







Anna Estival

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Unresectable stage III NSCLC



Viena, Austria





- Sugemalimab vs placebo after concurrent or sequencial Ch-Rt in patients with unresectable stage III NSCLC (GEMSTONE 301)
- Consolidation immunotherapy with nivolumab and ipilimumab or nivolumab alone after concurrent Ch-RT in unresectable stage IIIA/IIIB NSCLC
- Durvalumab + RT in unresectable locally advanced NSCLC





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

Presenter: Yi-Long Wu

Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, China

Yi-Long Wu¹, Qing Zhou¹, Ming Chen^{2,3}, Ou Jiang⁴, Yi Pan¹, Desheng Hu⁵, Qin Lin⁶, Gang Wu⁷, Jiuwei Cui⁸, Jianhua Chang^{9,10}, Yufeng Cheng¹¹, Cheng Huang¹², Anwen Liu¹³, Nong Yang¹⁴, Youling Gong¹⁵, Chuan Zhu¹⁶, Zhiyong Ma¹⁷, Jian Fang¹⁸, Gongyan Chen¹⁹, Jun Zhao¹⁸, Anhui Shi¹⁸, Yingcheng Lin²⁰, Guanghui Li²¹, Yunpeng Liu²², Dong Wang²³, Rong Wu²⁴, Xinhua Xu²⁵, Jianhua Shi²⁶, Zhihua Liu²⁷, Rumei Chen²⁸, Qiang Wang²⁸, Mengmeng Qin²⁸, Yiding Ma²⁸, Jingru Wang²⁸, Jason Yang²⁸

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Study Design

Key Eligibility Criteria

Screening

- 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 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

N = 381

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2:1

STRATIFICATION:

CRT (cCRT vs sCRT)

(<60 Gy vs ≥60 Gy)

ECOG PS (0 vs 1)

Total RT dose

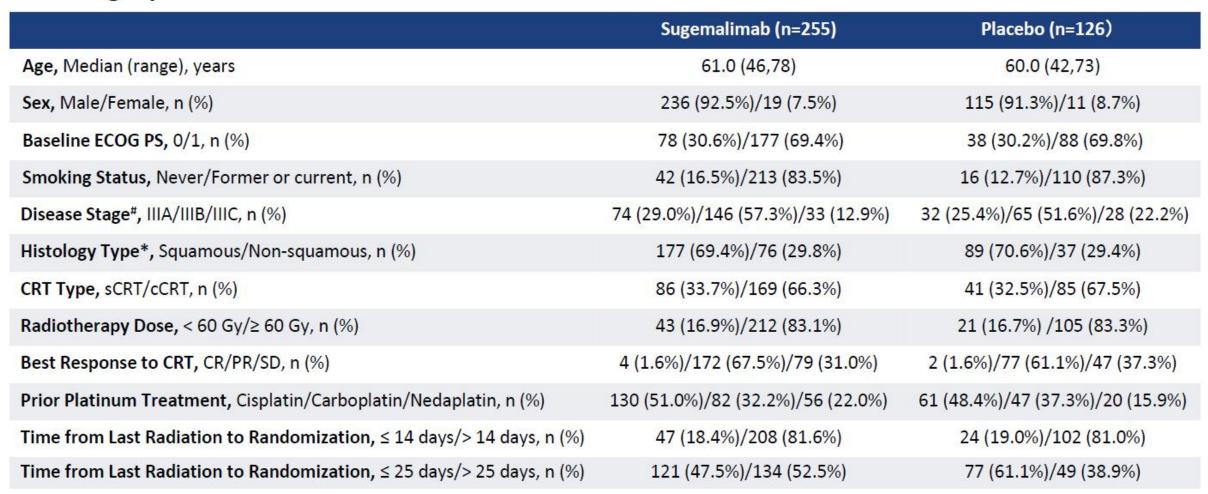
Interim and final OS analysis were planned when approximately 175 and 260 OS events occurred, respectively

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.

