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Phase II Study of iza-bren (BL-B01D1) in Combination with Serplulimab in Patients with Small Cell Lung Cancer (SCLC)

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Declaration

- ❑ The author declares no financial or non-financial conflicts of interest related to this presentation.

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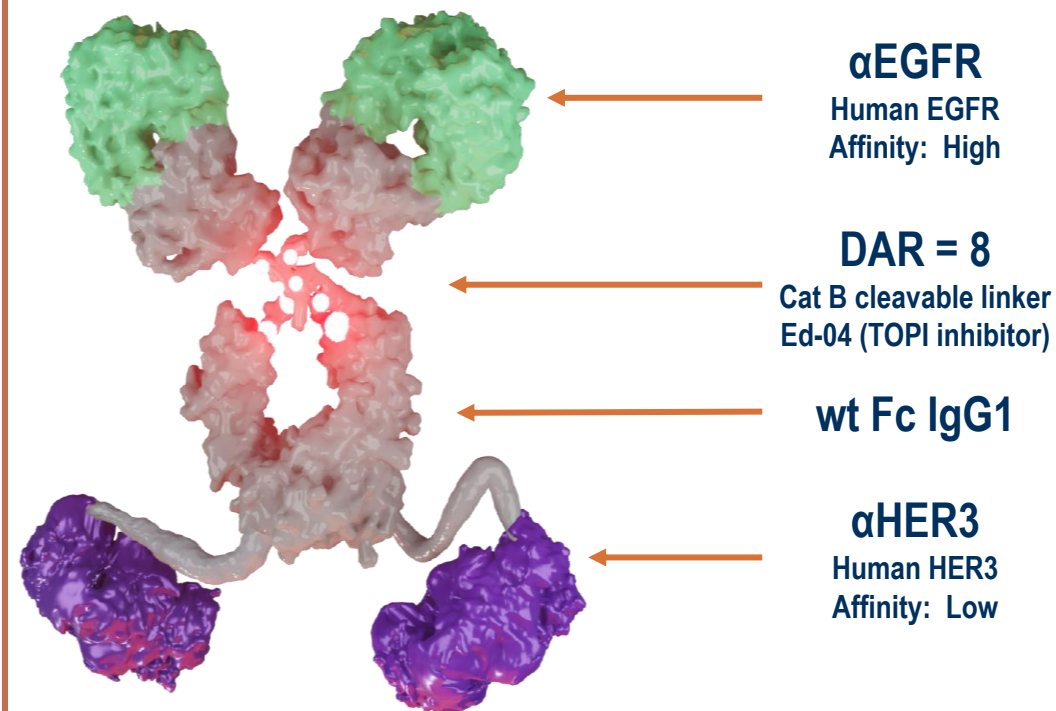


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Background

Iza-bren, an EGFR x HER3 bispecific ADC



wt: wild type; **Cat B**: cathepsin B; **TOPI**: Topoisomerase I.

- ❑ Iza-bren is a potentially first-in-class ADC comprised of an EGFR x HER3 bispecific antibody conjugated to a novel topoisomerase I inhibitor payload (Ed-04) via a stable tetrapeptide-based cleavable linker.
- ❑ Iza-bren uniquely targets EGFR and HER3, which are commonly expressed in SCLC¹⁻⁵.
- ❑ In a phase Ib study in patients with locally advanced or metastatic SCLC, iza-bren resulted in an ORR of 55.2% (confirmed ORR, 44.8%).

Results for safety, tolerability and efficacy from a phase II study evaluating iza-bren in combination with serplulimab⁶, an anti-PD-1 antibody, in treatment-naïve patients with extensive-stage small cell lung cancer (ES-SCLC) are presented (NCT06437509).

