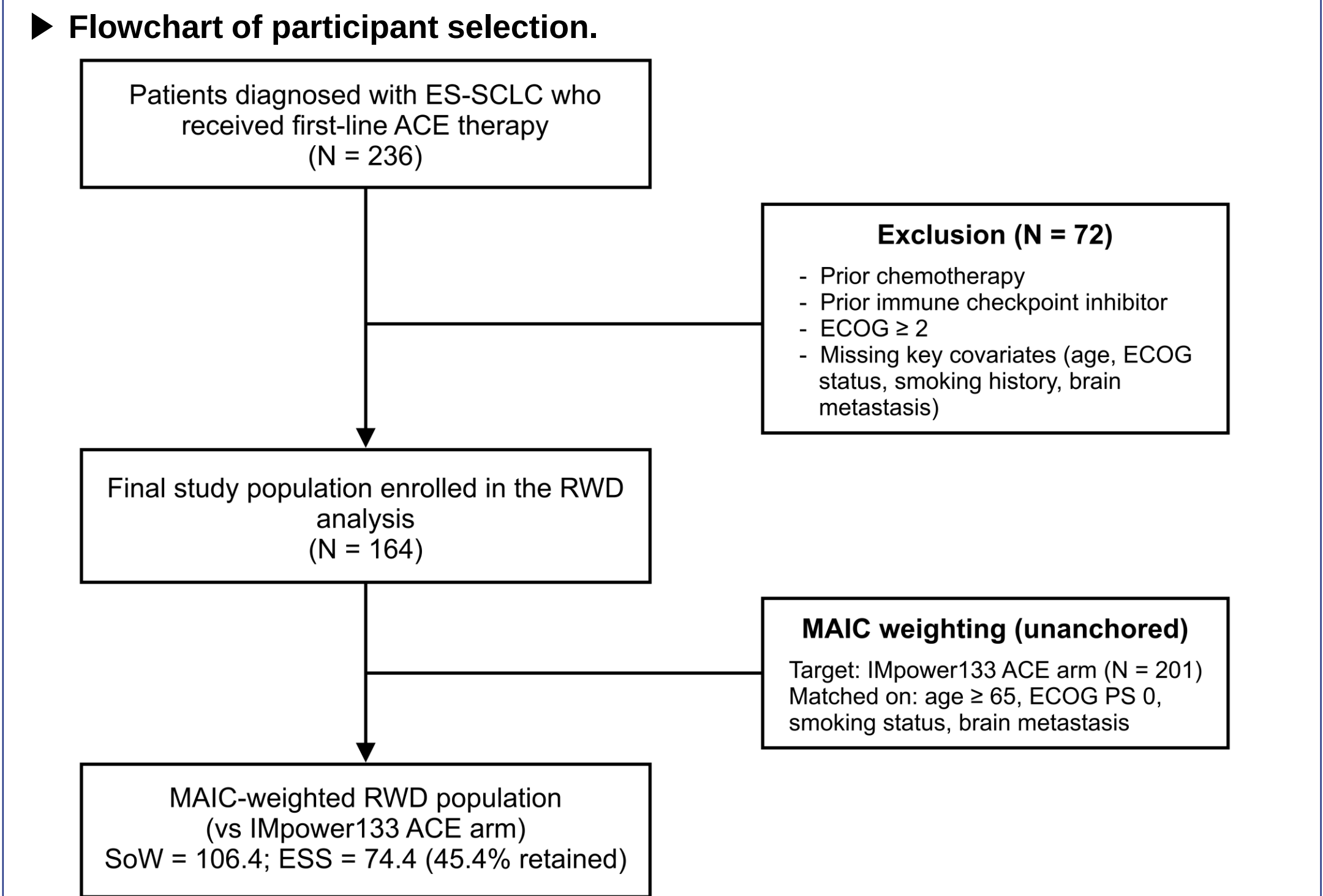


INTRODUCTION

- IMpower133 trial** established **ACE** as the standard first-line treatment for ED-SCLC, but its stringent eligibility criteria may limit generalizability.
- Therefore , the **real-world effectiveness of ACE** and the prognostic impact of **consolidative thoracic RT** were assessed.

