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Sugemalimab vs placebo after concurrent or sequential chemoradiotherapy in patients with unresectable stage III NSCLC (GEMSTONE-301): final progression-free survival analysis of a phase 3 study

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DISCLOSURES

Y-L W reports advisory services for AstraZeneca, Boehringer Ingelheim, Novartis, Takeda; personal fees from AstraZeneca, Beigene, Boehringer Ingelheim, BMS, Eli Lilly, MSD, Pfizer, Roche, Sanofi; grants from AstraZeneca, Boehringer Ingelheim, BMS, Hengrui, and Roche, outside the submitted work.

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All other authors declare no competing interests.

Background

- Concurrent chemoradiotherapy (cCRT) followed by immunotherapy is the standard of care for patients with unresectable stage III NSCLC. However, a substantial proportion of patients cannot tolerate or access cCRT, and thus sequential chemoradiotherapy (sCRT) is commonly utilized
- GEMSTONE-301 is the first phase 3 trial in this setting to include patients who received either cCRT or sCRT
- Sugemalimab is a full-length, fully human IgG4 monoclonal antibody targeting PD-L1
- At the pre-planed interim progression-free survival (PFS) analysis, sugemalimab showed a statistically significant and clinically meaningful improvement compared with placebo (median PFS 9.0 vs 5.8 months, HR 0.64, p=0.0026)[1]
- In June 2022, sugemalimab was approved for the treatment of patients with unresectable stage III NSCLC whose disease was not progressed following cCRT or sCRT in China
- Here, we report the updated results from the final PFS analysis

1. Zhou Q, Wu YL et al. Lancet Oncol. 2022 Feb;23(2):209-219. PMID: 35038429.

Study Design

Screening

Key Eligibility Criteria

- Patients with unresectable stage III NSCLC whose disease was not progressed following cCRT or sCRT
- ECOG PS 0-1
- No known sensitizing *EGFR, ALK, or ROS1* genomic alterations

Randomization

N=381

R
2:1

STRATIFICATION:

- ECOG PS (0 vs 1)
- CRT (cCRT vs sCRT)
- Total RT dose (<60 Gy vs ≥60 Gy)

Treatment

Sugemalimab: 1200 mg IV Q3W

Placebo: IV Q3W

Both for up to 24 months*

PRIMARY ENDPOINT

- PFS by BICR according to RECIST v1.1

SECONDARY ENDPOINTS

- OS
- PFS by the investigators according to RECIST v1.1
- ORR
- DoR
- TTDM
- Safety
- PK

Statistical Considerations

- PFS by BICR is tested first at a two-sided alpha of 0.05; if PFS is significant, then OS would be tested at a two-sided alpha of 0.05
- Final PFS analysis were planned when approximately 262 PFS events occurred
- Interim and final OS analysis were planned when approximately 175 and 260 OS events occurred, respectively

DoR: duration of response; ORR: overall response rate; OS: overall survival; PFS: progression-free survival; PK: pharmacokinetics; Q3W: once every 3 weeks; TTDM: Time to death or distant metastasis

*At the discretion of the study investigator, patients without progression and with tolerance for Sugemalimab after 24 months of treatment may continue to receive the treatment.

