2022 ASCO® ANNUAL MEETING

SKYSCRAPER-02: Primary results of a phase III, randomized, double-blind, placebo-controlled study of atezolizumab + carboplatin + etoposide with or without tiragolumab in patients with untreated extensive-stage small cell lung cancer

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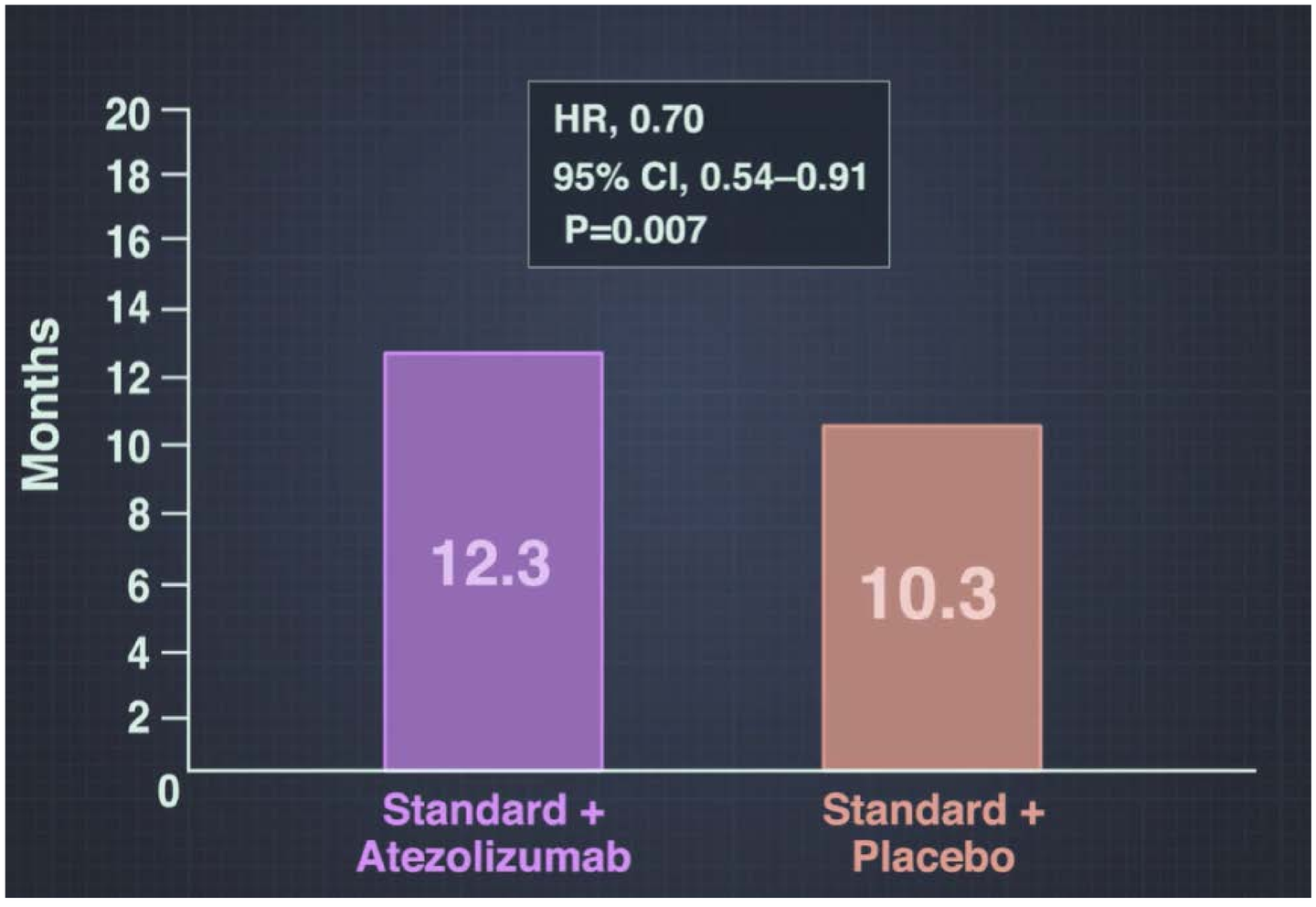
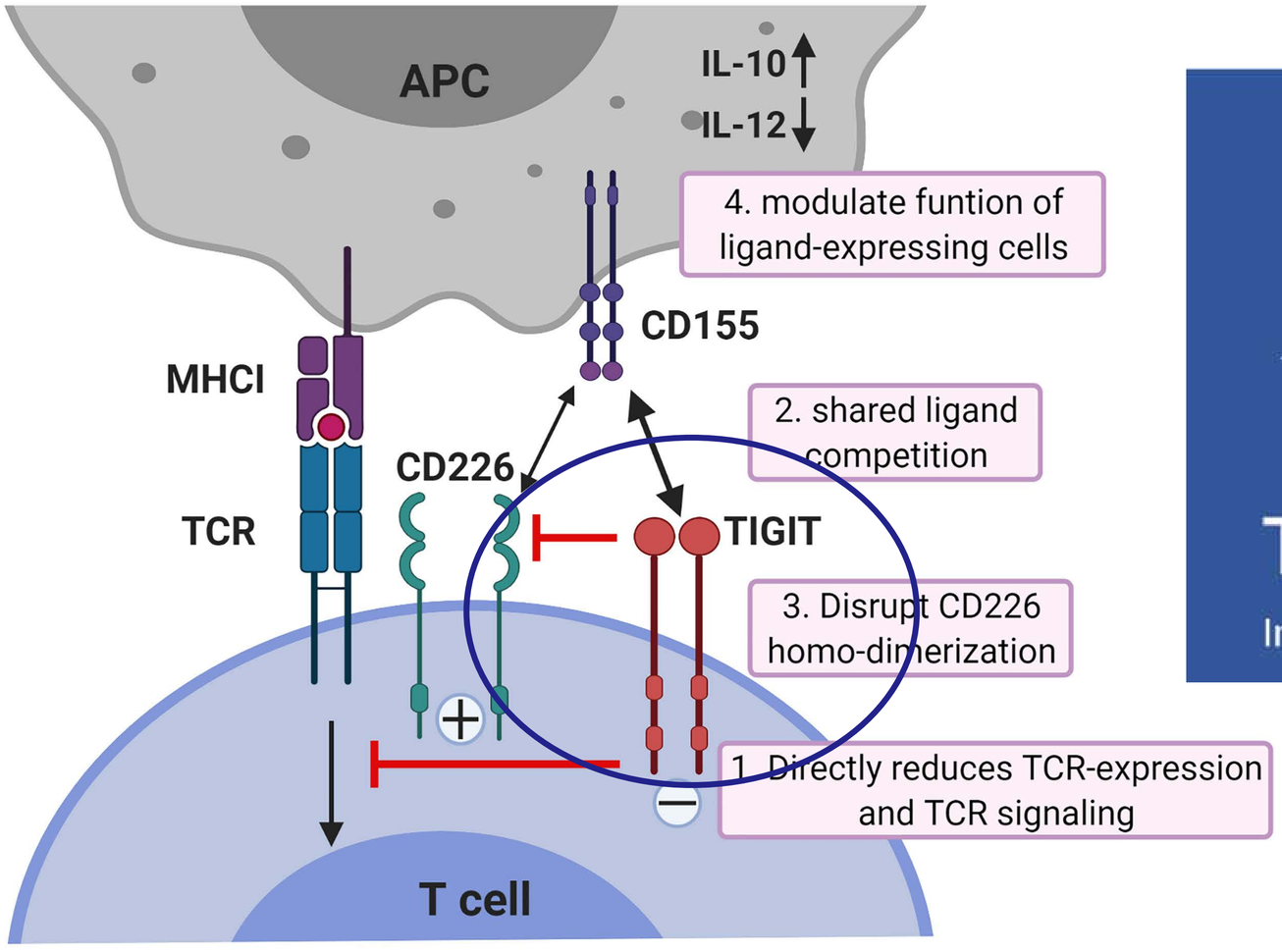
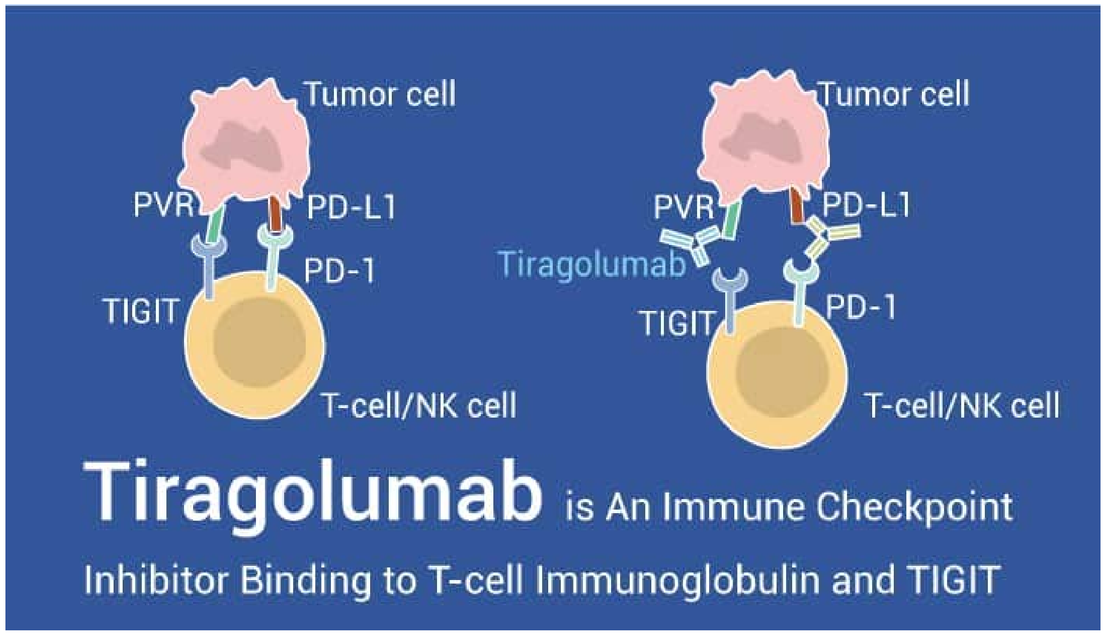
BACKGROUND

