Updated analysis and patient-reported outcomes from CITYSCAPE: a randomised, double-blind, Phase II study of the anti-TIGIT antibody tiragolumab + atezolizumab vs placebo + atezolizumab as first-line treatment for PD-L1+ NSCLC

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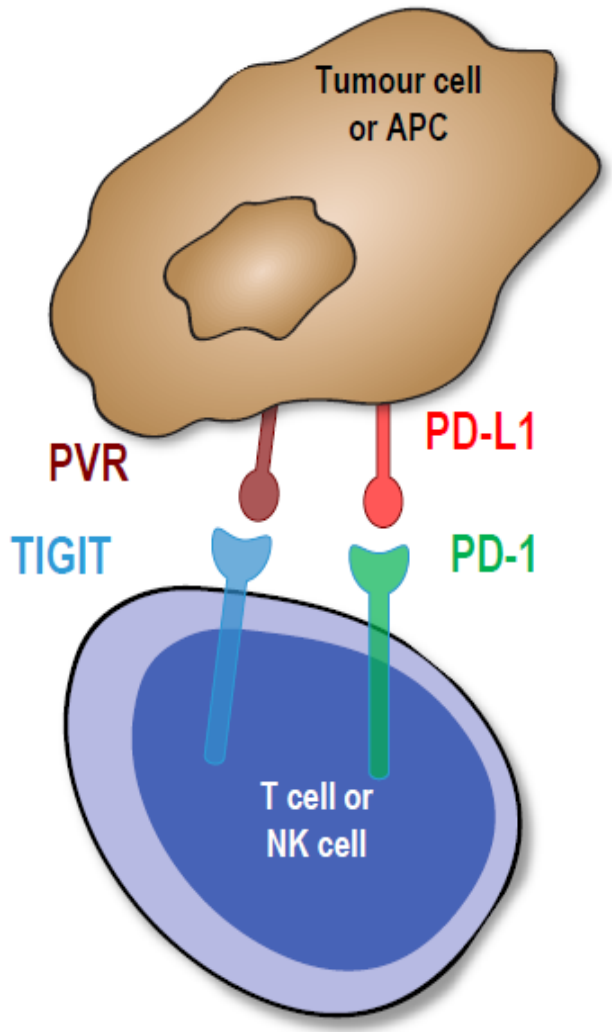
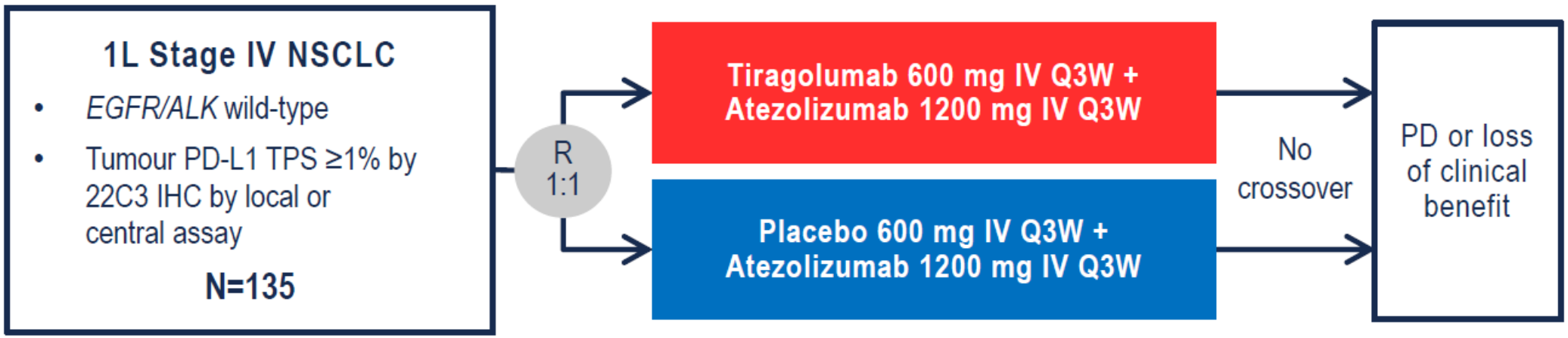
Background

- TIGIT (T cell immunoreceptor with Ig and ITIM domains) is a novel inhibitory immune checkpoint present on activated T cells and NK cells in multiple cancers.[1–3] TIGIT expression correlates with PD-1, especially in tumour-infiltrating T cells
- Tiragolumab is a fully human IgG1/kappa anti-TIGIT monoclonal antibody with an intact Fc region that blocks the binding of TIGIT to its receptor PVR
- We hypothesise that anti-TIGIT antibodies, such as tiragolumab, could restore the anti-tumour response and may amplify the activity of anti-PD-L1/PD-1 antibodies
- CITYSCAPE (NCT03563716) is the first randomised Phase II study of an anti-TIGIT antibody. At the primary analysis, tiragolumab + atezolizumab showed a clinically meaningful improvement in ORR and PFS in the ITT population compared with atezolizumab monotherapy. This was maintained after a further 5 months of follow-up, with a greater magnitude of improvement seen in the PD-L1 TPS ≥50% subgroup[4]
- Tiragolumab has been granted Breakthrough Therapy Designation (BTD) by the US FDA, in combination with atezolizumab for first-line treatment of patients with metastatic NSCLC whose tumours have high PD-L1 expression with no *EGFR* or *ALK* genomic tumour aberrations
- Here, we present an updated analysis with ~30 months of follow-up, including OS, updated PFS and safety analyses and patient-reported outcomes (PROs)



