ORIGINAL ARTICLE

Avelumab Versus Docetaxel in Patients With Platinum-Treated Advanced NSCLC: 2-Year Follow-Up From the JAVELIN Lung 200 Phase 3 Trial

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ABSTRACT

Introduction: In the JAVELIN Lung 200 trial, avelumab (anti-programmed death-ligand 1 [PD-L1] antibody) did not significantly prolong overall survival (OS) versus docetaxel in patients with platinum-treated PD-L1+ NSCLC. We report greater than 2-year follow-up data.

Methods: Patients with stage IIIB or IV or recurrent NSCLC with disease progression after platinum-doublet chemotherapy were randomized 1:1 to avelumab 10 mg/kg every 2 weeks or docetaxel 75 mg/m^2 every 3 weeks. The primary end point was OS in patients with PD-L1+ tumors (greater than or equal to 1% tumor cell expression; IHC 73-10 pharmDx assay).

Results: Of 792 patients, 529 had PD-L1+ tumors (264 versus 265 in the avelumab versus docetaxel arms, respectively). As of March 4, 2019, median duration of follow-up for OS in the PD-L1+ population was 35.4 months in the avelumab arm and 34.7 months in the docetaxel arm; study treatment was ongoing in 25 (9.5%) versus 0 patients, respectively. In the PD-L1+ population, 2-year OS rates (95% confidence interval [CI]) with avelumab versus docetaxel were 29.9% (24.5%–35.5%) versus 20.5% (15.6%–25.8%); in greater than or equal to 50% PD-L1+ subgroups, 2-year OS rates were 36.4% (29.1%–43.7%) versus 17.7% (11.8%–24.7%) and in the greater than or equal to 80% subgroup were 40.2% (31.3%–49.0%) versus 20.3% (12.9%–28.8%), respectively. Median duration of response (investigator assessed) was 19.1 months (95% CI: 10.8–34.8) versus 5.7 months (95% CI: 4.1–8.3). Safety profiles for both arms were consistent with the primary analysis.

Conclusions: Although the JAVELIN Lung 200 primary analysis (reported previously) revealed that avelumab did not significantly prolong OS versus docetaxel in patients with platinum-treated PD-L1+ NSCLC, posthoc analyses at 2 years of follow-up revealed that 2-year OS rates were doubled with avelumab in subgroups with higher PD-L1 expression (greater than or equal to 50% and greater than or equal to 80%).

Keywords: Avelumab; PD-L1; Non–small cell lung cancer; Second-line; Phase 3

Introduction

Since 2015, immune checkpoint inhibitors that inhibit the programmed cell death protein-1 (PD-1) or programmed death-ligand 1 (PD-L1) interaction have become established therapeutic options for the treatment of advanced NSCLC on the basis of data from randomized trials of nivolumab, pembrolizumab, and atezolizumab.[1–4]

Avelumab (anti–PD-L1) has been approved in metastatic Merkel cell carcinoma as first-line or later monotherapy, in advanced urothelial carcinoma as first-line maintenance and as second-line therapy after disease progression on platinum-based chemotherapy, and in combination with axitinib as first-line treatment for advanced renal cell carcinoma.[5,6]

Avelumab has also shown clinical activity in patients with advanced NSCLC as first-line or second-line treatment in two phase 1 cohorts.[7,8] In a subsequent phase 3 open-label trial, JAVELIN Lung 200, avelumab did not significantly improve overall survival (OS) (primary end point) compared with docetaxel in patients with stage IIIB or IV PD-L1+ (defined as expression on greater than or equal to 1% of tumor cells using the 73-10 PD-L1 assay [Agilent Technologies, Dako, Carpinteria, CA]) NSCLC who had progressed after treatment with platinum-containing doublet chemotherapy.[9] In the primary analysis, reported after a median follow-up of 18.3 months, median OS in the PD-L1+ population was 11.4 months (95% confidence interval [CI]: 9.4–13.9 mo) with avelumab versus 10.3 months (95% CI: 8.5–13.0 mo) with docetaxel (hazard ratio [HR] = 0.90 [96% CI: 0.72–1.12]). However, posthoc analyses suggested that OS was affected by the high frequency of poststudy immune checkpoint inhibitor use in the docetaxel arm.[10] Prespecified exploratory analyses from JAVELIN Lung

200 revealed longer OS with avelumab versus docetaxel in patients with tumors with higher PD-L1 expression[9]; median OS in patients with greater than or equal to 50% PD-L1 expression was 13.6 versus 9.2 months (HR = 0.67 [95% CI: 0.51–0.89]) and in patients with greater than or equal to 80% PD-L1 expression was 17.1 versus 9.3 months (HR = 0.59 [95% CI: 0.42–0.83]). The greater than or equal to 80% PD-L1 cutoff for the 73-10 assay is comparable to a tumor proportion score of greater than or equal to 50% with the 22C3 (pembrolizumab) assay, each identifying approximately 30% of patients with advanced NSCLC.[1,9,11]

We report updated data from the JAVELIN Lung 200 study with an additional 16 months of median follow-up (greater than or equal to 24 months in all patients).