IMPOWER
133 in SCLC

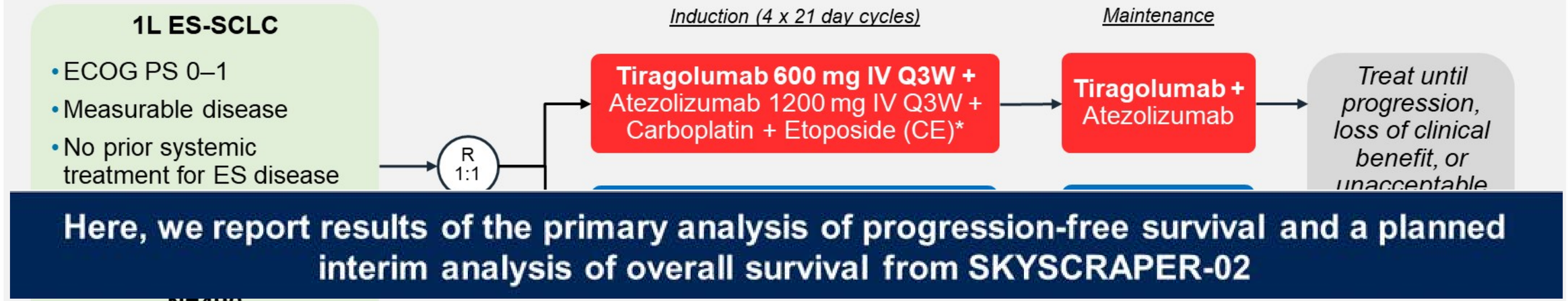


TIGIT


APC
IL-10
IL-12
4. modulate funtion of ligand-expressing cells
CD155
MHCI
2. shared ligand competition
CD226
TCR
TIGIT
3. Disrupt CD226 homo-dimerization
1. Directly reduces TCR-expression and TCR signaling
T cell


