Subgroup Analysis of Japanese Patients in a Phase III Study of Atezolizumab in Extensive-stage Small-cell Lung Cancer (IMpower133)

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Abstract

Atezolizumab is effective and well-tolerated in patients with extensive-stage small-cell lung cancer (ES-SCLC). We examined atezolizumab's efficacy and safety in 42 Japanese patients with ES-SCLC via a subanalysis of the phase I/III IMpower133 trial. Addition of atezolizumab to chemotherapy improved overall survival and was generally well-tolerated, thus offering a potentially new treatment for Japanese patients with ES-SCLC.

Background: Atezolizumab is effective and well-tolerated in patients with extensive-stage small-cell lung cancer (ES-SCLC), but differences in response to systemic therapy exist between Asian and Caucasian patients. Here, we assess the efficacy and tolerability of atezolizumab in Japanese patients from the IMpower133 trial (NCT02763579). **Patients and Methods:** Key eligibility criteria for this multicenter, double-blind, placebo-controlled, randomized study included age $\geq$ 18 years; histologically or cytologically confirmed ES-SCLC, measurable per Response Evaluation Criteria in Solid Tumors version 1.1; an Eastern Cooperative Oncology Group performance status of 0/1; and no prior systemic treatment for ES-SCLC. Patients were treated with either atezolizumab 1200 mg or placebo with carboplatin (area under the curve of 5 mg/mL/min) and etoposide (100 mg/m^2). Primary endpoints were overall survival and investigator-assessed progression-free survival in the intention-to-treat population. Of the 403 patients randomized in the IMpower133 trial, 42 were enrolled at Japanese centers. **Results:** In Japanese patients in the intention-to-treat population, the median overall survival in the atezolizumab group (n = 20) was longer than that in the placebo group (n = 22; 14.6 months; 95% confidence interval [CI], 11.8-17.8 months vs. 11.9 months; 95% CI, 8.4-15.8, respectively; hazard ratio, 0.72; 95% CI, 0.31-1.67). The median progression-free survival was 4.5 months (95% CI, 4.2-8.1 months) versus 4.0 months (95% CI, 2.9-5.6 months; hazard ratio, 0.47; 95% CI, 0.23-0.96), respectively. Atezolizumab was generally well-tolerated, with no treatment-related deaths. **Conclusion:** The addition of atezolizumab to carboplatin and etoposide was effective and well-tolerated in Japanese patients with ES-SCLC. Results are consistent with the primary analysis of the IMpower133 trial.

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Introduction

Limited progress has been made in the development of new treatments for extensive-stage small-cell lung cancer (ES-SCLC) in the past 30 years.[1] The current standard-of-care first-line treatment is platinum chemotherapy with etoposide.[2,3] Despite good response rates to first-line treatment, patient outcomes remain poor, with a median overall survival (OS) of approximately 10 months.[4,5]

SCLC has a high mutation rate, which may render it susceptible to immune checkpoint inhibition.[6-8] Atezolizumab is a humanized monoclonal anti-programmed death-ligand 1 (PD-L1) antibody that inhibits PD-L1—programmed death-1 protein and PD-L1—B7-1 signaling and restores tumor-specific T-cell immunity.[9,10] In patients with non—small-cell lung cancer, the combination of atezolizumab with bevacizumab and chemotherapy has shown better outcomes than bevacizumab and chemotherapy alone.[11] This supports the rationale for exploring treatment combinations with chemotherapy for patients with ES-SCLC.

The IMpower133 trial evaluated the efficacy and safety of adding atezolizumab or placebo to first-line treatment with carboplatin and etoposide in patients with ES-SCLC.[12] Overall, the trial met its primary endpoints of OS and progression-free survival (PFS). In patients treated with atezolizumab compared with placebo, the data showed improvements in OS (12.3 vs. 10.3 months) and PFS (5.2 vs. 4.3 months). At the time of data cutoff, more patients had an ongoing response in the atezolizumab group than the placebo group. Additionally, the safety profile of the atezolizumab treatment regimen (atezolizumab + carboplatin + etoposide) was in line with the defined toxic effects of its individual agents.