Materials and Methods

Study Design and Treatment

JAVELIN Lung 200 is an open-label, multicenter, randomized phase 3 trial evaluating avelumab versus docetaxel as second-line treatment in patients with advanced NSCLC. Full eligibility criteria for this trial were reported previously.[9] Briefly, eligibility criteria included patients with histologically confirmed stage IIIB or IV or recurrent NSCLC with disease progression after platinum-doublet treatment and tumor material available for biomarker assessment, an Eastern Cooperative Oncology Group performance status of 0 or 1, and adequate hematologic, renal, and hepatic function. Patients were not eligible if they had received an immune checkpoint inhibitor therapy or systemic anticancer treatment previously after disease progression with platinum-based therapy.

The study protocol was approved by institutional review boards and ethics committees at each institution. The study was done in accordance with the trial protocol, Good Clinical Practice guidelines, and the Declaration of Helsinki, and all patients provided written informed consent.

Procedures and Assessments

All procedures, assessments, and statistical methodologies were reported previously.[9] Patients were randomized 1:1 to receive either avelumab 10 mg/kg every 2 weeks or docetaxel 75 mg/m^2 every 3 weeks. Allocation was stratified by PD-L1 status (PD-L1+ versus PD-L1−) and NSCLC histology (squamous versus nonsquamous). PD-L1+ status was defined as PD-L1 expression on greater than or equal to 1% of tumor cells, evaluated centrally using the 73-10 assay. No crossover to the avelumab arm was permitted. The primary end point was OS, and the primary analysis population was patients with PD-L1+ tumors. Analyses of PD-L1+ subgroups defined by greater than or equal to 50% and greater than or equal to 80% expression were prespecified exploratory end points. Tumors were evaluated by radiographic imaging at baseline, every 6 weeks for the first 12 months, and then every 12 weeks thereafter. In this update, tumor responses were determined by investigator assessment according to Response Evaluation Criteria in Solid Tumors version 1.1. Safety was evaluated at each treatment visit, and adverse events (AEs) were coded in accordance with Medical Dictionary for Regulatory Activities (MedDRA) version 21.1 and graded according to the National Cancer Institute Common Terminology Criteria for AEs version 4.03. Infusion-related reactions with avelumab were evaluated as AEs of special interest and identified according to a prespecified list of MedDRA-preferred terms, including infusion-related reaction, drug hypersensitivity, hypersensitivity, type 1 hypersensitivity, and anaphylactic reaction occurring on the day of or the day after the study drug infusion or various signs and symptoms of infusion-related reaction (including abdominal pain, back pain, chills, dyspnea, flushing, hypotension, pyrexia, urticaria, and wheezing) occurring on the day of the study drug infusion and resolving within 2 days. Immune-related AEs (irAEs) were identified using a prespecified list of MedDRA-preferred terms followed by a comprehensive medical review.

Results

Patient Characteristics and Disposition

In total, 792 patients were enrolled (intention-to-treat population) and randomized 1:1 to avelumab or docetaxel (396 per arm). Of these, 529 (66.8%) had PD-L1+ tumors (primary population, defined as expression on greater than or equal to 1% of tumor cells; 264 patients in the avelumab arm and 265 patients in the docetaxel arm).

Patient demographics and disease characteristics were similar between avelumab and docetaxel arms and were reported previously.[9] Briefly, in the avelumab and docetaxel arms of the PD-L1+ population, 182 (68.9%) versus 185 (69.8%) were of male sex, Eastern Cooperative Oncology Group performance status was 0 in 96 (36.4%) versus 91 (34.3%) and 1 in 168 (63.6%) versus 174 (65.7%), tumor histology was squamous in 88 (33.3%) versus 92 (34.7%) and nonsquamous in 176 (66.7%) versus 173 (65.3%), and smoking status was ever smoker in 220 (83.3%) versus 224 (84.5%), respectively. Of 792 total patients, 315 (39.8%) had greater than or equal to 50% PD-L1+ tumors (168 [21.2%] in the avelumab arm and 147 patients [18.6%] in the docetaxel arm) and 226 (28.5%) had greater than or equal to 80% PD-L1+ tumors (120 [15.2%] in the avelumab arm and 106 patients [13.4%] in the docetaxel arm).