CITYSCAPE: randomised Phase II study of tiragolumab + atezolizumab in PD-L1+ patients with NSCLC



Stratification factors
- PD-L1 TPS (1–49% vs ≥50%)
- Histology (non-squamous vs squamous)
- Tobacco use (yes vs no)

Co-primary endpoints
- ORR and PFS

Key secondary endpoints
- Safety, DOR, OS

Exploratory endpoints
- Efficacy analysis by PD-L1 status, PROs

Primary analysis[1]
- Cut-off date of 30 June 2019
- Median follow-up of 5.9 months

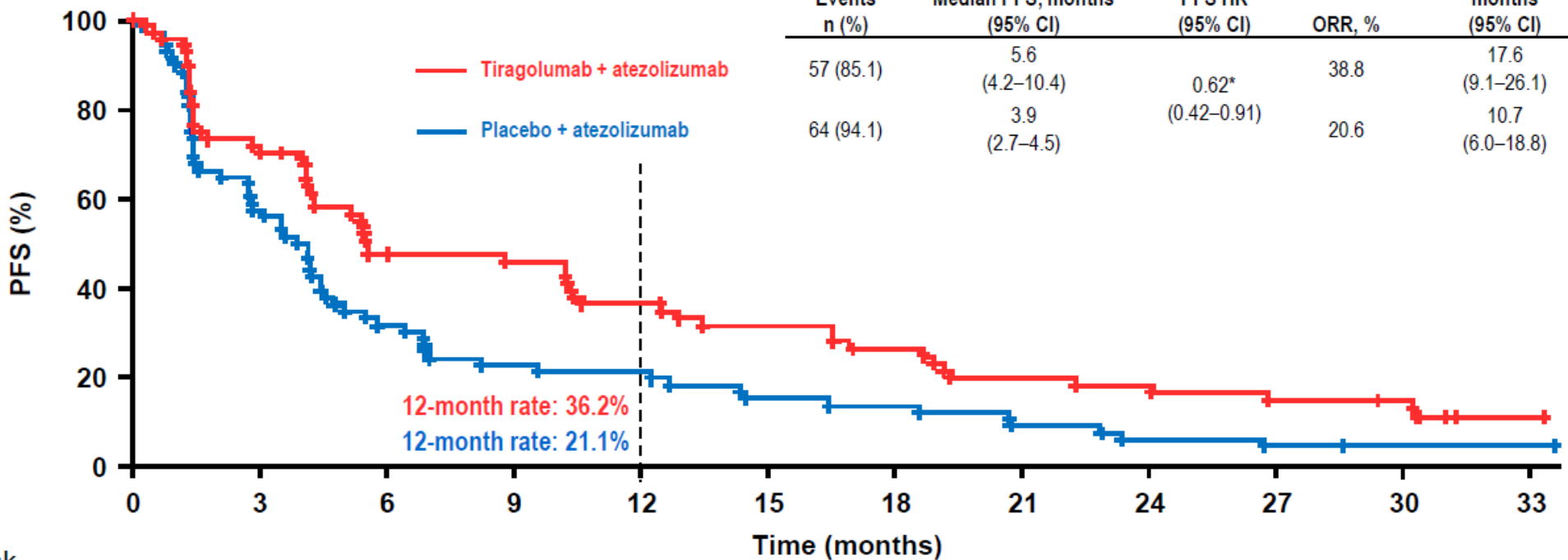
Updated analysis
- Follow-up performed to assess safety and efficacy
- Cut-off date of 16 August 2021
- Median follow-up of 30.4 months

1. Rodriguez-Abreu et al. ASCO 2020

Baseline characteristics (ITT population)

n, (%)	Tiragolumab + atezolizumab (n=67)	Placebo + atezolizumab (n=68)
Age <65 years	28 (41.8)	28 (41.2)
Male	39 (58.2)	48 (70.6)
White	42 (62.7)	40 (58.8)
Asian	18 (26.9)	23 (33.8)
ECOG PS 0	20 (29.9)	19 (27.9)
Never used tobacco*	7 (10.4)	7 (10.3)
Non-squamous histology*	40 (59.7)	40 (58.8)
PD- L1 TPS ≥50%*	29 (43.3)	29 (42.6)
PD-L1 TPS 1–49%*	38 (56.7)	39 (57.4)

Investigator-assessed PFS: ITT population



	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
T + A	57 (85.1)	5.6 (4.2–10.4)	0.62* (0.42–0.91)	38.8	17.6 (9.1–26.1)
P + A	64 (94.1)	3.9 (2.7–4.5)		20.6	10.7 (6.0–18.8)