1. K Schmid et al. *Br J Cancer*. 2010 Aug 3;103(5):622–628. 2. Cerami et al. *Cancer Discovery*. May 2012 2; 401. 3. Gao et al. *Sci. Signal*. 6, p1 (2013). 4. de Bruijn et al. *Cancer Res* (2023). 5. https://www.cbiportal.org/study/summary?id=sclc_clcgp%2Cscld_jhu%2Cscld_ucologne_2015%2Cscld_cancercell_gardner_2017. 6. Y Cheng et al. *JAMA* 2022 Sep 27;328(12):1223-1232

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Study Design

Presented

Key Eligibility Criteria

- ❑ ES-SCLC confirmed by histopathology and/or cytology
- ❑ Failed standard treatment (Stage I) or treatment-naïve (Stage II)
- ❑ ECOG performance status of 0-1
- ❑ At least one measurable lesion per RECIST v1.1
- ❑ Adequate organ and marrow function

Stage I

Pts who failed standard treatment

Iza-bren 2.75 mg/kg D1D8Q3W
+ Serplulimab* 4.5 mg/kg Q3W

Stage II

Treatment-naïve pts

Iza-bren 2.5 mg/kg D1D8Q3W
+ Serplulimab 4.5 mg/kg Q3W

Iza-bren 2.75 mg/kg D1D8Q3W
+ Serplulimab 4.5 mg/kg Q3W

- **Primary:** ORR, RP2D (for combination treatment)
- **Secondary:** PFS, DCR, DOR, OS, PK, immunogenicity, DDI, safety

Safety and efficacy results for stage II are presented.

ECOG: Eastern Cooperative Oncology Group; **ORR:** objective response rate; **RP2D:** recommended phase 2 dose; **PFS:** progression-free survival; **DCR:** disease control rate; **DOR:** duration of response; **OS:** overall survival; **PK:** pharmacokinetics; **DDI:** drug-drug interaction

*: PD-1 inhibitor, which has been approved in China as first-line treatment for ES-SCLC in combined with carboplatin/etoposide.

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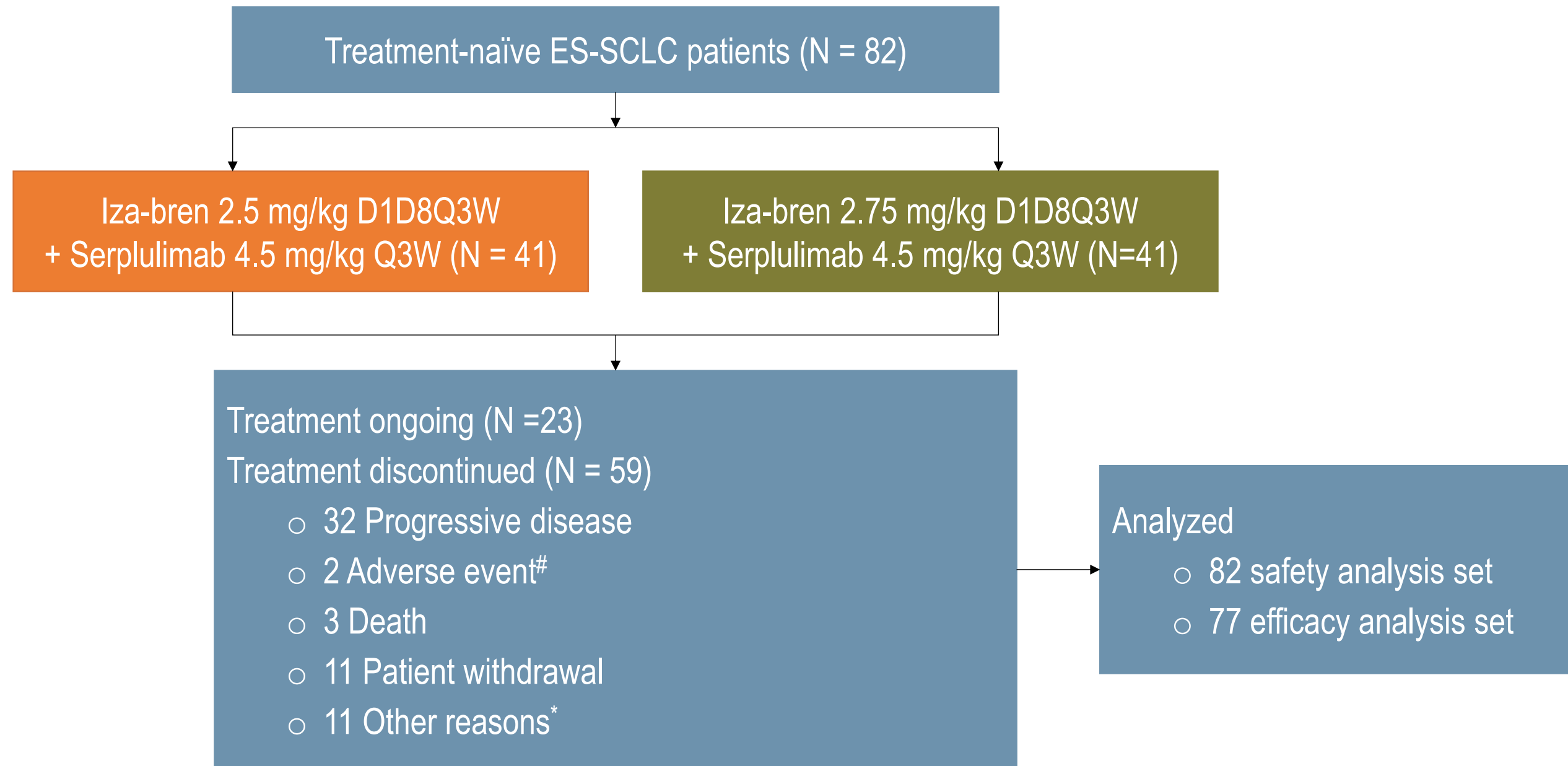
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Patient Disposition



