Sugemalimab vs Placebo after cCRT or sCRT in patients with Unresectable Stage III NSCLC: Final PFS Analysis of a Phase 3 Study


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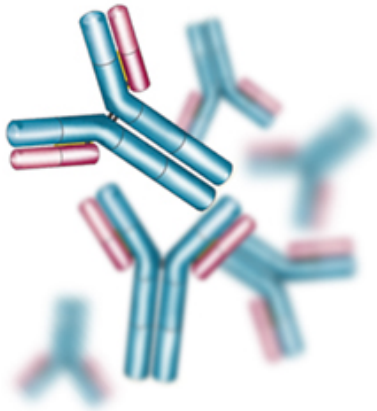
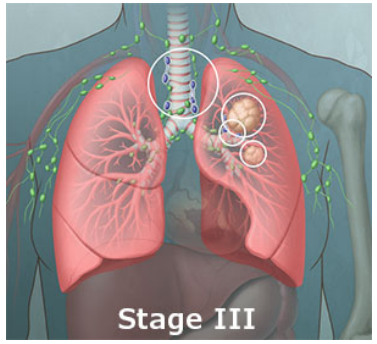
CSTONE PHARMACEUTICALS

Today's Discussion



Sugemalimab



Standard of care in Stage III unresectable lung cancers

Gemstone 301 (The Trial)

Data in perspective..

Conclusion

Sugemalimab - CStone Pharmaceuticals/EQRx

Generation and Selection of Human Monoclonal Antibodies from the OmniRat™

John S. Kenney, Glen Lin, Jennifer Somera, Leonel Santibanez-Vargas, Rick Chang, Joshua Lowitz, Billy Nguyen, Julie Ngo, and Roland Buelow^ *Antibody Solutions, Sunnyvale, CA, USA & ^Open Monoclonal Technologies (OMT), Palo Alto, CA, USA*

OmniMouse naturally optimized human antibodies®

OmniRat naturally optimized human antibodies®

OmniChicken naturally optimized human antibodies®

Sugemalimab (Cejemly)

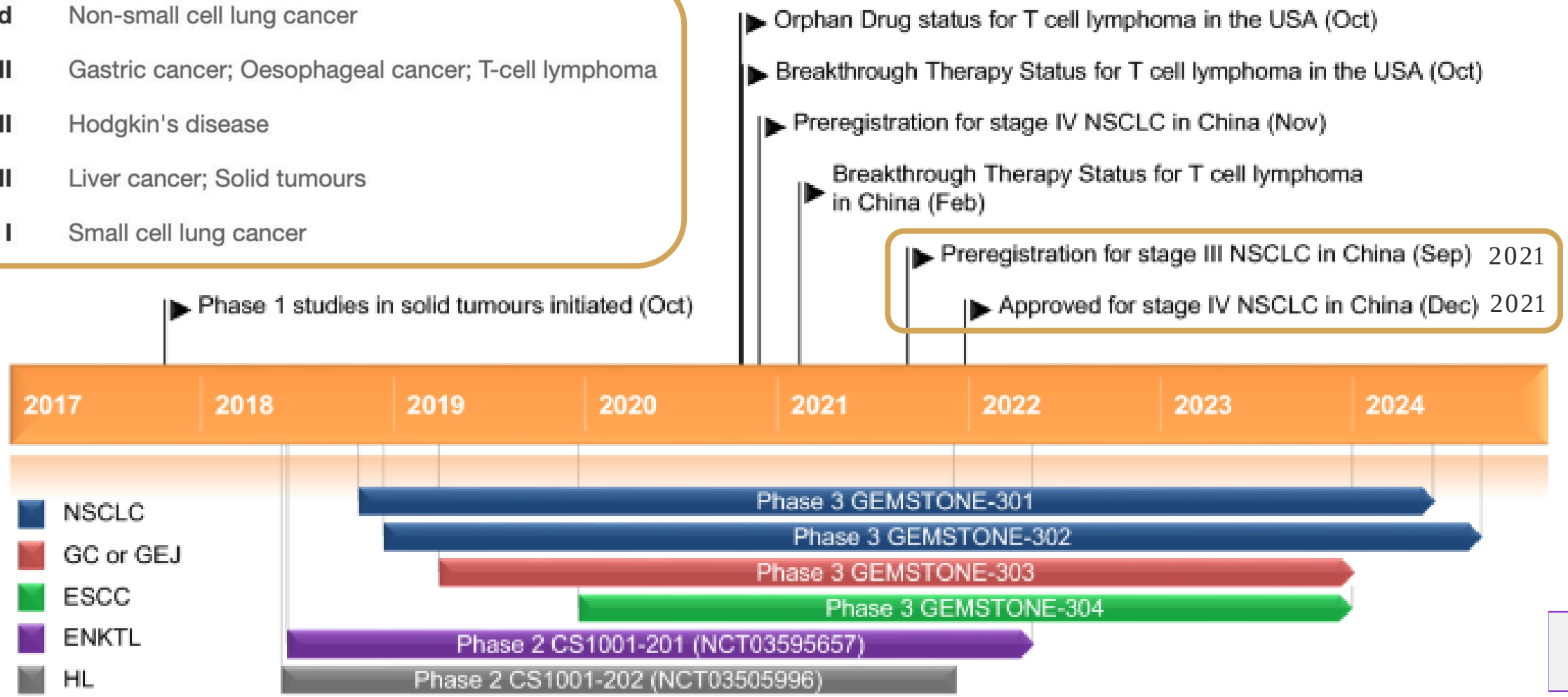
- Anti-PD-L1 mAb discovered using the OmniRat® transgenic animal platform, which can generate fully human antibodies
- As a fully human, full-length anti-PD-L1 mAb, Cejemly mirrors the natural G-type IgG4 human antibody, which may reduce the risk of immunogenicity and potential toxicities in patients
- Lacks ADCC and complement-dependent cytotoxicity (CDC)

Sugemalimab - CStone Pharmaceuticals/EQRx

Alternative Names: Cejemly; CS-1001; WBP-3155; ZEJIEMEI

Latest Information Update: 10 Aug 2022

Marketed	Non-small cell lung cancer
Phase III	Gastric cancer; Oesophageal cancer; T-cell lymphoma
Phase II	Hodgkin's disease
Phase I/II	Liver cancer; Solid tumours
Phase I	Small cell lung cancer



Sugemalimab - CStone Pharmaceuticals/EQRx

Alternative Names: Cejemly; CS-1001; WBP-3155; ZEJIEMEI

Latest Information Update: 10 Aug 2022

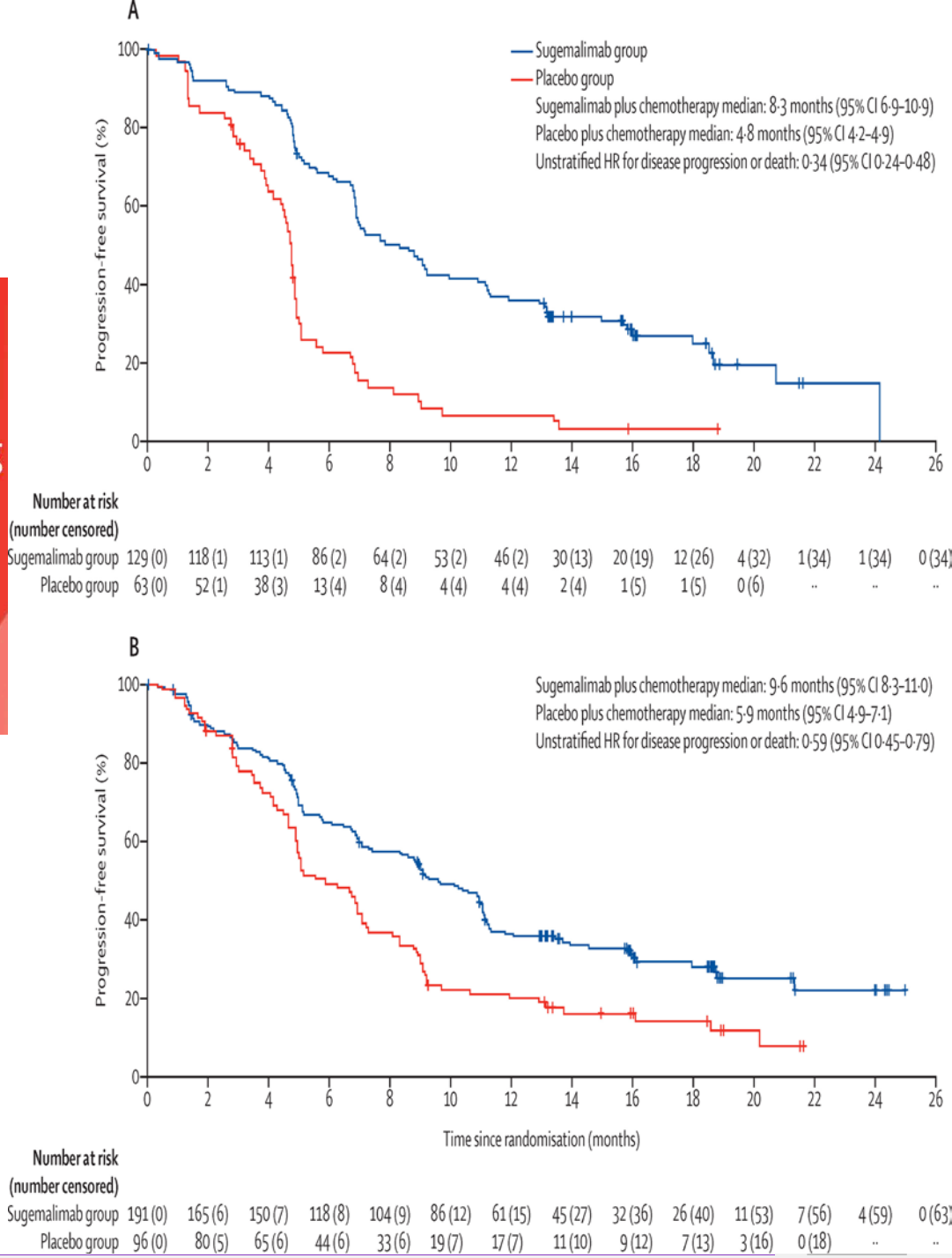
ARTICLES | VOLUME 23, ISSUE 2, P220-233, FEBRUARY 01, 2022

