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CONQUERING THORACIC CANCERS WORLDWIDE

IMpower133: exploratory analysis of maintenance therapy in patients with extensive-stage small cell lung cancer

Martin Reck,[1] Leora Horn,[2] Tony S. K. Mok,[3] Aaron S. Mansfield,[4] Richard De Boer,[5] Gyorgy Losonczy,[6] Shunichi Sugawara,[7] Rafal Dziadziuszko,[8] Maciej Krzakowski,[9] Alexey Smolin,[10] Maximilian Hochmair,[11] Marina Garassino,[12] Gilberto Castro,[13] Helge Bischoff,[14] Andres Cardona,[15] Stefanie Morris,[15] Stephen V. Liu[16]

[1] Lung Clinic Grosshansdorf, Airway Research Center North, German Center of Lung Research, Grosshansdorf, Germany; [2] Vanderbilt University Medical Center, Nashville, TN, USA; [3] The Chinese University of Hong Kong, Hong Kong; [4] Division of Medical Oncology, Mayo Clinic, Rochester, MN, USA; [5] Peter MacCallum Cancer Centre, Melbourne, Australia; [6] Semmelweis Egyetem ÁOK, Budapest, Hungary; [7] Sendai Kousei Hospital, Sendai, Japan; [8] Medical University of Gdansk, Gdansk, Poland; [9] Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [10] Burdenko Main Military Hospital, Moscow, Russia; [11] Karl Landsteiner Institute of Lung Research and Pulmonary Oncology, Vienna North Hospital – Klinik Floridsdorf, Vienna, Austria; [12] Thoracic Oncology Unit, Instituto Nazionale dei Tumori, Milan, Italy; [13] Instituto de Cancer do Estado de São Paulo, Hospital das Clínicas da FMUSP, São Paulo, Brazil; [14] Thoraxklinik Heidelberg gGmbH – Universität Heidelberg, Heidelberg, Germany; [15] F. Hoffmann-La Roche Ltd, Basel, Switzerland; [16] Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA

Disclosures

- Dr Reck has the following relationships to disclose:
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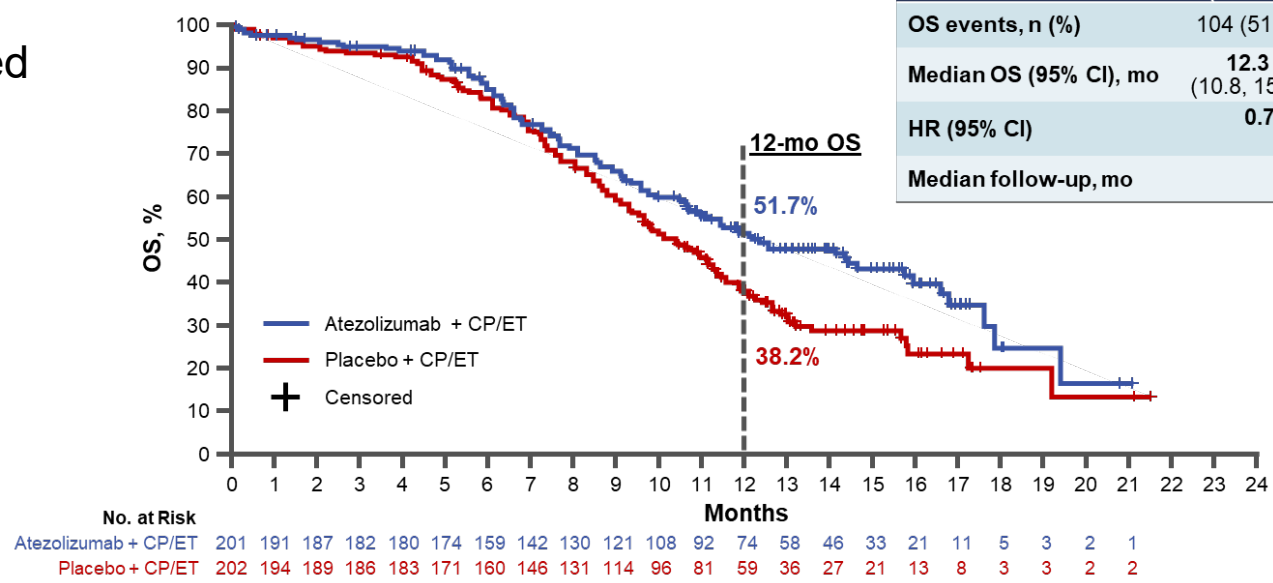
Background