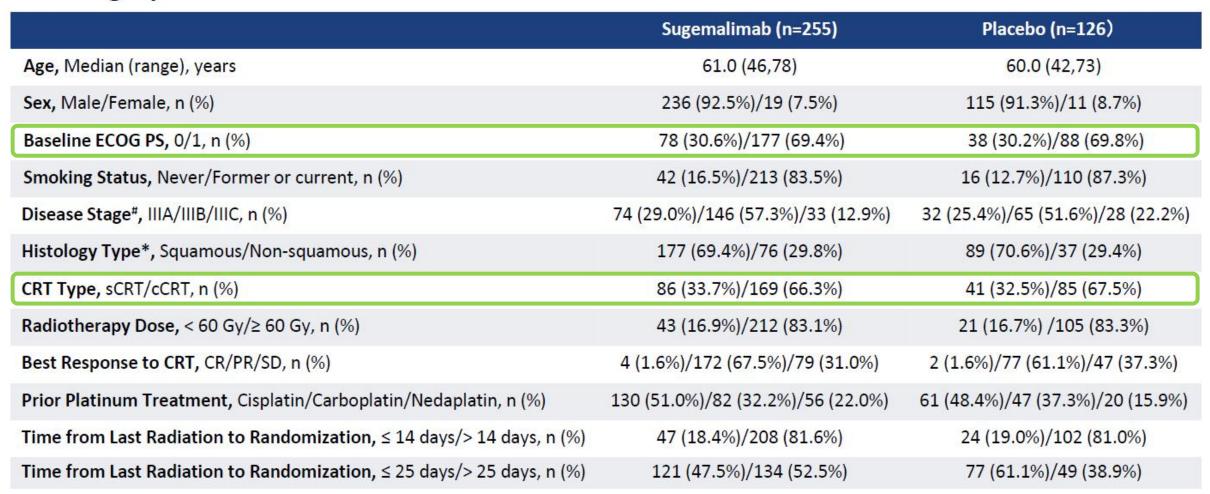


Demographics and Baseline Characteristics

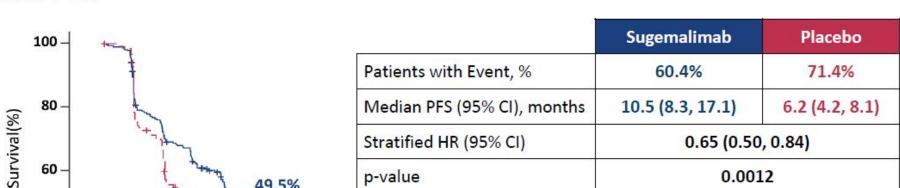


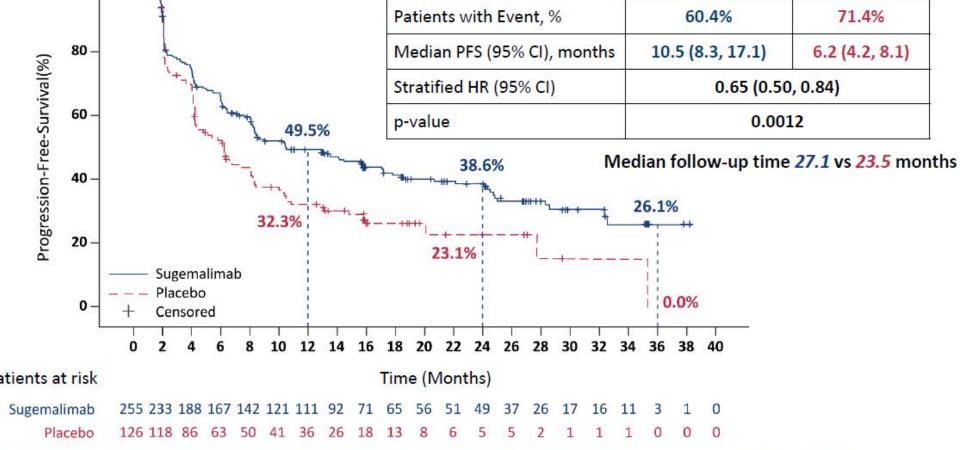


Demographics and Baseline Characteristics



BICR-assessed PFS

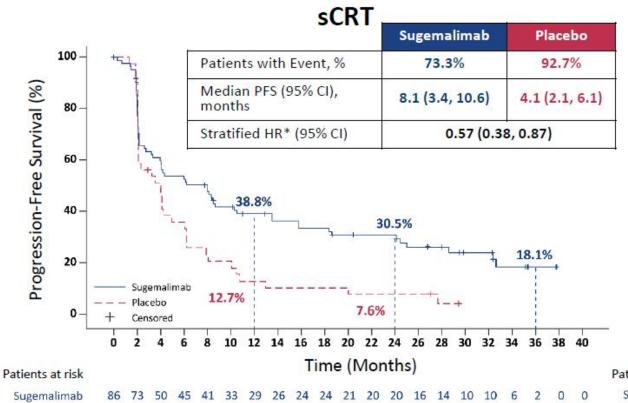


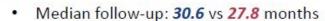


Patients at risk



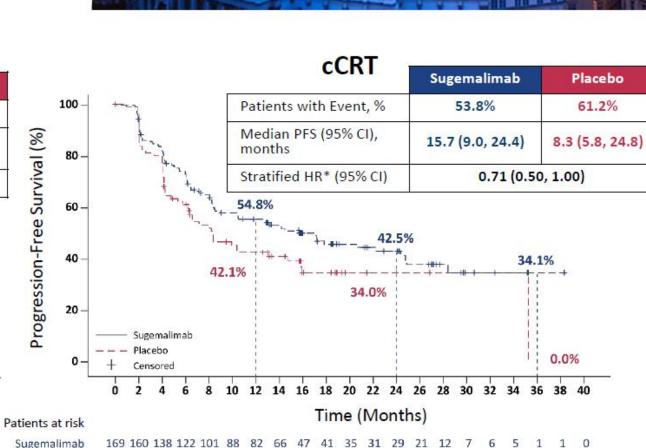
BICR-assessed PFS by CRT Type





Placebo

Median time from start date of CRT to randomization: 156.5 vs 168.0 days



Median follow-up: 22.4 vs 20.0 months

Placebo

Median time from start date of CRT to randomization: 72.0 vs 69.0 days

85 81 66 49 40 33 31 22 14 9 4 3 2 2 1 1



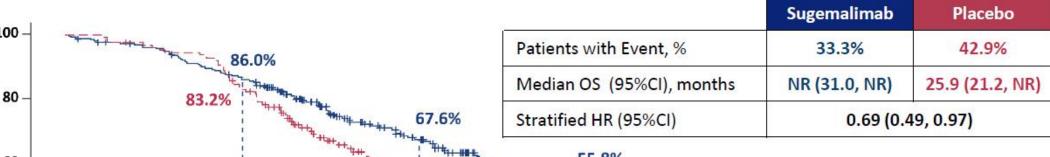
Subgroup Analyses of PFS

	Median PFS ,	months		
Subgroups	Sugemalimab (n=255)	Placebo (n=126)		HR* (95%CI)
All patients	10.5	6.2	Hard .	0.65 (0.50, 0.84
Sex				
Male	12.9	6.2		0.64 (0.49, 0.84
Female	6.5	7.1	I	→ 0.91 (0.38, 2.17)
Age			l de la constant de l	
<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	1	0.45 (0.22, 0.90
Former or current	10.5	6.2	H	0.70 (0.53, 0.93
ECOG PS				