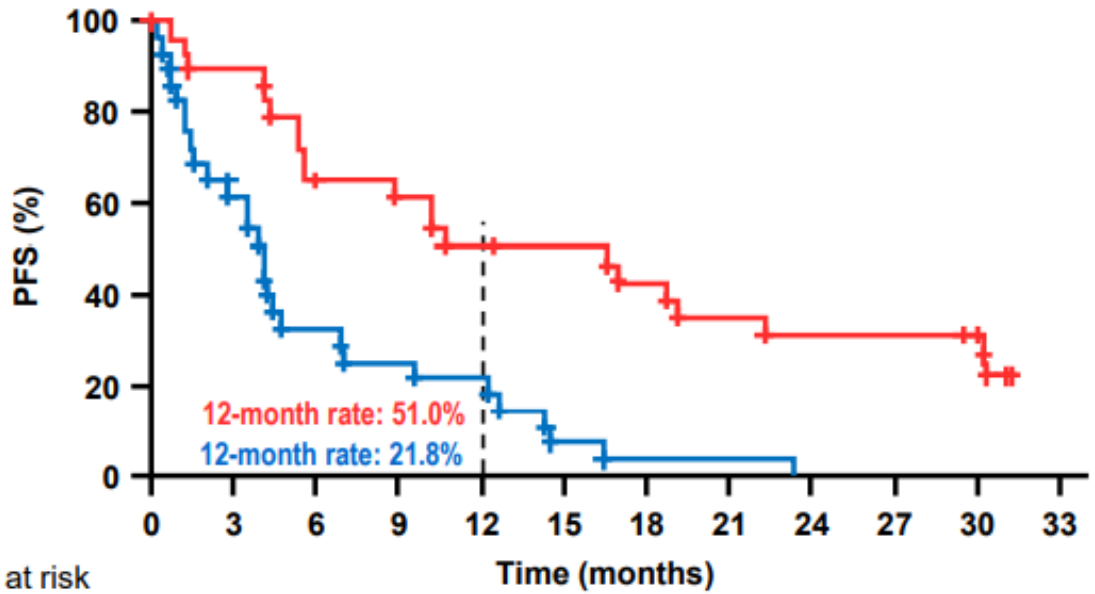
No. at risk

T + A	67	48	31	29	23	19	16	12	11	9	8	1
P + A	68	38	21	15	14	10	9	6	4	3	2	2

Investigator-assessed PFS: PD-L1 subgroups

PD-L1 TPS ≥50% (n=58)

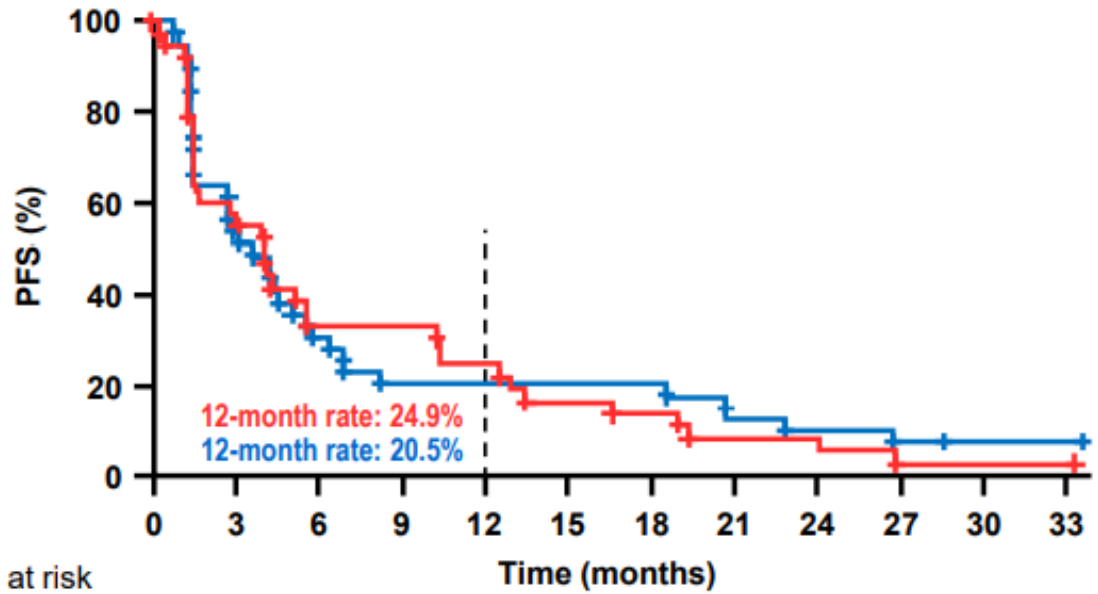
	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tira + atezo	21 (72.4)	16.6 (5.5–22.3)	0.29* (0.15–0.53)	69.0	15.7 (9.1–NE)
Placebo + atezo	28 (96.6)	4.1 (2.1–6.8)		24.1	8.2 (5.6–10.4)



No. at risk												
T + A	29	26	19	17	14	13	11	9	8	8	7	NE
P + A	29	17	9	7	6	2	1	1	NE	NE	NE	NE