- Several immunotherapies are the subject of investigation in patients with ES-SCLC[1]
- Studies of immunotherapy maintenance in patients with ES-SCLC who have completed chemotherapy only have not shown improvement in survival outcomes[2,3]
- In the Phase I/III IMpower133 study, atezolizumab + CP/ET followed by maintenance therapy with atezolizumab led to significant improvement in OS and PFS vs placebo + CP/ET[4]
- In this exploratory analysis, we assessed the benefit of atezolizumab vs placebo in the patients who reached the maintenance phase of IMpower133

IMpower133: OS in the ITT population[4]

	Atezolizumab + CP/ET (n=201)	Placebo + CP/ET (n=202)
OS events, n (%)	104 (51.7)	134 (66.3)
Median OS (95% CI), mo	**12.3** (10.8, 15.9)	**10.3** (9.3, 11.3)
HR (95% CI)	**0.70** (0.54, 0.91) *P*=0.007	
Median follow-up, mo	13.9	

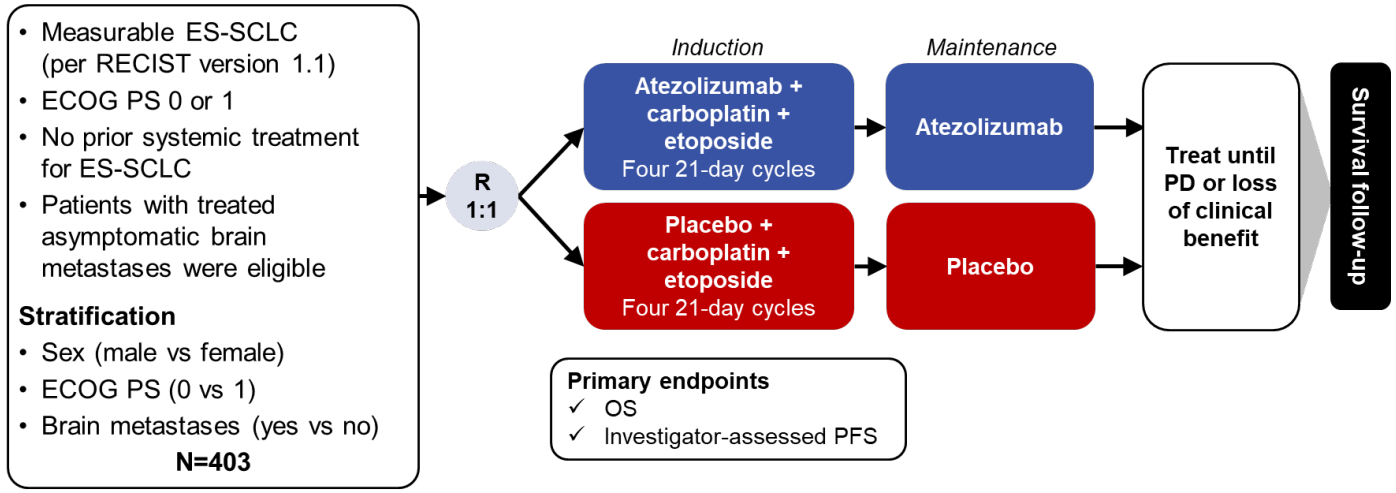


Data cutoff: 24 April 2018.