Tumor cell
PVR
PD-L1
PD-1
TIGIT
T-cell/NK cell
Tumor cell
PVR
PD-L1
Tiragolumab
TIGIT
PD-1
T-cell/NK cell
Tiragolumab is An Immune Checkpoint
Inhibitor Binding to T-cell Immunoglobulin and TIGIT

SKYSCRAPER-02: randomized, double-blind, placebo-controlled study of tiragolumab + atezolizumab + chemotherapy in patients with untreated ES-SCLC



Here, we report results of the primary analysis of progression-free survival and a planned interim analysis of overall survival from SKYSCRAPER-02

Stratification Factors:

- **ECOG PS** (0 vs. 1)
- **Brain metastases** (Yes vs. No)
- **LDH** (≤ ULN vs. > ULN)

Co-Primary Endpoints:

- OS and investigator-assessed PFS in **Primary Analysis Set** (all randomized patients without presence or history of brain metastases at baseline)

Secondary Endpoints:

- PFS and OS in **Full Analysis Set** (all randomized patients)
- Confirmed objective response rate
- Duration of response
- Safety
- Pharmacokinetics
- PROs

Primary analysis

- Cut-off date of 6 February 2022
- Median follow-up of 14.3 months (Primary Analysis Set)

NCT04256421

*Carboplatin IV AUC 5 mg/mL per min Q3W and etoposide IV 100mg/m^2 body surface area days 1–3 Q3W

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Baseline characteristics: Full Analysis Set

n (%)	Tiragolumab + atezolizumab + CE (n=243)	Placebo + atezolizumab + CE (n=247)
Age <65 years	117 (48.1)	116 (47.0)
Male	162 (66.7)	164 (66.4)
Race		
White	173 (71.2)	174 (70.4)
Asian	63 (25.9)	67 (27.1)
Other*	7 (2.9)	6 (2.4)
Tobacco Use		
Previous	153 (63.0)	161 (65.2)
Current	81 (33.3)	76 (30.8)
Never	9 (3.7)	10 (4)
Baseline ECOG PS‡		
0	86 (35.4)	82 (33.2)
1	156 (64.2)	165 (66.8)
LDH ≤ULN	99 (40.7)	101 (40.9)
Brain metastases	47 (19.3)	46 (18.6)
Treated§	14 (5.8)	19 (7.7)
Untreated	33 (13.6)	27 (10.9)
Liver metastases	89 (36.6)	94 (38.1)

Baseline characteristics in the Primary Analysis Set were similar to those in the Full Analysis Set

*Black or African American, Native Hawaiian or Pacific Islander, or Unknown; ‡One patient in the tiragolumab + atezolizumab + CE arm had baseline ECOG PS 2
§Previously treated with local CNS-directed therapy, with no ongoing requirement for anticonvulsants or corticosteroids

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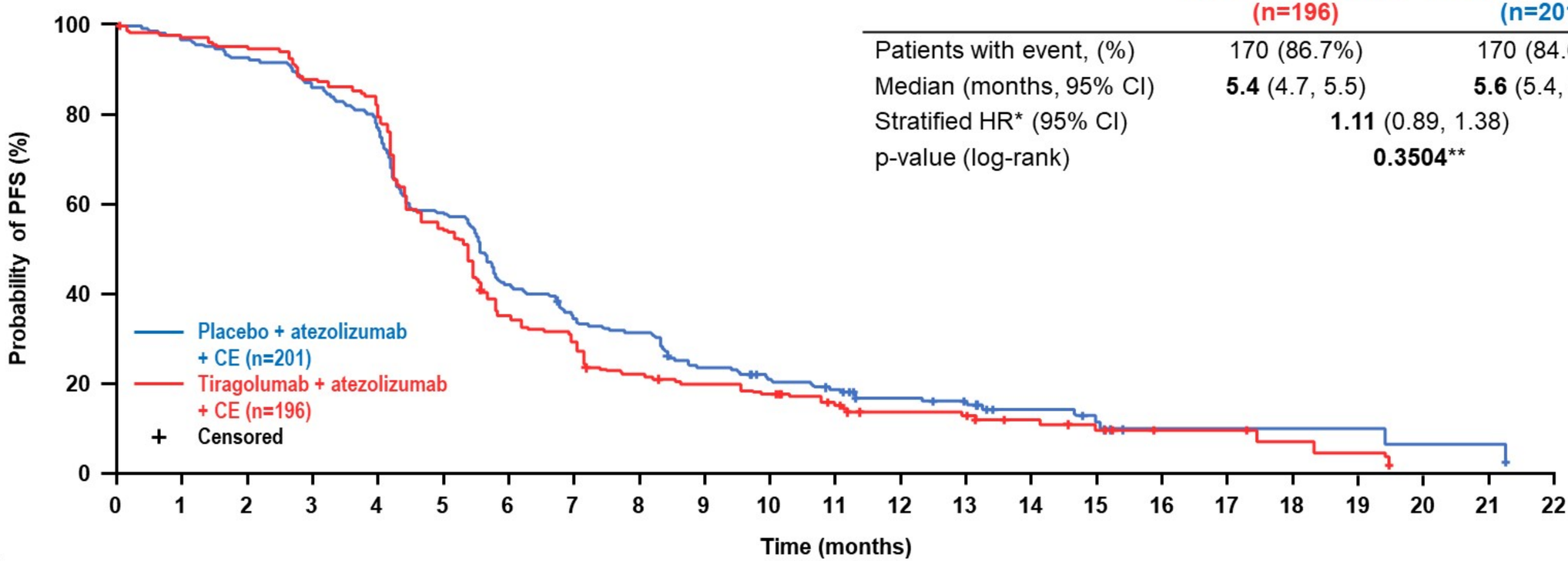
PFS: Primary Analysis Set