Pharmacokinetic modelling has suggested that ethnicity does not impact the pharmacokinetics of immune checkpoint inhibitors.[13] However, differences in systemic therapy outcomes and toxicities exist between Asian and Caucasian patients with lung cancer.[14] Genetic and physical differences, in terms of height and body weight, between Asian and Caucasian patient populations can alter the efficacy and incidence of treatment-related adverse events.[15] Therefore, it is of interest to assess whether the efficacy and tolerability of atezolizumab differ between Japanese patients and the global population. This subgroup analysis of the IMpower133 trial assesses the efficacy and safety of atezolizumab in the Japanese subpopulation.

Patients and Methods

Study Design

IMpower133 (NCT02763579) is a phase I/III, multicenter, double-blind, placebo-controlled, randomized study evaluating atezolizumab plus carboplatin and etoposide in treatment-naive patients with ES-SCLC. Details of the overall study design were previously reported.[12] The trial was conducted in accordance with Good Clinical Practice guidelines and the provisions of the Declaration of Helsinki. Ethics approval was obtained from each participating institution's institutional review board or ethics committee.

Patients

Key eligibility criteria included age ≥ 18 years; histologically or cytologically confirmed ES-SCLC as defined by the Veterans Administration Lung Study Group staging system,[16] which was measurable according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1; an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1; and no prior systemic treatment for ES-SCLC. Patients with treated asymptomatic central nervous system metastases were also eligible for enrollment. Key exclusion criteria were the presence of active or untreated central nervous system metastases, a history of autoimmune disease, and previous treatment with immune checkpoint blockade therapies or CD137 agonists. All patients provided written informed consent. Of the 403 patients randomized in the IMpower133 trial, 42 were enrolled at Japanese centers. Twenty patients were randomized to the atezolizumab group and 22 to the placebo group. Among the 361 (89.6%) non-Japanese patients in the IMpower133 trial, 27 (7.5%) were non-Japanese Asian (see Supplemental Table 1 in the online version).

Treatments

Enrolled patients were randomized in a 1:1 ratio to receive 4 21-day cycles of carboplatin (area under the curve of 5 mg/mL/min, day 1 of each cycle) and etoposide (100 mg/m^2 of body surface area, days 1-3 of each cycle) with either atezolizumab (1200 mg, day 1 of each cycle) or placebo in the induction phase. This was followed by a maintenance phase of atezolizumab or placebo, per randomization group, until disease progression per RECIST 1.1 or the occurrence of unacceptable toxicity. Continuation of study treatment beyond disease progression in either phase was allowed if there was evidence of clinical benefit. Prophylactic cranial irradiation was permitted during the maintenance phase, but thoracic radiation therapy was not. PD-L1 testing was not performed during screening for reasons previously described.[12]

Assessments and Endpoints

Tumor assessments were conducted at baseline, then every 6 weeks for the first 48 weeks, and every 9 weeks thereafter until disease progression per RECIST 1.1. Patients who continued treatment beyond disease progression were assessed every 6 weeks until treatment discontinuation. The primary endpoints were OS and investigator-assessed PFS in the intention-to-treat (ITT) population. Key secondary endpoints included investigator-assessed objective response rate (ORR) per RECIST 1.1 and duration of response. Adverse events (AEs) were assessed per National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0, and treatment-related AEs were determined by the investigators. In this subgroup analysis, we report the primary and secondary endpoints in Japanese patients. We also report the safety of the trial regimen in Japanese patients and compare it with that previously reported in the ITT population.[12]

Statistical Analysis

Details of the statistical analysis have been previously described.[12] Briefly, it was calculated that 306 deaths in the ITT population would be needed to provide 91% power at a 2-sided significance level of 0.045, using a log-rank test, to detect a hazard ratio (HR) of 0.68 for OS with atezolizumab compared with placebo. One interim analysis of OS was performed when 238 deaths had occurred (data cutoff date, April 24, 2018), with a 2-sided α level of 0.0193 (stopping boundary), computed on the basis of the

Lan-DeMets function approximating the O'Brien-Fleming boundary.[17] The primary analysis of PFS was conducted at the time of the interim analysis of OS. No interim analysis of PFS was planned.