Sugemalimab versus placebo, in combination with platinum-based chemotherapy, as first-line treatment of metastatic non-small-cell lung cancer (GEMSTONE-302): interim and final analyses of a double-blind, randomised, phase 3 clinical trial

Prof Caicun Zhou, MD • Prof Ziping Wang, MD • Prof Yuping Sun, MD • Prof Lejie Cao, MMed • Prof Zhiyong Ma, MMed • Prof Rong Wu, MD • et al. Show all authors

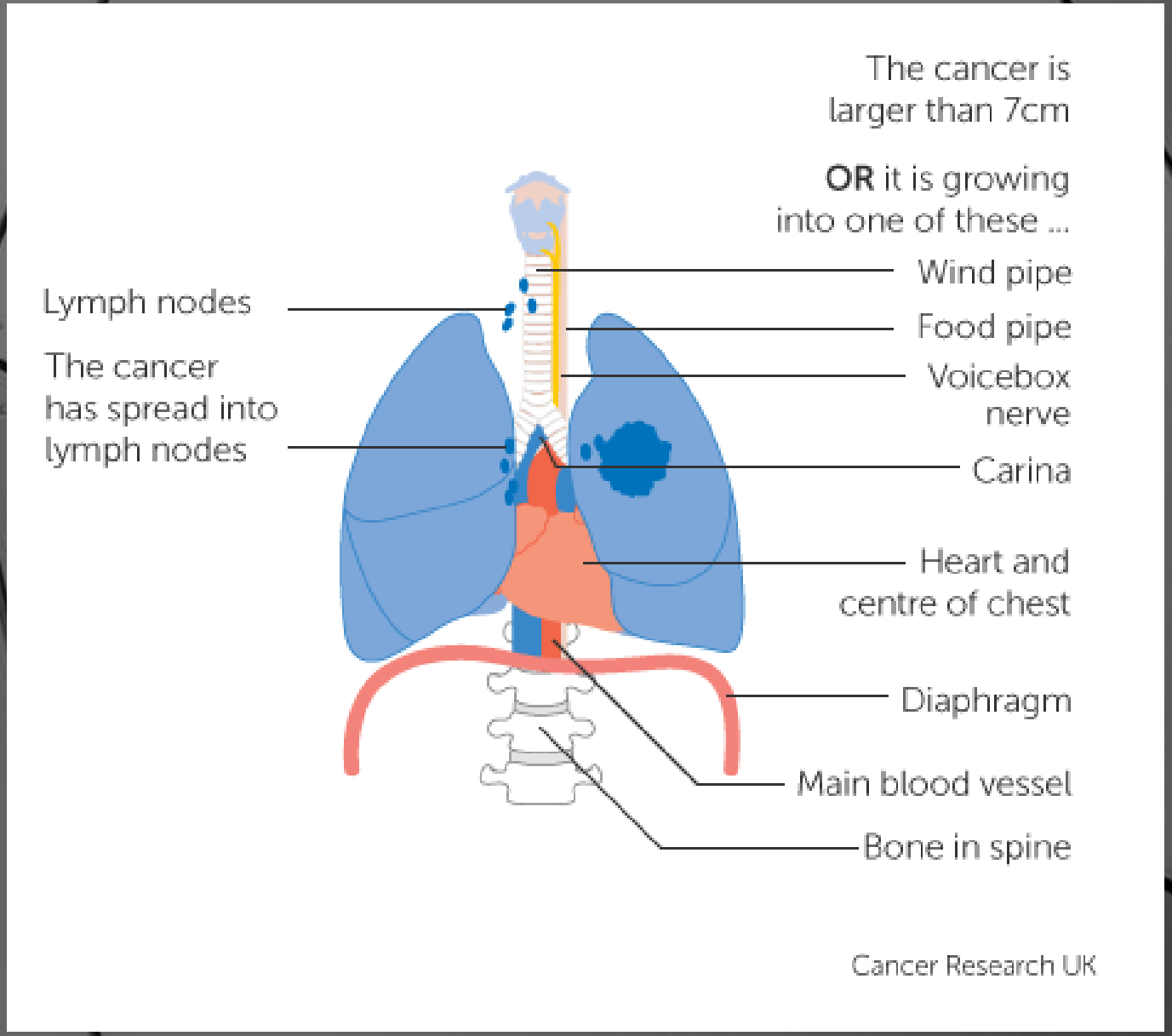
In the final analysis (March 15, 2021) with a median follow-up of 17·8 months (IQR 15·1–20·9), the improvement in progression-free survival was maintained

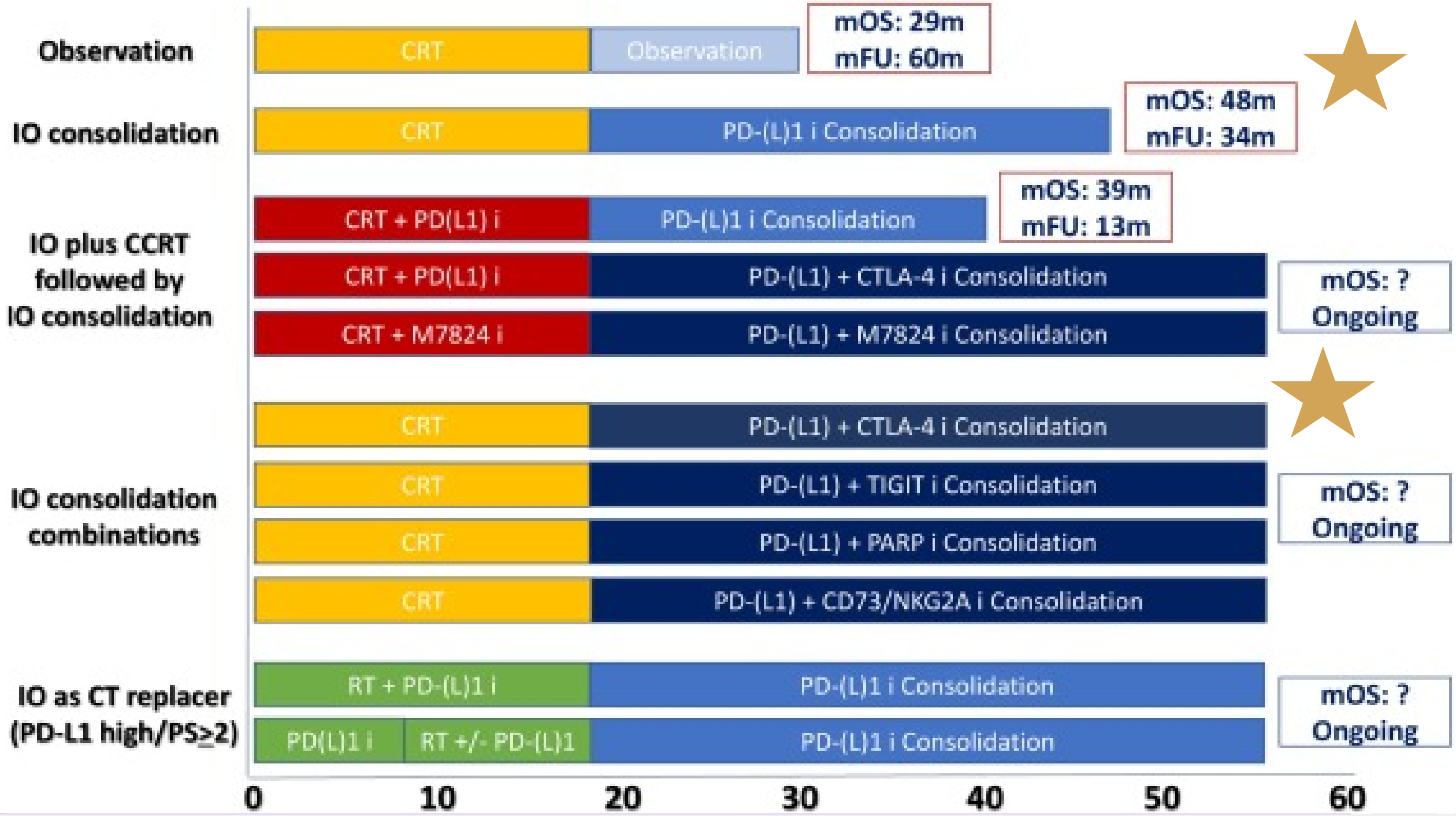
- median 9·0 months [95% CI 7·4–10·8] *vs* 4·9 months [4·8–5·1]
- stratified HR 0·48 [95% CI 0·39–0·60], p<0·0001)