*: Including 9 discontinued per physician decision; 2 with treatment delay >28 days

#: One discontinued due to G3 pneumonia, the other discontinued due to G4 respiratory failure. Both AEs were related to iza-bren and Serplulimab.

Data cutoff: November 30th, 2025

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Baseline Characteristics

	Total (N = 82)	Iza-bren D1D8 Q3W+Serplulimab 4.5 mg/kg Q3W	
		Iza-bren 2.5 mg/kg D1D8Q3W (N = 41)	Iza-bren 2.75 mg/kg D1D8Q3W (N = 41)
Median (Q1, Q3) age, years	61.5 (56.0, 67.0)	62.0 (60.0, 68.0)	59.0 (56.0, 66.0)
Male, n (%)	65 (79.3)	30 (73.2)	35 (85.4)
ECOG-PS score, n (%)			
0	24 (29.3)	10 (24.4)	14 (34.1)
1	58 (70.7)	31 (75.6)	27 (65.9)
Median (Q1, Q3) baseline SOD, mm	101.2 (75.1, 128.9)	96.0 (78.3, 126.9)	105.6 (72.0, 128.9)
Median (Q1, Q3) baseline BMI, kg/m²	23.3 (21.2, 25.6)	23.1 (21.3, 25.6)	23.9 (21.2, 25.6)
Smoking history, n (%)			
Never smoked	20 (24.4)	14 (34.1)	6 (14.6)
Previous smoking	54 (65.9)	23 (56.1)	31 (75.6)
Currently smoking	7 (8.5)	3 (7.3)	4 (9.8)
Missing	1 (1.2)	1 (2.4)	0
Brain metastasis at baseline, n (%)	1 (1.2)	1 (2.4)	0
Liver metastasis at baseline, n (%)	32 (39.0)	20 (48.8)	12 (29.3)