Results

Patients and Treatments

The median follow-up duration for Japanese patients was 16.5 months (range, 5.3-17.8 months) in the atezolizumab group and 15.3 months (range, 0.5-16.6 months) in the placebo group. The median duration of treatment was 4.7 months (range, 2.0-16.6 months) and 3.3 months (range, 0.0-15.2 months) in the atezolizumab and placebo groups, respectively. Baseline characteristics were largely balanced between both treatment groups apart from age, gender, baseline ECOG PS, and baseline brain metastases (Table 1). A greater proportion of Japanese patients received ≥ 2 subsequent lines of therapy compared with non-Japanese patients (2 subsequent lines, 69.0% vs. 52.1%; 3 subsequent lines, 40.5% vs. 13.9%; 4 subsequent lines: 16.7% vs. 3.0%, respectively) (Table 2).

Efficacy

In Japanese patients from the ITT population, the median OS in the atezolizumab group was 14.6 months (95% confidence interval [CI], 11.8-17.8 months) compared with 11.9 months (95% CI, 8.4-15.8 months) in the placebo group (HR, 0.72; 95% CI, 0.31-1.67) (Figure 1A). Japanese patients in the atezolizumab group had a longer PFS (4.5 months; 95% CI, 4.2-8.1 months) than those in the placebo group (4.0 months; 95% CI, 2.9-5.6 months) (Figure 1B). This was consistent with the findings from the overall IMpower133 population (Japanese population: HR, 0.47; 95% CI, 0.23-0.96; overall IMpower133 population: HR, 0.77; 95% CI, 0.62-0.96; $P = .02$).

Investigator-assessed confirmed ORRs were higher in the atezolizumab group than the placebo group for Japanese patients (Table 3). Fifteen (75%) patients in the atezolizumab group had a partial response compared with 11 (50%) patients in the placebo group. There were no complete responses. These data are numerically higher than the ORR of 60.2% for the atezolizumab group in the overall IMpower133 population. The duration of response between the atezolizumab and placebo groups in the ITT Japanese population was comparable (HR, 0.90; 95% CI, 0.38-2.09).

Safety

There was a numerically higher rate of all-cause grade 3/4 AEs in Japanese patients than non-Japanese patients (atezolizumab, 95.0% vs. 64.0%; placebo, 86.4% vs. 60.9%) and a higher rate of treatment-related grade 3/4 AEs (atezolizumab, 95.0% vs. 52.2%; placebo, 86.4% vs. 52.3%) (Table 4). There were no treatment-related deaths or AEs leading to treatment withdrawal in Japanese patients compared with 3 treatment-related deaths and 22 AEs leading to treatment withdrawal in non-Japanese patients. The rate of serious AEs was numerically lower in the Japanese atezolizumab group (25.0%) than in the non-Japanese atezolizumab group (38.8%).

The most frequent all-grade atezolizumab-related AEs were decreased neutrophil count (75.0%), alopecia (70.0%), constipation (65.0%), decreased platelet count (55.0%), and anemia and decreased appetite (50.0% each) (Table 5). Grade ≥ 3 AEs were reported in 19 (95.0%) patients in the atezolizumab group and 21 (95.5%) patients in the placebo group. All-grade AEs of special interest occurred in 14 (70.0%) patients in the atezolizumab group and 9 (40.9%) patients in the placebo group (Table 6). The most frequently occurring all-grade AEs of special interest in patients receiving atezolizumab were rash (20.0%) and dry skin and peripheral sensory neuropathy (15.0% each). Most AEs of special interest were grade 1/2, regardless of the treatment group.