At data cutoff (March 4, 2019), median duration of follow-up for OS in the PD-L1+ population was 35.4 months (range: 0.2–45.3 mo) for avelumab and 34.7 months (range: 0.03–44.4 mo) for docetaxel. In the PD-L1+ population, study treatment was ongoing in the avelumab arm only (25 patients [9.5%]). Reasons for permanent treatment discontinuation (avelumab versus docetaxel arm) were progressive disease (172 [65.2%] versus 153 [57.7%] patients), AE (40 [15.2%] versus 41 [15.5%]), loss to follow-up (0 versus 2 [0.8%]), withdrawal of consent (7 [2.7%] versus 17 [6.4%]), death (15 [5.7%] versus 11 [4.2%]), and other reasons (physician's decision in 2 [0.8%] versus 10 [3.8%], patient's decision in 1 [0.4%] versus 1 [0.4%], and maximum number of docetaxel cycles completed per local practice in 10 [3.8%]). Median duration of treatment was 3.4 months (range: 0.5–42.3 mo) with avelumab and 2.8 months (range: 0.7–21.8 mo) with docetaxel. In avelumab and docetaxel arms, subsequent immune checkpoint inhibitor was received by 17 patients (6.4%) versus 74 patients (27.9%), respectively. In the docetaxel arm, a higher proportion of patients received subsequent immune checkpoint inhibitor treatment among those with nonsquamous tumors (61 of 173 [35.3%]) versus squamous tumors (13 of 92 [14.1%]).

Efficacy

In the PD-L1+ population (greater than or equal to 1% expression), median OS with avelumab versus docetaxel was 11.4 months (95% CI: 9.4–13.8 mo) versus 10.6 months (95% CI: 8.5–12.9 mo), respectively (HR = 0.87 [95% CI: 0.71–1.05]; one-sided $p = 0.0721$) (Fig. 1*A*). In addition, 2-year OS rates were 29.9% (95% CI: 24.5%–35.5%) versus 20.5% (95% CI: 15.6%–25.8%), respectively. Of patients who had greater than or equal to 2-year OS in the PD-L1+ population, 10 of 77 patients (13.0%) in the avelumab arm and 30 of 45 patients (66.7%) in the docetaxel arm received subsequent immune checkpoint inhibitor therapy. The difference in OS increased with increasing PD-L1 expression (Fig. 1*B* and *C*). With avelumab versus docetaxel, 2-year OS rates in the greater than or equal to 50% PD-L1+ subgroup were 36.4% (95% CI: 29.1%–43.7%) versus 17.7% (95% CI: 11.8%–24.7%) and in the greater than or equal to 80% PD-L1+ subgroup were 40.2% (95% CI: 31.3%–49.0%) versus 20.3% (95% CI: 12.9%–28.8%), respectively. Median OS values were consistent with the primary analysis of these subgroups. In the full-analysis set (all patients irrespective of PD-L1 status), 2-year OS rates were 26.6% (95% CI: 22.3%–31.1%) in the avelumab arm versus 19.8% (95% CI: 15.9%–24.1%) in the docetaxel arm (Supplementary Fig. 1).

OS findings for avelumab versus docetaxel were different between patients with squamous versus nonsquamous NSCLC in the PD-L1+ population (Supplementary Fig. 2). In patients with squamous NSCLC, the HR for OS was 0.72 (95% CI: 0.52–1.01), and 2-year OS rates were 31.9% (95% CI: 22.4%–41.9%) with avelumab versus 16.6% (95% CI: 9.6%–25.3%) with docetaxel. In patients with squamous NSCLC with greater than or equal to 50% (n = 120) and greater than or equal to 80% (n = 80) PD-L1+ tumors, HRs were 0.64 (95% CI: 0.43–0.97) and 0.55 (95% CI: 0.34–0.90), respectively. In patients with nonsquamous NSCLC, the HR for OS was 0.95 (95% CI: 0.75–1.21), and 2-year OS rates were 28.9% (95% CI: 22.3%–35.7%) with avelumab versus 22.5% (95% CI: 16.3%–29.2%) with docetaxel. Nevertheless, in patients with nonsquamous NSCLC with greater than or equal to 50% (n = 195) and greater than or equal to 80% (n = 139) PD-L1+ tumors, HRs were 0.67 (95% CI: 0.49–0.93) and 0.67 (95% CI: 0.45–0.99), respectively. Analyses of OS in other subgroups of the PD-L1+ population were consistent with those reported previously (Fig. 2).[9] Subgroup analyses in the full-analysis set were similar.

In the PD-L1+ population, objective response rates (ORRs) by investigator assessment with avelumab and docetaxel were 18.9% (95% CI: 14.4%–24.2%) versus 10.6% (95% CI: 7.1%–14.9%), respectively. ORRs with avelumab increased with increasing PD-L1 expression (Fig. 3). ORRs in the full-analysis set were 15.2% (95% CI: 11.8%–19.1%) with avelumab versus 10.6% (95% CI: 7.8%–14.1%) with docetaxel. Median duration of response by investigator assessment in the avelumab and docetaxel arms in the PD-L1+ population was 19.1 months (95% CI: 10.8–34.8 mo) versus 5.7 months (95% CI: 4.1–8.3 mo), respectively, and differences were consistent across PD-L1 expression subgroups (Figs. 3 and 4*A* and *B*). Of responding patients in the PD-L1+ population in the avelumab (n = 50) and docetaxel (n = 28) arms, proportions with an objective response lasting greater than or equal to 2 years (calculated by Kaplan-Meier analysis) were 44.9% (95% CI: 30.3%–58.5%) in the avelumab arm compared with 4.9% (95% CI: 0.4%–19.5%) in the docetaxel arm. In the full-analysis set, median duration of response by investigator assessment in the avelumab and docetaxel arms was 15.4 months (95% CI: 10.6–30.4) versus 5.6 months (95% CI: 4.1–8.3) and responses lasted greater than or equal to 2 years in 40.6% (95% CI: 27.7%–53.1%) versus 6.1% (95% CI: 1.2%–17.2%) of responders, respectively.