Standard of care in Stage III unresectable lung cancers

T/M	Subcategory	N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
T3	T3	IIB	IIIA	IIIB	IIIC
T4	T4	IIIA	IIIA	IIIB	IIIC
M1	M1a	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA
	M1c	IVB	IVB	IVB	IVB




Observation
CRT
Observation
mOS: 29m
mFU: 60m
IO consolidation
CRT
PD-(L)1 i Consolidation
mOS: 48m
mFU: 34m
IO plus CCRT followed by IO consolidation
CRT + PD(L1) i
PD-(L)1 i Consolidation
mOS: 39m
mFU: 13m
CRT + PD(L1) i
PD-(L1) + CTLA-4 i Consolidation
mOS: ? Ongoing
CRT + M7824 i
PD-(L1) + M7824 i Consolidation
IO consolidation combinations
CRT
PD-(L1) + CTLA-4 i Consolidation
CRT
PD-(L1) + TIGIT i Consolidation
mOS: ? Ongoing
CRT
PD-(L1) + PARP i Consolidation
CRT
PD-(L1) + CD73/NKG2A i Consolidation
IO as CT replacer (PD-L1 high/PS≥2)
RT + PD-(L)1 i
PD-(L)1 i Consolidation
PD(L)1 i
RT +/- PD-(L)1
PD-(L)1 i Consolidation
mOS: ? Ongoing
0
10
20
30
40
50
60

Consolidation after cCTRT / sCTRT

CT RT → ICI

- PACIFIC (NCT02125461)*
- GEMSTONE 301 (NCT03728556)*
- PACIFIC-5 (NCT03706690)*

CT → RT → ICI

- GEMSTONE 301 (NCT03728556)*
- PACIFIC-5 (NCT03706690)*
- PACIFIC 6 (NCT03693300), cohort 1

Concurrent ICI + cCTRT

ICI
CT RT → ICI

- KEYNOTE-799 (NCT036311784)
- DETERRED (NCT02525757)
- NICOLAS (NCT02434081)
- PACIFIC 2 (NCT03519971)*
- EA5181 (NCT04092283)*
- CheckMate 73L (NCT04026412)*
- KEYLYNK-012 (NCT04380636)*#
- KEYVIBE-006 (NCT05298423)*
- NCT05386888

Patients with PS ≥2

CT → RT → ICI

- PACIFIC 6 (NCT03693300)

RT → ICI

- SWOG 1933 (NCT04310020)
- DUART trial (NCT04249362)

ICI RT

- TRADE-Hypo (NCT04351256)
- DART (NCT03999710)
- AIRING (NCT04577638

ICI-consolidation intensification

CT RT → ICI ICI

- COAST (NCT03822351)
- PACIFIC-9 (NCT05221840)*
- PACIFIC-8 (NCT05211895)*
- SKYSCRAPER-03 (NCT04513925)*
- BTCRC-LUN 16-081 (NCT03285321)
- CheckMate 73L (NCT04026412)*

Induction (CT)- ICI

CT ICI → CT RT → ICI

- APOLO trial (NCT04776447)
- (NCT04085250)
- DEDALUS (NCT05128630)
- BRIDGE (NCT04765709)
- PACIFIC-BRAZIL (NCT04230408)

ICI → CT RT → ICI ± CT

- AFT-16 (NCT03102242)

Chemotherapy-free

ICI → RT → ICI

- SPRINT (NCT03523702)
- NRG-LU004 (NCT03801902)

Consolidation with TKI

CT RT → TKI

- LAURA (NCT03521154)*
- BO42777 (NCT05170204)*

GEMSTONE 301 TRIAL

Journal of Thoracic Oncology

Volume 17, Issue 9, Supplement, September 2022, Pages S7-S8

OA02 FROM LOCALLY ADVANCED TO UNRESECTABLE NSCLC: IMPROVEMENT OF MULTIMODALITY TREATMENT, SUNDAY, AUGUST 7, 2022 - 12:00 - 13:00

OA02.05 Sugemalimab vs Placebo after cCRT or sCRT in pts with Unresectable Stage III NSCLC: Final PFS Analysis of a Phase 3 Study

Y.-L. Wu [1], Q. Zhou [2], M. Chen [3], Y. Pan [1], O. Jian [4], D. Hu [5], Q. Lin [6], G. Wu [7], J. Cui [8], J. Chang [9], Y. Cheng [10], C. Huang [11], A. Liu [12], N. Yang [13], Y. Gong [14], C. Zhu [15], Z. Ma [16], J. Fang [17], G. Chen [18], J. Zhao [19] ...J. Yang [29]

Introduction

- Patients with stage III NSCLC represent a heterogeneous population. For those with unresectable disease, concurrent chemoradiotherapy (cCRT) followed by an immune checkpoint inhibitor is the standard of care[1,2]

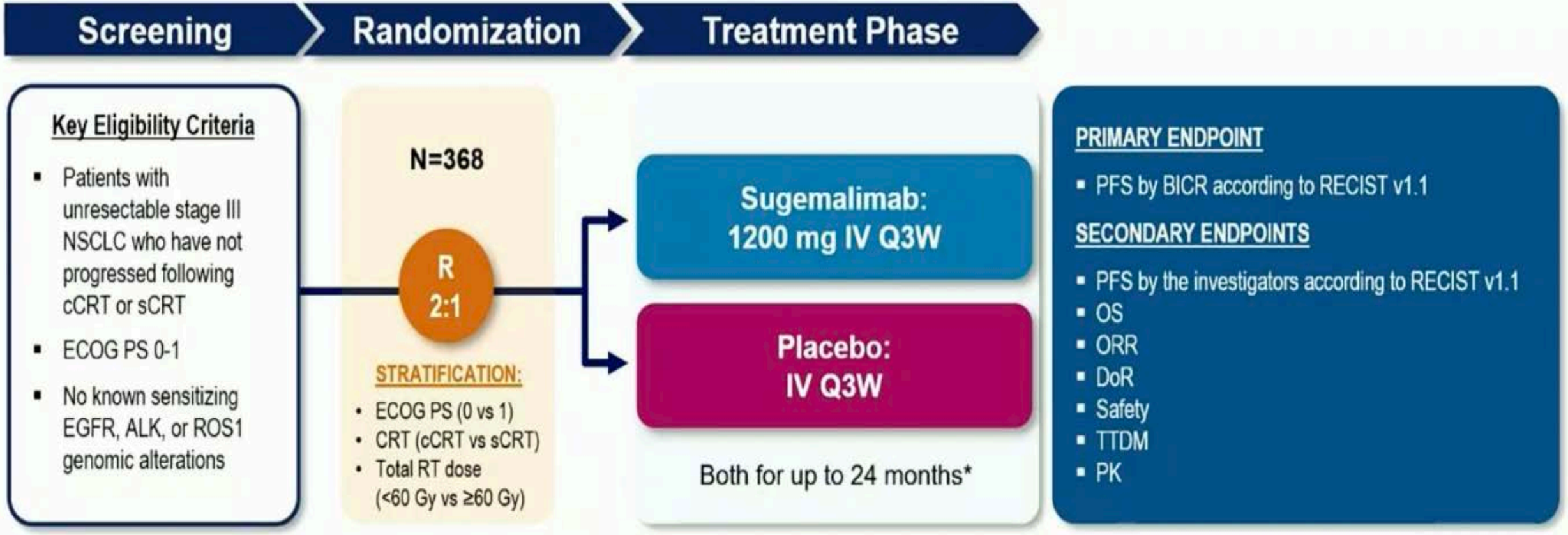
- However, cCRT is associated with significant toxicity and treatment-related mortality[3,4]
  - Patient comorbidities and lack of access to cCRT in certain areas often limit its use in the real-world setting
  - Observational data indicate a 30-55% utilization rate for cCRT globally[5-8]