METHODS

- Retrospectively analyzed **164 patients with ED-SCLC** treated with **first-line ACE** at a tertiary center
✓ 2020.9.22-2025.7.8
- Matching-adjusted indirect comparison (MAIC)** using age, ECOG performance status, smoking history, and brain metastasis was conducted against the **IMpower133 trial** cohort (*n* = 201).
- To adjust for **sequential thoracic RT-associated confounding** (*n* = 29), time-dependent multivariate Cox regression and time-origin reset analyses were conducted.



Abbreviations: ES-SCLC, extensive-stage small-cell lung cancer; ACE, atezolizumab plus carboplatin plus etoposide; ECOG PS, Eastern Cooperative Oncology Group performance status; RWD, real-world data.

S1. Application of Mpower133 Eligibility Criteria to the Real –World Data (RWD) Cohort

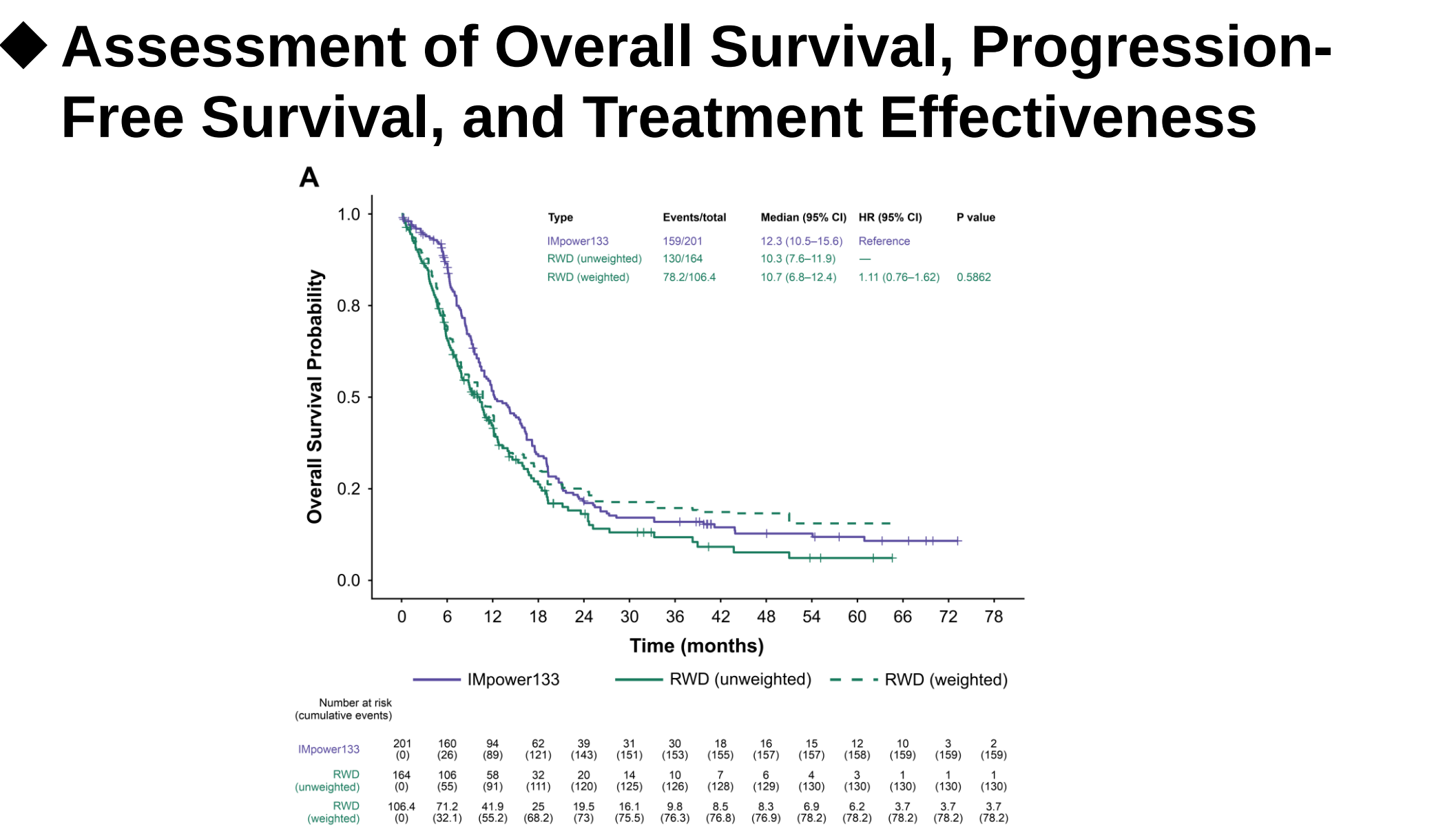
Eligibility criteria	IMpower133 Trial Arm	RWD Cohort
Inclusion criteria		
Histologically/cytologically confirmed	✓ Required	✓ Applied
ES-SCLC		
Age ≥18 years	✓ Required	✓ Applied
ECOG PS 0 or 1	✓ 0–1 only	✓ Applied (ECOG ≥2 excluded)
No prior systemic therapy for ES-	✓ Required	✓ Applied
SCLC		
Measurable disease per RECIST v1.1	✓ Required	Not assessed in RWD
Exclusion criteria		
Prior immune checkpoint inhibitor	✗ Excluded	✗ Applied
ECOG PS ≥2	✗ Excluded	✗ Applied
Active or prior autoimmune disease	✗ Excluded	Not routinely recorded
Missing values for MAIC covariates	N/A	✗ Excluded