Table 1 Demographics and Baseline Characteristics of the Japanese Subpopulation

	Atezolizumab (n = 20)	Placebo (n = 22)	All Patients (N = 42)
Age, y			
Median	67.5	69.0	68.5
Range	46-80	56-87	46-87
Age group (y), n (%)			
<65	9 (45.0)	6 (27.3)	15 (35.7)
≥65	11 (55.0)	16 (72.7)	27 (64.3)
Age group (y), n (%)			
<65	9 (45.0)	6 (27.3)	15 (35.7)
65-74	6 (30.0)	10 (45.5)	16 (38.1)
75-84	5 (25.0)	5 (22.7)	10 (23.8)
≥85	0	1 (4.5)	1 (2.4)
Gender, n (%)			
Male	17 (85.0)	17 (77.3)	34 (81.0)
Female	3 (15.0)	5 (22.7)	8 (19.0)
Baseline ECOG PS, n (%)			
0	8 (40.0)	5 (22.7)	13 (31.0)
1	12 (60.0)	17 (77.3)	29 (69.0)
Tobacco use history, n (%)			
Never	1 (5.0)	1 (4.5)	2 (4.8)
Current	5 (25.0)	3 (13.6)	8 (19.0)
Previous	14 (70.0)	18 (81.8)	32 (76.2)
Brain metastases, n (%)			
Yes	4 (20.0)	2 (9.1)	6 (14.3)
No	16 (80.0)	20 (90.9)	36 (85.7)
bTMB biomarker expression, n (%)			
<10	11 (57.9)	8 (40.0)	19 (48.7)
≥10	8 (42.1)	12 (60.0)	20 (51.3)
<16	17 (89.5)	15 (75.0)	32 (82.1)
≥16	2 (10.5)	5 (25.0)	7 (17.9)
SLD at baseline			
Median	98.6	100.5	100.5
Range	12.0-171.9	32.0-218.0	12.0-218.0