	Tiragolumab + atezolizumab + CE (n=196)	Placebo + atezolizumab + CE (n=201)
Patients with event, (%)	170 (86.7%)	170 (84.6%)
Median (months, 95% CI)	**5.4** (4.7, 5.5)	**5.6** (5.4, 5.9)
Stratified HR* (95% CI)	**1.11** (0.89, 1.38)	
p-value (log-rank)	**0.3504****	

No. at risk

Placebo + atezo + CE	201	192	184	171	152	115	84	68	62	46	39	34	26	20	11	8	3	3	3	3	2	2	NE
Tiragolumab + atezo + CE	196	189	183	170	154	105	67	54	41	37	33	25	17	17	11	8	5	5	3	2	NE	NE	NE

*Stratification factors are: ECOG, LDH; **Statistical boundary: 0.001
Data cut-off: 6 February 2022 (median follow-up:14.3 months)

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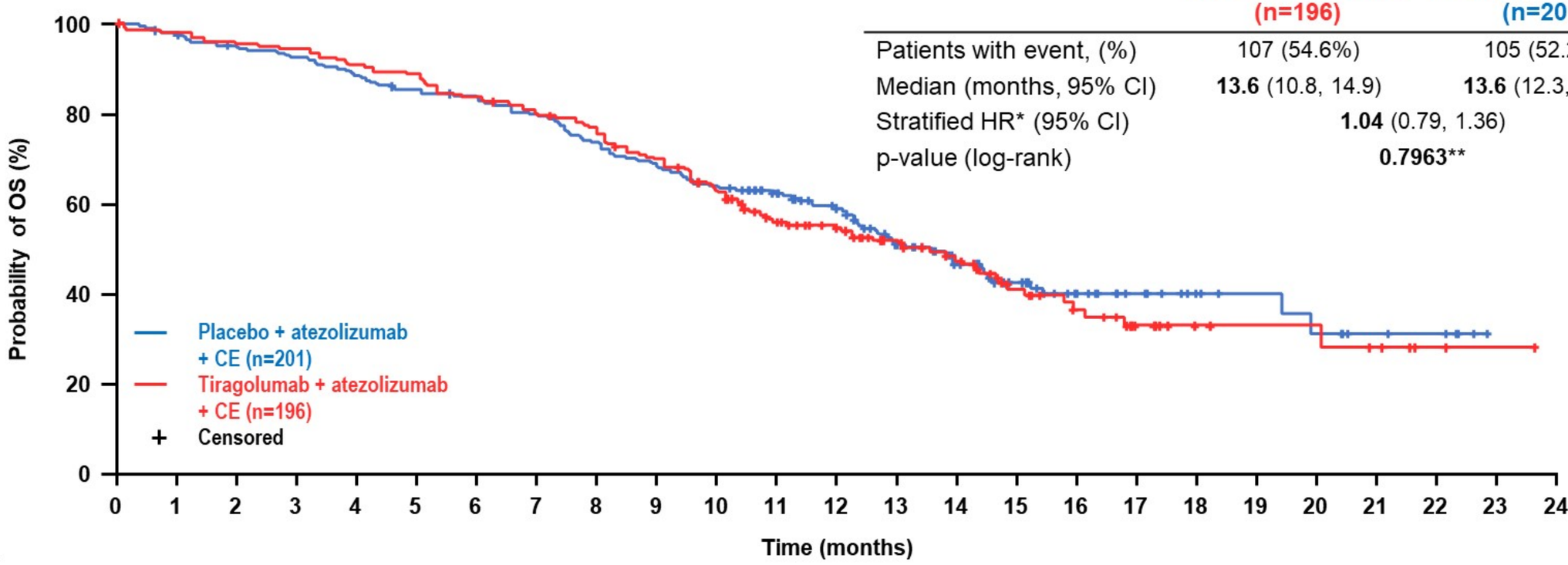
Interim OS: Primary Analysis Set

	Tiragolumab + atezolizumab + CE (n=196)	Placebo + atezolizumab + CE (n=201)
Patients with event, (%)	107 (54.6%)	105 (52.2%)
Median (months, 95% CI)	**13.6** (10.8, 14.9)	**13.6** (12.3, 15.2)
Stratified HR* (95% CI)	**1.04** (0.79, 1.36)	
p-value (log-rank)	**0.7963****	



No. at risk

Placebo + atezo + CE	201	195	188	183	175	168	164	156	144	134	125	115	97	70	47	36	26	19	12	9	7	5	4	NE	NE
Tiragolumab + atezo + CE	196	191	186	184	177	172	162	154	146	133	116	93	80	62	51	32	21	14	9	7	7	5	2	1	NE

*Stratification factors are: ECOG, LDH; **Statistical boundary: 0.0175
Data cut-off: 6 February 2022 (median follow-up:14.3 months)