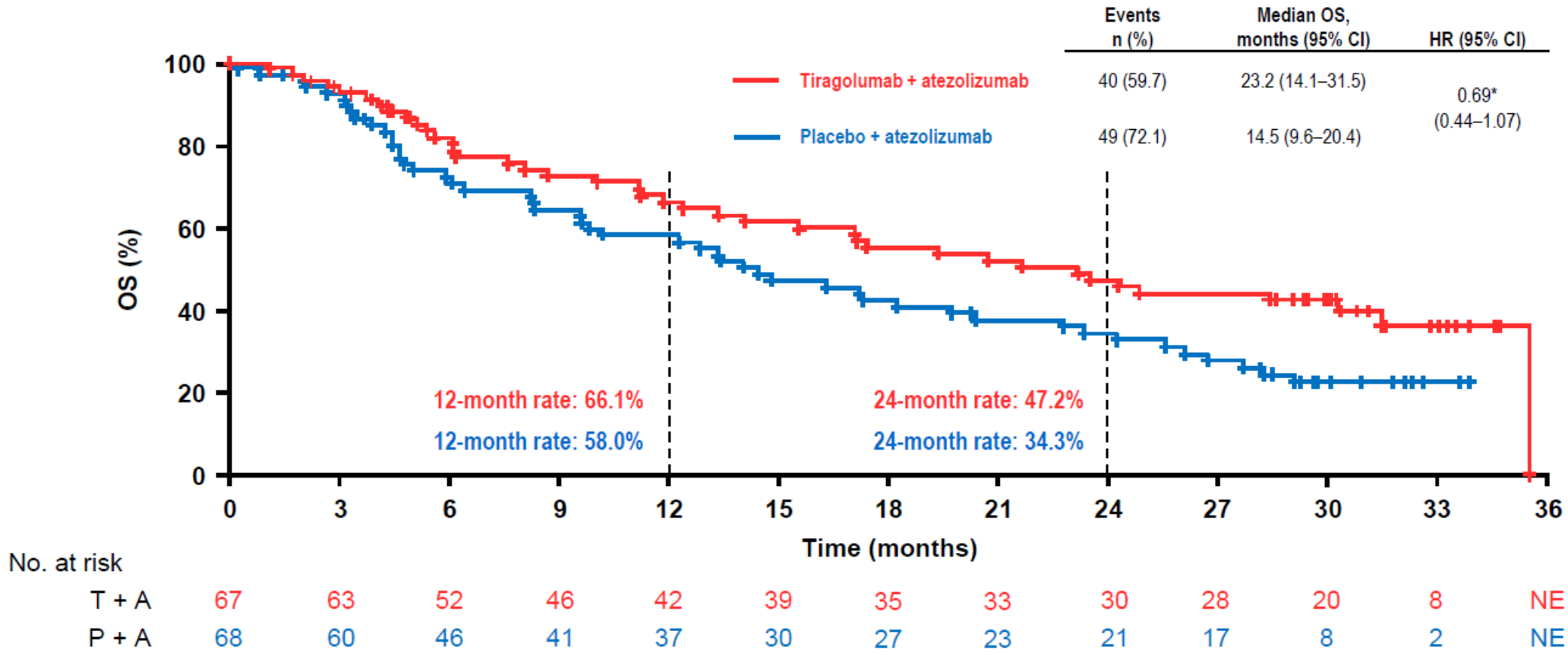
PD-L1 TPS 1–49% (n=77)

	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tira + atezo	36 (94.7)	4.0 (1.6–5.6)	1.07* (0.67–1.71)	15.8	17.8 (8.3–24.2)
Placebo + atezo	36 (92.3)	3.6 (1.4–5.5)		17.9	18.8 (15.9–22.8)



No. at risk												
T + A	38	22	12	12	9	6	5	3	3	1	1	1
P + A	39	21	12	8	8	8	8	5	4	3	2	2

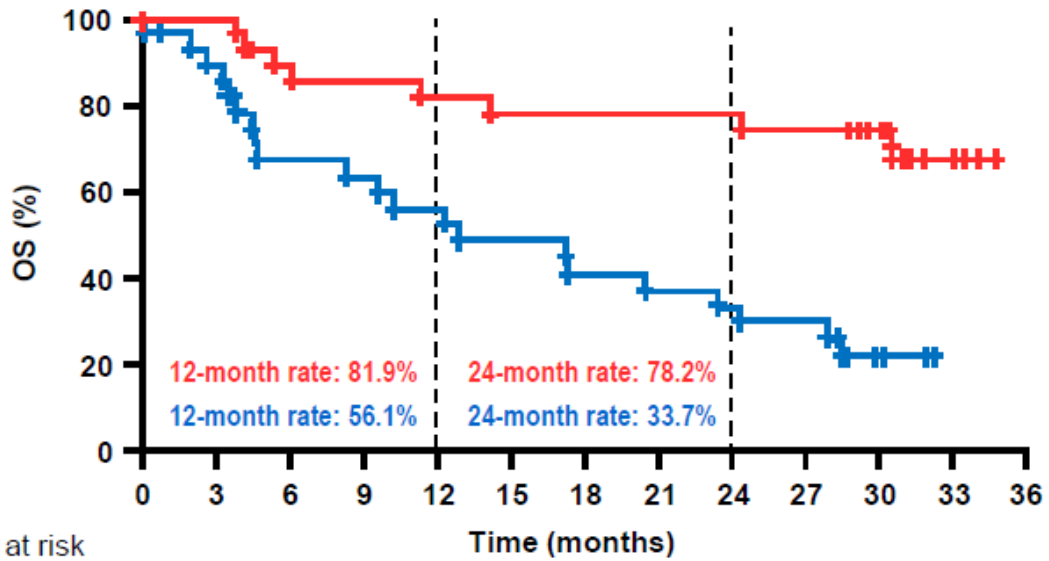
Overall survival: ITT population



Overall survival: PD-L1 subgroups

PD-L1 TPS ≥50% (n=58)