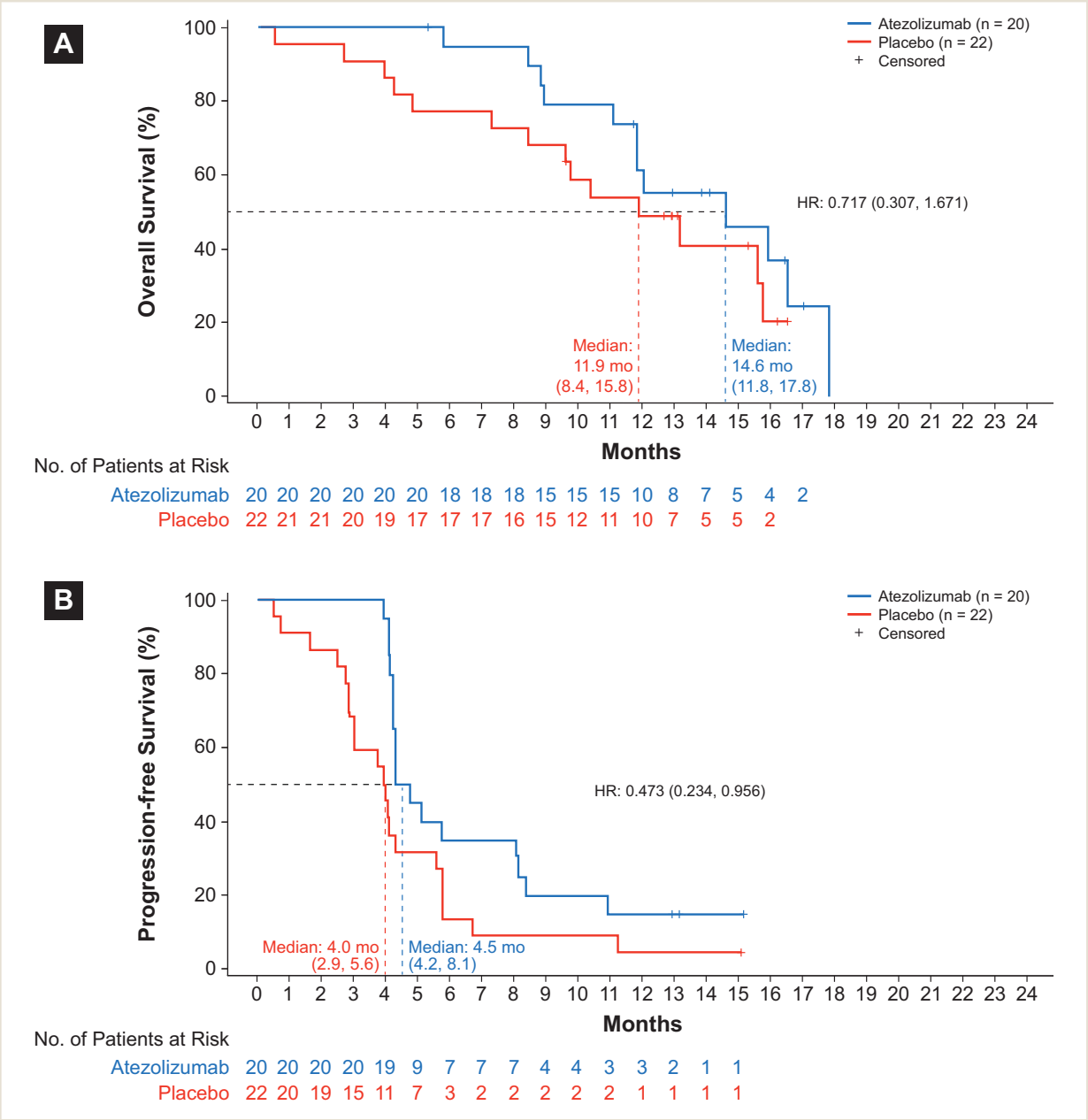
Abbreviations: bTMB = blood-based tumor mutational burden; ECOG PS = Eastern Cooperative Oncology Group performance status; SLD = sum of longest diameters.

Table 2 Subsequent Lines of Therapy Received

Subsequent Lines of Therapy Received	Japanese, n (%)			Non-Japanese, n (%)		
	Atezolizumab (n = 20)	Placebo (n = 22)	All Patients (N = 42)	Atezolizumab (n = 181)	Placebo[a] (n = 180)	All Patients (N = 361)
2	13 (65.0)	16 (72.7)	29 (69.0)	88 (48.6)	100 (55.6)	188 (52.1)
3	7 (35.0)	10 (45.5)	17 (40.5)	22 (12.2)	28 (15.6)	50 (13.9)
4	1 (5.0)	6 (27.3)	7 (16.7)	2 (1.1)	9 (5.0)	11 (3.0)

[a]Data missing for 1 patient in the placebo group.

Figure 1 Overall Survival (A) and Investigator-assessed Progression-free Survival (B) in the Japanese Population. Hazard ratios are shown with 95% confidence intervals



Abbreviation: HR = hazard ratio.

Table 3 Response Rate, Duration of Response, and Disease Progression

	Atezolizumab (n = 20)	Placebo (n = 22)
Objective confirmed response, n (%)		
Objective response	15 (75.0)	11 (50.0)
Complete response	0	0
Partial response	15 (75.0)	11 (50.0)
Stable disease	5 (25.0)	5 (22.7)
Progressive disease	0	5 (22.7)
Missing or unevaluable	0	1 (4.5)
Duration of response, mos		
Median (95% confidence interval)	3.4 (2.9-6.6)	4.2 (2.8-5.4)
Ongoing response at data cutoff		
Patients with response/ total patients, n/N (%)	3/15 (20)	1/11 (9.1)