Safety

The overall safety profile of avelumab with long-term follow-up was consistent with the primary analysis. Among all treated patients, AEs (related or unrelated) occurred in 375 of 393 patients (95.4%) in the avelumab

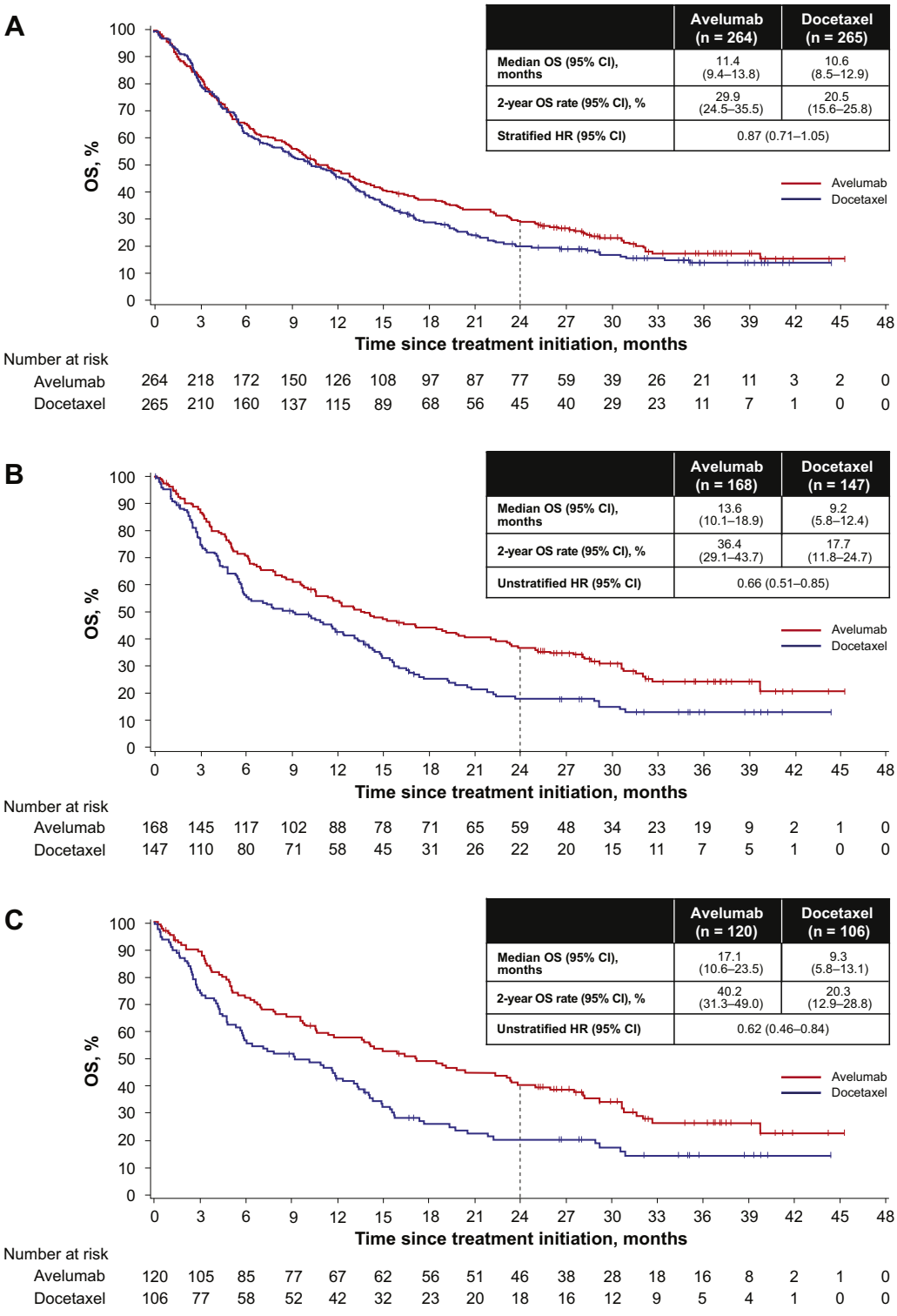


Figure 1. OS with avelumab versus docetaxel in patients with (*A*) greater than or equal to 1% PD-L1+ tumors (primary population), (*B*) greater than or equal to 50% PD-L1+ tumors, and (*C*) greater than or equal to 80% PD-L1+ tumors. CI, confidence interval; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1.

arm and 346 of 365 patients (94.8%) in the docetaxel arm (Table 1 and Supplementary Table 1). Treatment-related AEs (TRAEs) of any grade occurred in 252 patients (64.1%) in the avelumab arm (one additional patient compared with the primary analysis) and 313 patients (85.8%) in the docetaxel arm (identical to the primary analysis). In the avelumab and docetaxel arms, a grade 3 or greater TRAE occurred in 41 (10.4%) versus