- Sequential CRT (sCRT) is a widely used alternative in a large subset of patients who cannot tolerate or access cCRT; thus, there remains a high unmet need to improve outcomes for patients without disease progression following sCRT

- Sugemalimab is a full-length, fully human immunoglobulin G4 (s228p) monoclonal antibody that targets PD-L1
  - Sugemalimab plus chemotherapy demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared with chemotherapy in patients with metastatic NSCLC (GEMSTONE-302 study)

- GEMSTONE-301 (NCT03728556) is a randomized, phase 3 trial comparing sugemalimab with placebo as a consolidation treatment in patients with unresectable stage III NSCLC without progression after cCRT or sCRT
  - This is the first phase 3 trial evaluating an anti–PD-1/PD-L1 agent in both populations in this setting

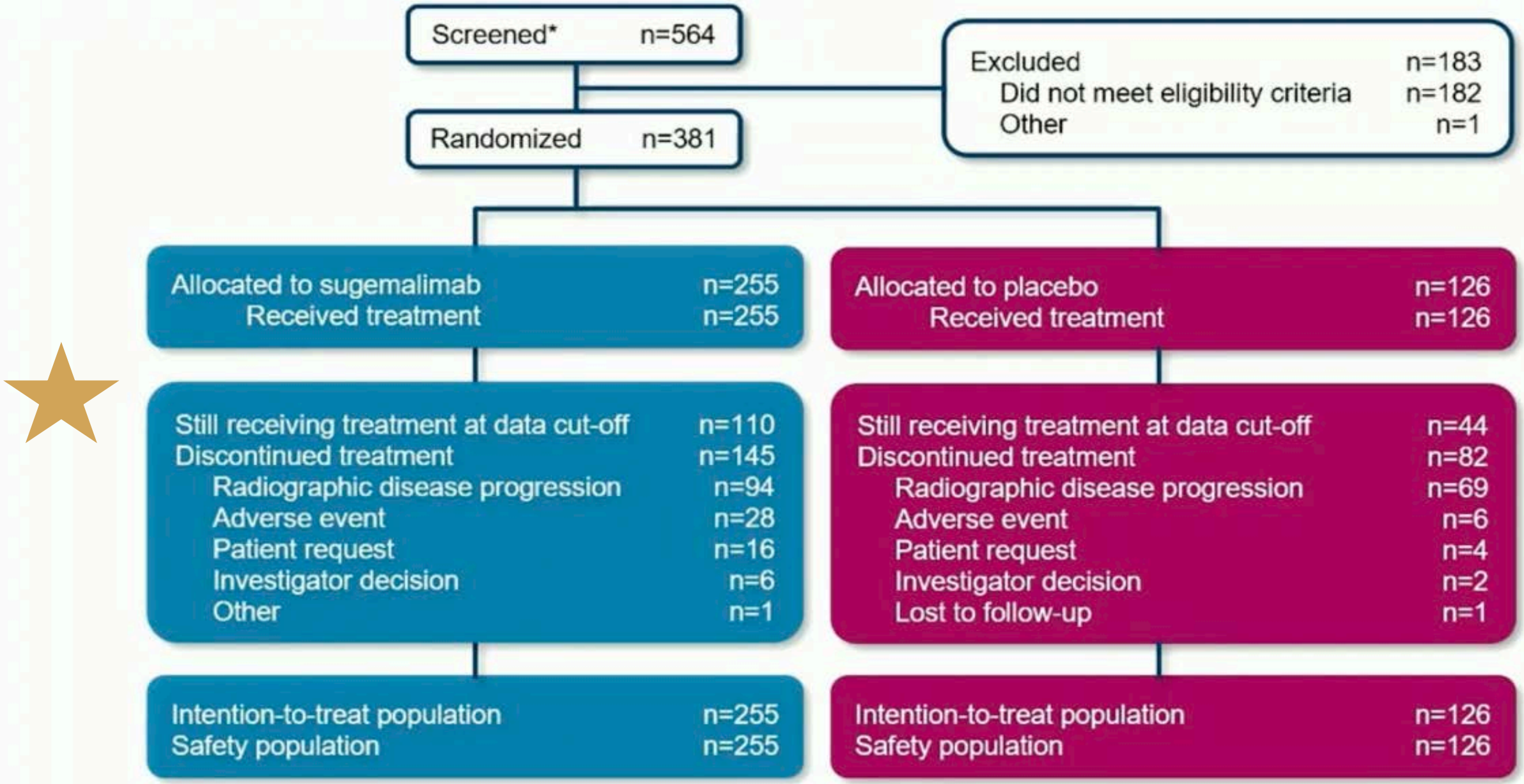
GEMSTONE-301 Study Design



Statistical Considerations

- PFS 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
- Interim and final PFS analysis were planned when approximately 194 and 262 PFS events occurred, respectively. O'Brien-Fleming method was used to control the type I error
- Interim and final OS analysis were planned when approximately 175 and 260 OS events occurred, respectively.

Patient Disposition



Baseline Characteristics

	Sugemalimab (N=255)	Placebo (N=126)
Sex		
Male	93%	91%
Female	7%	9%
Age, years – median (range)	61 (46–78)	60 (42–73)
Age ≥65 years	29%	25%
Smoking history		
Never	16%	13%
Former or current	84%	87%
ECOG performance status		
0	31%	30%
1	69%	70%
Radiotherapy dose		
<60 Gy	17%	16%
≥60 Gy	83%	84%

	Sugemalimab (N=255)	Placebo (N=126)
Pathologic type*		
Squamous cell carcinoma	69%	68%
Nonsquamous cell carcinoma	30%	32%
CRT type		
Sequential	34%	33%
Concurrent	66%	67%
Disease stage#		
IIIA	29%	25%
IIIB	57%	52%
IIIC	13%	22%
Best response to CRT		
Complete response	2%	2%
Partial response	67%	61%
Stable disease	31%	37%