0	24.5	8.1	1 I	0.43 (0.26, 0.70
1	8.4	6.1	H	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	H-1	0.73 (0.39, 1.36
Histology type				
Squamous	8.4	4.3	H-	0.63 (0.47, 0.86
Non-Squamous	24.5	9.9	1	0.65 (0.38, 1.10
		0.1	0.5 1	3 5 7 9
		4	malimab better Pla	cebo better



	Median PFS ,	, months		
Subgroups	Sugemalimab (n=255)	Placebo (n=126)		HR* (95%CI)
All patients	10.5	6.2	-	0.65 (0.50, 0.84)
CRT type Sequential Concurrent	8.1 15.7	4.1 8.3	-	0.56 (0.37, 0.85 0.70 (0.50, 0.99
Radiotherapy dose <60 Gy ≥60 Gy	15.8 10.5	4.3 6.2		0.49 (0.26, 0.92 0.69 (0.52, 0.93
Best response to CRT Complete response Partial response Stable disease	5.8 10.5 13.5	8.1 4.2	⊢	(, 0.73 (0.52, 1.03 0.50 (0.32, 0.77
Prior platinum treatm Cisplatin Carboplatin Nedaplatin	12.9 10.6 9.0	8.0 6.1 4.1	1	0.71 (0.49, 1.03 0.67 (0.43, 1.05 0.45 (0.25, 0.83
Time from last radiati to randomization [#] ≤14 days >14 days	14.2 10.5	9.9 4.8	-	0.88 (0.45, 1.72 0.62 (0.46, 0.82
Time from last radiati to randomization # ≤25days >25days	14.2 10.5	8.1 4.2	-	0.69 (0.48, 0.99 0.58 (0.39, 0.86
		0.1	0.5 1	3 5 7 9
		Sugem	alimab better	Placebo better