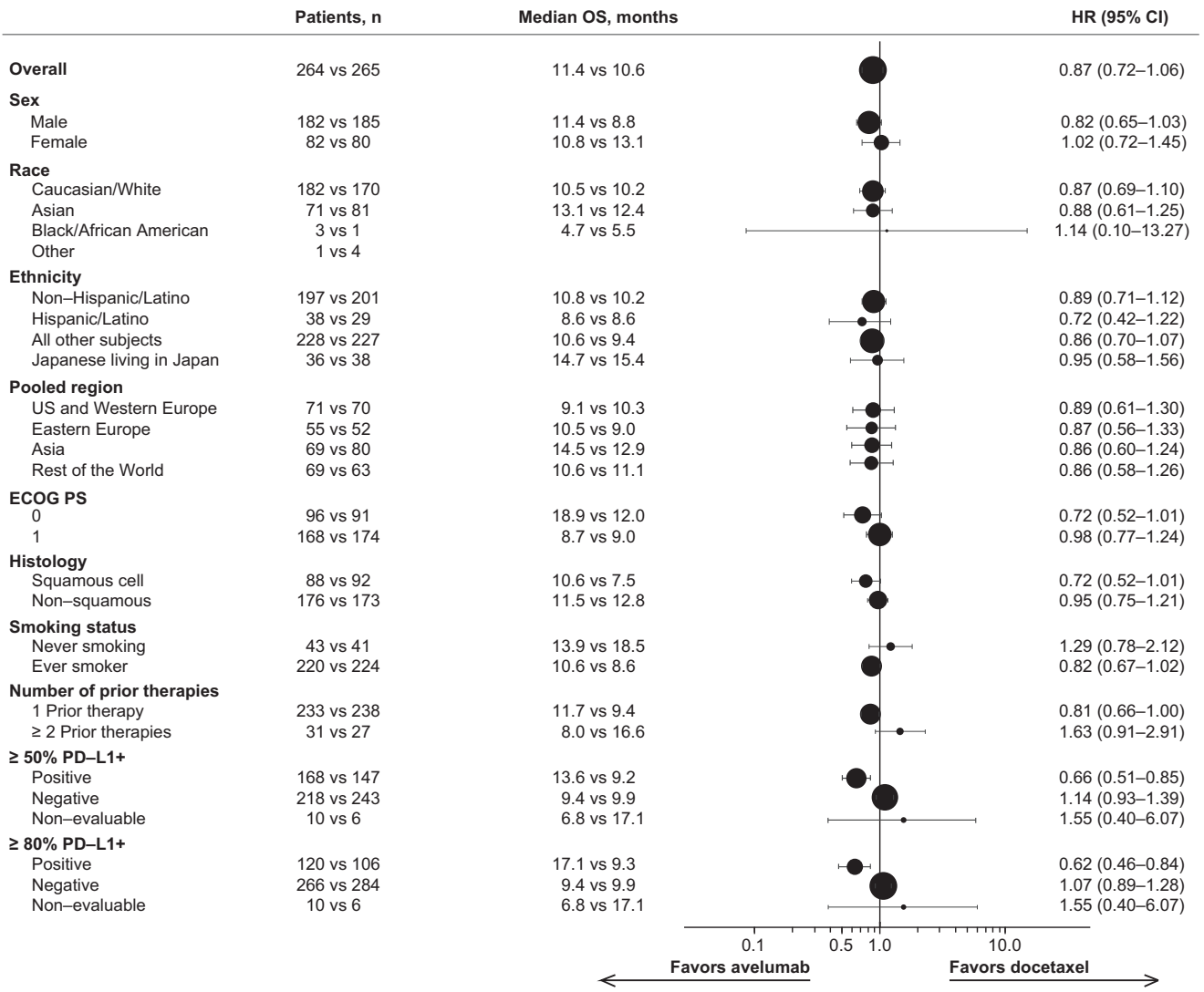
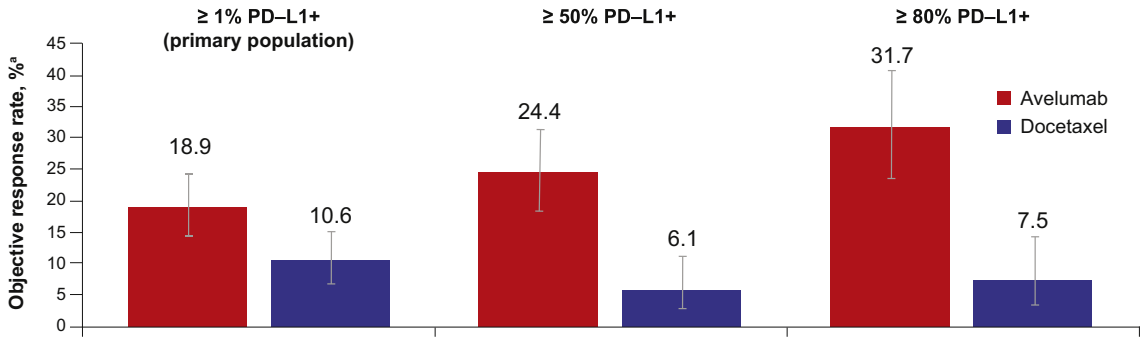


Figure 2. Subgroup analysis of OS in the PD-L1+ population. CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1.