RESULTS

◆ **Patients and baseline characteristics**

Characteristic	RWD unweighted (<i>n</i> = 164)	RWD weighted (SoW = 106.4;	IMpower133 ACE (<i>n</i> = 201)	SMD before weighting	SMD after weighting
ESS = 74.4) ^a					
Median age, year (range)	70 (51–88)		64 (28–90)		
Age ≥ 65 years, <i>n</i> (%)	120 (73.2%)	44.8%	90 (44.8%)	0.638	0.000
Male sex, <i>n</i> (%)	149 (90.9%)		129 (64.2 %)		
ECOG PS 0, <i>n</i> (%)	43 (26.2%)	36.3%	73 (36.3%)	0.229	0.000
Smoking status					
Never smoker, <i>n</i> (%)	15 (9.1%)	4.5%	9 (4.5%)	0.161	0.000
Current smoker, <i>n</i> (%)	70 (42.7%)	36.8%	74 (36.8%)	0.119	0.000
Former smoker, <i>n</i> (%) ^b	79 (48.2%)	58.7%	118 (58.7%)	—	—
Brain metastasis, <i>n</i> (%)	49 (29.9%)	8.5%	17 (8.5%)	0.466	0.000

- Abbreviations: ACE, atezolizumab plus carboplatin plus etoposide; ECOG PS, Eastern Cooperative Oncology Group performance status; ESS, effective sample size; MAIC, matching-adjusted indirect comparison; RWD, real-world data; SMD, standardized mean difference; SoW, sum of weights.
- ✓ Real-world data (RWD) cohort was **older** (median age, 70 vs. 64 years) and had more **brain metastases** (29.9% vs. 8.5%).
 - ✓ **MAIC** achieved complete covariate balance.