BMI: body mass index; SOD: sum of diameters of target lesions

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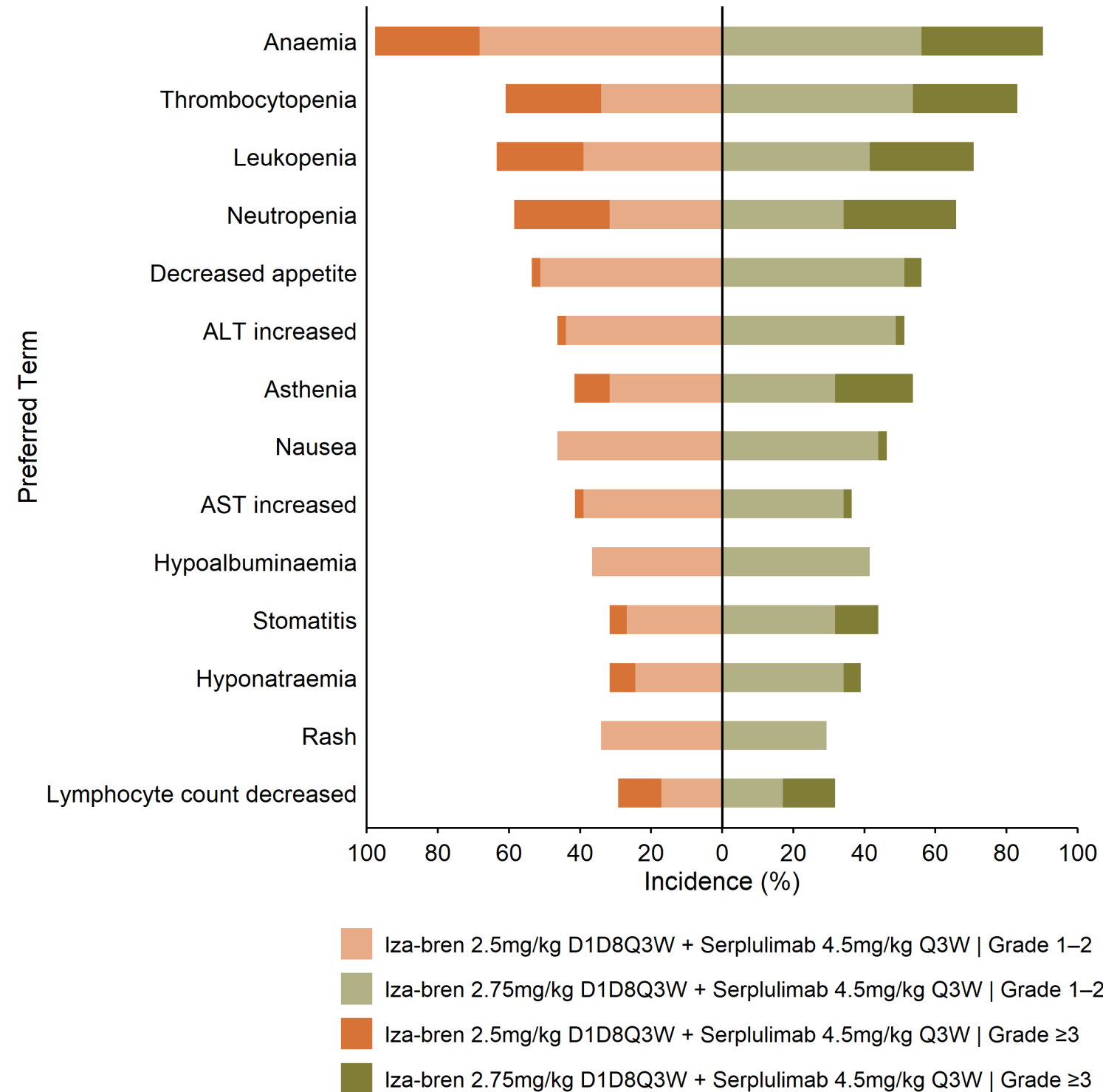
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TRAEs with Frequency $\geq 30\%$