CP/ET, carboplatin + etoposide; ES-SCLC, extensive-stage small cell lung cancer. 1. Saltos A, et al. *Front Oncol* 2020;10:1074; 2. Gadgeel SM, et al. *J Thorac Oncol* 2018;13:1393-99; 3. Owonikoko TK, et al. ESMO 2019 [abstract 683]; 4. Horn L, et al. *N Engl J Med* 2018;379:2220-9.

Methods

IMpower133 study design



Maintenance population: patients who received at least the first dose of maintenance therapy, regardless of the number of chemotherapy cycles received

Characteristic	Atezolizumab + CP/ET (n=201)	Placebo + CP/ET (n=202)
Maintenance, n (%)	**154 (77)**	**164 (81)**
95% CI	70, 82	75, 86
Non-maintenance, n (%)	47 (23)	38 (19)
95% CI	18, 30	14, 25

- A generalised linear model was used to identify patient and disease characteristics that could be prognostic or predictive of reaching the maintenance phase
- A multivariate Cox model from the start of maintenance treatment was used to evaluate the treatment effect on OS and PFS to account for potential lead-time bias

Atezolizumab, 1200 mg IV, day 1; carboplatin, AUC 5 mg/mL/min IV, day 1; etoposide, 100 mg/m^2 IV, days 1-3.
NCT02763579. Data cutoff: 24 April 2018.

Baseline characteristics in the maintenance population

	Maintenance population (n=318)	
Characteristic[a]	Atezolizumab + CP/ET (n=154)	Placebo + CP/ET (n=164)
Age, median (range), y	64 (38-90)	63 (26-83)
Male, n (%)[b]	101 (65)	107 (65)
ECOG PS 0, n (%)[b]	61 (40)	65 (40)
ECOG PS 1, n (%)[b]	93 (60)	99 (60)
Current/previous tobacco use, n (%)	150 (97)	162 (99)
LDH >ULN, n (%)[c]	85 (56)	87 (53)
Median SLD (range), mm	113 (12-325)	104 (15-353)
≥3 metastatic sites, n (%)	110 (71)	111 (68)
Presences of brain metastases, n (%)[b]	11 (7)	14 (9)
Received 4 cycles of CP/ET, n (%)	152 (98)	161 (99)

- Baseline characteristics were balanced between arms in the maintenance population

LDH, lactate dehydrogenase; SLD, sum of the longest diameters; ULN, upper limit of normal.
[a] At time of randomisation. [b] Per interactive voice/web response system. [c] Three missing values in the atezolizumab + CP/ET arm (n=151). Data cutoff: 24 April 2018.