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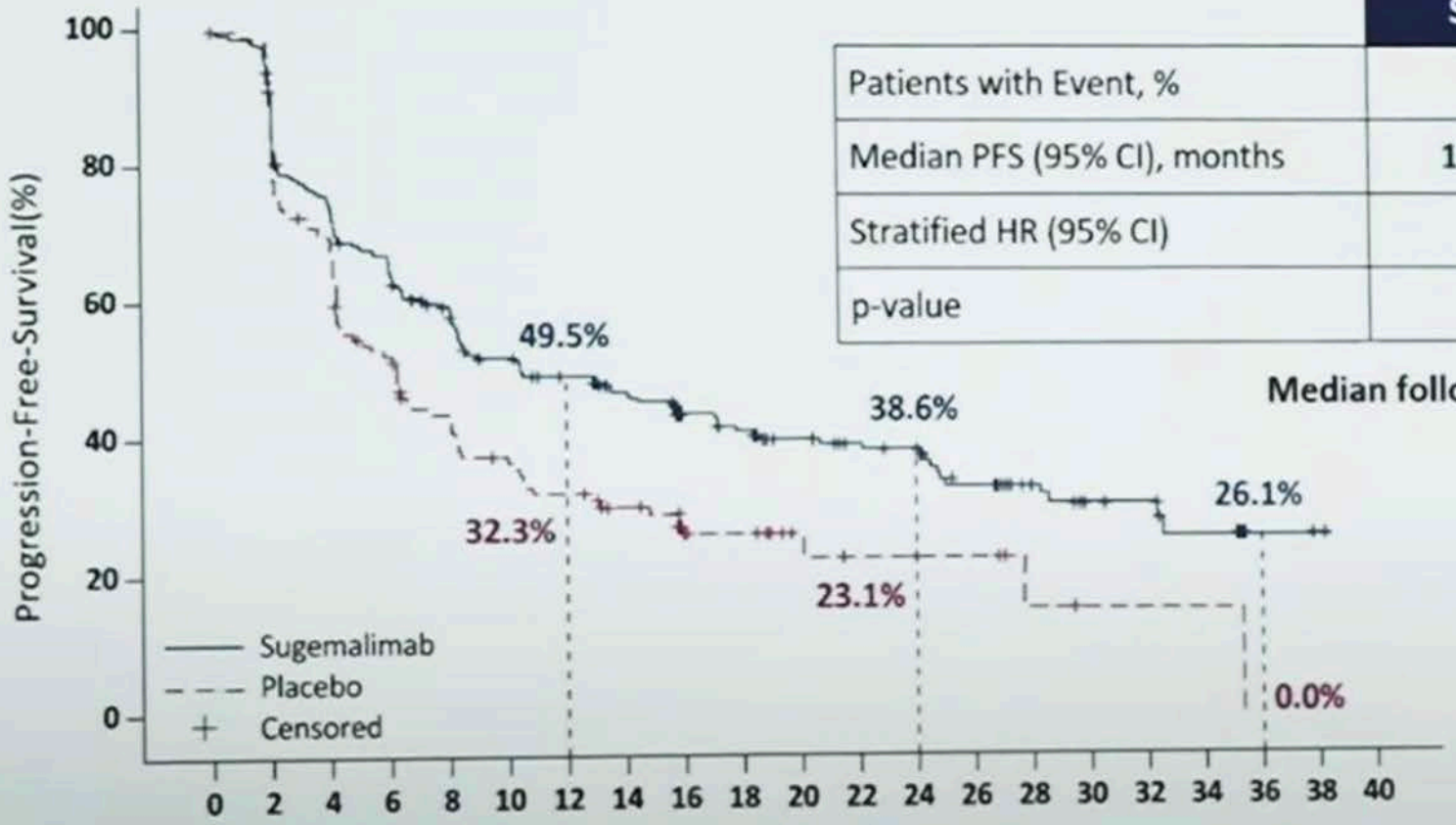
BICR-assessed PFS

	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



Patients at risk

Sugemalimab	255	233	188	167	142	121	111	92	71	65	56	51	49	37	26	17	16	11	3	1	0
Placebo	126	118	86	63	50	41	36	26	18	13	8	6	5	5	2	1	1	1	0	0	0

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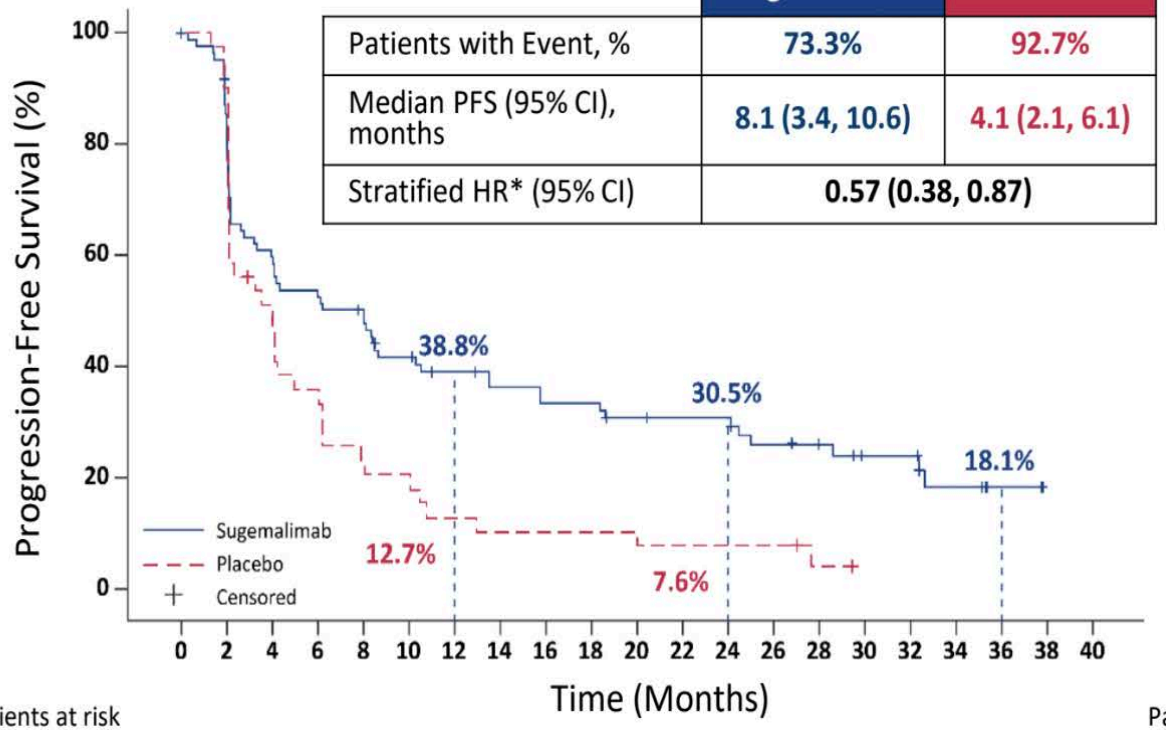
BICR-assessed PFS by CRT Type

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)	



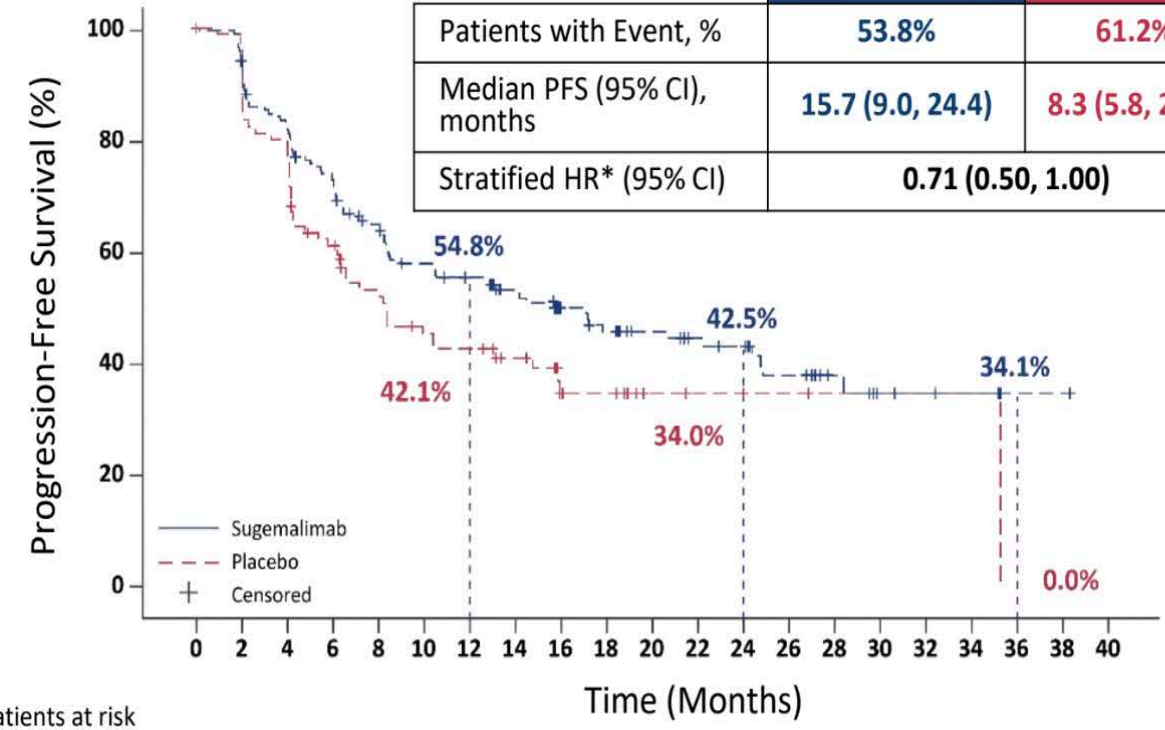
Patients at risk

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)	