Discussion

Several studies in Japan have investigated various drug combinations for the treatment of ES-SCLC—irinotecan with cisplatin,[18] amrubicin with carboplatin,[19] topotecan with cisplatin,[20] and amrubicin and topotecan[21]—but no trials have included immune checkpoint inhibitors. To our knowledge, the current subanalysis of the IMpower133 trial is the first investigation of the efficacy and safety of atezolizumab in Japanese patients with ES-SCLC. Atezolizumab was found to be efficacious in Japanese patients and resulted in a longer PFS than placebo. Although the median PFS in Japanese patients who received atezolizumab was lower (4.5 months) than the overall ITT population (5.4 months), the positive HR for PFS (HR, 0.47; 95% CI, 0.23-0.96) in this analysis suggests that atezolizumab may be equally effective in both populations. Response rates with atezolizumab were also higher than those with placebo. These data are similar to the findings from the overall IMpower133 population.[12] A numerically longer OS was observed in Japanese patients who received atezolizumab than in Japanese patients who received placebo. The numerically longer OS observed in Japanese patients is greater than the OS reported in patients treated with atezolizumab in the overall IMpower133 population, possibly owing to a greater proportion of Japanese patients receiving $\geq$ 2 subsequent lines of therapy.

Atezolizumab was generally well-tolerated with no treatment-related deaths. Although there were numerically higher rates of all-cause and treatment-related grade 3/4 AEs in the Japanese population than in the non-Japanese IMpower133 population, the rate of serious AEs was numerically lower.[12] This difference is likely due to the increased hematotoxicity observed in Japanese patients who receive carboplatin and etoposide. In this study, grade $\geq$ 3 neutrophil count decrease was observed in 68.2% of patients in the placebo group compared with 16.8% in the placebo group from the overall IMpower133 population.[12] Differences in the incidence of AEs between Japanese and non-Japanese patients may also be attributed to the lower body weights of the former, which may affect the physiologic concentrations of fixed-dose drug formulations.[15]

It has been noted that Japanese patients may be more vulnerable to immune checkpoint inhibitor-induced interstitial lung disease than Caucasian patients.[22] In this subanalysis, only 1 (5%) patient from the atezolizumab-treated group was reported to have pneumonitis. However, the incidence of pneumonitis in the overall IMpower133 ITT population was 2%, which is equivalent to < 1 case for every 40 patients. Given the small sample size in this subanalysis (n = 42), one cannot conclude that there was a lower rate of interstitial lung disease in the Japanese ITT population.

The limitations of this analysis include its small sample size, which limits direct comparisons between Japanese and non-Japanese subpopulations and the overall IMpower133 population. Also, the current analysis of the Japanese subpopulation was not powered for

Table 4 Summary of AEs in Japanese and Non-Japanese Patients

	Japanese, n (%) (n = 42)		Non-Japanese, n (%) (n = 352)	
	Atezolizumab (n = 20)	Placebo (n = 22)	Atezolizumab (n = 178)	Placebo (n = 174)
All-cause AEs	20 (100)	22 (100)	178 (100)	167 (96.0)
Treatment-related AEs	20 (100)	22 (100)	168 (94.4)	159 (91.4)
All-cause grade 3/4 AEs	19 (95.0)	19 (86.4)	114 (64.0)	106 (60.9)
Treatment-related grade 3/4 AEs	19 (95.0)	19 (86.4)	93 (52.2)	91 (52.3)
All deaths	0	2 (9.1)	4 (2.2)	9 (5.2)
Treatment-related deaths	0	0	3 (1.7)	3 (1.7)
Serious AEs	5 (25.0)	8 (36.4)	69 (38.8)	60 (34.5)
AEs leading to withdrawal from any treatment	0	0	22 (12.4)	6 (3.4)
AEs leading to withdrawal from carboplatin	0	0	5 (2.8)	1 (0.6)
AEs leading to withdrawal from etoposide	0	0	8 (4.5)	2 (1.1)

Abbreviation: AE = adverse event.