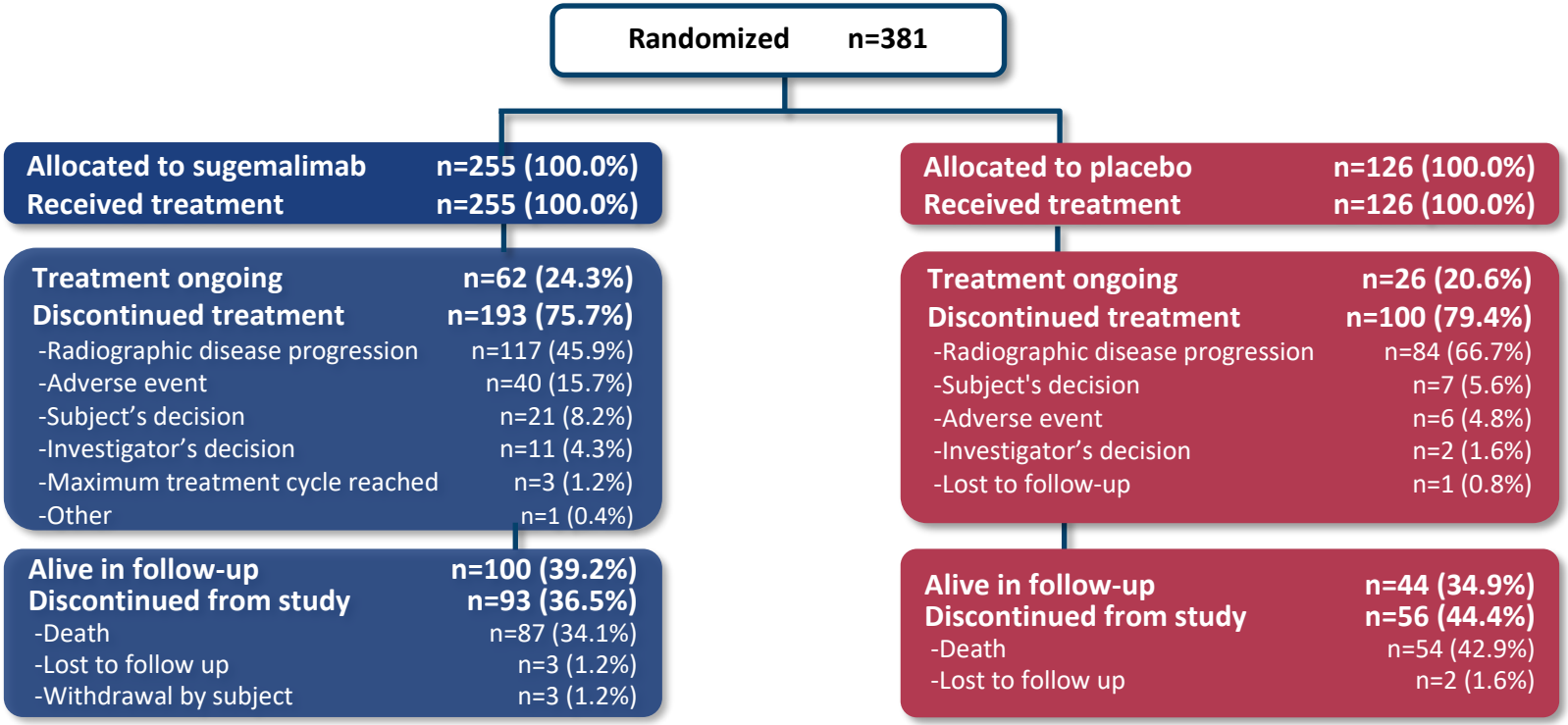
Demographics and Baseline Characteristics

	Sugemalimab (n=255)	Placebo (n=126)
Age, Median (range), years	61.0 (46,78)	60.0 (42,73)
Sex, Male/Female, n (%)	236 (92.5%)/19 (7.5%)	115 (91.3%)/11 (8.7%)
Baseline ECOG PS, 0/1, n (%)	78 (30.6%)/177 (69.4%)	38 (30.2%)/88 (69.8%)
Smoking Status, Never/Former or current, n (%)	42 (16.5%)/213 (83.5%)	16 (12.7%)/110 (87.3%)
Disease Stage#, IIIA/IIIB/IIIC, n (%)	74 (29.0%)/146 (57.3%)/33 (12.9%)	32 (25.4%)/65 (51.6%)/28 (22.2%)
Histology Type*, Squamous/Non-squamous, n (%)	177 (69.4%)/76 (29.8%)	89 (70.6%)/37 (29.4%)
CRT Type, sCRT/cCRT, n (%)	86 (33.7%)/169 (66.3%)	41 (32.5%)/85 (67.5%)
Radiotherapy Dose, < 60 Gy/≥ 60 Gy, n (%)	43 (16.9%)/212 (83.1%)	21 (16.7%) /105 (83.3%)
Best Response to CRT, CR/PR/SD, n (%)	4 (1.6%)/172 (67.5%)/79 (31.0%)	2 (1.6%)/77 (61.1%)/47 (37.3%)
Prior Platinum Treatment, Cisplatin/Carboplatin/Nedaplatin, n (%)	130 (51.0%)/82 (32.2%)/56 (22.0%)	61 (48.4%)/47 (37.3%)/20 (15.9%)
Time from Last Radiation to Randomization, ≤ 14 days/> 14 days, n (%)	47 (18.4%)/208 (81.6%)	24 (19.0%)/102 (81.0%)
Time from Last Radiation to Randomization, ≤ 25 days/> 25 days, n (%)	121 (47.5%)/134 (52.5%)	77 (61.1%)/49 (38.9%)

