

Efficacy/Safety of Atezolizumab + Chemo in 1L ES-SCLC by Age & Comorbidity: Pooled Analysis of Four Phase 3 Trials



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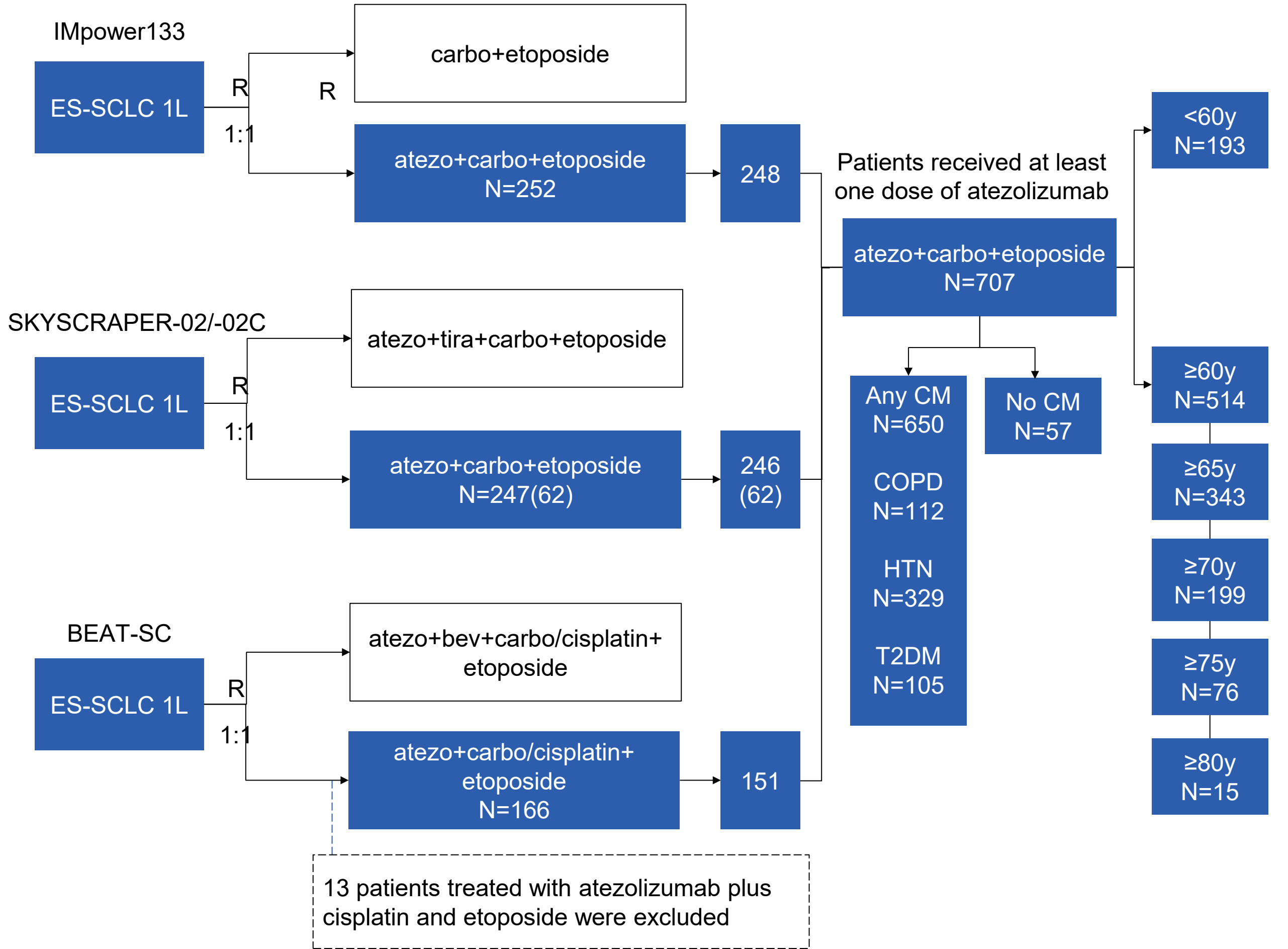
Background