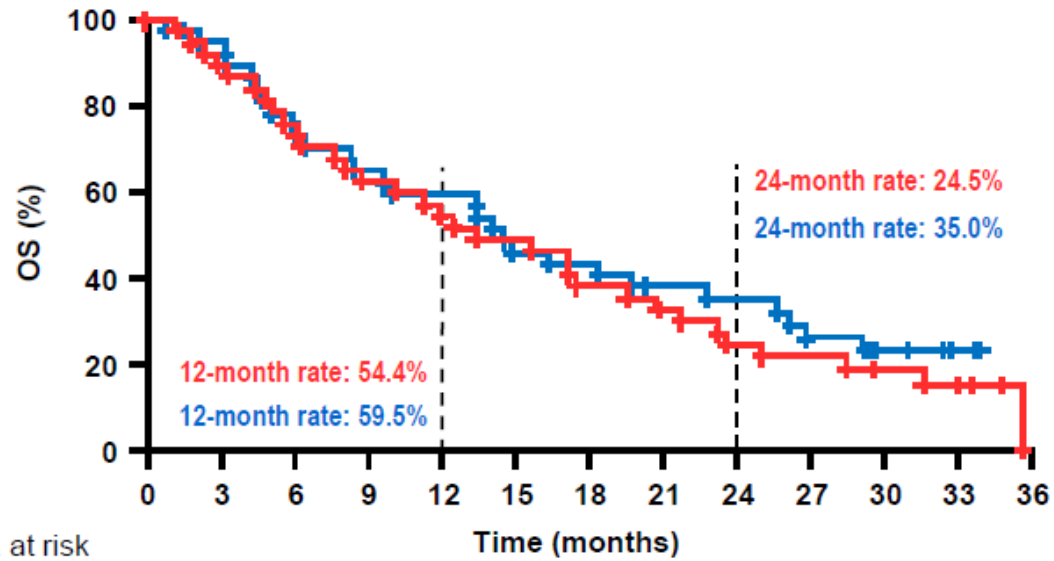
	Events n (%)	Median OS, months (95% CI)	HR (95% CI)
Tira + atezo	8 (27.6)	NE (30.3–NE)	0.23* (0.10–0.53)
Placebo + atezo	21 (72.4)	12.8 (4.7–24.2)	



No. at risk													
T + A	29	29	24	23	22	21	21	21	21	20	15	4	NE
P + A	29	25	18	17	15	13	11	10	9	8	3	NE	NE

PD-L1 TPS 1–49% (n=77)

	Events n (%)	Median OS, months (95% CI)	HR (95% CI)
Tira + atezo	32 (84.2)	13.3 (8.0–20.7)	1.16* (0.70–1.94)
Placebo + atezo	28 (71.8)	14.5 (8.3–25.6)	



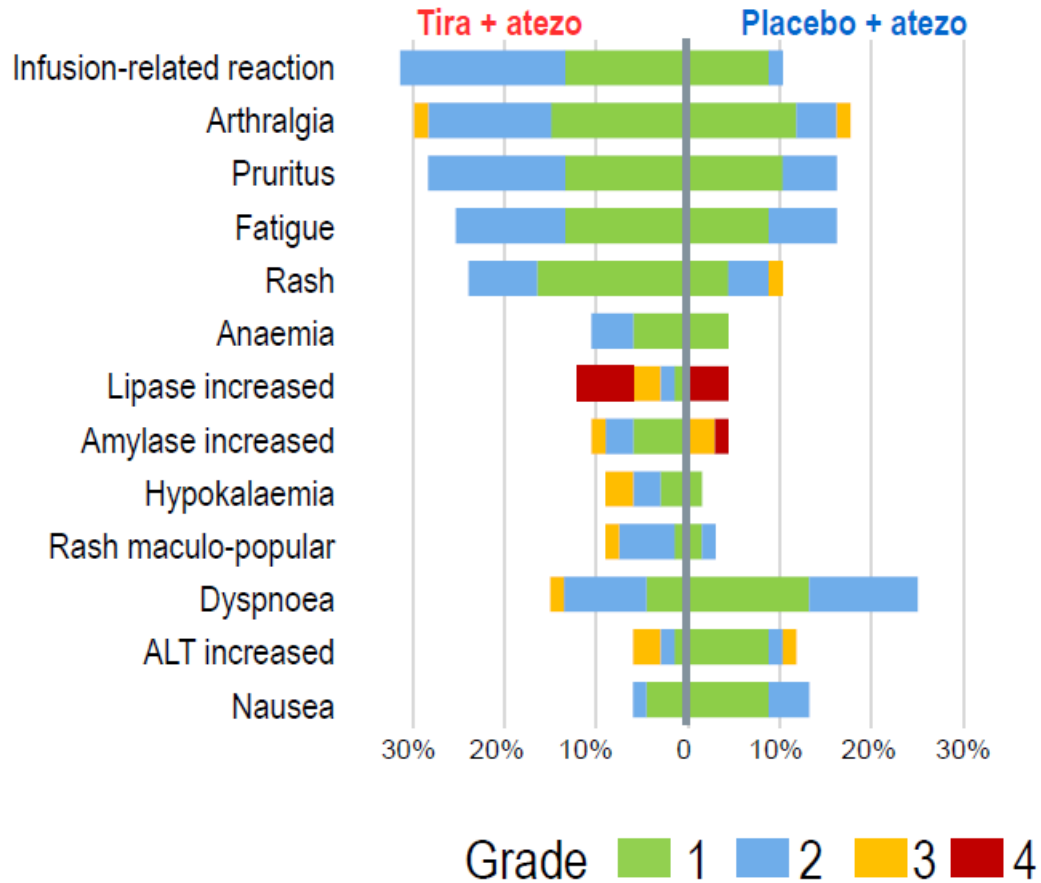
No. at risk													
T + A	38	34	28	23	20	18	14	12	9	8	5	4	NE
P + A	39	35	28	24	22	17	16	13	12	9	5	2	NE

