

Atezolizumab plus Chemotherapy in ES-SCLC with or without Brain Metastases: A Pooled Analysis of Four Phase 3 Trials

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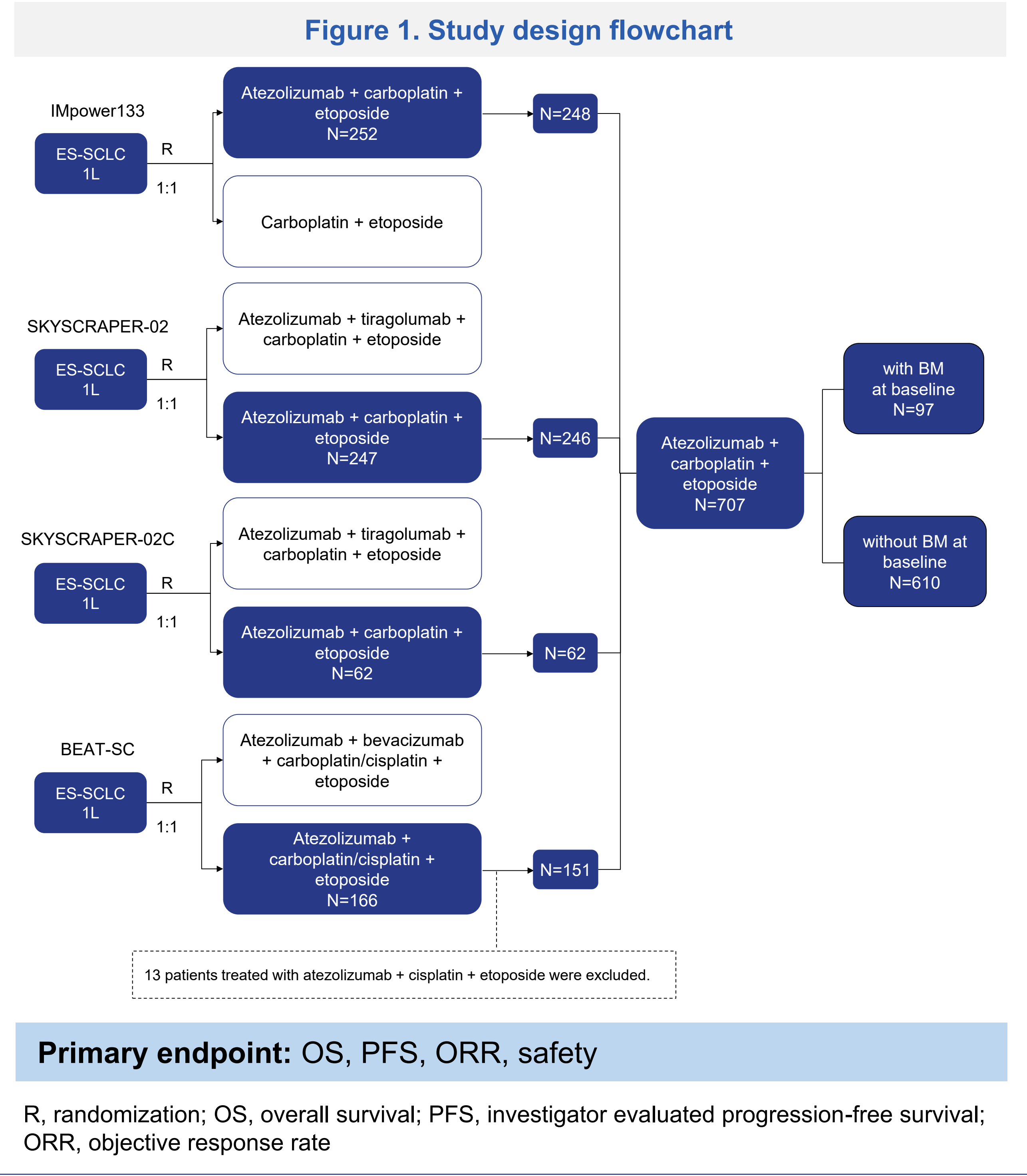
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INTRODUCTION