Cutoff date: 1 Mar 2022

*Two patients in the sugemalimab group had NSCLC not otherwise specified and NSCLC poorly differentiated carcinoma.
#Three patients had disease stage other than III

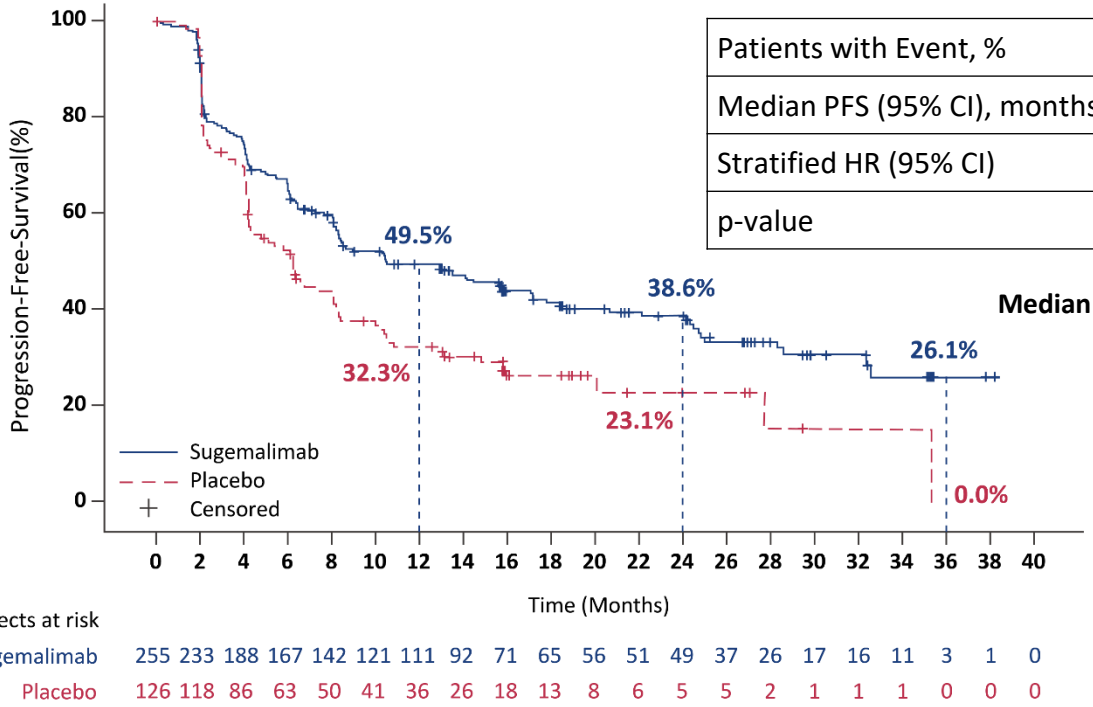
Patient Disposition



Cutoff date: 1 Mar 2022

BICR-assessed PFS

	Sugemalimab	Placebo
Patients with Event, %	60.4%	71.4%
Median PFS (95% CI), months	10.5 (8.3, 17.1)	6.2 (4.2, 8.1)
Stratified HR (95% CI)	0.65 (0.50, 0.84)	
p-value	0.0012	



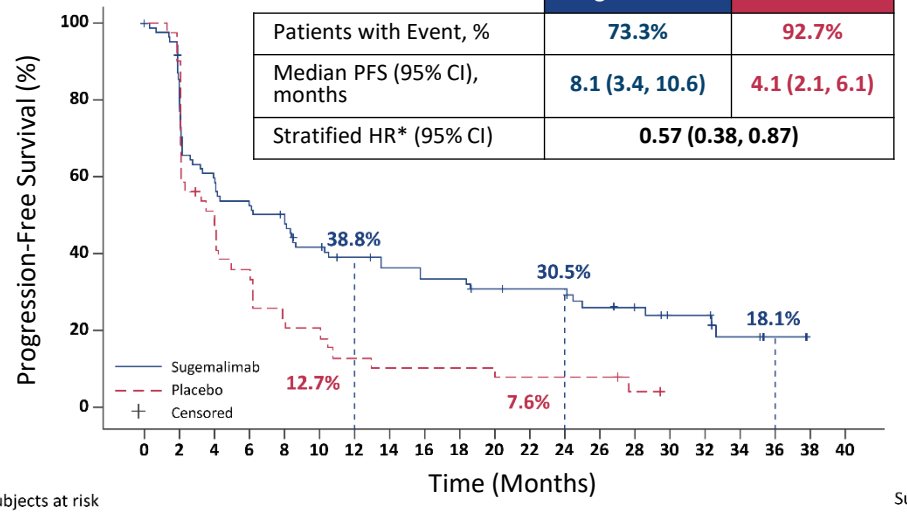
Median follow-up time *27.1* vs *23.5* months