180 (49.3%), respectively, representing two additional patients in the avelumab arm compared with the primary analysis. In the avelumab arm, the most common TRAEs of any grade were decreased appetite (34 [8.7%]), asthenia (31 [7.9%]), and fatigue (31 [7.9%]) and of grade 3 or greater were increased lipase (5 [1.3%]), increased alanine aminotransferase (3 [0.8%]; one additional patient versus the primary analysis), increased γ-glutamyltransferase (3 [0.8%]), and pneumonitis (3 [0.8%]). In the docetaxel arm, the most common TRAEs of any grade were alopecia (97 [26.6%]), anemia (69 [18.9%]), and decreased appetite (66 [18.1%]) and of grade 3 or greater were neutropenia (51 [14.0%]), febrile neutropenia (37 [10.1%]), and decreased neutrophil count (36 [9.9%]), with incidences of these TRAEs unchanged since the primary analysis.

Infusion-related reactions in the avelumab arm using an expanded definition (see Methods for signs and symptoms included) occurred at any grade in 107 patients (27.2%) and at grade 3 or greater in six patients (1.5%), unchanged from the primary analysis. In avelumab-treated patients, irAEs of any grade occurred in 68 patients (17.3%) (Supplementary Table 2). The most common irAEs were hypothyroidism (20 [5.1%]), rash (14 [3.6%], and pneumonitis (9 [2.3%]). Three additional patients had an irAE in this analysis compared with the primary analysis. Newly reported irAEs were increased blood thyroid-stimulating hormone, dermatitis acneiform, drug eruption, and skin toxicity, which each occurred in one patient (0.3%). Compared with the primary analysis, rates of the after irAEs were reported each in one additional patient: hypothyroidism, rash, increased alanine aminotransferase, increased aspartate



	Avelumab (n = 264)	Docetaxel (n = 265)	Avelumab (n = 168)	Docetaxel (n = 147)	Avelumab (n = 120)	Docetaxel (n = 106)
Odds ratio for objective response rate (95% CI)	1.98 (1.20–3.26)		4.95 (2.31–10.59)		5.68 (2.51–12.85)	
Responding patients, n	50	28	41	9	38	8
Median duration of response (95% CI), months	19.1 (10.8–34.8)	5.7 (4.1–8.3)	19.4 (10.8–34.8)	6.9 (2.8–22.3)	19.4 (10.8–34.8)	7.2 (2.8–22.3)
Duration of response ≥ 1 year (95% CI), %[b]	60.8 (45.6–73.0)	14.8 (4.7–30.4)	62.8 (46.0–75.7)	22.2 (3.4–51.3)	62.5 (45.1–75.9)	25.0 (3.7–55.8)
Duration of response ≥ 2 years (95% CI), %[b]	44.9 (30.3–58.5)	4.9 (0.4–19.5)	46.4 (30.2–61.1)	0	45.5 (29.0–60.6)	0

Figure 3. Objective response rate and duration of response by investigator assessment with avelumab versus docetaxel by PD-L1 expression. [a]Error bars reveal 95% CIs. [b]On the basis of Kaplan-Meier estimates. CI, confidence interval; PD-L1, programmed death-ligand 1.

aminotransferase, and increased blood creatine phosphokinase. Grade 3 or greater irAEs occurred in 12 patients (3.1%) with avelumab treatment in this analysis, an increase of one patient compared with the primary analysis (Supplementary Table 2). The only newly reported grade 3 or greater irAE was increased aspartate aminotransferase (1 [0.3%]). Compared with the primary analysis, rates of the following grade 3 or greater irAEs were reported each in one additional patient: increased alanine aminotransferase and increased blood creatine phosphokinase.

Discussion

Consistent with the primary analysis, 2-year follow-up from the JAVELIN Lung 200 trial showed no improvement in OS with avelumab versus docetaxel in the primary population of patients with PD-L1+ tumors (greater than or equal to 1% cutoff); however, 2-year follow-up data from this trial substantiate the previous finding of markedly increased efficacy for avelumab versus docetaxel in subgroups with higher levels of tumor PD-L1 expression (greater than or equal to 50% and greater than or equal to 80% expression cutoffs). Furthermore, 2-year OS rates for avelumab versus docetaxel in the greater than or equal to 1% PD-L1+ population were 29.9% versus 20.5%, whereas 2-year OS rates were doubled in higher PD-L1+ subgroups: 36% versus 18% in the greater than or equal to 50% subgroup and 40% versus 20% in the greater than or equal to 80% subgroup (equivalent to a tumor proportion score of greater than or equal to 50% in pembrolizumab trials[11]), respectively. Furthermore, in the greater than or equal to 80% subgroup, the ORR was increased by greater than fourfold for avelumab versus docetaxel (31.7% versus 7.5%, respectively). Of note, more than two-thirds of patients in the greater than or equal to 50% subgroup had greater than or equal to 80% PD-L1 expression, suggesting the greater than or equal to 80% subgroup may be the main driver of improved efficacy. Randomization of patients in the trial was stratified by PD-L1 status (greater than or equal to 1% expression) but not by higher PD-L1 expression, which is a limitation of the comparisons between arms in the higher PD-L1+ subgroups.