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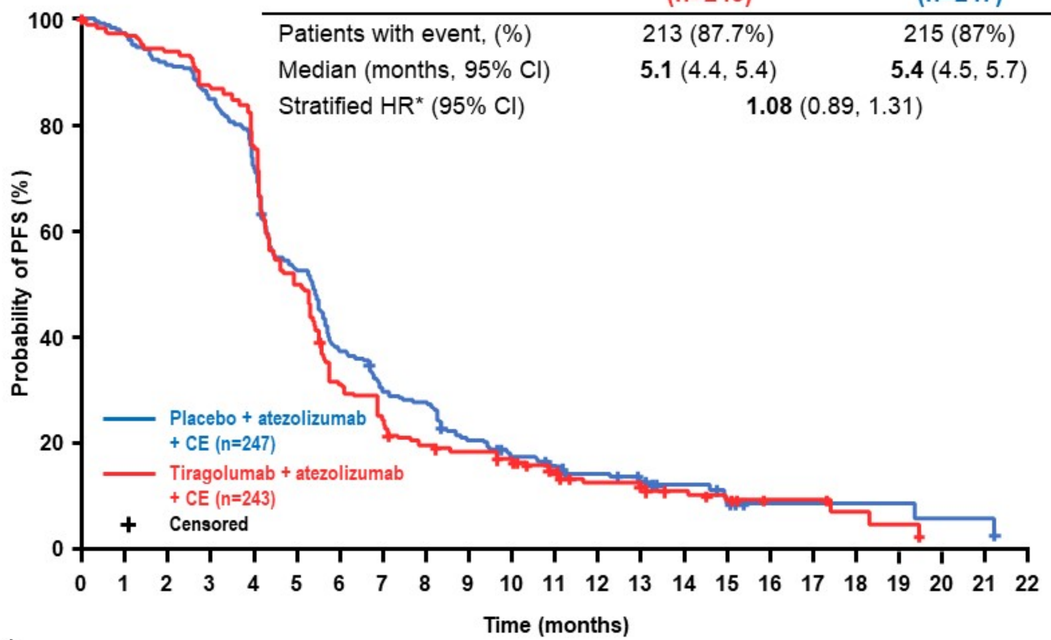
PFS and OS: Full Analysis Set

PFS in the Full Analysis Set

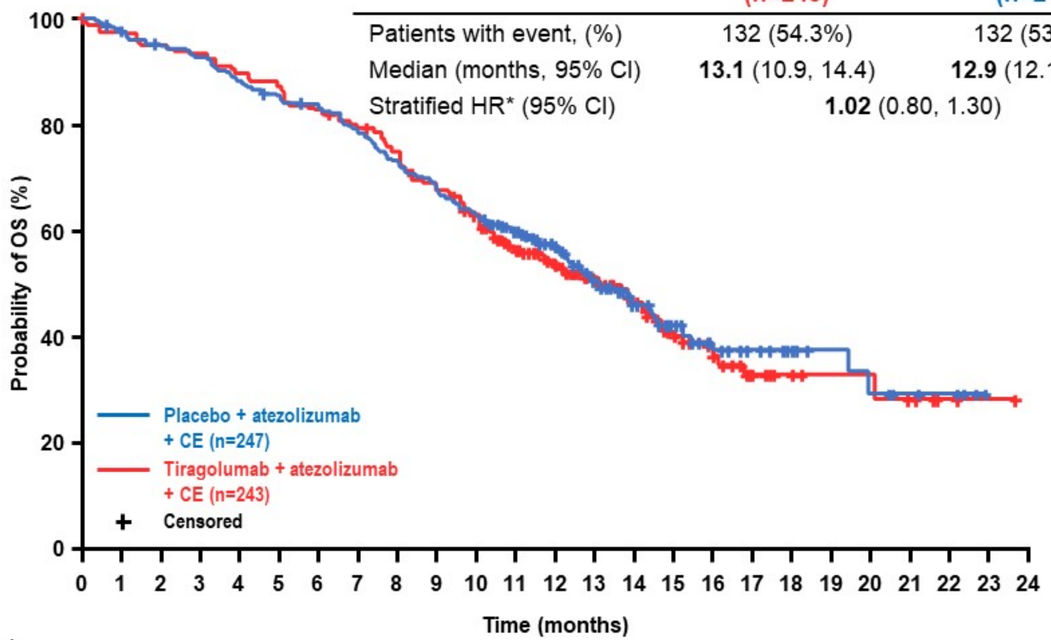
	Tiragolumab + atezolizumab + CE (n=243)	Placebo + atezolizumab + CE (n=247)
Patients with event, (%)	213 (87.7%)	215 (87%)
Median (months, 95% CI)	**5.1** (4.4, 5.4)	**5.4** (4.5, 5.7)
Stratified HR* (95% CI)	**1.08** (0.89, 1.31)	



No. at risk																						
Placebo + atezo + CE	247	237	224	207	185	128	92	73	66	49	40	34	26	20	11	8	3	3	3	3	2	2	NE
Tiragolumab + atezo + CE	243	232	224	209	188	120	74	59	45	41	35	27	18	18	12	9	5	5	3	2	NE	NE	NE

Interim OS in the Full Analysis Set

	Tiragolumab + atezolizumab + CE (n=243)	Placebo + atezolizumab + CE (n=247)
Patients with event, (%)	132 (54.3%)	132 (53.4%)
Median (months, 95% CI)	**13.1** (10.9, 14.4)	**12.9** (12.1, 14.5)
Stratified HR* (95% CI)	**1.02** (0.80, 1.30)	



No. at risk																									
Placebo + atezo + CE	247	240	232	226	215	207	202	190	176	165	152	134	109	80	52	40	26	19	12	9	7	5	4	NE	NE
Tiragolumab + atezo + CE	243	235	228	225	216	210	199	190	176	161	141	114	90	70	56	36	24	14	9	7	7	5	2	1	NE

*Stratification factors are: ECOG, LDH
Data cut-off: 6 February 2022 (median follow-up:13.9 months)