Cutoff date: 1 Mar 2022

BICR-assessed PFS by CRT Type

sCRT

	Sugemalimab	Placebo
Patients with Event, %	73.3%	92.7%
Median PFS (95% CI), months	8.1 (3.4, 10.6)	4.1 (2.1, 6.1)
Stratified HR* (95% CI)	0.57 (0.38, 0.87)	



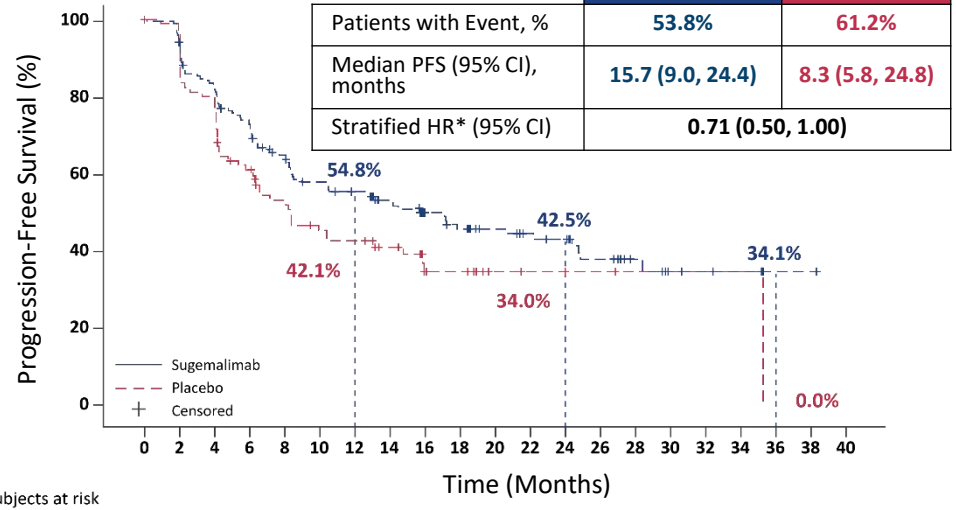
Subjects at risk

Sugemalimab	86	73	50	45	41	33	29	26	24	24	21	20	20	16	14	10	10	6	2	0	0
Placebo	41	37	20	14	10	8	5	4	4	4	4	3	3	3	1	0	0	0	0	0	0

- Median follow-up: ***30.6*** vs ***27.8*** months
- Median time from start date of CRT to randomization: ***156.5*** vs ***168.0*** days

cCRT

	Sugemalimab	Placebo
Patients with Event, %	53.8%	61.2%
Median PFS (95% CI), months	15.7 (9.0, 24.4)	8.3 (5.8, 24.8)
Stratified HR* (95% CI)	0.71 (0.50, 1.00)	



Subjects at risk

Sugemalimab	169	160	138	122	101	88	82	66	47	41	35	31	29	21	12	7	6	5	1	1	0
Placebo	85	81	66	49	40	33	31	22	14	9	4	3	2	2	1	1	1	1	0	0	0

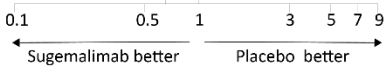
- Median follow-up: ***22.4*** vs ***20.0*** months
- Median time from start date of CRT to randomization: ***72.0*** vs ***69.0*** days

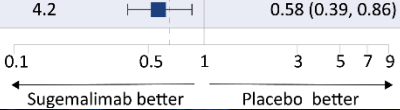
Cutoff date: 1 Mar 2022

*Hazard ratio was estimated by stratified Cox regression model with stratification factors from IxRS.