- Grade ≥ 3 TRAEs which were predominantly hematologic in nature, were able to be effectively managed with standard supportive measures including dose reductions and growth factor support.
- 9.8% of patients had dose reduction and 1.2% of patients had dose discontinuation due to neutropenia. The median time to resolution of Grade 3 or 4 neutropenia was 3 days. Most only had 1 episode.
- Neutropenic fever rate was 2.4%.
- 6.1% of patients had dose reduction and 0 patient had dose discontinuation due to anaemia. The median time to resolution of Grade 3 anaemia was 7 days. Most had 2 episodes.
- All grade and grade ≥ 3 infection related AEs rate were 20.7% and 8.9%.
- Two deaths related to iza-bren (one due to multiple organ dysfunction syndrome, and one due to pneumonia and respiratory failure) were reported.
- Two cases (2.4%) of ILD were reported (one Grade 2, iza-bren 2.5 mg/kg D1D8Q3W cohort; one Grade 3, 2.75 mg/kg D1D8Q3W cohort).
- No new safety signals were identified.

TRAE: treatment related adverse event;

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Promising Efficacy Seen in Treatment-naïve Patients

	Total (N = 77)	Iza-bren D1D8 Q3W+Serplulimab 4.5 mg/kg Q3W	
		Iza-bren 2.5 mg/kg D1D8Q3W (N = 40)	Iza-bren 2.75 mg/kg D1D8Q3W (N = 37)
BOR, n (%)			
PR	68 (88.3)	34 (85.0)	34 (91.9)
Confirmed PR	60 (77.9)	31 (77.5)	29 (78.4)
PR pending confirmation ^[1]	1 (1.3)	0	1 (2.7)
SD	5 (6.5)	3 (7.5)	2 (5.4)
PD	4 (5.2)	3 (7.5)	1 (2.7)
ORR, % (95% CI)	88.3 (79.0, 94.5)	85.0 (70.2, 94.3)	91.9 (78.1, 98.3)
cORR, % (95% CI)	77.9 (67.0, 86.6)	77.5 (61.5, 89.2)	78.4 (61.8, 90.2)
DCR, % (95% CI)	94.8 (87.2, 98.6)	92.5 (79.6, 98.4)	97.3 (85.8, 99.9)
mDOR, mo (95% CI)	7.3 (5.6, 8.3)	7.3 (5.3, 8.3)	8.0 (5.5, 8.6)
mPFS, mo (95% CI)	8.2 (6.7, 9.6)	8.2 (4.4, 9.6)	8.3 (6.9, 9.7)
Median FU for PFS, mo (95% CI)	10.8 (8.3, 12.3)	9.8 (8.1, 12.4)	10.8 (8.3, 12.5)
12-mo OS rate, % (95% CI)	80.8 (66.1, 89.6)	85.7 (68.7, 93.9)	76.5 (51.4, 89.8)
Median FU for OS, mo (95% CI)	10.5 (9.7, 11.3)	10.5 (9.7, 11.6)	10.4 (9.2, 11.7)

Patients with at least one post baseline scan were included in the analysis.

[1] Patients still on study with tumor assessment of PR who have not yet reached to the next time point of tumor assessment.

CI: confidence interval; cORR: confirmed objective response rate; PR: partial response; SD: stable disease; PD: progressive disease; FU: follow-up time.