- Extensive-stage small cell lung cancer (ES-SCLC) is a highly aggressive neuroendocrine tumor characterized by rapid proliferation, early systemic dissemination, and a poor prognosis. A substantial proportion of patients are elderly, frequently presenting with significant smoking-related comorbidities and frailty.
- A comprehensive network meta-analysis of eight phase III randomized controlled trials, encompassing approximately 2,000 elderly patients (≥65 years), has demonstrated that adding PD-L1/PD-1 inhibitors to etoposide-platinum (EP) chemotherapy significantly improves overall survival (OS, hazard ratio [HR] 0.75, 95% confidence interval [CI] 0.67-0.84) and progression-free survival (PFS, HR=0.53, 95% CI 0.40-0.71) compared with chemotherapy alone in this population, with the atezolizumab–EP combination ranking highest for OS¹.
- However, the definition of the "elderly" remains a persistent challenge, given the heterogeneity of age thresholds (ranging from 60 to 80 years) across different regions and clinical trials. Furthermore, chronological age often pales in significance compared to the impact of comorbidities on the safety and efficacy of immunotherapy.
- To address these gaps, this study utilizes a pooled individual patient data (IPD) analysis from four pivotal trials—IMpower133 (NCT02763579)², SKYSCRAPER-02 (NCT04256421)³, SKYSCRAPER-02C (NCT04665856)⁴, and BEAT-SC (JRCT2080224946)⁵— to systematically evaluate the survival and safety outcomes of first-line atezolizumab plus chemotherapy in elderly ES-SCLC patients.

Methods

- We conducted a pooled IPD analysis of 707 patients from four pivotal trials: IMpower133, SKYSCRAPER-02, SKYSCRAPER-02C, and BEAT-SC. Patients received first-line atezolizumab plus carboplatin/etoposide. Efficacy and safety were evaluated across predefined age subgroups (<60, ≥60, ≥65, ≥70, ≥75, and ≥80 years) and according to baseline comorbidities, including hypertension (HTN), chronic obstructive pulmonary disease (COPD), and type 2 diabetes (T2DM).

Figure 1. Study design flowchart



Age subgroups are based on overlapping/cumulative age thresholds.

References

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Abbreviations

1L, first-line; AE, adverse event; AESI, adverse event of special interest; Atezo, atezolizumab; Bev, bevacizumab; Carbo, carboplatin; CI, confidence interval; CM, comorbidity; COPD, chronic obstructive pulmonary disease; ECOG PS, Eastern Cooperative Oncology Group performance status; EP, etoposide-platinum; ES-SCLC, extensive-stage small cell lung cancer; HR, hazard ratio; HTN, hypertension; IPD, individual patient data; MedDRA, Medical Dictionary for Regulatory Activities; SCLC, small cell lung cancer; SLD, sum of longest diameters; T2DM, type 2 diabetes mellitus; Tira, tiragolumab.

Results

Baseline characteristics

- A total of 707 patients were included in the analysis. Baseline characteristics across the cumulative age-threshold subgroups are summarized in Table 1A. Brain metastases were more frequent in the <60-year subgroup (Table 1A). 650 (91.9%) patients presented at least one ongoing medical condition and the most prevalent comorbidities were HTN, COPD, and T2DM (Table 2). Notably, fewer Asian patients (25.9%) in the COPD group were observed (Table 1B).