Subgroup Analyses of PFS

Subgroups	Median PFS, months: Sugemalimab (n=255)	Median PFS, months: Placebo (n=126)	HR* (95%CI)
All patients	10.5	6.2	0.65 (0.50, 0.84)
Sex			
Male	12.9	6.2	0.64 (0.49, 0.84)
Female	6.5	7.1	0.91 (0.38, 2.17)
Age			
<65years	12.9	7.1	0.72 (0.53, 0.99)
≥65years	10.5	4.1	0.47 (0.29, 0.78)
Smoking status			
Never	14.1	5.8	0.45 (0.22, 0.90)
Former or current	10.5	6.2	0.70 (0.53, 0.93)
ECOG PS			
0	24.5	8.1	0.43 (0.26, 0.70)
1	8.4	6.1	0.76 (0.56 ,1.04)
Disease stage			
Stage IIIA	13.1	6.2	0.79 (0.46, 1.35)
Stage IIIB	10.5	6.2	0.57 (0.40, 0.81)
Stage IIIC	8.4	5.4	0.73 (0.39, 1.36)
Histology type			
Squamous	8.4	4.3	0.63 (0.47, 0.86)
Non-Squamous	24.5	9.9	0.65 (0.38, 1.10)
CRT type			
Sequential	8.1	4.1	0.56 (0.37, 0.85)
Concurrent	15.7	8.3	0.70 (0.50, 0.99)
Radiotherapy dose			
<60 Gy	15.8	4.3	0.49 (0.26, 0.92)
≥60 Gy	10.5	6.2	0.69 (0.52, 0.93)
Best response to CRT			
Complete response	5.8	-	— (— , —)
Partial response	10.5	8.1	0.73 (0.52, 1.03)
Stable disease	13.5	4.2	0.50 (0.32, 0.77)
Prior platinum treatment			
Cisplatin	12.9	8.0	0.71 (0.49, 1.03)
Carboplatin	10.6	6.1	0.67 (0.43, 1.05)
Nedaplatin	9.0	4.1	0.45 (0.25, 0.83)
Time from last radiation to randomization#			
≤14 days	14.2	9.9	0.88 (0.45, 1.72)
>14 days	10.5	4.8	0.62 (0.46, 0.82)
Time from last radiation to randomization#			
≤25days	14.2	8.1	0.69 (0.48, 0.99)
>25days	10.5	4.2	0.58 (0.39, 0.86)

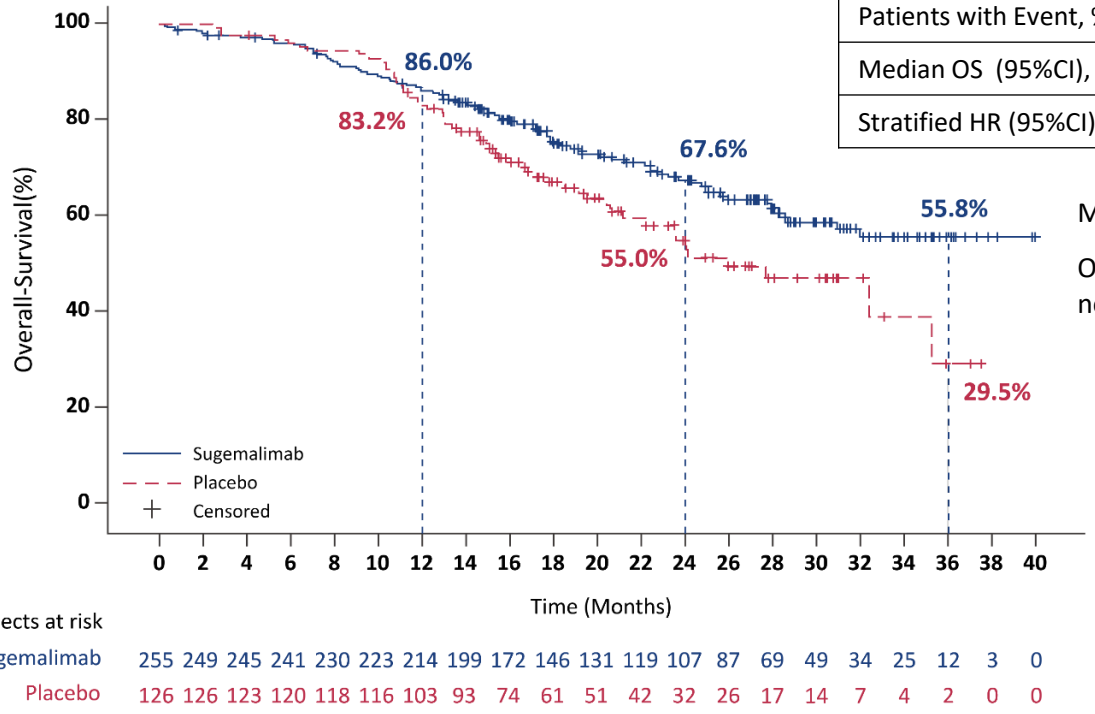




Cutoff date: 1 Mar 2022

*Hazard ratio and 95% CI were calculated using unstratified univariate Cox regression, except for the analysis for all patients which used stratified Cox regression with the stratification factors from the IxRS; #Post-hoc exploratory analysis