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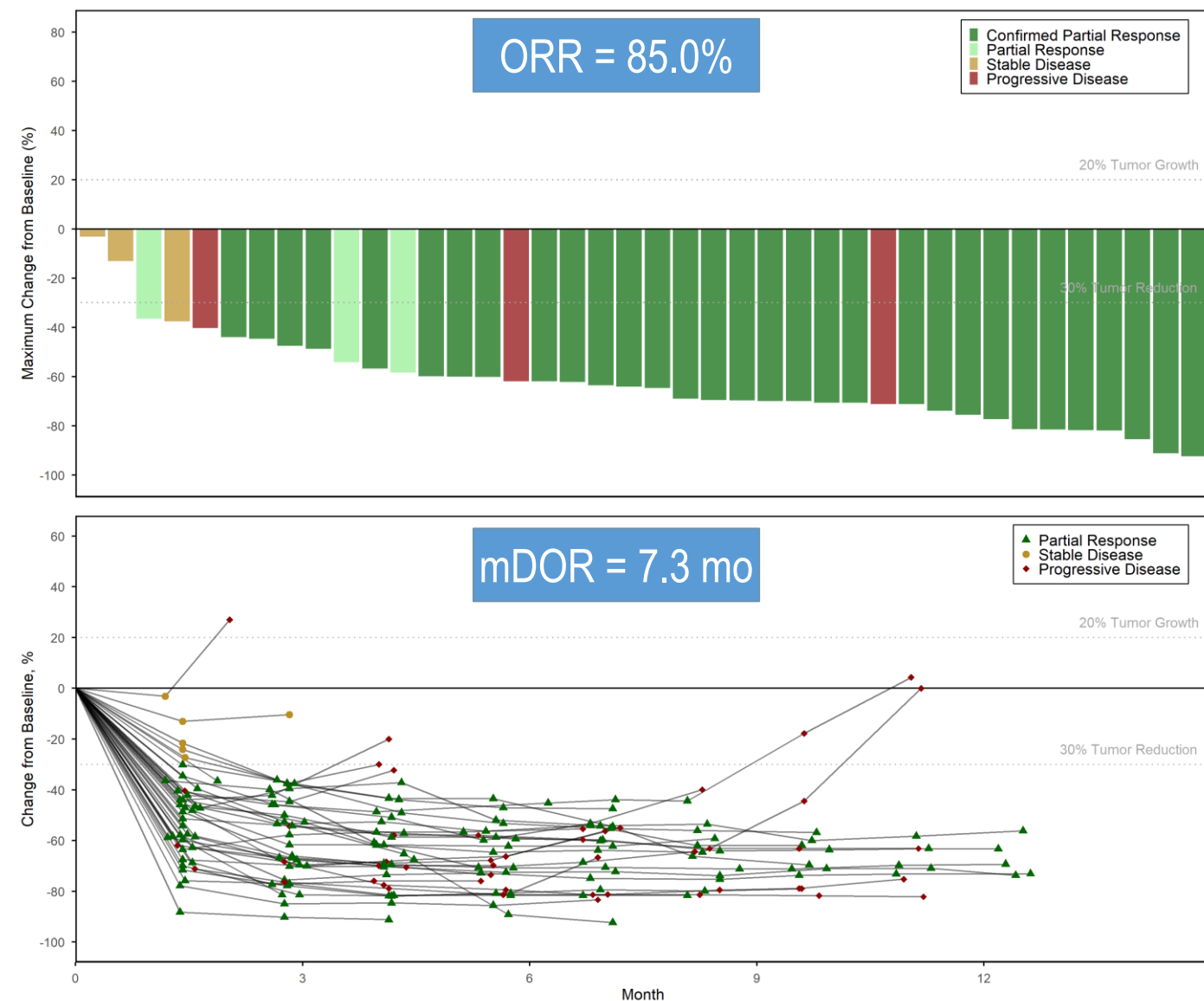


