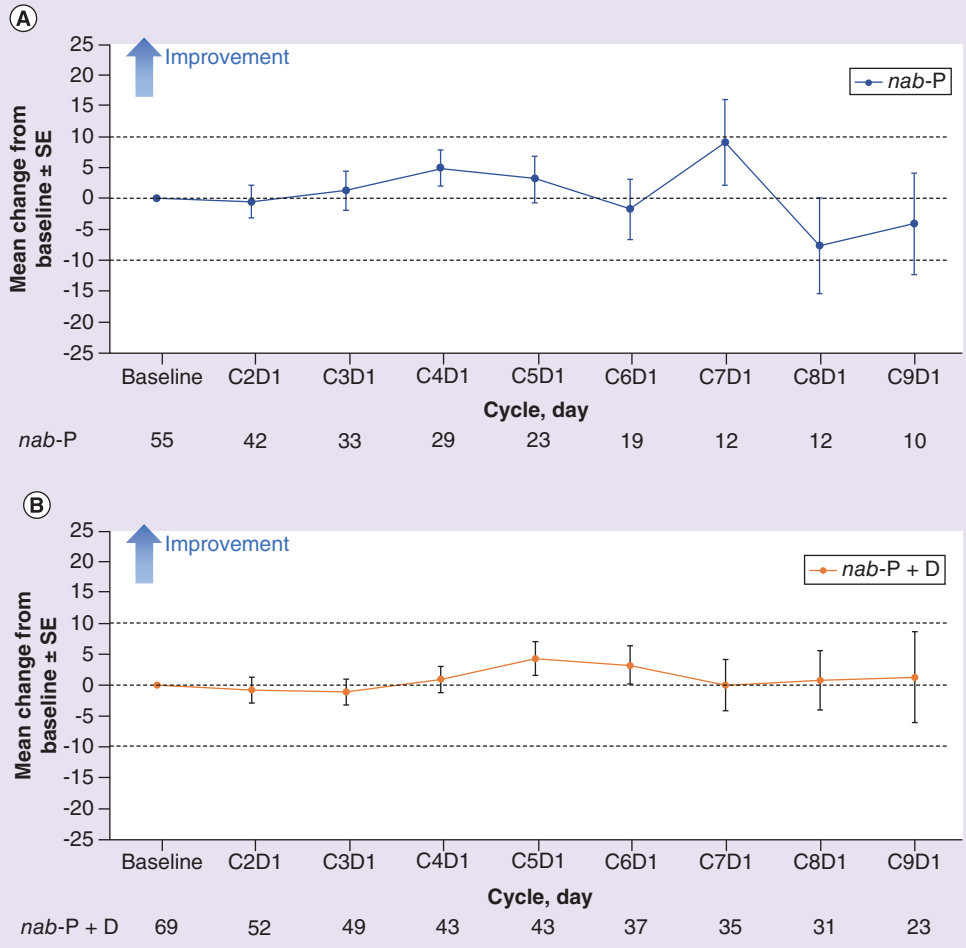

Figure 1. Change from baseline in quality of life (Lung Cancer Symptom Scale total score[†]). (A) Patients who received *nab*-P alone and **(B)** Patients who received *nab*-P + D. A higher score represents a better health status.
[†]Average of appetite, fatigue, cough, dyspnea, hemoptysis, pain, lung cancer symptoms, normal activity and global QoL scores.
C: Cycle; D: Day; *nab*-P: *nab*-paclitaxel; *nab*-P + D: *nab*-paclitaxel + durvalumab; QoL: Quality of life.

functioning and global health status/QoL in both arms (Figure 5A & B), and in pain (decreased score denotes improvement) in the *nab*-paclitaxel + durvalumab arm. Physical, role, cognitive and social functioning, as well as fatigue and nausea/vomiting were stable in both arms.

Performance status deterioration

Among those who received *nab*-paclitaxel alone and had a baseline ECOG PS 0, 18 (78.3%) patients experienced a performance status deterioration of ≥1; among those who had a baseline ECOG PS 1, 15 (26.3%) patients experienced a performance status deterioration of ≥1. Among those who received *nab*-paclitaxel + durvalumab and had a baseline ECOG PS 0, 15 (83.3%) patients experienced a performance status deterioration of ≥1; among those who had a baseline ECOG PS 1, 22 (36.1%) patients experienced a performance status deterioration of ≥1.