Safety overview

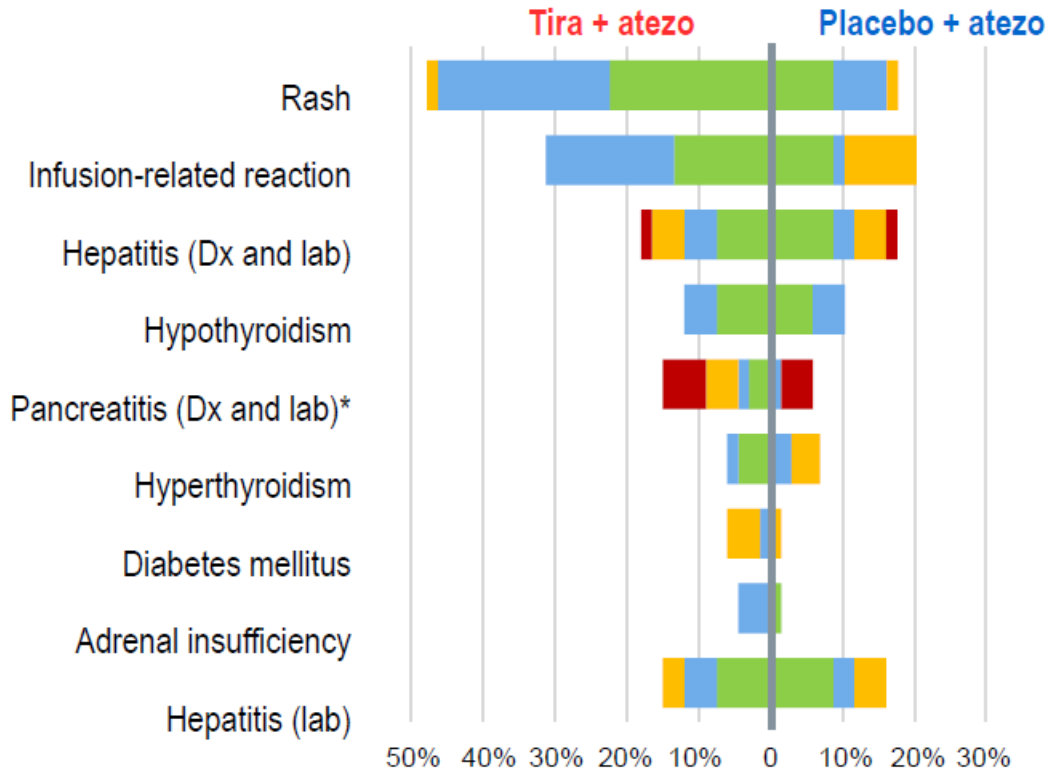
	Tiragolumab + atezolizumab (n=67)	Placebo + atezolizumab (n=68)
Median treatment duration, months (min–max)	4.99 (0–34.5)	2.81 (0–30.3)
Any-cause AEs, n (%)	66 (98.5)	66 (97.1)
Grade 3–4 AEs	35 (52.2)	27 (39.7)
Grade 5	3 (4.5)	7 (10.3)
Serious AEs	35 (52.2)	28 (41.2)
Treatment-related AEs, n (%)	55 (82.1)	48 (70.6)
Grade 3–4 AEs	15 (22.4)	17 (25.0)
Grade 5*	2 (3.0)	0
Serious AEs	14 (20.9)	12 (17.6)
Immune-mediated AEs, n (%)	51 (76.1)	32 (47.1)
Grade 3–4	13 (19.4)	11 (16.2)
AEs leading to dose modification/interruption, n (%)	33 (49.3)	24 (35.3)
AEs leading to treatment withdrawal, n (%)	10 (14.9)	9 (13.2)

Incidence of AEs overview

All cause AEs (>5% difference between arms)



Immune-mediated AEs (>5% in at least one arm)

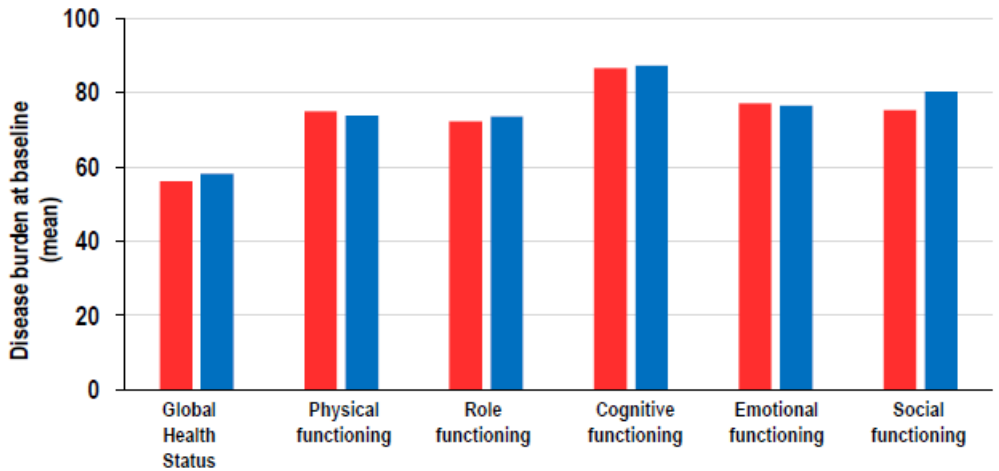


*Single case of diagnosed pancreatitis was reported in the placebo + atezolizumab arm