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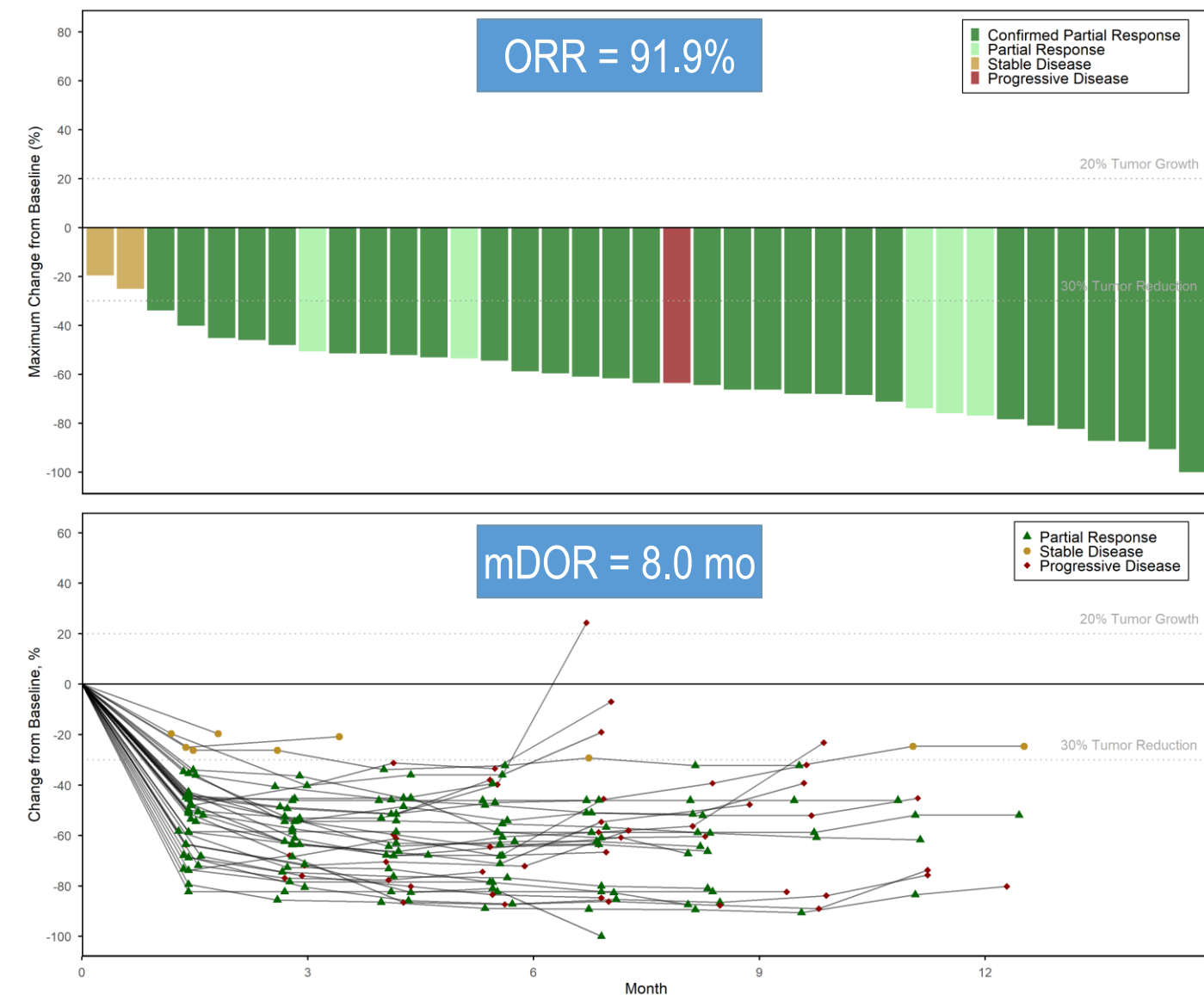


Depth & Duration of Response

Iza-bren 2.5 mg/kg D1D8Q3W+Serplulimab 4.5 mg/kg Q3W



Iza-bren 2.75 mg/kg D1D8Q3W+Serplulimab 4.5 mg/kg Q3W



- ❑ Iza-bren 2.5 mg/kg D1D8Q3W+Serplulimab: 100% of patients with tumor shrinkage and the median (range) shrinkage (%) was -64.4 (-92.4, -3.1).
- ❑ Iza-bren 2.75 mg/kg D1D8Q3W+Serplulimab: 100% of patients with tumor shrinkage and the median (range) shrinkage (%) was -63.6 (-100.0, -19.6).