Discussion

The results of this analysis show that in general, QoL scores were stable or improved through the first eight cycles of treatment with two *nab*-paclitaxel-based regimens used in the ABOUND.2L+ study: *nab*-paclitaxel alone and *nab*-paclitaxel + durvalumab. Clinically meaningful improvement in mean maximum improvement occurred in both treatment arms in the LCSS components of fatigue, cough, dyspnea, appetite, pain, normal activity and global QoL.

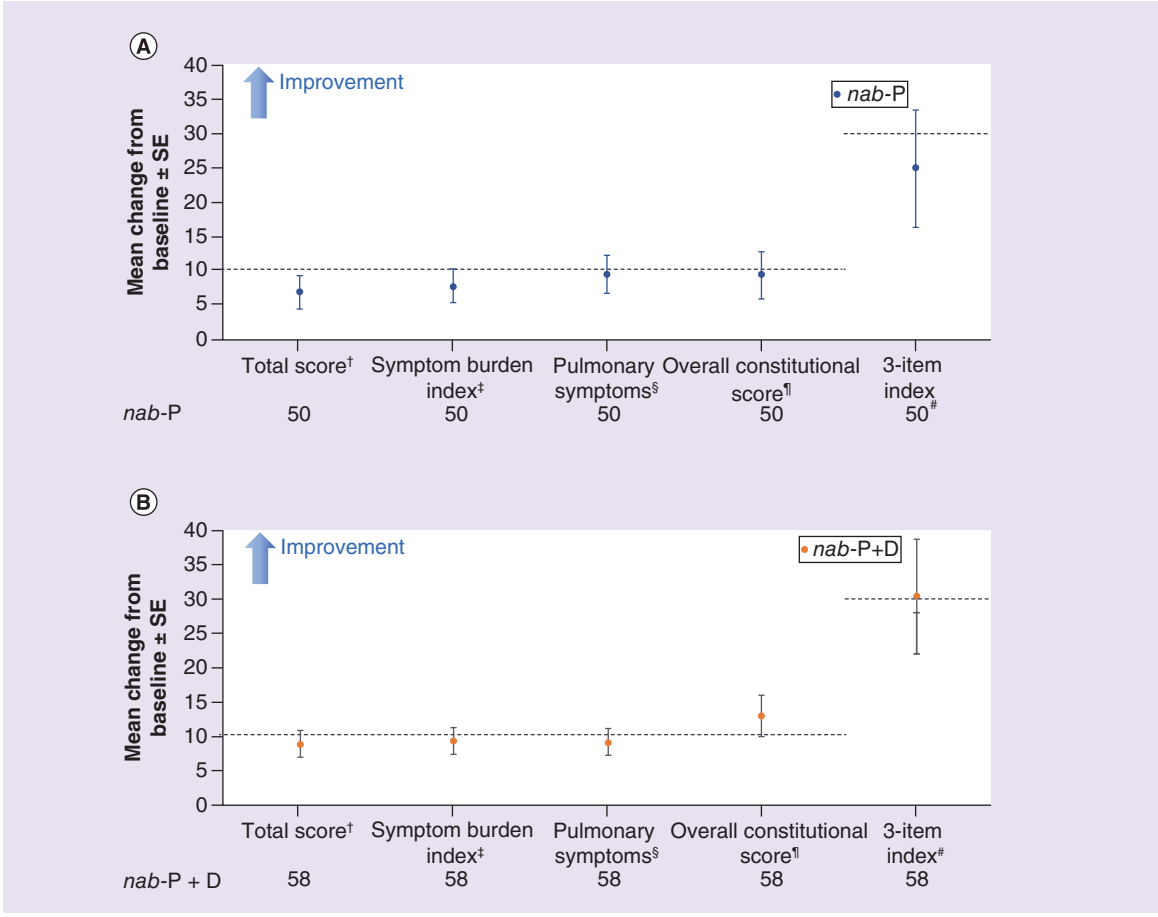

Figure 2. Improvement from baseline in Lung Cancer Symptom Scale composite scores (mean maximum). (A) Patients who received *nab*-P alone and **(B)** Patients who received *nab*-P + D. A higher score represents a better health status.
†Average of appetite, fatigue, cough, dyspnea, hemoptysis, pain, lung cancer symptoms, normal activity and global QoL scores.
‡Average of appetite, fatigue, cough, dyspnea, hemoptysis and pain scores.
§Average of cough, dyspnea and hemoptysis scores.
¶Sum of lung cancer symptoms, normal activity and global QoL scores. This item is measured on a 300-mm scale, with clinically meaningful improvement defined as ≥30 mm.
#Average of appetite and fatigue scores.
nab-P: *nab*-paclitaxel; *nab*-P + D: *nab*-paclitaxel + durvalumab; QoL: Quality of life.

Clinically meaningful improvement was also noted in lung cancer symptoms in the *nab*-paclitaxel + durvalumab arm. In the EQ-5D-5L domains, 19–56% of patients reported stable or improved status, while 9–51% of patients reported complete resolution of a problem in a domain at least once. Clinically meaningful improvement in mean maximum improvement also occurred in EORTC QLQ-C30 emotional functioning and global health status/QoL (*nab*-paclitaxel alone and *nab*-paclitaxel + durvalumab) and pain (*nab*-paclitaxel + durvalumab) scores. The impact of *nab*-paclitaxel-based regimens on QoL observed in our study is supported by a previous report of *nab*-paclitaxel + carboplatin for frontline treatment of patients with squamous NSCLC, which reported stable QoL through four cycles of induction treatment based on LCSS scores, and stable or improved status in the EQ-5D-5L domains in ≥83% of patients [6].

Given the high symptom burden in patients with advanced NSCLC [2] as well as the significantly worse QoL associated with disease progression [3,4], it is important to consider the impact of treatment on specific symptoms as well as overall QoL and other clinical outcomes. The *nab*-paclitaxel-based regimens employed in this trial generally kept symptom severity, as assessed by LCSS component scores, stable throughout treatment, with little clinically meaningful deterioration.