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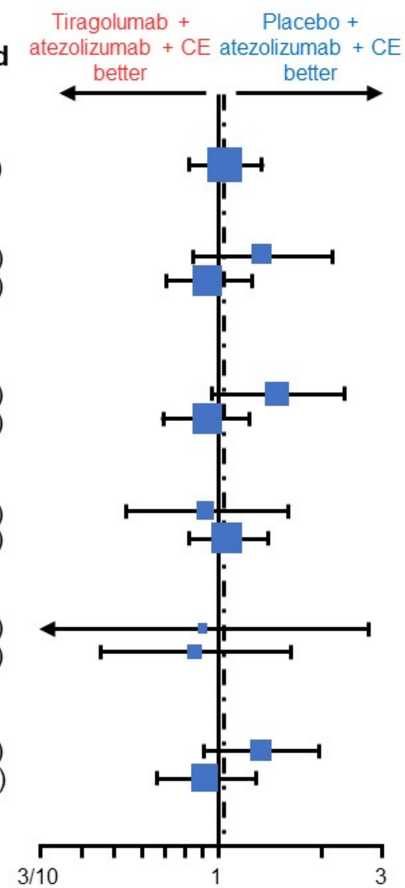
Subgroup analysis of OS: Full Analysis Set

Baseline risk factors	Total n	Placebo + atezolizumab + CE (n=247) n	Events	Median (months)	Tiragolumab + atezolizumab + CE (n=243) n	Events	Median (months)	Unstratified hazard ratio	Unstratified 95% CI
All patients	490	247	132	12.9	243	132	13.1	1.04	(0.82, 1.32)
Baseline ECOG									
0	168	82	31	NE	86	41	14.9	1.34	(0.84, 2.14)
1	321	165	101	12.0	156	90	11.7	0.93	(0.70, 1.24)
LDH									
≤ULN	199	94	34	19.4	105	48	14.8	1.48	(0.95, 2.31)
>ULN	291	153	98	9.9	138	84	10.3	0.92	(0.68, 1.23)
Brain metastasis									
Yes	93	46	27	10.6	47	25	11.7	0.92	(0.53, 1.59)
No	397	201	105	13.6	196	107	13.6	1.06	(0.81, 1.39)
Brain metastasis: Yes									
Treated	33	19	9	16.0	14	5	NE	0.89	(0.29, 2.69)
Untreated	60	27	18	10.2	33	20	11.7	0.85	(0.45, 1.62)
Liver metastasis at enrollment									
Yes	183	94	54	12.3	89	57	9.9	1.32	(0.91, 1.92)
No	307	153	78	13.8	154	75	14.2	0.92	(0.67, 1. 26)



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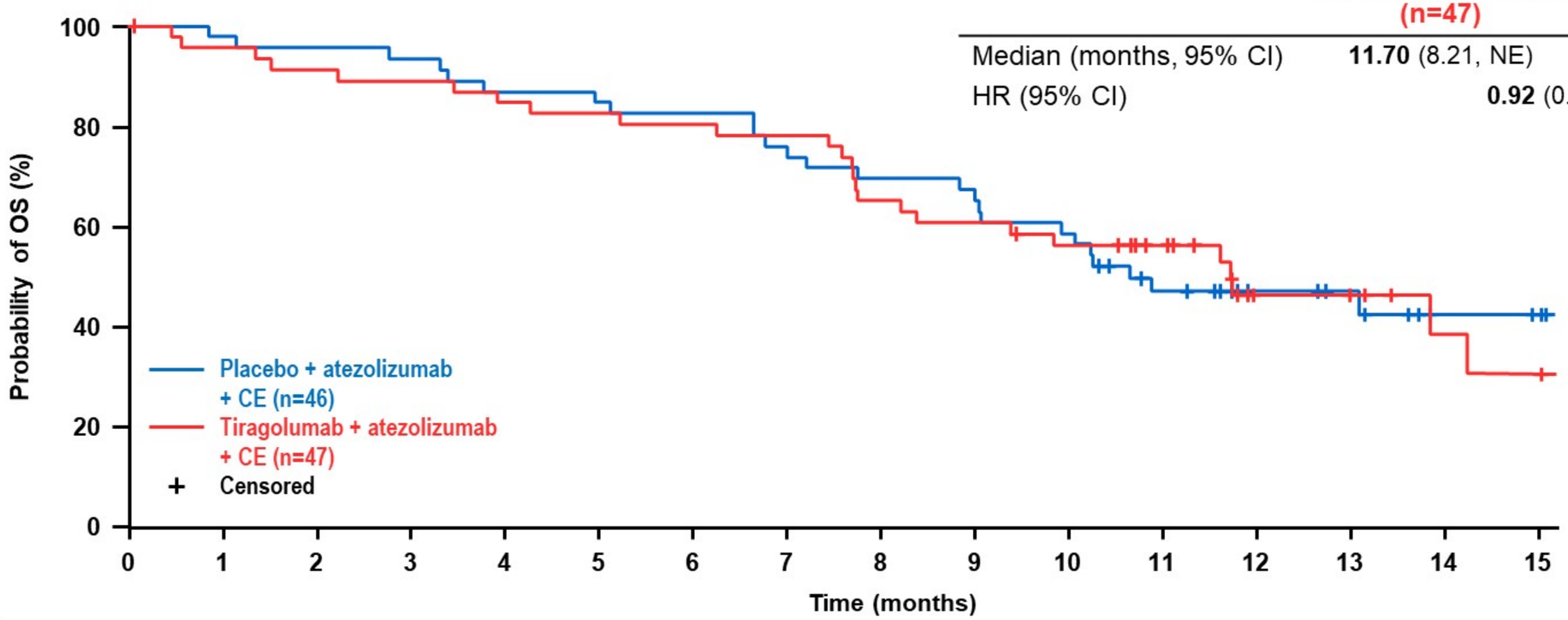
Subgroup OS: patients with brain metastases

	Tiragolumab + atezolizumab + CE (n=47)	Placebo + atezolizumab + CE (n=46)
Median (months, 95% CI)	**11.70** (8.21, NE)	**10.64** (9.03, NE)
HR (95% CI)	**0.92** (0.53, 1.59)	



No. at risk

Placebo + atezo + CE	46	45	44	43	40	39	38	34	32	31	27	19	12	10	5	4
Tiragolumab + atezo + CE	47	44	42	41	39	38	37	36	30	28	25	21	10	8	5	4