Table 1A. Baseline Characteristics by Age Subgroup

Parameters	<60 (N=193)	≥60 (N=514)	≥65 (N=343)	≥70 (N=199)	≥75 (N=76)	≥80 (N=15)
Age (years)†	55.0 (25-59)	67.0 (60-90)	70.0 (65-90)	73.0 (70-90)	77.0 (75-90)	81.0 (80-90)
Sex (Male/Female), n (%)	143 (74.1) / 50 (25.9)	366 (71.2) / 148 (28.8)	242 (70.6) / 101 (29.4)	139 (69.8) / 60 (30.2)	61 (80.3) / 15 (19.7)	10 (66.7) / 5 (33.3)
Race, n (%)						
Asian	108 (56.0)	255 (49.6)	175 (51.0)	107 (53.8)	49 (64.5)	6 (40.0)
White	84 (43.5)	249 (48.4)	159 (46.4)	88 (44.2)	26 (34.2)	9 (60.0)
Black or African American	1 (0.5)	2 (0.4)	1 (0.3)	1 (0.5)	0	0
Unknown	0	8 (1.6)	8 (2.3)	3 (1.5)	1 (1.3)	0
Baseline Weight (kg)†	67.75 (39.0-181.0)	67.00 (39.8-135.0)	66.00 (39.8-135.0)	65.00 (42.0-116.0)	62.95 (42.4-113.0)	64.00 (45.5-113.0)
Tobacco Use History (Yes), n (%)	170 (88.1)	480 (93.4)	324 (94.5)	190 (95.5)	75 (98.7)	15 (100)
Baseline ECOG PS (0/1), n (%)	60 (31.1) / 133 (68.9)	153 (29.8) / 361 (70.2)	97 (28.3) / 246 (71.7)	61 (30.7) / 138 (69.3)	21 (27.6) / 55 (72.4)	4 (26.7) / 11 (73.3)
Organ Metastases (Yes), n (%)						
Brain Metastases	33 (17.1)	64 (12.5)	39 (11.4)	21 (10.6)	8 (10.5)	1 (6.7)
Liver Metastases	70 (36.3)	186 (36.2)	132 (38.5)	74 (37.2)	27 (35.5)	2 (13.3)
No. of Metastatic Sites†	3.0 (1-8)	3.0 (1-8)	3.0 (1-8)	3.0 (1-8)	3.0 (1-8)	3.0 (1-4)
Baseline SLD (mm)†,‡	109.95 (10.0-308.1)	105.00 (12.0-325.0)	106.55 (12.0-310.0)	102.50 (12.0-292.6)	96.50 (12.0-292.6)	119.00 (20.8-279.0)

Table 1B. Baseline Characteristics by Comorbidity Subgroup

Parameters	Any CM (N=650)	No CM (N=57)	COPD (N=112)	HTN (N=329)	T2DM (N=105)
Age (years)†	65.0 (25-90)	61.0 (28-79)	67.0 (43-84)	67.0 (43-90)	67.0 (44-83)
Sex (Male/Female), n (%)	462 (71.1) / 188 (28.9)	47 (82.5) / 10 (17.5)	68 (60.7) / 44 (39.3)	228 (69.3) / 101 (30.7)	77 (73.3) / 28 (26.7)
Race, n (%)					
Asian	329 (50.6)	34 (59.6)	29 (25.9)	144 (43.8)	48 (45.7)
White	310 (47.7)	23 (40.4)	80 (71.4)	179 (54.4)	56 (53.3)
Black or African American	3 (0.5)	0 (0.0)	2 (1.8)	0 (0.0)	0 (0.0)
Unknown	8 (1.2)	0 (0.0)	1 (0.9)	4 (1.2)	1 (1.0)
Baseline Weight (kg)†	67.0 (39.0-181.0)	67.0 (39.8-94.0)	65.9 (41.0-181.0)	70.0 (41.0-181.0)	75.0 (45.5-120.0)
Tobacco Use History (Yes), n (%)	600 (92.3)	50 (87.7)	110 (98.2)	313 (95.1)	103 (98.1)
Baseline ECOG PS (0/1), n (%)	197 (30.3) / 453 (69.7)	16 (28.1) / 41 (71.9)	30 (26.8) / 82 (73.2)	106 (32.2) / 223 (67.8)	33 (31.4) / 72 (68.6)
Organ Metastases (Yes), n (%)					
Brain Metastases	86 (13.2)	11 (19.3)	14 (12.5)	39 (11.9)	13 (12.4)
Liver Metastases	243 (37.4)	13 (22.8)	39 (34.8)	121 (36.8)	39 (37.1)
No. of Metastatic Sites†	3.0 (1-8)	3.0 (1-8)	3.0 (1-7)	3.0 (1-7)	3.0 (1-7)
Baseline SLD (mm)†,‡	109.0 (10.0-325.0)	95.5 (12.0-278.0)	112.5 (13.0-310.0)	109.0 (12.0-325.0)	114.7 (25.0-308.1)

† Data are presented as median (range). * Baseline SLD available for N=648 (Any CM), N=56 (No CM), N=112 (COPD), N=327 (HTN), N=105 (T2DM).