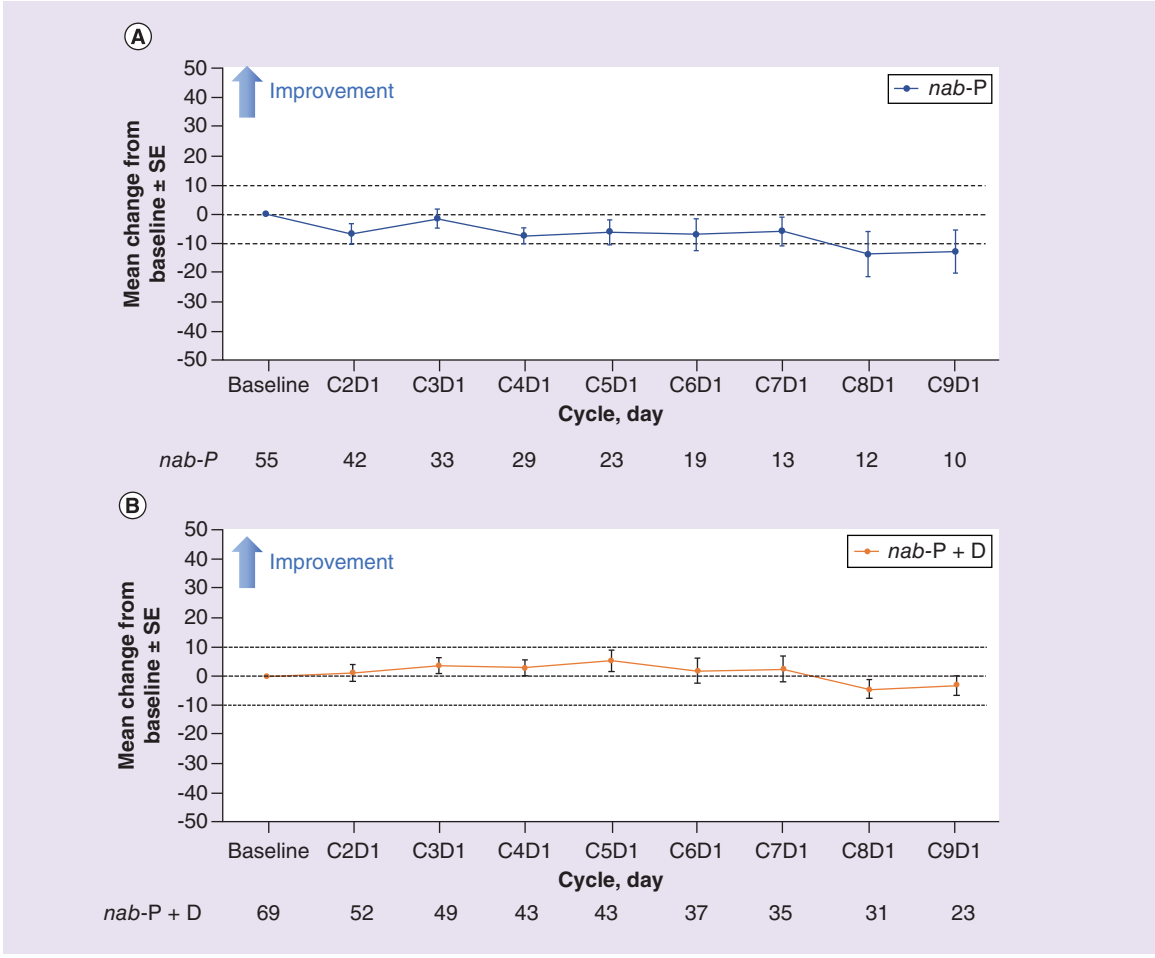

Figure 3. Change from baseline in quality of life (EuroQoL Five-Dimensions Five-Levels Visual Analog Scale score†). **(A)** Patients who received *nab*-P alone and **(B)** Patients who received *nab*-P + D. A higher score represents a better health status.
†EQ-5D-5L VAS score records the patient's self-rated health on a VAS with end points 'The best health you can imagine' and 'The worst health you can imagine'. VAS score was calculated using the US Crosswalk Index Value set.
C: Cycle; D: Day; EQ-5D-5L: EuroQoL Five-Dimensions Five-Levels; *nab*-P: *nab*-paclitaxel; *nab*-P + D: *nab*-paclitaxel + durvalumab; QoL: Quality of life; VAS: Visual analog scale.

Beyond the physical impact of NSCLC, the assessments reported here also examined the psychological and social impacts of the disease. Previous studies revealed the presence of psychological and social problems facing patients with NSCLC, including anxiety, lung cancer-related stigma and depression and have suggested an association between anxiety and depression with mortality in these patients [26–28]. In the current study, based on EORTC QLQ-C30, emotional functioning showed clinically meaningful improvement compared with baseline at several time points throughout the treatment in the *nab*-paclitaxel alone arm and remained stable in the *nab*-paclitaxel + durvalumab arm. Additionally, the anxiety/depression domain of the EQ-5D-5L was completely resolved at least once in 37 and 50% of patients in the *nab*-paclitaxel alone and *nab*-paclitaxel + durvalumab arms, respectively. Although our findings cannot be compared directly with those from previous studies, a possible explanation could be the promising activity with treatment, but such interpretations must be made cautiously due to potential survivor selection bias in longitudinal QoL analyses.

The current National Comprehensive Cancer Network guidelines for NSCLC include ICIs (nivolumab, pembrolizumab and atezolizumab) as category 1, preferred subsequent therapy options for patients without prior ICI therapy [15]. In addition, docetaxel, pemetrexed (nonsquamous), gemcitabine, or ramucirumab plus docetaxel are category 2A options. Given the major impact of ICIs plus chemotherapy in the first-line setting, there will con-