Overall Survival



	Sugemalimab	Placebo
Patients with Event, %	33.3%	42.9%
Median OS (95%CI), months	NR (31.0, NR)	25.9 (21.2, NR)
Stratified HR (95%CI)	0.69 (0.49, 0.97)	

Median follow-up time ***27.1*** vs ***23.5*** months

OS data were immature at the data cutoff date, no formal analysis was performed

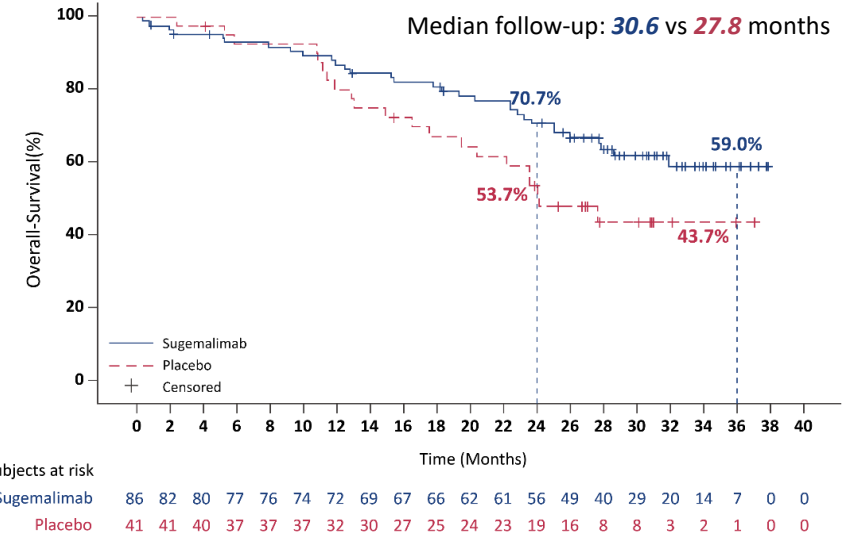
Cutoff date: 1 Mar 2022

NR: not reached

OS by CRT type

sCRT

	Sugemalimab	Placebo
Patients with Event, %	36.0%	51.2%
Median OS (95%CI), months	NR (31.9, NR)	24.1 (19.5, NR)
Stratified HR (95% CI)	0.60 (0.34, 1.05)	

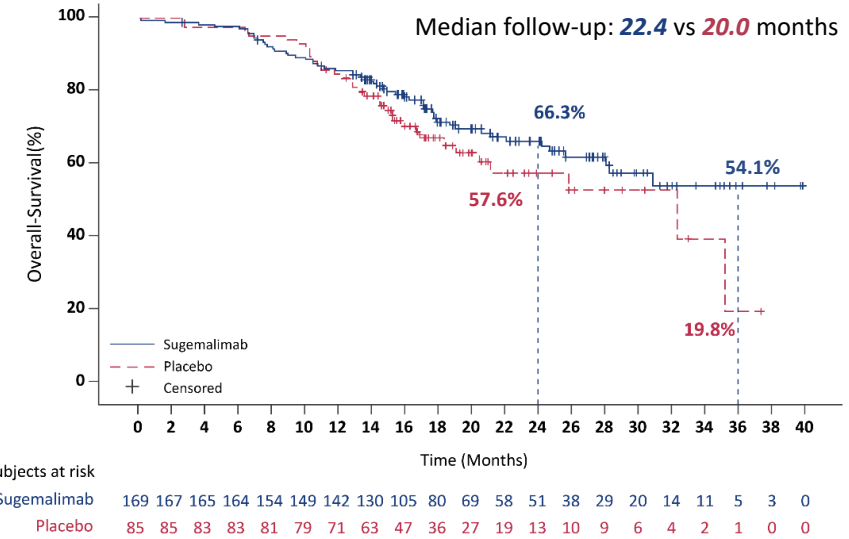


Subjects at risk

Sugemalimab	86	82	80	77	76	74	72	69	67	66	62	61	56	49	40	29	20	14	7	0	0
Placebo	41	41	40	37	37	37	32	30	27	25	24	23	19	16	8	8	3	2	1	0	0

cCRT

	Sugemalimab	Placebo
Patients with Event, %	32.0%	38.8%
Median OS (95%CI), months	NR (28.2, NR)	32.4 (20.6, NR)
Stratified HR (95% CI)	0.75 (0.48, 1.15)	