Overall Survival



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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(9							3.2/		THE PERSON NAMED IN	The same		H I 111	**-+	67	.6%		5	Strat	tifie	d HI	R (95	5%CI)
Overall-Survival(%)	60 –											⁺⁻ ф++- ₋ -,	+ -++	#+	 	18-1 ₂		"	 	55.8	% 		N
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ients a	t risk										Time	e (Mo	onths	s)									
ugemal	imab	255	249	245	241	230	223	214	199	172	146	131	119	107	87	69	49	34	25	12	3	0	
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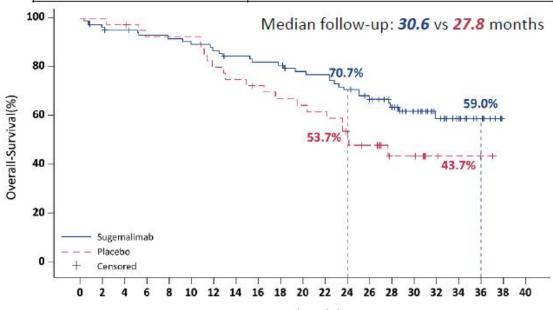
Placebo 126 126 123 120 118 116 103 93 74 61 51 42 32 26 17 14



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 (0.3	34, 1.05)

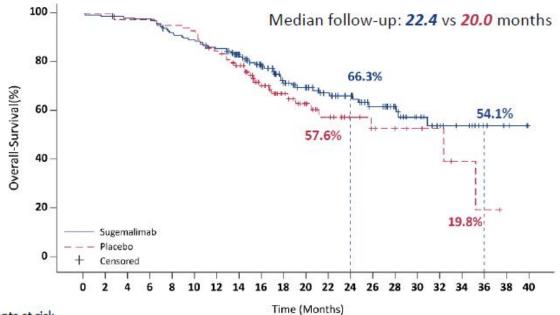


Patients at risk										Time	e (Mc	onth	5)								
Sugemalimab	86	82	80	77	76	74	72	69	67	66	62	61	56	49	40	29	20	14	7	0	0
Placebo	41	41	40	37	37	37	32	30	27	25	24	23	19	16	8	8	3	2	1	0	0



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)



Patients at risk

Sugemalimab 169 167 165 164 154 149 142 130 105 80 69 58 51 38 29 20 14 11 5 3

Placebo 85 85 83 83 81 79 71 63 47 36 27 19 13 10 9 6 4 2 1 0



ORR and **DoR**

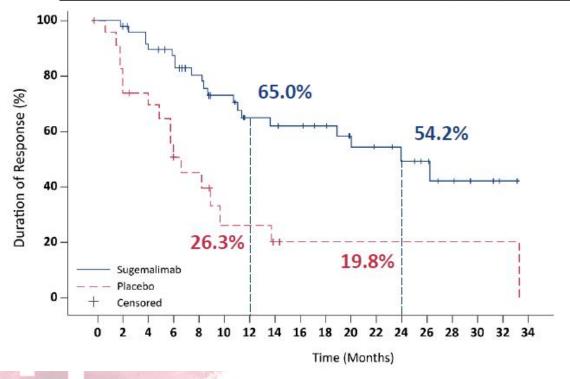
	Sugemalimab (n=204)+	Placebo (n=103)+
ORR (CR+PR)*, n(%) (95%CI)	50 (24.5) (18.8, 31.0)	26 (25.2) (17.2, 34.8)
Complete response, n(%)	0	1 (1.0)
Partial response, n(%)	50 (24.5)	25 (24.3)
Stable disease, n(%)	104 (51.0)	48 (46.6)
Progression of disease, n(%)	43 (21.1)	27 (26.2)
Not applicable#	7 (3.4)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

^{*}Results are based on Intent-to-Treat Analysis Set with Measurable Disease at Baseline