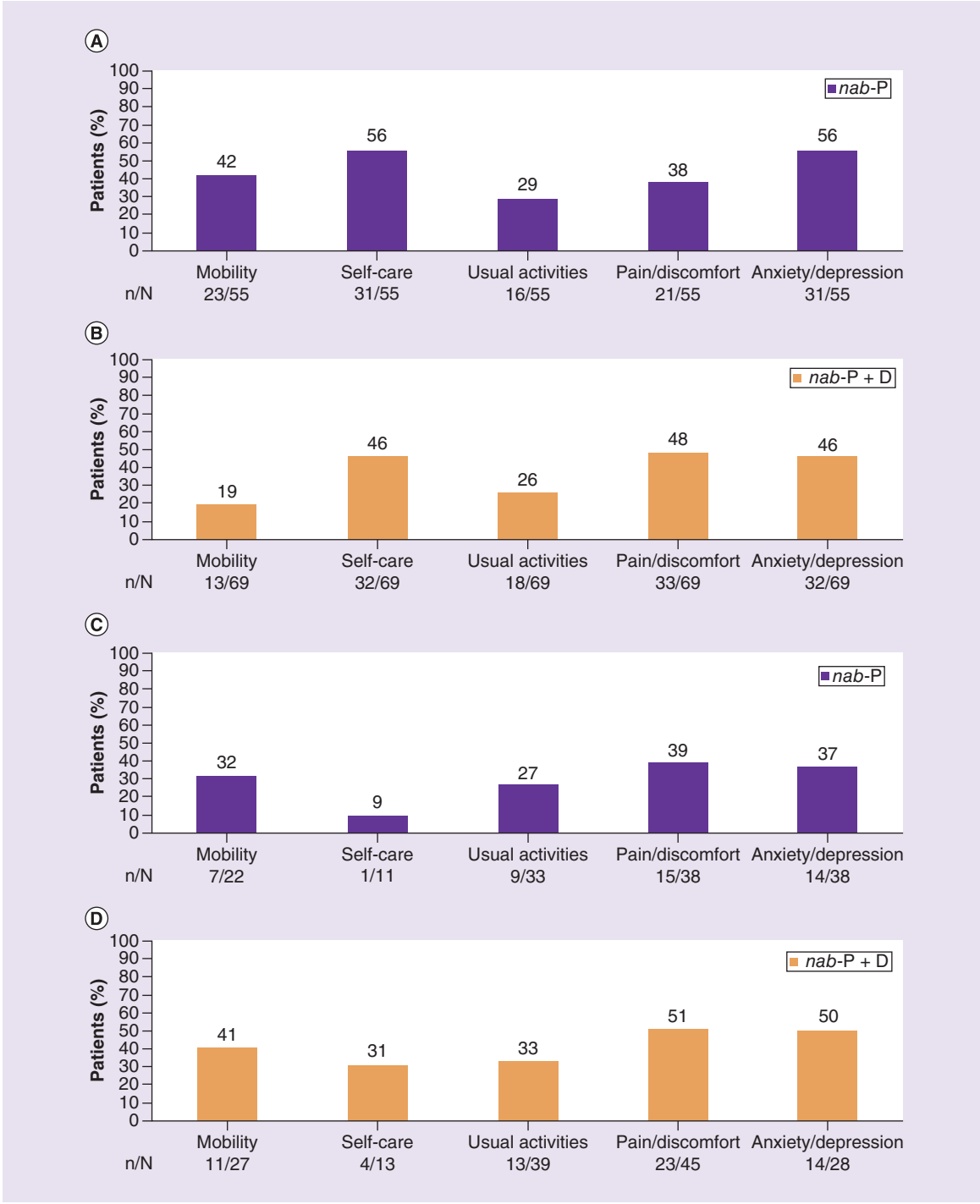

Figure 4. Resolution of problems[†] (EuroQoL Five-Dimensions Five-Levels). Stable or improved from baseline (*nab*-P alone **[A]** or *nab*-P + D **[B]**) or complete resolution of symptoms at least once (*nab*-P alone **[C]** or *nab*-P + D **[D]**). The percentage of patients with a stable or improved dimension is based on the population with a baseline assessment. The percentage of patients with a dimension completely resolved at least once is based on the population with a problem in the given dimension at baseline. **(A)** Stable or improved from baseline (*nab*-P alone). **(B)** Stable or improved from baseline (*nab*-P + D). **(C)** Complete resolution of symptoms at least once (*nab*-P alone). **(D)** Complete resolution of symptoms at least once (*nab*-P + D).

[†]Patients rate their health state in each domain as 'no problems', 'slight problems', 'moderate problems', 'severe problem' and 'extreme problems'. A dimension is stable or improved if it stays the same or improves compared with baseline during the study. A dimension is completely resolved if the score becomes 'no problems'.

nab-P: *nab*-paclitaxel; *nab*-P + D: *nab*-paclitaxel + durvalumab.