Several trials of other immune checkpoint inhibitor monotherapies in the first-line and postplatinum NSCLC settings have also reported the greatest efficacy benefits in subgroups with the highest PD-L1 expression.[1,2,12–15] Duration of response was longer with avelumab versus docetaxel irrespective of PD-L1 status (median 19.1 versus 5.7 mo in the PD-L1+ population and 15.4 versus 5.6 mo in the full-analysis set, respectively). The safety profile of avelumab after extended treatment remained consistent with the earlier analysis,[10] including a lower rate of grade 3 or greater TRAEs versus docetaxel (10.4% versus 49.3%, respectively) and only small increases in AE rates; no new safety signals were identified with prolonged treatment.

Long-term survival in a subset of patients has been reported for other anti–PD-1 and anti-PD-L1 agents in the second-line NSCLC treatment setting after 2 to 3 years of follow-up. In the phase 3 KEYNOTE-010 trial,

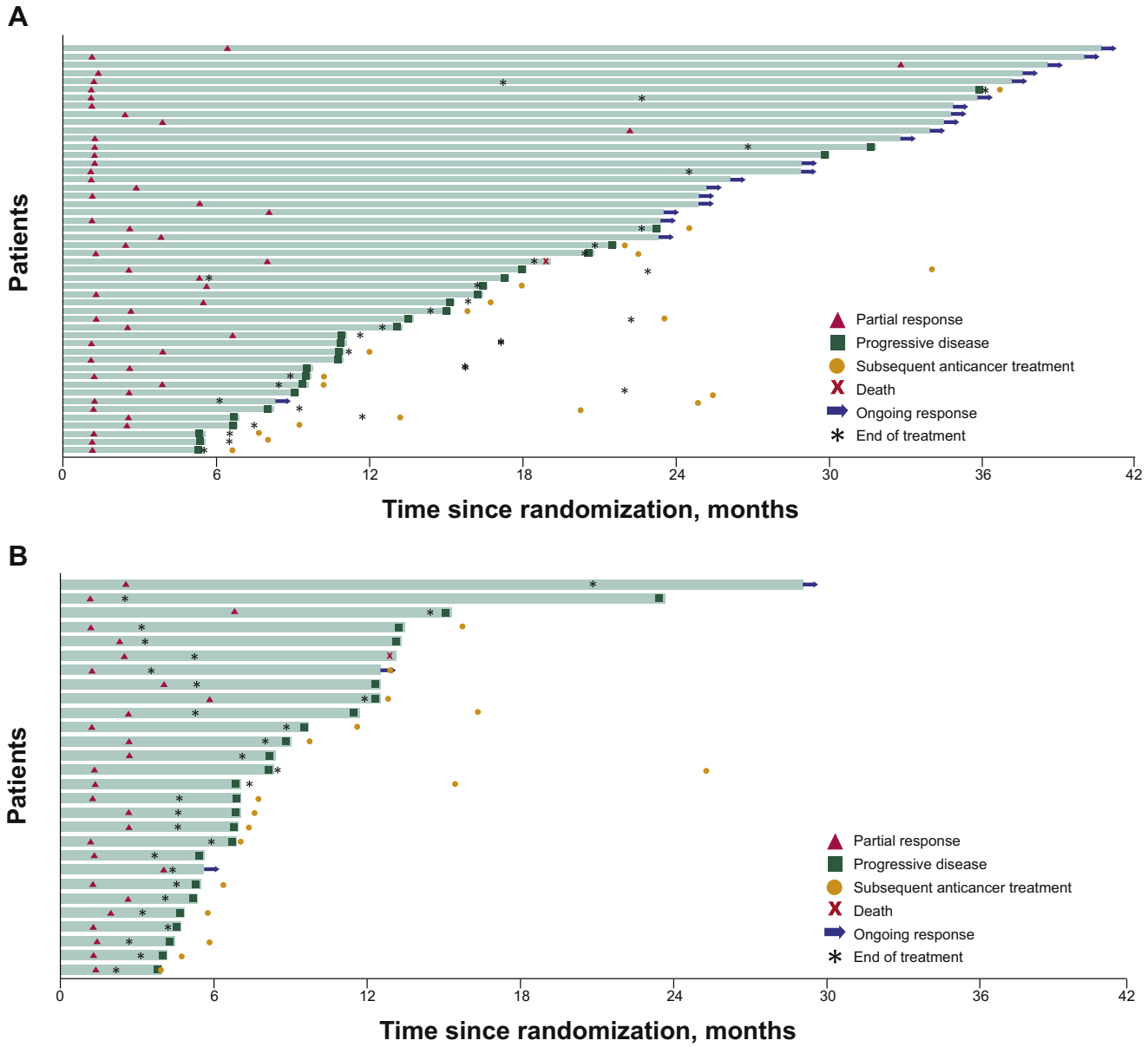


Figure 4. Time to and duration of response with (*A*) avelumab (n = 50) and (*B*) docetaxel (n = 28) by investigator assessment in the PD-L1+ population. PD-L1, programmed death-ligand 1.