Patients 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

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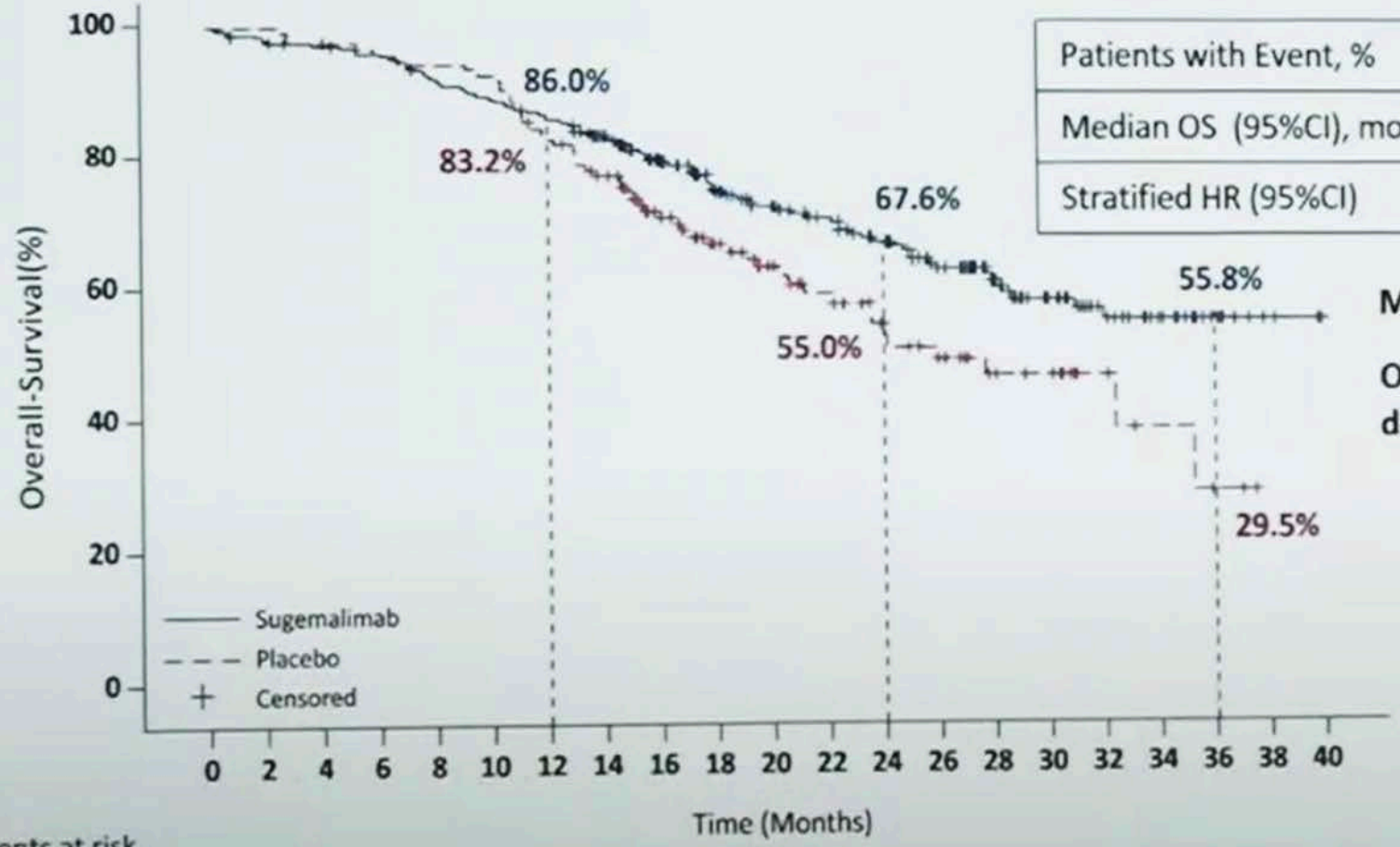
Overall Survival

	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)	



Patients at risk

Sugemalimab	255	249	245	241	230	223	214	199	172	146	131	119	107	87	69	49	34	25	12	3	0
Placebo	126	126	123	120	118	116	103	93	74	61	51	42	32	26	17	14	7	4	2	0	0

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

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

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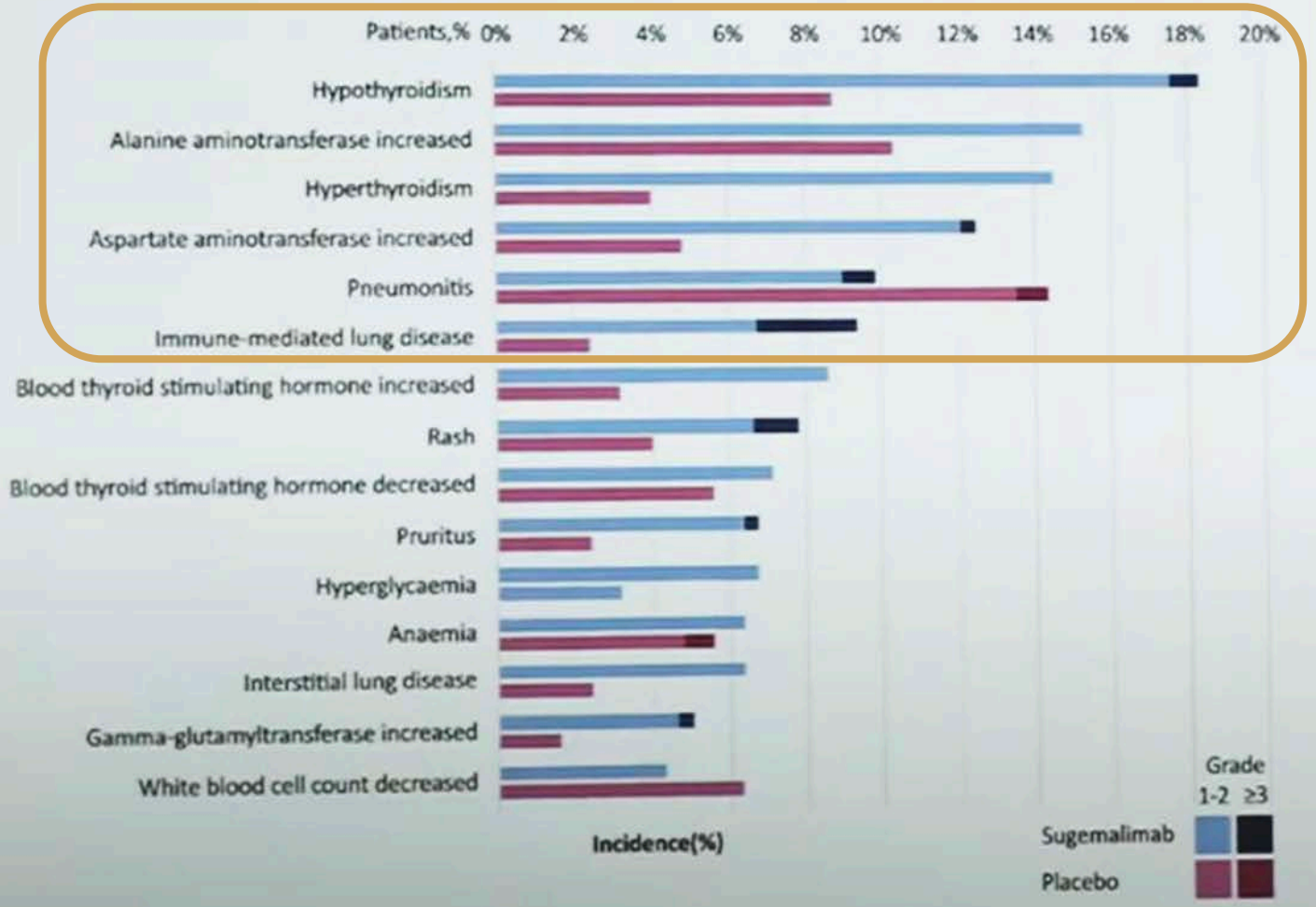
Summary of Adverse Events



	Total	
	Sugemalimab (n=255)	Placebo (n=126)
Treatment Emergent Adverse Event (TEAE)	248 (97.3%)	121 (96.0%)
Treatment-related TEAE	200 (78.4%)	81 (64.3%)
Serious TEAE	88 (34.5%)	35 (27.8%)
Treatment-related serious TEAE	44 (17.3%)	11 (8.7%)
Grade 3-5 TEAE	79 (31.0%)	36 (28.6%)
Treatment-related Grade 3-5 TEAE	29 (11.4%)	7 (5.6%)
TEAE leading to drug permanently discontinued	41 (16.1%)	6 (4.8%)
TEAE leading to infusion interruption	1 (0.4%)	1 (0.8%)
TEAE leading to treatment cycle delay	90 (35.3%)	32 (25.4%)
TEAE leading to death	12 (4.7%)	3 (2.4%)

Conclusion

- PFS final analysis showed sustained improvement in PFS with sugemalimab versus placebo for 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
- No new safety signals were found in PFS final analysis

Let us put the data in perspective..