- Brain metastases (BM) occur in approximately 20% of patients with extensive-stage small cell lung cancer (ES-SCLC) at diagnosis, serving as a frequent site of distant failure¹⁻³. The presence of BM is historically associated with poor prognosis and progressive neurological decline, including cognitive impairment and focal deficits, underscoring the urgent need for effective therapeutic strategies in this high-risk population⁴.
- Atezolizumab plus chemotherapy is a standard treatment for ES-SCLC, validated by IMpower133⁵ and confirmed in subsequent trials including SKYSCRAPER-02⁶, SKYSCRAPER-02C⁷, and BEAT-SC⁸. However, its specific efficacy in the high-risk BM population remains a subject of clinical debate due to limited sample sizes in individual trials.
- This individual patient data (IPD) pooled analysis aims to evaluate the survival outcomes and safety profile of atezolizumab in ES-SCLC patients with and without baseline BM. By aggregating patient-level data across multiple trials, this approach enables more precise estimation of treatment effects in clinically relevant subgroups and addresses the critical evidence gap for this historically understudied population.

METHODS

- The IPD of patients who received at least one dose of atezolizumab plus carboplatin and etoposide were pooled from IMpower133 (NCT02763579)⁵, SKYSCRAPER-02 (NCT04256421)⁶, SKYSCRAPER-02C (NCT04665856)⁷, and BEAT-SC (JRCT2080224946)⁸ (Figure 1). Efficacy and safety outcomes were assessed, stratified by baseline BM status. The impact of radiotherapy (RT) timing on survival was also explored.



RESULTS

Baseline characteristics

- A total of 707 patients were analyzed, including 97 patients with baseline BM and 610 without (Table 1). There were no significant differences in duration of treatment between the BM group and the non-BM group, despite significant baseline imbalances.

Table 1. Baseline characteristics

	BM (N=97)	Non-BM (N=610)
Age (years)		
Mean (SD)	62.8 (8.4)	64.3 (8.6)
Age group (years)		
<65	58 (59.8)	306 (50.2)
≥65	39 (40.2)	304 (49.8)
Sex		
Male	72 (74.2)	437 (71.6)
Female	25 (25.8)	173 (28.4)
Race		
Asian	52 (53.6)	311 (51.0)
White	43 (44.3)	290 (47.5)
Black or African American	0	3 (0.5)
Unknown	2 (2.1)	6 (1.0)
Weight (kg)		
Mean (SD)	67.92 (14.18)	70.10 (16.42)
History of tobacco use		
Yes	90 (92.8)	560 (91.8)
ECOG PS		
0	34 (35.1)	179 (29.3)
1	63 (64.9)	431 (70.7)
Liver metastases		
Yes	32 (33.0)	224 (36.7)
Number of metastatic sites		
Mean (SD)	4.0 (1.6)	3.3 (1.2)
Sum of longest diameters (mm)		
Mean (SD)	129.58 (70.14)	114.08 (58.32)
Received radiotherapy		
Enrollment radiotherapy	39 (40.2)	35 (5.7)
On-study radiotherapy	11 (11.3)	42 (6.9)
Follow-up radiotherapy	36 (37.1)	159 (26.1)
Not received radiotherapy	26 (26.8)	393 (64.4)

Safety

- The incidence of grade 3/4 adverse events (AEs) was 79.4% in the BM group and 74.8% in the non-BM group. Rates of grade 5 AEs and serious AEs were also comparable between the two groups (BM vs. non-BM: 4.1% vs. 3.9%; 42.3% vs. 40.5%). No new safety signals were observed (Table 2).