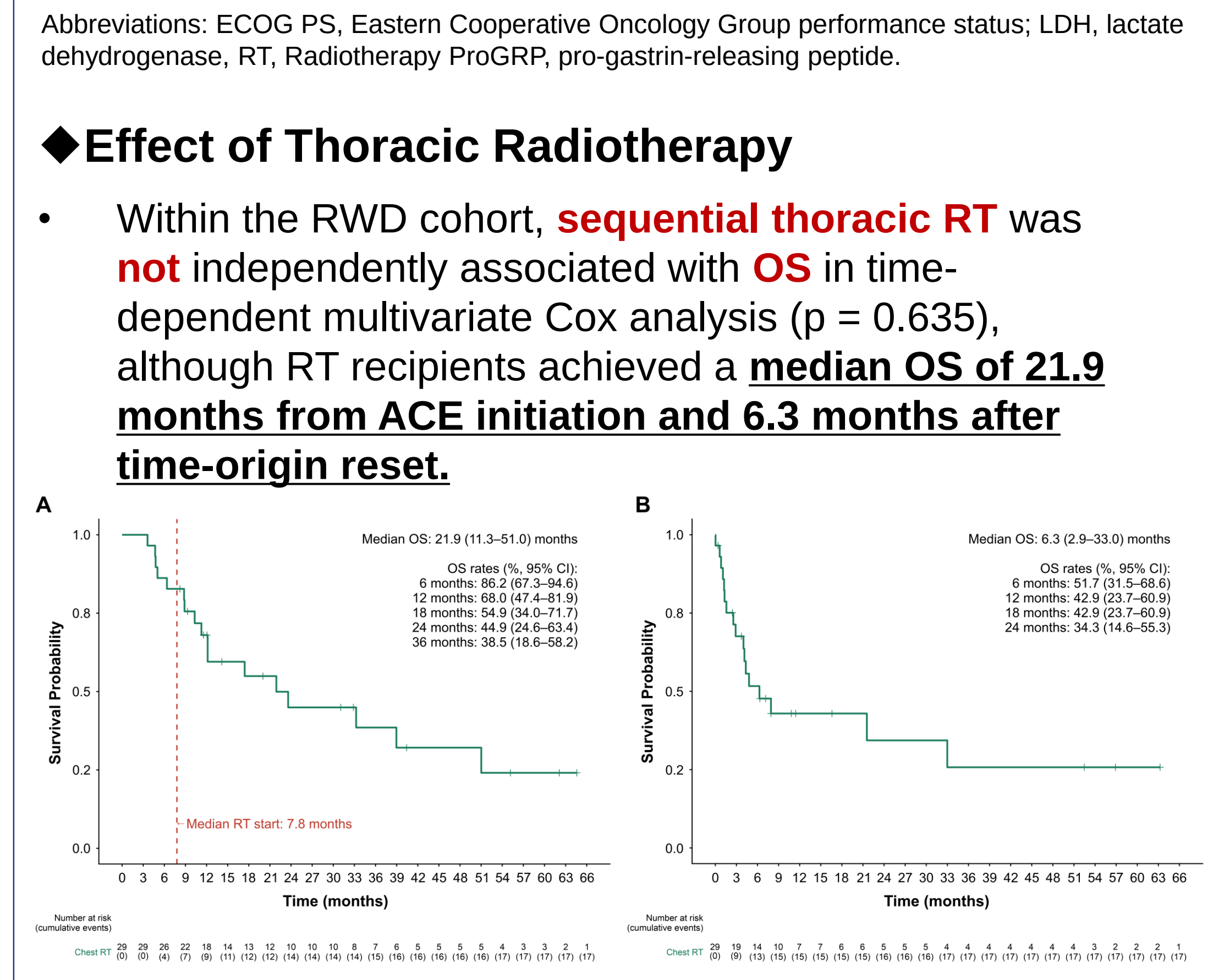
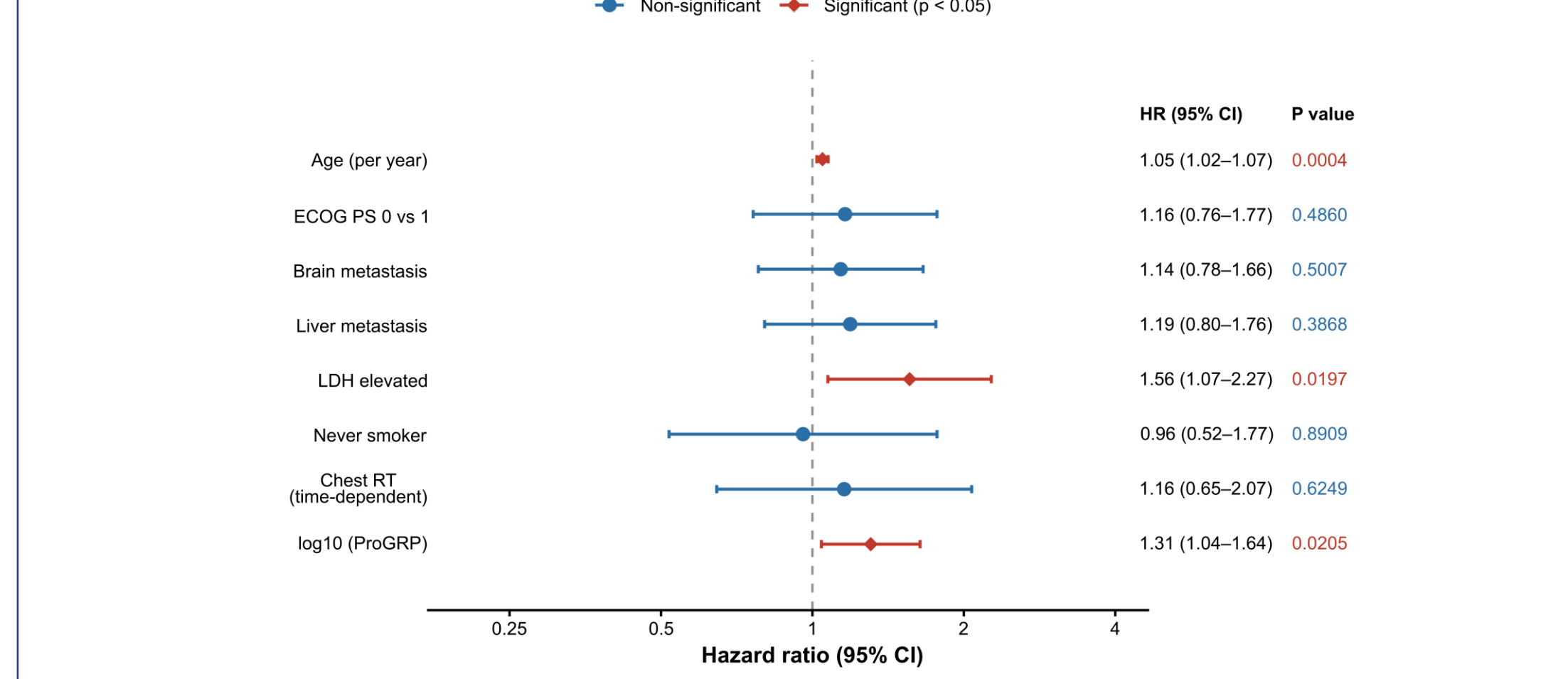
- Weighted median OS was 10.7 months vs. 12.3 months**
✓ **aHR** for death of **1.11** (95% CI, 0.76–1.62).
- Five-year OS** was numerically **higher** in the RWD cohort (15.5% vs. 11.9%).