36-month OS rates for pembrolizumab versus docetaxel in patients with greater than or equal to 50% PD-L1 expression were 35% versus 13%, respectively.[16] In a 2-year updated analysis from the CheckMate 017 and CheckMate 057 phase 3 trials, 2-year OS rates for nivolumab versus docetaxel were 23% versus 8% for squamous NSCLC and 29% versus 16% for nonsquamous NSCLC (both trials included patients with NSCLC unselected for PD-L1 expression).[13] In an updated analysis from the phase 3 OAK trial, 2-year OS rates for atezolizumab versus docetaxel in patients with greater than or equal to 50% PD-L1 expression (evaluated using the Ventana SP142 IHC assay) were 43% versus 17%.[17] OS rates in docetaxel arms across different studies seem to have increased over time, consistent with the increasing availability of immune checkpoint inhibitors as subsequent treatment.[17] Direct cross-trial comparison of OS rates should be interpreted with caution owing to differences in study designs and patient populations.

In this trial, patients with squamous NSCLC had a non-significant trend for longer OS with avelumab versus docetaxel, whereas OS was similar between arms in patients with nonsquamous NSCLC, as noted in the primary analysis. In the docetaxel arm, the proportion of patients who received subsequent immune checkpoint

Table 1. Overview of Safety in All Treated Patients: Comparison Between the Updated Analysis and the Primary Analysis

Category	Primary Analysis (Data Cutoff: November 22, 2017)		≥24-Mo Follow-Up (Data Cutoff: March 4, 2019)	
	Avelumab (n = 393)	Docetaxel (n = 365)	Avelumab (n = 393)	Docetaxel (n = 365)
AE (related or unrelated), n (%)				
Any grade	375 (95.4)	346 (94.8)	375 (95.4)	346 (94.8)
Grade ≥ 3	201 (51.1)	247 (67.7)	209 (53.2)	247 (67.7)
TRAE, n (%)				
Any grade	251 (63.9)	313 (85.8)	252 (64.1)	313 (85.8)
Grade ≥ 3	39 (9.9)	180 (49.3)	41 (10.4)	180 (49.3)
Serious AE, n (%)	163 (41.5)	143 (39.2)	167 (42.5)	145 (39.7)
Serious TRAE, n (%)	34 (8.7)	75 (20.5)	35 (8.9)	75 (20.5)
AE leading to permanent treatment discontinuation, n (%)	84 (21.4)	89 (24.4)	91 (23.2)	90 (24.7)
TRAE leading to permanent treatment discontinuation, n (%)	28 (7.1)	51 (14.0)	31 (7.9)	52 (14.2)
irAE, n (%)				
Any grade	65 (16.5)	NA	68 (17.3)	NA
Grade ≥ 3	11 (2.8)	NA	12 (3.1)	NA
Death owing to AE, n (%)	64 (16.3)	49 (13.4)	64 (17.3)	51 (14.0)
Death owing to TRAE, n (%)	3 (0.8)	14 (3.8)	3 (0.8)	14 (3.8)

AE, adverse event; irAE, immune-related adverse event; NA, not applicable; TRAE, treatment-related adverse event.

inhibitor treatment was lower in those with squamous versus nonsquamous histology (14% versus 35%).

Since the JAVELIN Lung 200 trial was initiated, use of ICIs as first-line treatment for NSCLC without *EGFR* or *ALK* genomic tumor aberrations, either as monotherapy or within combination regimens, has become standard.[18] A phase 3 trial, JAVELIN Lung 100 (NCT02576574), is evaluating avelumab monotherapy as first-line treatment versus platinum-based doublet therapy in patients with PD-L1+ NSCLC. The primary-analysis population is patients with high PD-L1–expressing tumors (greater than or equal to 80% expression on tumor cells using the 73-10 assay).[19]

In conclusion, 2-year follow-up data from the JAVELIN Lung 200 trial suggested that a subset of patients experienced long-term efficacy benefits with avelumab, which were increased with increasing tumor PD-L1 expression. No new safety signals were observed, and avelumab continued to have a lower rate of TRAEs compared with docetaxel.

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Supplementary Data

To access the supplementary material accompanying this article, visit the online version of the *Journal of Thoracic Oncology* at www.jto.org and at https://doi.org/10.1016/j.jtho.2021.03.009.

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