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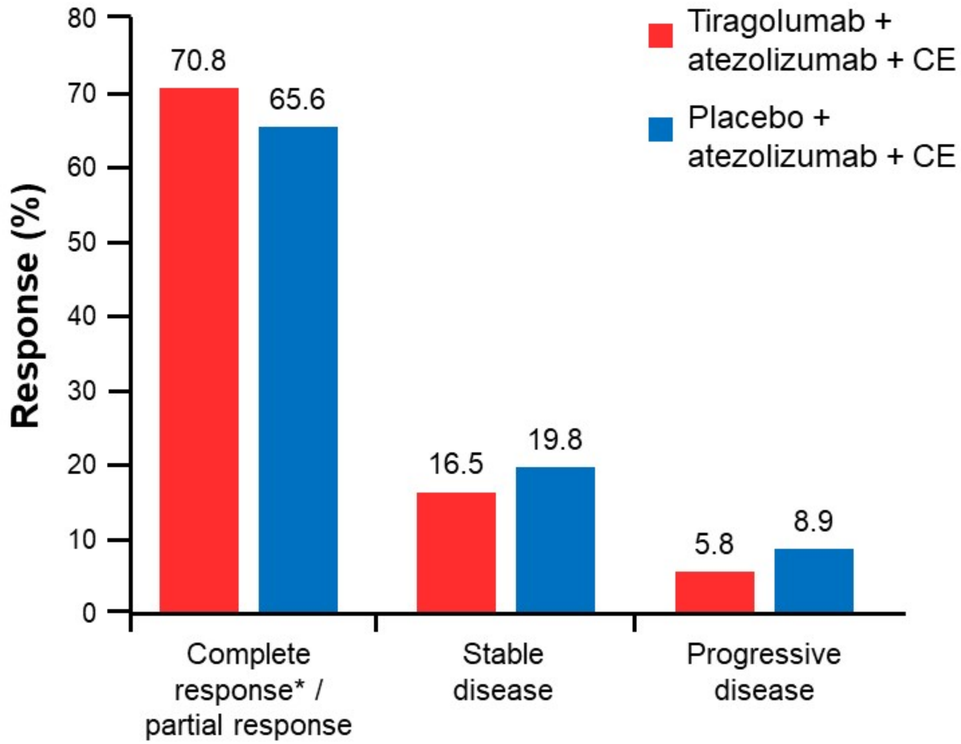
Objective response rate and duration of response: Full Analysis Set



	Tiragolumab + atezolizumab + CE (n=243)	Placebo + atezolizumab + CE (n=247)
Objective response rate, % (95% CI)	**70.8** (64.6, 76.3)	**65.6** (59.3, 71.4)
Duration of response		
Responders, n	172	162
With subsequent event, n (%)	147 (85.5)	135 (83.3)
Median, months (95% CI)	**4.2** (4.1, 4.4)	**5.1** (4.4, 5.8)

*1 patient (0.4%) in the tiragolumab + atezolizumab + CE arm and 2 patients (0.8%) in the placebo + atezolizumab + CE arm had complete response
Data cut-off: 6 February 2022