• **OS at 1–5 years in the weighted RWD**

Landmark	Weighted RWD OS, % (95% CI)	IMpower133 OS, % (95% CI)	Difference, % points (95% CI) ^b	<i>P</i>
1-year	45.8% (33.5–57.2)	51.7% (44.2–58.7)	–5.9 (–19.9, +8.1)	0.1477
2-year	24.7% (13.9–37.2)	21.7% (16.0–27.9)	3.1 (–10.3, +16.4)	0.4377
3-year	19.7% (9.3–33.0)	16.0% (11.0–21.7)	3.8 (–9.5, +17.1)	0.5249
4-year	18.3% (8.0–31.9)	12.8% (8.2–18.4)	5.5 (–7.8, +18.9)	0.5890
5-year	15.5% (5.6–30.0)	11.9% (7.4–17.5)	3.7 (–9.9, +17.3)	0.5611

Abbreviations: CI, confidence interval; OS, overall survival; RWD, real-world data.

- Weighted median PFS was 5.7 months vs. 5.2 months**
✓ **aHR** for progression or death of **0.86** (95% CI, 0.63–1.18).
- In multivariable analysis, **advanced age**, **elevated LDH**, and **higher log10-transformed pro-GRP levels** were independent **adverse prognostic factors**.
- Forest plot of the multivariable Cox proportional hazards regression analysis with thoracic radiotherapy modeled as a time-dependent covariate.



DISCUSSION AND CONCLUSION

- This real-world Korean cohort study reports **long-term outcomes of first-line ACE therapy in ES-SCLC, including 5-year OS**.
- An **unanchored MAIC** achieved complete balance of key baseline prognostic variables versus the IMpower133 trial population.
- After adjustment, an **older, less favorable real-world cohort** achieved **survival comparable to the IMpower133 trial**.
- Although **sequential consolidative thoracic RT** showed a favorable survival trend, **no** independent survival benefit was demonstrated..
- Older age, elevated LDH, and higher proGRP levels** independently predicted **poorer survival** in this cohort.

REFERENCES & ACKNOWLEDGEMENTS

Reference

- Rudin CM, Brambilla E, Faivre-Finn C, Sage J. Small-cell lung cancer. Nat Rev Dis Primers. 2021;7(1):3.
- Gazdar AF, Bunn PA, Minna JD. Small-cell lung cancer: what we know, what we need to know and the path forward. Nat Rev Cancer. 2017;17(12):725–737.
- Horn L, Mansfield AS, Szczesna A, et al. First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. N Engl J Med. 2018;379(23):2220–2229.

Acknowledgments

This study was conducted within the **K-HOPE** (Korea-Hwasun Oncology Precision Biomedicine & Experimental Trials) Consortium.

Funding

This work was supported by the Chonnam National University Hospital Biomedical Research Institute [grant number BCR122015] and the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea [grant number RS-2025-19252970].