The challenger.. **Our choice..**

GEMSTONE-301 VS PACIFIC

	GEMSTONE-301	PACIFIC[1]
Patient area	China	Non-China
Prior CRT	cCRT or sCRT	cCRT only
Treatment period	24 months*	12 months
EGFR/ALK/ROS1	Exclude EGFR/ALK/ROS1+	Not exclude EGFR/ALK/ROS1+
Disease Stage	IIIA: 29%	IIIA: 53%
Histology	SCC:69%	SCC:46%

The challenger..

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[a]	7 (3.4)	2 (1.9)

Our choice..

Table S3. Updated Antitumor Activity by Blinded Independent Central Review (ITT Population).

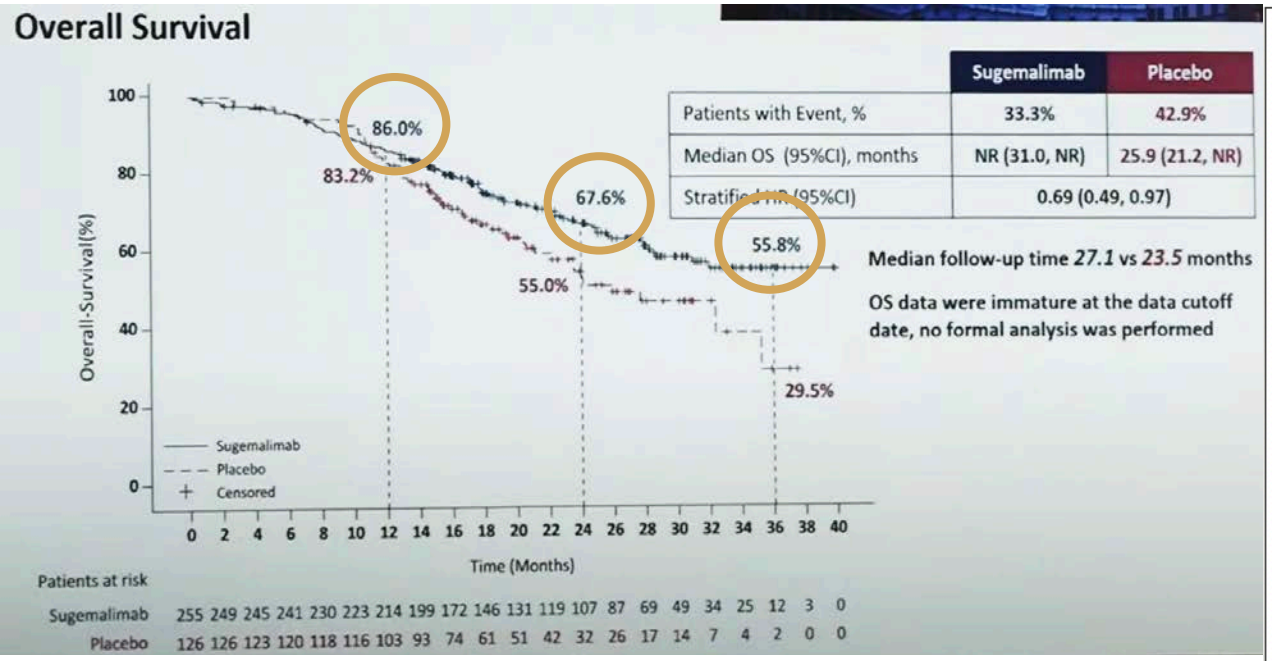
	Durvalumab (N=443)*	Placebo (N=213)*
Objective response		
No. of patients	133	38
% of patients (95% CI)	30.0 (25.79–34.53)	17.8 (12.95–23.65)
P value	<0.001	
Best overall response – no. (%)		
Complete response	8 (1.8)	1 (0.5)
Partial response	125 (28.2)	37 (17.4)
Stable disease	227 (51.2)	115 (54.0)
Progressive disease	73 (16.5)	59 (27.7)
Non-evaluable	10 (2.3)	1 (0.5)
Duration of response, months		
Median (95% CI)	Not reached (27.4–not reached)	18.4 (6.7–24.5)

Best response to previous CRT – no. (%)			
Complete response	9 (1.9)	7 (3.0)	16 (2.2)
Partial response	237 (49.8)	112 (47.3)	349 (48.9)
Stable disease	223 (46.8)	115 (48.5)	338 (47.4)
Progression	2 (0.4)	0	2 (0.3)
Non-evaluable	5 (1.1)	2 (0.8)	7 (1.0)

The challenger..

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)	

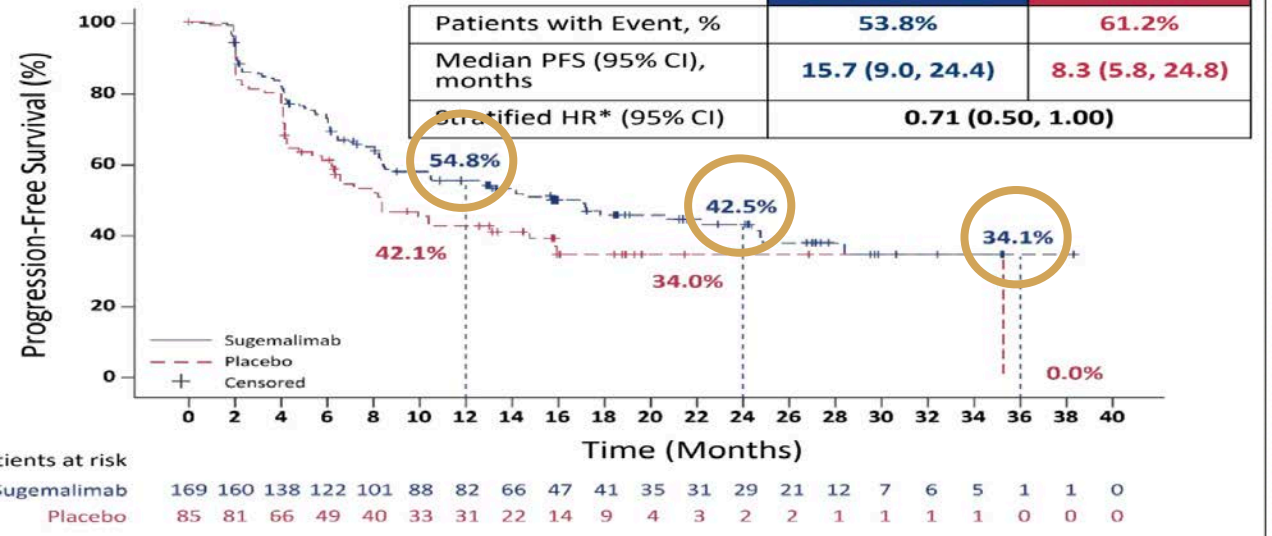


Median follow-up time *27.1* vs *23.5* months

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

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)	



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

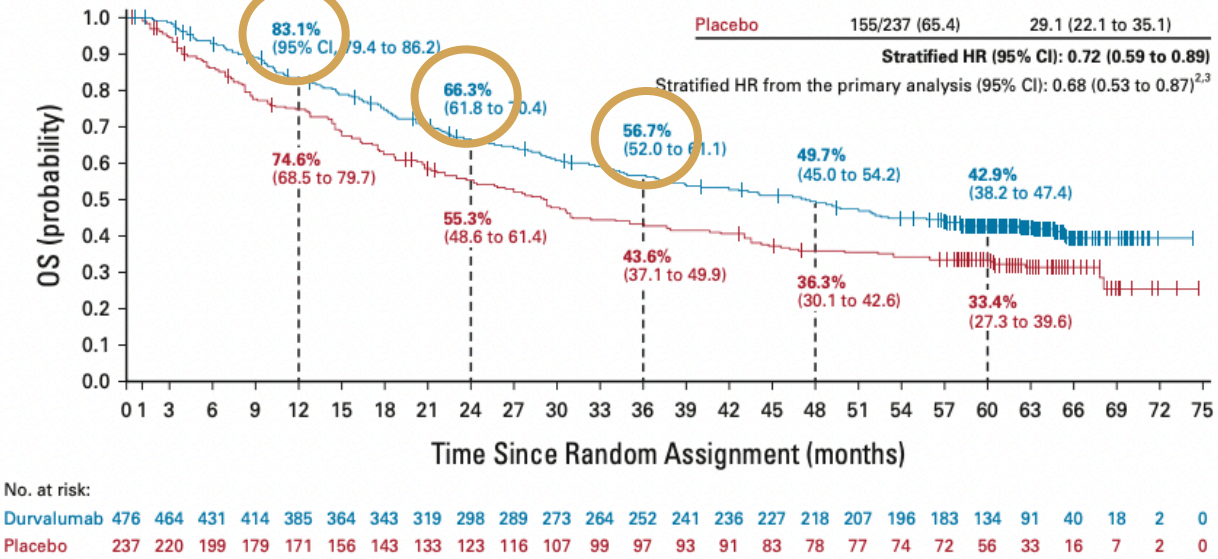
Our choice..