Table 2. Summary of safety

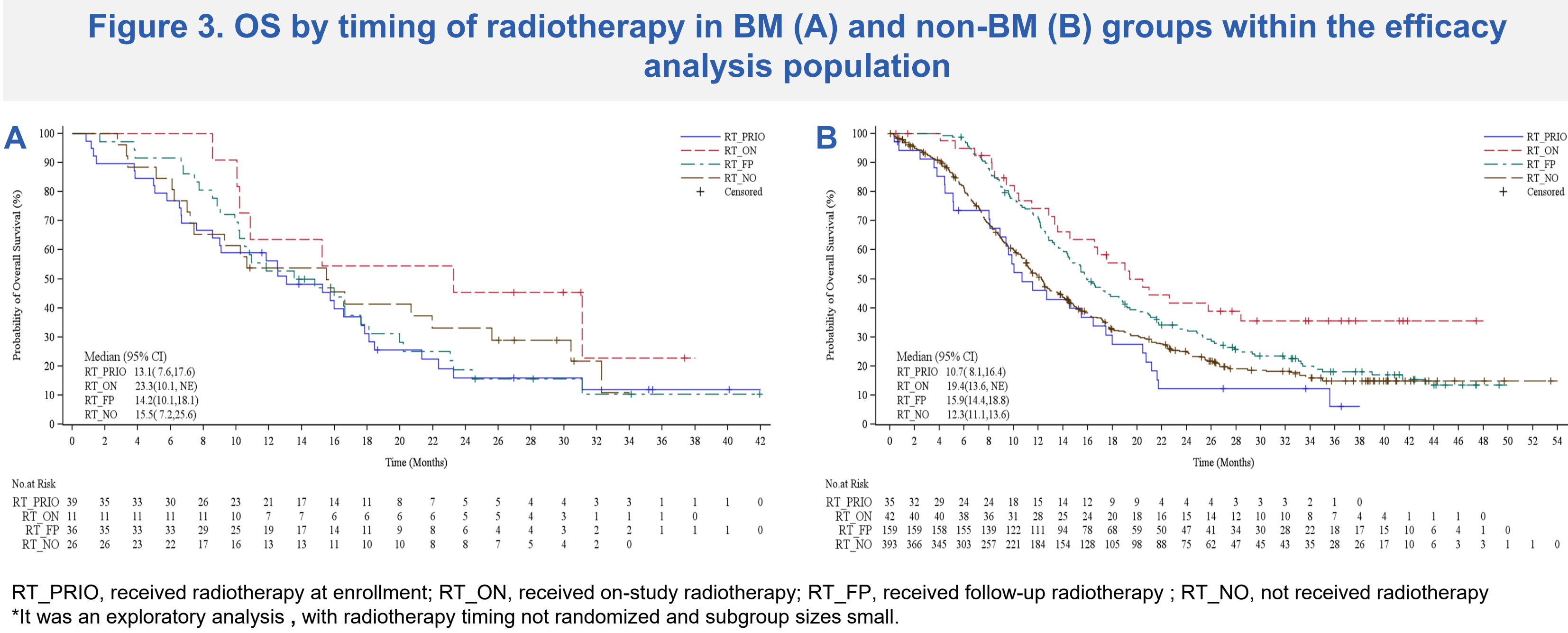
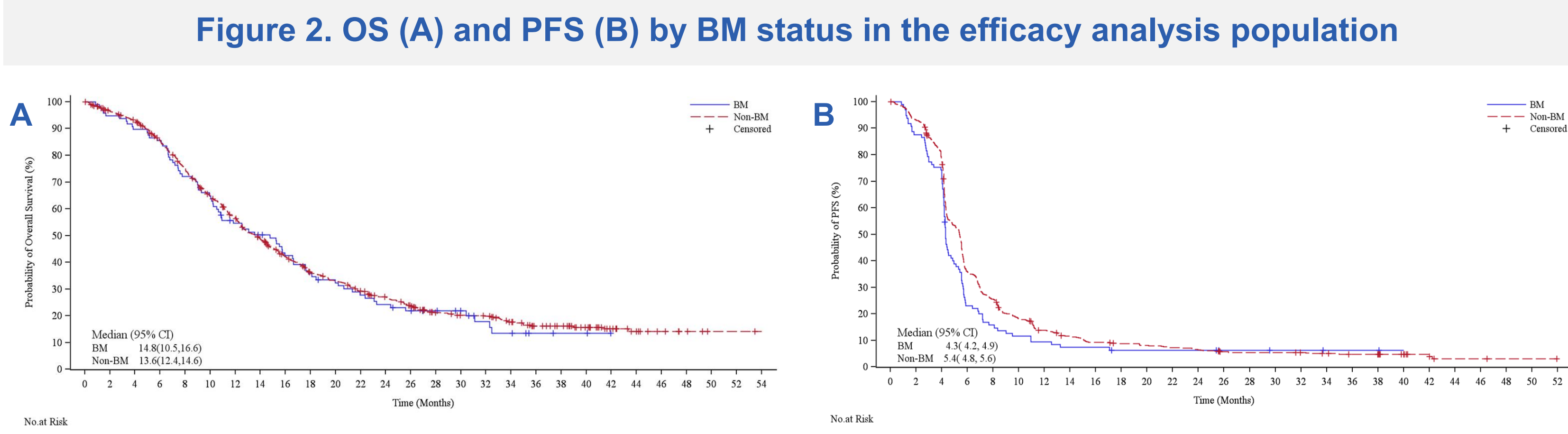
	BM (N=97)	Non-BM (N=610)
Patients with ≥1 AE	97 (100)	605 (99.2)
AE related to any study treatment	67 (69.1)	458 (75.1)
Grade 3/4 AE	77 (79.4)	456 (74.8)
Treatment-related Grade 3/4 AE	47 (48.5)	300 (49.2)
Grade 5 AE	4 (4.1)	24 (3.9)
Treatment-related Grade 5 AE	0	11 (1.8)
Serious AE	41 (42.3)	247 (40.5)
Treatment-related serious AE	18 (18.6)	112 (18.4)
AE leading to withdrawal from atezolizumab	4 (4.1)	60 (9.8)