Subjects at risk

Sugemalimab	169	167	165	164	154	149	142	130	105	80	69	58	51	38	29	20	14	11	5	3	0
Placebo	85	85	83	83	81	79	71	63	47	36	27	19	13	10	9	6	4	2	1	0	0

Cutoff date: 1 Mar 2022

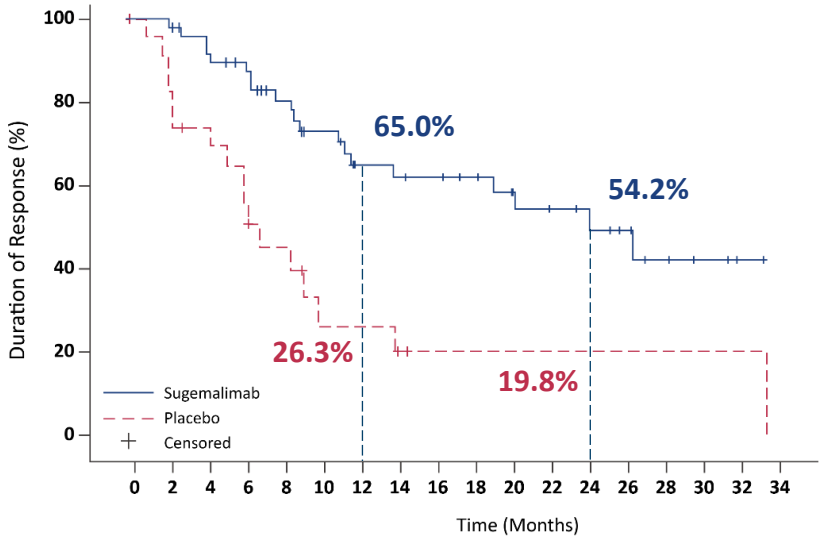
ORR and DoR

	Sugemalimab (n=204)+	Placebo (n=103)+
ORR (CR+PR)*, n(%) (95%CI)	**50 (24.5) (18.8, 31.0)**	**26 (25.2) (17.2, 34.8)**
Complete response, n(%)	0	1 (1.0)
Partial response, n(%)	50 (24.5)	25 (24.3)
Stable disease, n(%)	104 (51.0)	48 (46.6)
Progression of disease, n(%)	43 (21.1)	27 (26.2)
Not applicable#	7 (3.4)	2 (1.9)

+Results are based on Intent-to-Treat Analysis Set with Measurable Disease at Baseline
*BICR-accessed, RECIST v1.1
#Patients were classified as not applicable if no post-baseline response assessments were available

Kaplan-Meier Plot of DoR Assessed by BICR

	Sugemalimab	Placebo
Median DoR* (95%CI), months	24.1 (11.6, NR)	6.9 (4.2, 9.9)