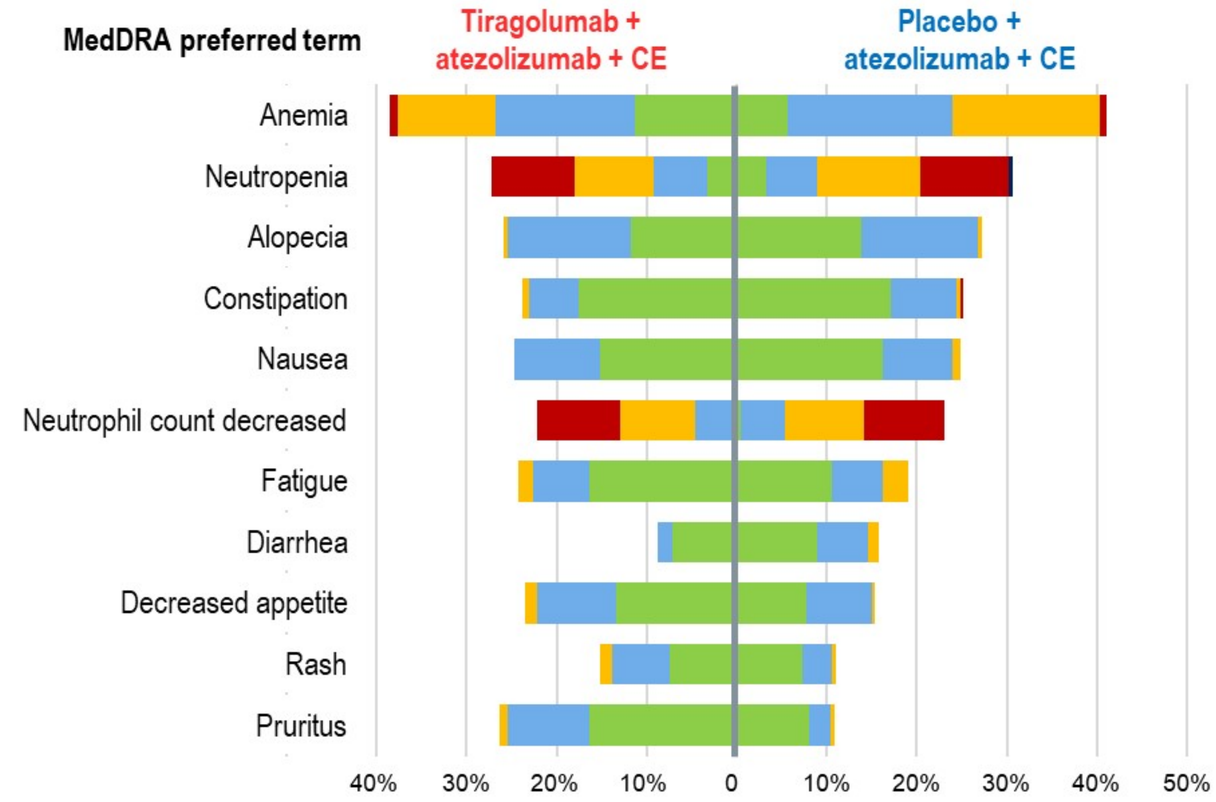
Safety overview: Safety Evaluable Set

n (%)	Tiragolumab + atezolizumab + CE (n=239)	Placebo + atezolizumab + CE (n=246)
All grade AEs, any cause	**238 (99.6)**	**245 (99.6)**
Grade 3–4 AEs	154 (64.4)	158 (64.2)
Grade 5 AEs	12 (5.0)	15 (6.1)
Treatment-related AEs	**221 (92.5)**	**227 (92.3)**
Grade 3–4 TRAEs	125 (52.3)	137 (55.7)
Grade 5 TRAEs	1 (0.4)	5 (2.0)
AEs of special interest*	**128 (53.6)**	**118 (48.0)**
Grade 3–4	19 (7.9)	17 (6.9)
Grade 5‡	1 (0.4)	2 (0.8)
Required systemic corticosteroids	30 (12.6)	26 (10.6)
Serious AEs	**105 (43.9)**	**97 (39.4)**
AEs leading to any treatment withdrawal	**17 (7.1)**	**23 (9.3)**
TRAEs leading to any treatment withdrawal	12 (5.0)	13 (5.3)

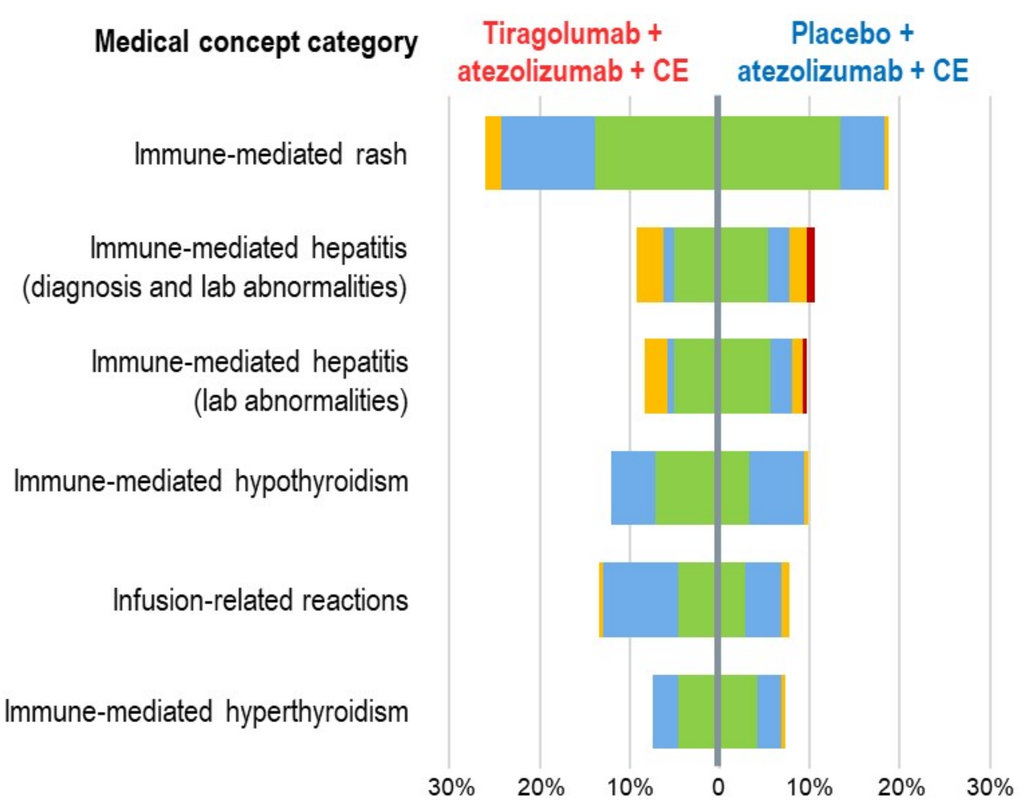
*Immune-mediated AEs; ‡Grade 5 AEs of special interest were 2 cases of interstitial lung disease (placebo + atezolizumab + CE arm) and 1 case of hepatorenal syndrome (tiragolumab + atezolizumab + CE arm); Safety Evaluable Set included all randomized patients who received at least one dose of any study drug; Data cut-off: 6 February 2022

Incidence of adverse events: Safety Evaluable Set

All cause AEs (>15% in at least one arm)



AEs of special interest (>5% in at least one arm)



Grade 1 2 3 4 5

Safety Evaluable Set included all randomized patients who received at least one dose of any study drug; Data cut-off: 6 February 2022

Conclusions

- The addition of tiragolumab to atezolizumab and chemotherapy did not provide further benefit over atezolizumab + chemotherapy in patients with untreated ES-SCLC
  - No difference in PFS or OS was observed between treatment arms in the Primary Analysis Set (patients without history or presence of brain metastases) or the Full Analysis Set (all patients)
- Tiragolumab + atezolizumab + chemotherapy was well tolerated
  - The safety profile was similar to that of atezolizumab + chemotherapy and was consistent with previous observations for the combination
  - No new safety signals were identified
- PFS and OS observed in the control arm (placebo + atezolizumab + chemotherapy) support the results observed in the IMpower133 trial and further confirms this combination as a standard-of-care for 1L treatment of patients with ES-SCLC
- The SKYSCRAPER-02 study will continue to the planned primary OS analysis and biomarker analyses are ongoing
- Based on these data, targeting TIGIT in ES-SCLC does not appear to be therapeutically relevant
- Investigation of tiragolumab is ongoing in NSCLC and other tumor types, including esophageal cancer