A

Arm	No. of Events/ Total No. of Patients (%)	Median OS (95% CI), Months
Durvalumab	264/476 (55.5)	47.5 (38.1 to 52.9)
Placebo	155/237 (65.4)	29.1 (22.1 to 35.1)

Stratified HR (95% CI): 0.72 (0.59 to 0.89)

Stratified HR from the primary analysis (95% CI): 0.68 (0.53 to 0.87)[2,3]



No. at risk:

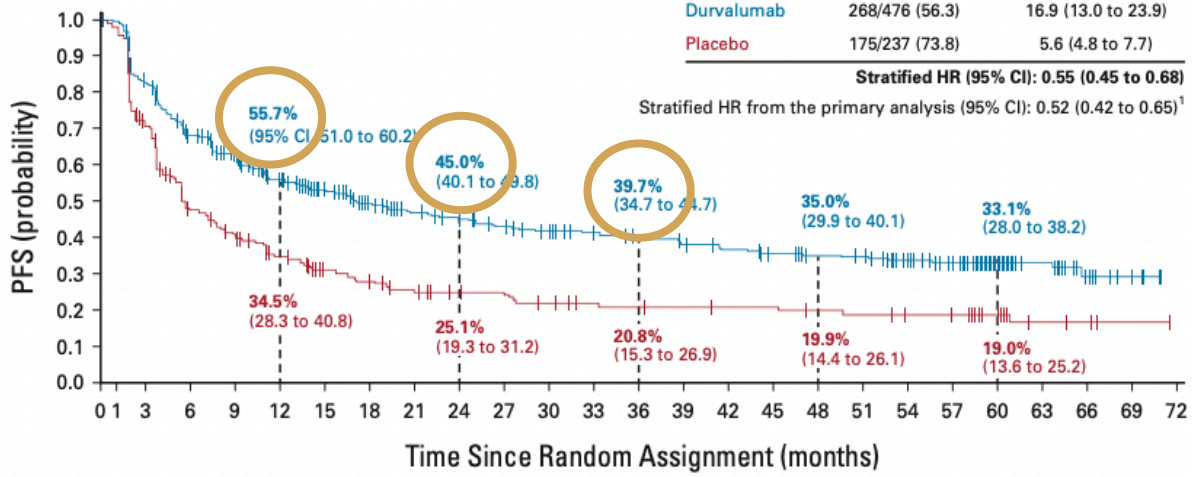
Durvalumab	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33	16	7	2	0

B

Arm	No. of Events/ Total No. of Patients (%)	Median PFS (95% CI), Months
Durvalumab	268/476 (56.3)	16.9 (13.0 to 23.9)
Placebo	175/237 (73.8)	5.6 (4.8 to 7.7)

Stratified HR (95% CI): 0.55 (0.45 to 0.68)

Stratified HR from the primary analysis (95% CI): 0.52 (0.42 to 0.65)[1]



No. at risk:

Durvalumab	476	377	301	267	215	190	165	147	137	128	119	110	103	97	92	85	81	78	67	57	34	22	11	5	0
Placebo	237	164	105	87	68	56	48	41	37	36	30	27	26	25	24	24	22	21	19	19	14	6	4	1	0

The challenger..

	Total	
	Sugemalimab (n=255)	Placebo (n=126)
Treatment Emergent Adverse Event (TEAE)	248 (97.3%)	121 (96.0%)
Treatment-related TEAE	200 (78.4%)	81 (64.3%)
Serious TEAE	88 (34.5%)	35 (27.8%)
Treatment-related serious TEAE	44 (17.3%)	11 (8.7%)
Grade 3-5 TEAE	79 (31.0%)	36 (28.6%)
Treatment-related Grade 3-5 TEAE	29 (11.4%)	7 (5.6%)
TEAE leading to drug permanently discontinued	41 (16.1%)	6 (4.8%)
TEAE leading to infusion interruption	1 (0.4%)	1 (0.8%)
TEAE leading to treatment cycle delay	90 (35.3%)	32 (25.4%)
TEAE leading to death	12 (4.7%)	3 (2.4%)

Our choice..

Event	Durvalumab (N=475)		Placebo (N=234)	
	Any Grade*	Grade 3 or 4	Any Grade*	Grade 3 or 4
	number of patients with event (percent)			
Any event	460 (96.8)	145 (30.5)	222 (94.9)	61 (26.1)
Cough	167 (35.2)	2 (0.4)	59 (25.2)	1 (0.4)
Fatigue	114 (24.0)	1 (0.2)	48 (20.5)	3 (1.3)
Dyspnea	106 (22.3)	7 (1.5)	56 (23.9)	6 (2.6)
Radiation pneumonitis†	96 (20.2)	7 (1.5)	37 (15.8)	1 (0.4)
Diarrhea	88 (18.5)	3 (0.6)	46 (19.7)	3 (1.3)
Pyrexia	72 (15.2)	1 (0.2)	22 (9.4)	0
Nausea	68 (14.3)	0	31 (13.2)	0
Decreased appetite	68 (14.3)	1 (0.2)	30 (12.8)	2 (0.9)
Pneumonia	63 (13.3)	21 (4.4)	18 (7.7)	9 (3.8)
Pneumonitis†	60 (12.6)	9 (1.9)	18 (7.7)	4 (1.7)
Arthralgia	59 (12.4)	0	26 (11.1)	0
Upper respiratory tract infection	59 (12.4)	1 (0.2)	24 (10.3)	0
Pruritus	59 (12.4)	0	12 (5.1)	0
Rash	58 (12.2)	1 (0.2)	18 (7.7)	0
Constipation	56 (11.8)	1 (0.2)	20 (8.5)	0
Hypothyroidism	55 (11.6)	1 (0.2)	4 (1.7)	0
Headache	52 (10.9)	1 (0.2)	21 (9.0)	2 (0.9)
Asthenia	51 (10.7)	3 (0.6)	31 (13.2)	1 (0.4)
Back pain	50 (10.5)	1 (0.2)	27 (11.5)	1 (0.4)
Musculoskeletal pain	39 (8.2)	3 (0.6)	24 (10.3)	1 (0.4)
Anemia	36 (7.6)	14 (2.9)	26 (11.1)	8 (3.4)

IO Consolidation combinations / Intensification

Meeting Abstract | 2022 ASCO Annual Meeting I

LUNG CANCER—NON-SMALL CELL LOCAL-REGIONAL/SMALL CELL/OTHER THORACIC CANCERS

Consolidation nivolumab plus ipilimumab or nivolumab alone following concurrent chemoradiation for patients with unresectable stage III non-small cell lung cancer: BTCRC LUN 16-081.

- **<u>The optimal duration of consolidation IO therapy in this setting is undefined</u>**
- 6 months: BTCRC Lun Trial
- 12 months: PACIFIC Trial
- 24 months: GEMSTONE 301 Trial

- Post CTRT, patients were randomised to Nivo 480mg IV q4wks (Arm A) or N 3mg/kg IV q2 wks + IPI 1mg/kg IV q6 wks (Arm B) for up to 24 weeks

- The percentage of patients completing the full treatment was 70.4% with Nivo and 56.9% with Nivo+IPI

- Median PFS was 25 months in both arms

- trAE on arm A/B were 72.2%/80.4%, and grade ≥3 trAEs on arm A/B were 38.9%/52.9%

Summary

Sugemalimab vs Durvalumab (Primarily)

<u>Subject to availability and pricing, Sugemalimab:</u>

- Can be used post cCTRT or sCTRT, in those with atleast a stable disease post CTRT
- Has shown comparible efficacy to durvalumab, with a PFS benefit and trend towards OS benefit
- No new red flag signs, but a longer follow up and real world data will be necessary

Thank you

Team

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