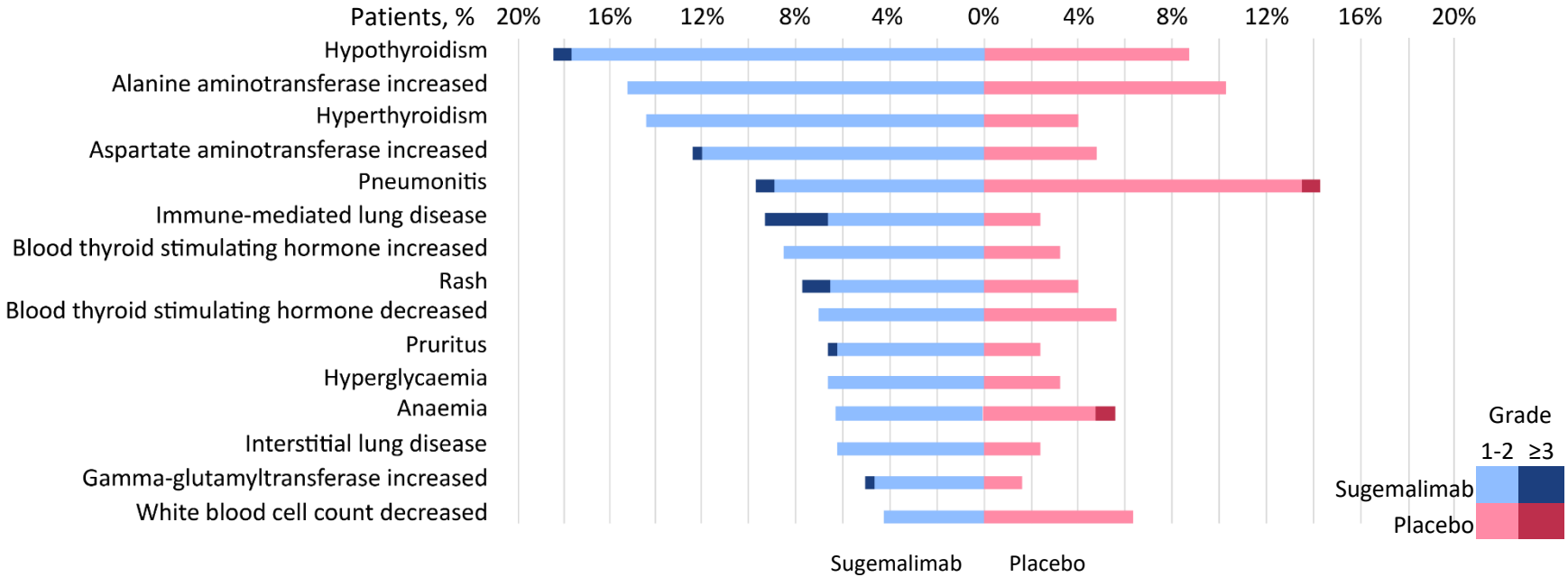


Summary of Adverse Events

	Total		sCRT		cCRT	
	Sugemalimab (n=255)	Placebo (n=126)	Sugemalimab (n=86)	Placebo (n=41)	Sugemalimab (n=169)	Placebo (n=85)
Treatment Emergent Adverse Event (TEAE)	248 (97.3%)	121 (96.0%)	82 (95.3%)	38 (92.7%)	166 (98.2%)	83 (97.6%)
Treatment-related TEAE	200 (78.4%)	81 (64.3%)	64 (74.4%)	20 (48.8%)	136 (80.5%)	61 (71.8%)
Serious TEAE	88 (34.5%)	35 (27.8%)	27 (31.4%)	11 (26.8%)	61 (36.1%)	24 (28.2%)
Treatment-related serious TEAE	44 (17.3%)	11 (8.7%)	12 (14.0%)	4 (9.8%)	32 (18.9%)	7 (8.2%)
Grade 3-5 TEAE	79 (31.0%)	36 (28.6%)	26 (30.2%)	9 (22.0%)	53 (31.4%)	27 (31.8%)
Treatment-related Grade 3-5 TEAE	29 (11.4%)	7 (5.6%)	8 (9.3%)	1 (2.4%)	21 (12.4%)	6 (7.1%)
TEAE leading to drug permanently discontinued	41 (16.1%)	6 (4.8%)	13 (15.1%)	2 (4.9%)	28 (16.6%)	4 (4.7%)
TEAE leading to infusion interruption	1 (0.4%)	1 (0.8%)	0	0	1 (0.6%)	1 (1.2%)
TEAE leading to treatment cycle delay	90 (35.3%)	32 (25.4%)	26 (30.2%)	10 (24.4%)	64 (37.9%)	22 (25.9%)
TEAE leading to death	12 (4.7%)	3 (2.4%)	5 (5.8%)	3 (7.3%)	7 (4.1%)	0

Cutoff date: 1 Mar 2022

Treatment-related Adverse Event (All Grade ≥5%)



Conclusion

- PFS final analysis showed sustained improvement in PFS with sugemalimab versus placebo among patients with unresectable stage III NSCLC who had not progressed following cCRT or sCRT
  - BICR-assessed mPFS: 10.5 vs 6.2 months, HR= 0.65
  - sCRT mPFS: 8.1 vs 4.1 months, HR=0.57
  - cCRT mPFS: 15.7 vs 8.3 months, HR=0.71
- Preliminary overall survival data showed a trend for benefit favoring sugemalimab
  - mOS: not reached vs 25.9 months, HR= 0.69
  - sCRT mOS: not reached vs 24.1 months, HR=0.60
  - cCRT mOS: not reached vs 32.4 months, HR=0.75
- Similar ORR between sugemalimab and placebo but DoR was longer in sugemalimab
  - ORR: 24.5% vs 25.2%
  - DoR: 24.1 vs 6.9 months
- No new safety signals were found in PFS final analysis

Take Home Message

Sugemalimab could be safely and effectively used after cCRT or sCRT and become a standard of care in this setting for stage III inoperable NSCLC

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