Acknowledgements

We thank the patients and investigators who participated in IMpower133 [NCT02763579], SKYSCRAPER-02 [NCT04256421], SKYSCRAPER-02C [NCT04665856], BEAT-SC [JRCT2080224946]. Medical writing support for the development of this poster, under the direction of the authors, was provided by Shanghai Medical Insight, and was funded by Shanghai Roche Pharmaceuticals Ltd., in accordance with Good Publication Practice guidelines (<http://www.ismpp.org/gpp-2022>).

Efficacy

- The median follow-up duration was 35.5 months (95% CI: 33.6–37.7). In this population, the median OS was 13.6 months (95% CI: 12.5–14.8). Atezolizumab plus chemotherapy showed similar OS outcomes in patients with and without baseline BM, with a median OS of 14.8 months (95% CI: 10.5–16.6) in the BM group versus 13.6 months (95% CI: 12.4–14.6) in the non-BM group. Median PFS was 4.3 months (95% CI: 4.2–4.9) in the BM group and 5.4 months (95% CI: 4.8–5.6) in the non-BM group (Figure 2).
- ORRs were similar between patients in the BM and non-BM groups (61.9% vs 65.4%).
- Compared with patients receiving follow-up radiotherapy, no radiotherapy, or radiotherapy at enrollment, patients who received on-study radiotherapy appeared to have longer OS, although these exploratory findings should be interpreted cautiously (Figure 3). The median OS was 23.3 months (95% CI: 10.1-NE) for patients with BM at baseline (n=11) and 19.4 months (95% CI: 13.6-NE) for those without BM at baseline (n=42).



RT_Prio, received radiotherapy at enrollment; RT_On, received on-study radiotherapy; RT_FP, received follow-up radiotherapy; RT_No, not received radiotherapy

*It was an exploratory analysis, with radiotherapy timing not randomized and subgroup sizes small.

CONCLUSION

- In this exploratory analysis, frontline atezolizumab plus chemotherapy showed similar efficacy and safety in ES-SCLC patients with or without baseline BM.

LIMITATION

- The inherent heterogeneity of small cell lung cancer may exert an influence on the observed outcomes.
- Disparities in the timing of trial conduct across the studies potentially reflect temporal evolutions in standards of supportive care.
- The exclusive reliance on data from interventional trials may constrain the generalizability of the findings to real-world clinical practice.

Disclosures

Shun Lu declares receiving research support from AstraZeneca, Duality Biologics, and D3S, and serving as an advisor and consultant for AstraZeneca, Pfizer, and Takeda. Yanjun Shi and Dandan Hu are employees of Shanghai Roche Pharmaceuticals Ltd.; Marcela Oancea is an employee of F. Hoffmann-La Roche Ltd.

Funding This study was sponsored by Shanghai Roche Pharmaceuticals Ltd./F. Hoffmann-La Roche.

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