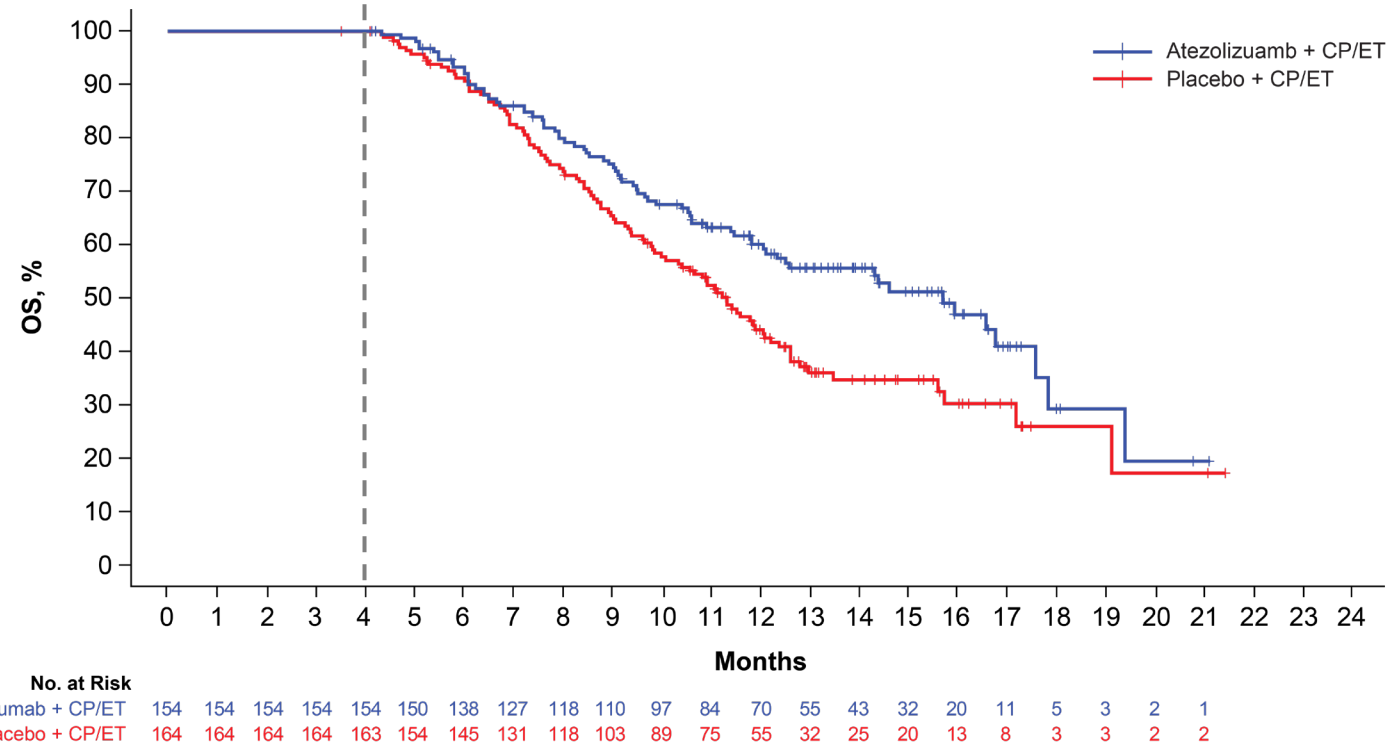
Likelihood of reaching maintenance phase

Covariate[a]	Odds ratio	*P* value	
		Main effect	Interaction
Treatment comparison (atezolizumab [ref] vs placebo)	0.759	0.261	
Sex (male [ref] vs female)	1.086	0.747	0.708
Age (10-year increase)[b]	**0.459**	**0.001**	**0.004**
ECOG PS (1 [ref] vs 0)[c]	**0.439**	**0.004**	0.473
LDH (>ULN [ref] vs ≤ULN)	**0.589**	**0.053**	0.167
SLD (10-mm increase)	0.980	0.257	0.607
No. of metastatic sites (1-site increase)	1.013	0.896	0.618
Presence of brain metastases (yes [ref] vs no)	0.951	0.910	0.321

- Main effects and interactions were modeled separately using generalised linear models
- Age, ECOG PS and LDH were identified as prognostic factors for the likelihood of reaching the maintenance phase
- A significant treatment interaction was also seen with age

Ref, reference; SLD, sum of the longest diameters; ULN, upper limit of normal.
[a] ECOG PS, sex and presence of brain metastases determined per interactive voice/web response system. [b] Older patients were less likely to reach the maintenance phase than younger patients. [c] ECOG PS 1 patients were less likely to reach the maintenance phase than ECOG PS 0 patients. Data cutoff: 24 April 2018.