Updated analysis data cut-off: 16 August 2021 (median follow-up: 30.4 months)

Patient-reported outcomes assessed by EORTC QLQ-C30 – Global Health Status and functioning

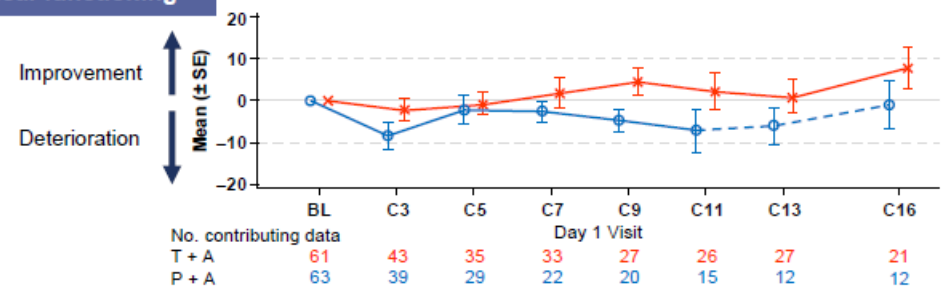
Patients generally reported moderate Global Health Status and moderately high functioning at baseline in both arms



Score 0–100 (Higher scores = better QoL and functioning)

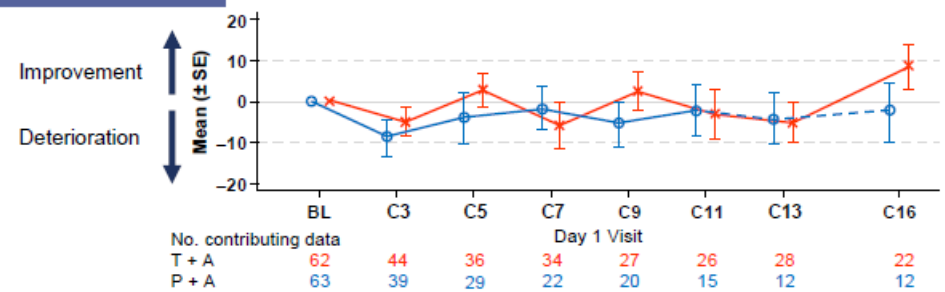
Changes from baseline scores of physical and role functioning were maintained and comparable between arms. Similar patterns were generally seen for Global Health Status and other functioning scales

Physical functioning



No. contributing data	BL	C3	C5	C7	C9	C11	C13	C16
T + A	61	43	35	33	27	26	27	21
P + A	63	39	29	22	20	15	12	12

Role functioning



No. contributing data	BL	C3	C5	C7	C9	C11	C13	C16
T + A	62	44	36	34	27	26	28	22
P + A	63	39	29	22	20	15	12	12