Table 5 Adverse Events Occurring in ≥ 10% of Patients

	Atezolizumab, n (%) (n = 20)		Placebo, n (%) (n = 22)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Patients with ≥ 1 event	20 (100)	19 (95.0)	22 (100)	21 (95.5)
Neutrophil count decreased	15 (75.0)	14 (70.0)	15 (68.2)	15 (68.2)
Alopecia	14 (70.0)	0	11 (50.0)	0
Constipation	13 (65.0)	2 (10.0)	15 (68.2)	0
Platelet count decreased	11 (55.0)	4 (20.0)	13 (59.1)	4 (18.2)
Anemia	10 (50.0)	3 (15.0)	12 (54.5)	2 (9.1)
Decreased appetite	10 (50.0)	0	5 (22.7)	0
Nausea	9 (45.0)	0	5 (22.7)	0
White blood cell count decreased	8 (40.0)	3 (15.0)	13 (59.1)	7 (31.8)
Leukopenia	6 (30.0)	3 (15.0)	3 (13.6)	1 (4.5)
Neutropenia	4 (20.0)	4 (20.0)	6 (27.3)	6 (27.3)
Malaise	4 (20.0)	0	4 (18.2)	0
Rash	4 (20.0)	0	0	0
Stomatitis	3 (15.0)	0	2 (9.1)	0
Dysgeusia	3 (15.0)	0	1 (4.5)	0
Peripheral sensory neuropathy	3 (15.0)	0	0	0
Dry skin	3 (15.0)	0	0	0
Diarrhea	2 (10.0)	0	4 (18.2)	0
Hiccups	2 (10.0)	0	3 (13.6)	0
Vomiting	2 (10.0)	0	2 (9.1)	0
Thrombocytopenia	2 (10.0)	0	2 (9.1)	0
Hyperglycemia	2 (10.0)	1 (5.0)	1 (4.5)	1 (4.5)
Pharyngitis	2 (10.0)	0	1 (4.5)	0
Blood creatinine increased	2 (10.0)	0	1 (4.5)	0
Rash, maculopapular	2 (10.0)	0	0	0
Pruritus	2 (10.0)	0	0	0
Febrile neutropenia	1 (5.0)	1 (5.0)	4 (18.2)	4 (18.2)
Pyrexia	1 (5.0)	0	4 (18.2)	0
Pneumonia	1 (5.0)	0	3 (13.6)	3 (13.6)
Lung infection	1 (5.0)	0	3 (13.6)	2 (9.1)

efficacy comparisons. Notably, the dosages of carboplatin and etoposide used in this study were higher than those in the Japanese treatment guidelines for ES-SCLC, which recommend carboplatin area under the curve of 5 mg/mL/min and etoposide 80 mg/m^2 for patients > 70 years with ECOG PS 0 to 2 or for patients with ECOG PS 3.[23] Despite this, there were no treatment-related deaths or AEs leading to treatment withdrawal in Japanese patients. The rate of serious AEs was numerically lower in the Japanese atezolizumab group (25.0%) than in the non-Japanese atezolizumab group (38.8%). The current analysis provides additional insights into the efficacy and safety of atezolizumab in Japanese patients.[24]

Platinum chemotherapy plus etoposide is the most frequently prescribed first-line therapy for ES-SCLC, although its use is less common in Japan than in the United States and Europe (73.3% vs. 87.0% and 82.1%, respectively).[25] Data from the Japan Clinical Oncology Group trial JCOG 9511 reported improved outcomes with cisplatin and irinotecan compared with cisplatin and etoposide.[18] As a result, Japanese patients with ES-SCLC tend to receive either cisplatin (60 mg/m^2) and irinotecan (60 mg/m^2) or cisplatin (80 mg/m^2) and etoposide (100 mg/m^2).[23] However, enrollment to JCOG 9511 was stopped early, and the data have never been confirmed in other trials outside of Japan.[26-29] This difference in prescribed chemotherapy regimens for ES-SCLC between Japan and the United States and Europe may be due to differences in response to chemotherapy, which may arise from pharmacogenomic differences between the Japanese and non-Japanese patient populations.[30] Our data suggest that response to atezolizumab does not seem to differ between Japanese and non-Japanese patients, although we note numerical increases in OS and PFS despite the small cohort size. Additionally, the efficacy of atezolizumab with different chemotherapy backbones (eg, carboplatin + etoposide vs. cisplatin + irinotecan) in Japanese patients with ES-SCLC warrants further investigation. The findings of this subanalysis could help to broaden therapeutic options for Japanese patients with ES-SCLC.