OS in the maintenance population

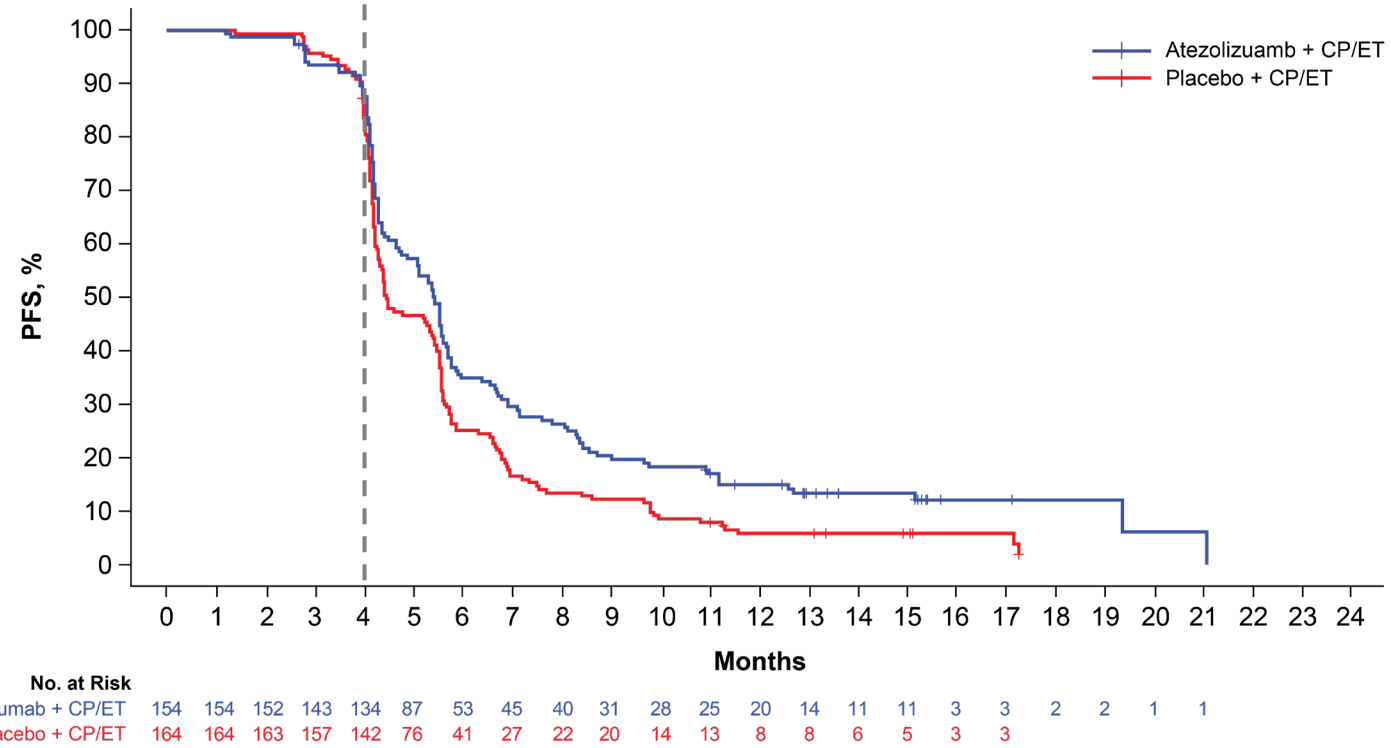


	Atezolizumab + CP/ET (n=154)	Placebo + CP/ET (n=164)
OS HR[a] from start of maintenance (95% CI)	0.59 (0.43, 0.81)	
Median OS from start of maintenance (95% CI), mo	12.5 (9.0, 14.5)	8.4 (7.0, 9.4)
Median OS from randomisation (95% CI), mo	15.7 (12.3, 17.6)	11.3 (10.1, 12.2)

- Among patients in the maintenance population, median OS was longer in the atezolizumab + CP/ET vs placebo + CP/ET arm

[a] Covariates used in the multivariate model: ECOG PS, LDH, SLD, age, number of metastatic sites, sex and presence of brain metastases.
Grey dotted line represents approximate start of maintenance therapy. Data cutoff: 24 April 2018.