Table 2. Ongoing Medical Conditions Reported in ≥10% of Patients in Any Age Subgroup

MedDRA Preferred Term, n (%)	<60 (N=193)	≥60 (N=514)	≥65 (N=343)	≥70 (N=199)	≥75 (N=76)	≥80 (N=15)
Total number of patients with at least one medical history	166 (86.0)	484 (94.2)	327 (95.3)	191 (96.0)	70 (92.1)	15 (100)
HTN	59 (30.6)	270 (52.5)	196 (57.1)	119 (59.8)	45 (59.2)	9 (60.0)
Cough	56 (29.0)	131 (25.5)	82 (23.9)	41 (20.6)	11 (14.5)	3 (20.0)
COPD	20 (10.4)	92 (17.9)	68 (19.8)	43 (21.6)	20 (26.3)	6 (40.0)
T2DM	22 (11.4)	83 (16.1)	61 (17.8)	37 (18.6)	12 (15.8)	3 (20.0)
Dyspnoea	27 (14.0)	80 (15.6)	54 (15.7)	31 (15.6)	9 (11.8)	3 (20.0)
Constipation	8 (4.1)	66 (12.8)	57 (16.6)	39 (19.6)	17 (22.4)	2 (13.3)
Back pain	21 (10.9)	53 (10.3)	38 (11.1)	21 (10.6)	9 (11.8)	4 (26.7)
Hyperlipidaemia	13 (6.7)	54 (10.5)	38 (11.1)	24 (12.1)	10 (13.2)	4 (26.7)
Benign prostatic hyperplasia	14 (7.3)	41 (8.0)	35 (10.2)	27 (13.6)	18 (23.7)	3 (20.0)
Insomnia	10 (5.2)	47 (9.1)	37 (10.8)	26 (13.1)	9 (11.8)	2 (13.3)
Anaemia	10 (5.2)	37 (7.2)	27 (7.9)	17 (8.5)	9 (11.8)	3 (20.0)
Arthralgia	11 (5.7)	35 (6.8)	27 (7.9)	17 (8.5)	7 (9.2)	2 (13.3)
Dyslipidaemia	8 (4.1)	32 (6.2)	25 (7.3)	21 (10.6)	9 (11.8)	2 (13.3)
Hypercholesterolaemia	4 (2.1)	33 (6.4)	27 (7.9)	18 (9.0)	10 (13.2)	2 (13.3)
Decreased appetite	7 (3.6)	34 (6.6)	24 (7.0)	12 (6.0)	4 (5.3)	2 (13.3)
Fatigue	12 (6.2)	29 (5.6)	18 (5.2)	13 (6.5)	6 (7.9)	5 (33.3)
Chest pain	21 (10.9)	29 (5.6)	17 (5.0)	7 (3.5)	2 (2.6)	0
Atrial fibrillation	3 (1.6)	26 (5.1)	22 (6.4)	16 (8.0)	5 (6.6)	2 (13.3)

Conclusions

- In this exploratory pooled analysis, observed survival and safety outcomes with atezolizumab plus chemotherapy were generally consistent across the evaluated age and comorbidity subgroups. These findings should be interpreted descriptively.

Limitations

- SCLC is biologically highly heterogeneous, which may influence treatment responses across subgroups. The constituent trials were conducted over different time periods. All pooled patients were derived from interventional trials, and the findings may not fully represent real-world clinical practice. Age-threshold groups were nested and comorbidity groups overlapped; therefore, the displayed estimates should not be interpreted as independent between-group comparisons. Findings in the ≥80-year subgroup should be interpreted cautiously due to the small sample size.

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Disclosures

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