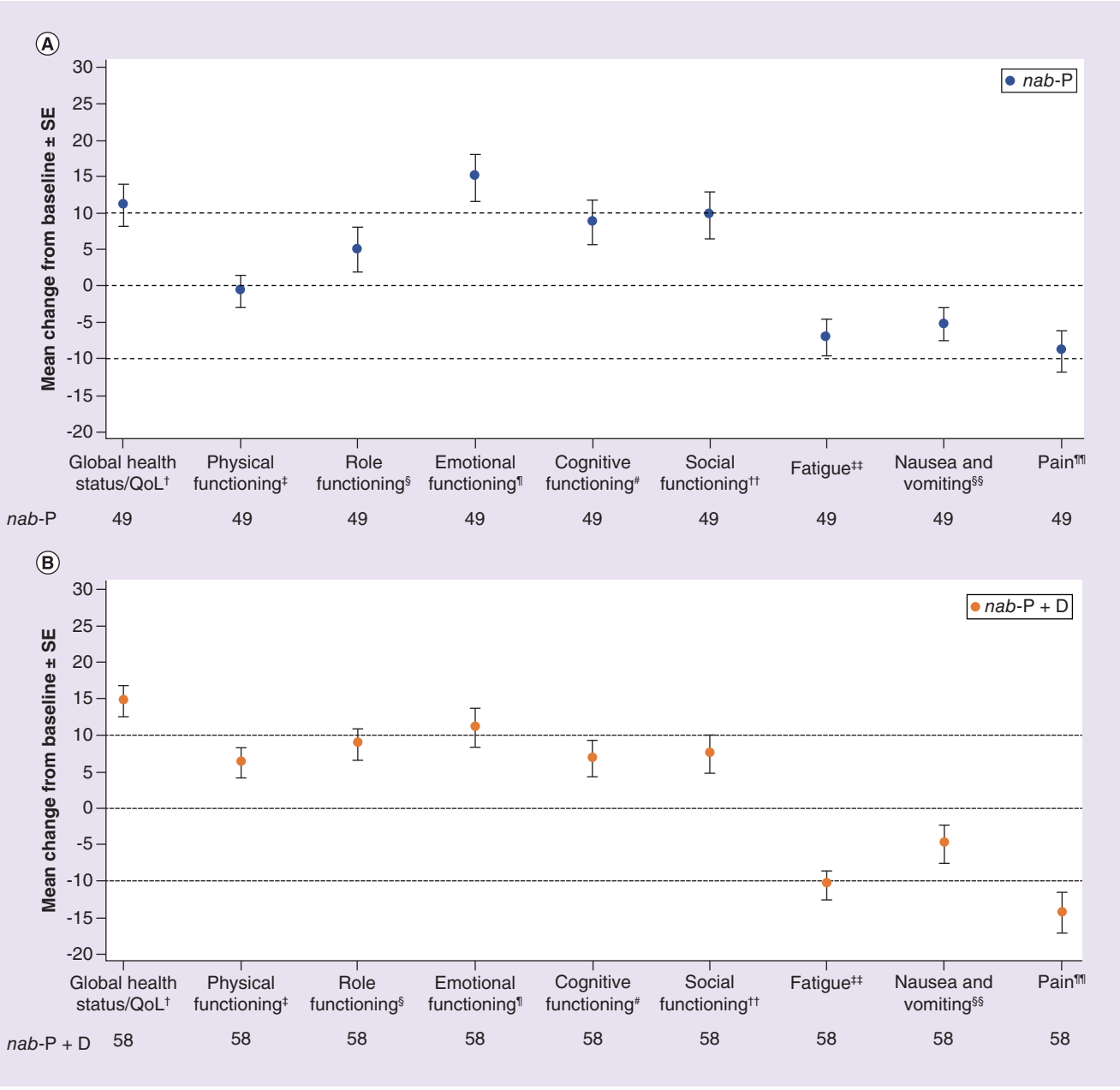

Figure 5. Improvement from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-item core scores (mean maximum). (A) Patients who received *nab*-P alone and **(B)** Patients who received *nab*-P + D. For global health status/QoL and functioning scales, a higher score represents a better health status. For symptom scales, a lower score represents a better health status.