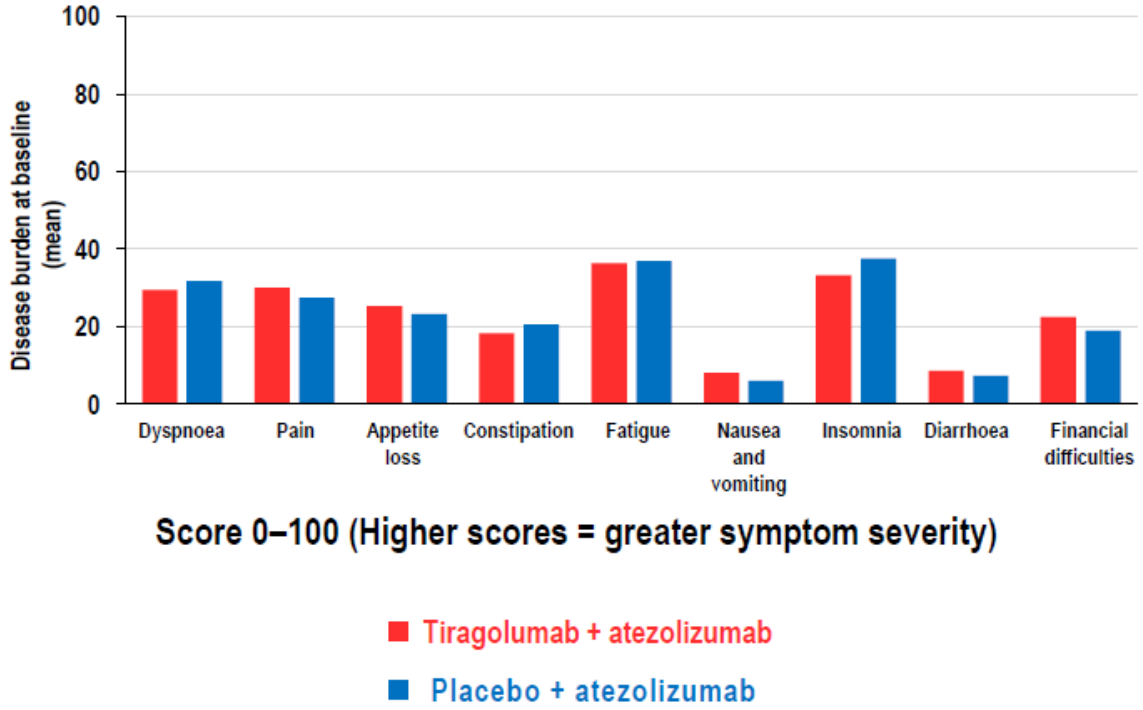
Tiragolumab + atezolizumab

Placebo + atezolizumab

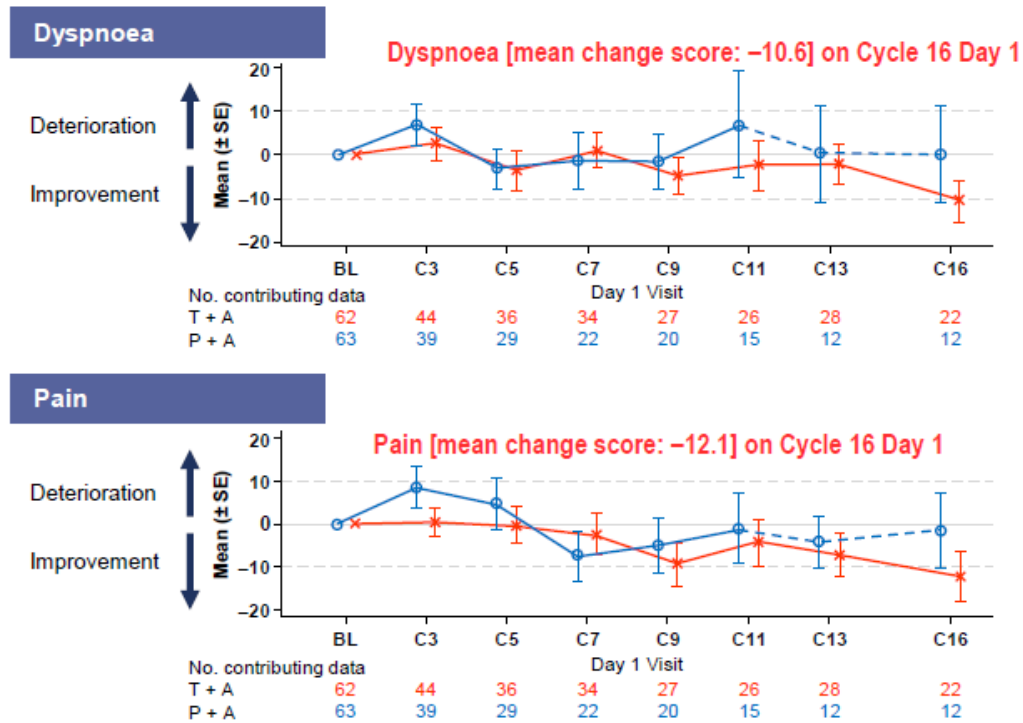
Note 1 - At baseline, patients in both arms had over 92% completion rates (as defined by patients who answered at least one question of the EORTC QLQ-C30) Note 2 - A ≥10-point change in the EORTC scale score is perceived as clinically significant (Osaba et al. 1998); Note 3 - Completion rates (as defined by patients who answered at least one question of the EORTC QLQ-C30) were ≥80% up to Cycle 16 in both arms, and remained ≥75% at most of study visits; Note 4 - Interpretation of change from baseline

Patient-reported outcomes assessed by EORTC QLQ-C30 – lung cancer-related symptoms

Patients generally reported minimal-to-moderate symptom burden at baseline, comparable between arms



Lung cancer-related symptom burden remained minimal-to-moderate over time in patients treated with tiragolumab + atezolizumab. Other symptoms showed similar patterns at most of these visits



Note 1 - At baseline, patients in both arms had over 92% completion rates (as defined by patients who answered at least one question of the EORTC QLQ-C30)
Note 2 - A ≥10-point change in the EORTC scale score is perceived as clinically significant (Osaba et al. 1998); **Note 3** - Completion rates (as defined by patients who answered at least one question of the EORTC QLQ-C30) were ≥80% up to Cycle 16 in both arms, and remained ≥75% at most of study visits; **Note 4** - Interpretation of change from baseline

CONCLUSIONS

- At this updated analysis, tiragolumab + atezolizumab provided a clinically meaningful improvement in PFS, ORR and OS in the ITT population compared with placebo + atezolizumab
- With ~30 months of follow-up, the median OS was not reached in the PD-L1 TPS ≥50% subgroup. Consistent with the primary analysis, this subgroup achieved the greatest clinical benefit
- Tiragolumab + atezolizumab was well-tolerated. Following longer follow-up, no new safety signals were observed with the combination of tiragolumab + atezolizumab
- Patients generally maintained their baseline Global Health Status/QoL and functioning scores in both arms over time
- Lung cancer-related symptom burden remained minimal-to-moderate over time in patients treated with tiragolumab + atezolizumab
- Durable response and encouraging OS continue to support evaluating tiragolumab + atezolizumab as a chemotherapy-free regimen in metastatic PD-L1-high NSCLC. The observed activity and safety is to be confirmed in an ongoing Phase III study (SKYSCRAPER-01) in first-line PD-L1 TPS ≥50% NSCLC (NCT04294810)