Conclusion

The addition of atezolizumab to carboplatin and etoposide was effective and well-tolerated in Japanese patients with ES-SCLC.

Table 6 Summary of Adverse Events of Special Interest

	Atezolizumab Group, n (%) (n = 20)		Placebo Group, n (%) (n = 22)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Patients with ≥ 1 event	14 (70.0)	2 (10.0)	9 (40.9)	2 (9.1)
Rash	4 (20.0)	0	0	0
Dry skin	3 (15.0)	0	0	0
Peripheral sensory neuropathy	3 (15.0)	0	0	0
Diarrhea	2 (10.0)	0	4 (18.2)	0
Pruritus	2 (10.0)	0	0	0
Rash, maculopapular	2 (10.0)	0	0	0
Alanine aminotransferase increased	1 (5.0)	1 (5.0)	2 (9.1)	0
Cheilitis	1 (5.0)	0	1 (4.5)	0
Aspartate aminotransferase increased	1 (5.0)	0	1 (4.5)	0
γ-glutamyltransferase increased	1 (5.0)	1 (5.0)	0	0
Liver function test increased	1 (5.0)	1 (5.0)	0	0
Pancreatitis acute	1 (5.0)	1 (5.0)	0	0
Pneumonitis	1 (5.0)	1 (5.0)	0	0
Angular cheilitis	1 (5.0)	0	0	0
Toxic skin eruption	1 (5.0)	0	0	0
Hypothyroidism	1 (5.0)	0	0	0
Hyperthyroidism	1 (5.0)	0	0	0
Lipase increased	0	0	1 (4.5)	1 (4.5)
Oliguria	0	0	1 (4.5)	1 (4.5)

Results are consistent with the primary analysis of the IMpower133 trial.

Clinical Practice Points

- Patients with ES-SCLC have poor outcomes and few treatment options.
- The addition of atezolizumab to carboplatin and etoposide was shown to be safe and effective in the IMpower133 patient population, but there are recognized differences in response to systemic therapy between Asian and white patients with lung cancer.
- The present analysis shows that the addition of atezolizumab to carboplatin and etoposide is effective and well-tolerated in Japanese patients with ES-SCLC, and these results are consistent with the primary analysis of the IMpower133 trial.
- The findings of this subanalysis could help to broaden therapeutic options and may make the addition of atezolizumab to carboplatin and etoposide the standard-of-care for Japanese patients with ES-SCLC.

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Disclosure

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Supplemental Data

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Supplemental Data

Supplemental Table 1 Patients in the Non-Japanese ITT Population

	Atezolizumab, n (%) (n = 201)	Placebo, n (%) (n = 202)	All Patients, n (%) (N = 403)
Japanese in ITT	20 (10.0)	22 (10.9)	42 (10.4)
Non-Japanese in ITT	181 (90.0)	180 (89.1)	361 (89.6)
Asian[a,b]	13 (7.2)	14 (7.8)	27 (7.5)
American Indian or Alaska Native[a]	0 (0)	1 (0.6)	1 (0.3)
Black or African American[a]	1 (0.6)	2 (1.1)	3 (0.8)
White[a]	163 (90.0)	159 (88.3)	322 (89.2)
Unknown[a]	4 (2.2)	4 (2.2)	8 (2.2)

Abbreviation: ITT = intention to treat.
[a]Percentage values calculated using the non-Japanese ITT patient numbers as a denominator.
[b]Does not include Japanese patients.