†Includes items 29 and 30 on the EORTC QLQ-C30. † ‡ § ¶ #

‡Includes items 1–5.

§Includes items 6 and 7.

¶Includes items 21–24.

#Includes items 20 and 25.

††Includes items 26 and 27.

‡‡Includes items 10, 12 and 18.

§§Includes items 14 and 15.

¶¶Includes items 9 and 19.

EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-item core; *nab*-P: *nab*-paclitaxel; *nab*-P + D: *nab*-paclitaxel + durvalumab; QoL: Quality of life.

Table 5. Mean change from baseline over time in patients treated with *nab*-paclitaxel alone (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-item core).

Assessment	C2,D1 (n = 42)	C3,D1 (n = 33)	C4,D1 (n = 29)	C5,D1 (n = 23)	C6,D1 (n = 19)	C7,D1 (n = 12)	C8,D1 (n = 12)	C9,D1 (n = 10)
Global health status/QoL†	0.60	7.07	1.72	1.81	0.00	0.00	-1.39	-6.67
Physical functioning‡	-4.44	-3.03	-5.98	-3.48	-6.32	-0.56	-8.89	-16.67
Role functioning§	-2.38	-7.58	-7.47	-5.80	-10.53	-4.17	-13.89	-21.67
Emotional functioning¶	5.56	7.32	10.34	14.86	18.42	17.36	10.42	6.67
Cognitive functioning#	3.57	7.58	6.90	11.59	10.53	11.11	11.11	13.33
Social functioning††	1.59	3.54	-5.17	2.90	-1.75	13.89	5.56	5.00
Fatigue‡‡	3.44	5.05	6.13	1.45	-1.17	-3.70	2.78	5.56
Nausea and vomiting§§	0.79	1.01	2.87	0.72	3.51	1.39	6.94	8.33
Pain¶¶	-0.40	0.00	2.30	-7.97	-0.88	2.78	9.72	15.00

For global health status/QoL and functioning scales, a higher score represents a better health status. For symptom scales, a lower score represents a better health status.
†Includes items 29 and 30 on the EORTC QLQ-C30.
‡Includes items 1–5.
§Includes items 6 and 7.
¶Includes items 21–24.
#Includes items 20 and 25.
††Includes items 26 and 27.
‡‡Includes items 10, 12 and 18.
§§Includes items 14 and 15.
¶¶Includes items 9 and 19.
C: Cycle; D: Day; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-item core; *nab*-P: *nab*-paclitaxel; *nab*-P + D: *nab*-paclitaxel + durvalumab; QoL: Quality of life.

Table 6. Mean change from baseline over time in patients treated with *nab*-paclitaxel + durvalumab (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-item core).

Assessment	C2,D1 (n = 52)	C3,D1 (n = 49)	C4,D1 (n = 43)	C5,D1 (n = 43)	C6,D1 (n = 37)	C7,D1 (n = 35)	C8,D1 (n = 31)	C9,D1 (n = 23)
Global health status/QoL†	2.08	4.59	1.55	4.07	0.45	-1.19	-1.88	0.00
Physical functioning‡	-0.90	-2.04	0.16	-0.16	-4.50	-5.14	-9.03	-9.28
Role functioning§	-5.13	-2.38	-1.55	-4.65	-4.50	-7.14	-11.83	-15.22
Emotional functioning¶	2.72	1.53	5.43	5.62	4.73	5.24	8.06	0.36
Cognitive functioning#	1.60	-0.34	0.78	2.71	0.00	3.81	-0.54	-2.17
Social functioning††	-4.49	-5.78	-1.55	-2.71	-1.80	-4.76	-5.38	-2.17
Fatigue‡‡	1.28	0.45	0.26	-1.03	5.11	5.71	9.32	12.56
Nausea and vomiting§§	-0.64	0.68	-2.33	-2.71	-4.05	-1.90	0.00	-5.07
Pain¶¶	-2.56	-0.68	0.39	-3.49	-5.41	-2.86	1.61	1.45

For global health status/QoL and functioning scales, a higher score represents a better health status. For symptom scales, a lower score represents a better health status.
†Includes items 29 and 30 on the EORTC QLQ-C30.
‡Includes items 1–5.
§Includes items 6 and 7.
¶Includes items 21–24.
#Includes items 20 and 25.
††Includes items 26 and 27.
‡‡Includes items 10, 12 and 18.
§§Includes items 14 and 15.
¶¶Includes items 9 and 19.
C: Cycle; D: Day; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-item core; *nab*-P: *nab*-paclitaxel; *nab*-P + D: *nab*-paclitaxel + durvalumab; QoL: Quality of life.

tinue to be a need for subsequent treatment options. Therefore, the promising activity [19] and QoL results of the ABOUND.2L+ trial suggest *nab*-paclitaxel monotherapy could be considered following disease progression.