PFS in the maintenance population



	Atezolizumab + CP/ET (n=154)	Placebo + CP/ET (n=164)
PFS HR[a] from start of maintenance (95% CI)	0.64 (0.50, 0.82)	
Median PFS from start of maintenance (95% CI), mo	2.6 (2.3, 2.9)	1.8 (1.4, 2.3)
Median PFS from randomisation (95% CI), mo	5.5 (4.9, 5.6)	4.5 (4.3, 5.4)

- Among patients in the maintenance population, median PFS was longer in the atezolizumab + CP/ET vs placebo + CP/ET arm

[a] Covariates used in the multivariate model: ECOG PS, LDH, SLD, age, number of metastatic sites, sex and presence of brain metastases.
Grey dotted line represents approximate start of maintenance therapy. Data cutoff: 24 April 2018.

Safety summary in the maintenance population

n (%)	From randomisation (induction and maintenance)		From start of maintenance[a]	
	Atezolizumab + CP/ET (n=155)	Placebo + CP/ET (n=163)	Atezolizumab + CP/ET (n=155)	Placebo + CP/ET (n=163)
Patients with ≥1				
Any AE	155 (100)	159 (98)	127 (82)	118 (72)
Treatment-related AE	151 (97)	153 (94)	76 (49)	61 (37)
Atezolizumab/placebo	100 (65)	86 (53)	64 (41)	41 (25)
Grade 3/4 AE	105 (68)	105 (64)	43 (28)	37 (23)
Treatment-related Grade 5 AE	0	1 (<1)	0	1 (<1)
Serious AE	52 (34)	47 (29)	24 (15)	19 (12)
AE leading to dose modification or interruption	111 (72)	100 (61)	30 (19)	17 (10)
Atezolizumab/placebo	96 (62)	85 (52)	28 (18)	17 (10)
Immune-related AE	64 (41)	46 (28)	41 (26)	24 (15)

[a] Any, Grade 3/4, serious and immune-related AEs previously reported in Mansfield AS, et al. Annal Oncol. 2020;31:310-7.
Data cutoff: 24 April 2018.

Immune-related AEs in the maintenance population

n (%)[b]	From randomisation (induction and maintenance)				From start of maintenance[a]			
	Atezolizumab + CP/ET (n=155)		Placebo + CP/ET (n=163)		Atezolizumab + CP/ET (n=155)		Placebo + CP/ET (n=163)	
	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Rash	34 (22)	3 (2)	19 (12)	0	21 (14)	2 (1)	6 (4)	0
Hypothyroidism	24 (16)	0	1 (<1)	0	16 (10)	0	1 (<1)	0
Pneumonitis	3 (2)	1 (<1)	5 (3)	2 (1)	1 (<1)	1 (<1)	5 (3)	2 (1)
Pancreatitis	1 (<1)	1 (<1)	2 (1)	2 (1)	0	0	2 (1)	2 (1)

- Grade 3/4 immune-related AEs were not commonly reported; no Grade 5 immune-related events occurred

[a] Any grade immune-related AEs previously reported in Mansfield AS, et al. Annal Oncol. 2020;31:310-7.
[b] Events of any grade occurring in ≥10% of patients and Grade 3/4 events occurring in ≥1%. Data cutoff: 24 April 2018.

Conclusions

- In IMpower133, a similar proportion of patients received maintenance treatment in the atezolizumab + CP/ET (77%) and placebo + CP/ET (81%) arms, as evidenced by the overlapping 95% CIs
- There was an OS and PFS benefit in the maintenance population in patients receiving atezolizumab + CP/ET vs placebo + CP/ET
  - This effect was analysed with a multivariate Cox model from the start of maintenance therapy
  - OS HR, 0.59 (95% CI: 0.43, 0.81); PFS HR, 0.64 (95% CI: 0.50, 0.82)
- Three prognostics factors for reaching the maintenance phase were identified (generalised linear model): age, ECOG PS and LDH; age appeared to show a trend for treatment interaction
- Safety results were comparable between treatment arms despite the continuation of atezolizumab monotherapy in the maintenance phase
- Both induction treatment with atezolizumab + CP/ET as well as maintenance treatment with atezolizumab appear to contribute to the OS benefit observed in IMpower133

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