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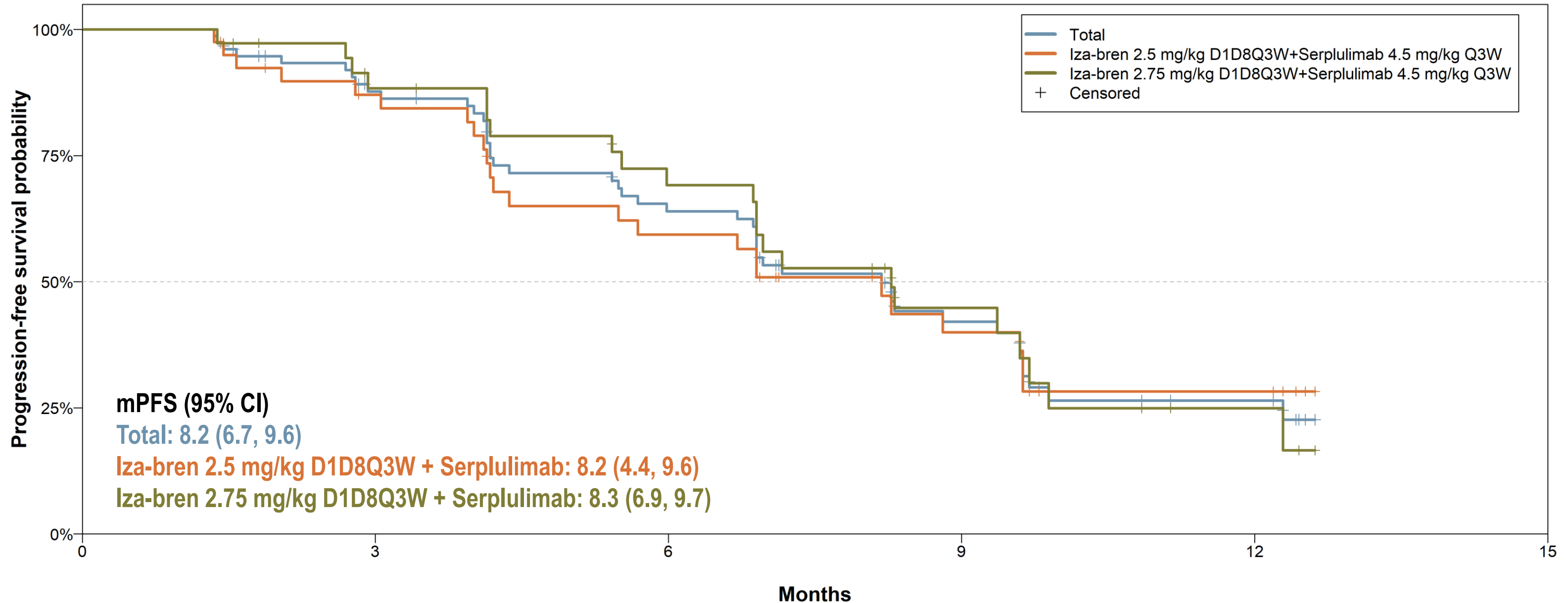
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PFS



Subjects at risk
 77
 40
 37

61
 32
 29

42
 21
 21

20
 11
 9

8
 5
 3

0
 0
 0

OS was immature at the time of DCO.

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Conclusions

- ❑ Iza-bren combined with serplulimab as a first-line treatment showed a tolerable and manageable safety profile in patients with ES-SCLC.
 - Hematologic toxicities were the most common AEs, but were effectively managed by supportive care and growth factor support.
 - Rate of iza-bren treatment discontinuation due to TRAEs was low overall (7.3%), with rates of 2.4% in the iza-bren 2.5 mg/kg D1D8Q3W cohort and 12.2% in the 2.75 mg/kg D1D8Q3W cohort .
- ❑ Encouraging antitumor activity was observed with iza-bren combined with serplulimab in 1L ES-SCLC:
 - In the cohort of iza-bren 2.5 mg/kg D1D8Q3W, ORR: 85.0%, cORR: 77.5%; mDOR: 7.3 mo; mPFS: 8.2 mo.
 - In the cohort of iza-bren 2.75 mg/kg D1D8Q3W, ORR: 91.9%, cORR: 78.4%; mDOR: 8.0 mo; mPFS: 8.3 mo.
- ❑ Iza-bren at 2.5 mg/kg D1D8 Q3W was selected as RP3D for combination with a PD-1 inhibitor and phase III study in China is in preparation for ES-SCLC.

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