There are some limitations to our study. First, 63–73% of patients completed baseline and ≥1 postbaseline QoL assessment, which may affect the interpretation of the results. As is the case in any longitudinal QoL study, patients who continue to receive treatment and whose QoL is measured tend to be those with better outcomes, and this potential survivor selection bias needs to be considered. Second, patients were not randomized to the *nab*-paclitaxel + durvalumab arm, as was done for the other arms of the ABOUND.2L+ study, and certain differences

between the arms reported here exist. Most notably, the *nab*-paclitaxel + durvalumab arm included patients with both squamous and nonsquamous histology, while the *nab*-paclitaxel alone arm only included nonsquamous histology.

Conclusion

At present, neither *nab*-paclitaxel monotherapy nor *nab*-paclitaxel + durvalumab are standards of care as subsequent therapy for NSCLC. When the ABOUND.2L+ trial was designed, pemetrexed and docetaxel were considered standards of care for subsequent therapy in NSCLC. However, an increased trend in first-line pemetrexed and potential concerns with second-line docetaxel fueled the need for more subsequent therapy options. Although *nab*-paclitaxel monotherapy or in combination with durvalumab are not standards of care for subsequent therapy, the primary publication of the ABOUND.2L+ trial reported encouraging outcomes with *nab*-paclitaxel alone [19], and the present findings suggest promising QoL trends. However, additional data are required to further support the potential use of these regimens as treatment options in this setting. Furthermore, these results may encourage future trials of additional *nab*-paclitaxel-based regimens in advanced NSCLC.

Summary points

- Quality of life (QoL) is an important consideration during treatment in patients with advanced non-small cell lung cancer (NSCLC).
- The aim of this analysis was to evaluate QoL in patients with advanced NSCLC who received *nab*-paclitaxel alone or *nab*-paclitaxel + durvalumab in the second or third line setting in the ABOUND.2L+ trial.
- A total of 80 and 79 patients were enrolled to receive *nab*-paclitaxel alone or *nab*-paclitaxel + durvalumab, respectively; 50 (62.5%) and 58 (73.4%) patients, respectively, completed a baseline and ≥1 postbaseline QoL assessment.
- Lung Cancer Symptom Scale (LCSS) total score was stable through eight treatment cycles in both arms. LCSS component and composite scores were largely stable or improved. Clinically meaningful improvement was noted in the three-item index and overall constitutional score in the *nab*-paclitaxel + durvalumab arm. Mean maximum component scores showed clinically meaningful improvement in both the *nab*-paclitaxel alone (seven of nine items) and *nab*-paclitaxel + durvalumab (eight of nine items) arms.
- EuroQoL Five-Dimensions Five-Levels scores were stable through eight treatment cycles in both arms, except for clinically meaningful deterioration in the *nab*-paclitaxel alone arm beginning with cycle 8. All domains were stable or improved in 19–56% of patients and completely resolved at least once in 9–51% of patients.
- European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-item core scores were stable or improved through eight treatment cycles, except for clinically meaningful deterioration in role functioning at later cycles. Mean maximum scores showed clinically meaningful improvement in emotional functioning and global health status/QoL in both arms, and in pain reduction in the *nab*-paclitaxel + durvalumab arm.
- QoL was generally stable or improved through eight cycles of *nab*-paclitaxel alone or *nab*-paclitaxel + durvalumab as second or third line treatment in patients with NSCLC.

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Data sharing statement

The authors certify that this manuscript reports original clinical trial data. Data requests may be submitted to Celgene, A Bristol-Myers Squibb Company at https://vivli.org/ourmember/celgene/ and must include a description of the research proposal. The source of this data is: NCT02250326.

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