Kaplan-Meier Plot of DoR Assessed by BICR

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

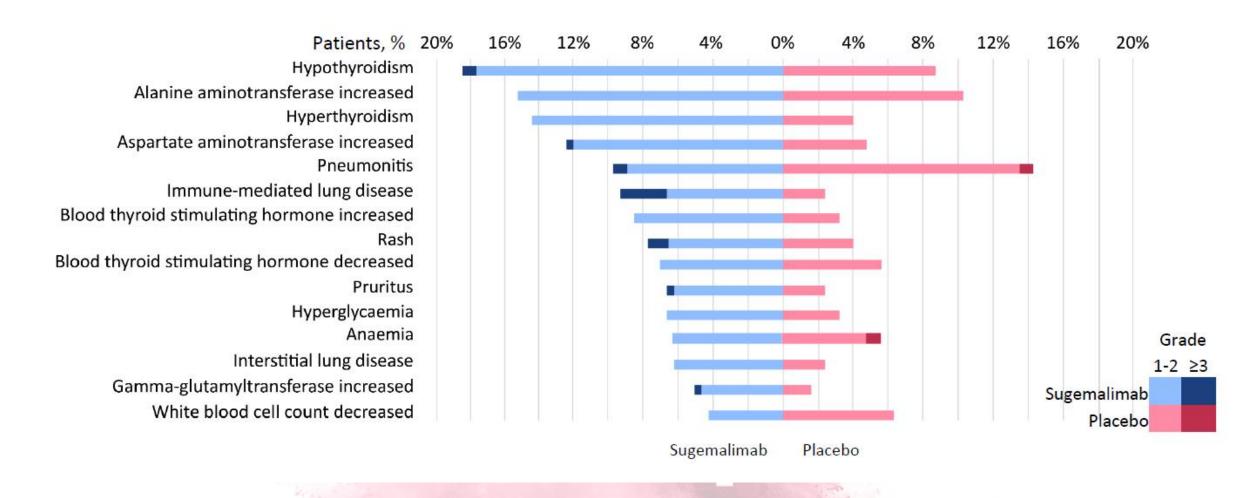


^{*}BICR-accessed, RECIST v1.1

^{*}Patients were classified as not applicable if no post-baseline response assessments were available

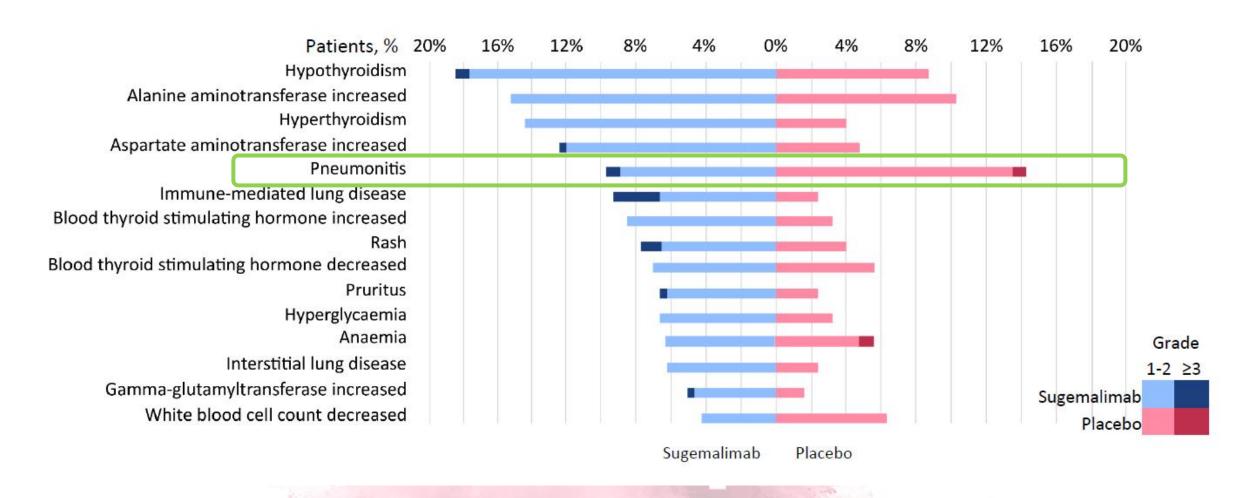


Treatment-related Adverse Event (All Grade ≥5%)





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







Phase II Study of Consolidation Immunotherapy with Nivolumab and Ipilimumab or Nivolumab alone following Concurrent Chemoradiation for Unresectable Stage IIIA/IIIB NSCLC

Nasser Hanna, MD
Indiana University Simon Comprehensive Cancer Center
United States



Unresectable Stage IIIA/IIIB
NSCLC

Concurrent Chemoradiation
Plt Doublet + 59.4-66.6 Gy XRT

/

1:1 Randomization

Nivolumab 480mg IV q4 weeks Nivolumab 240mg
IV q2 weeks
+
Ipilimumab
1mg/kg IV q6 wks

- Multi-center, open label randomized phase II trial
- Pts enrolled following completion of CCRT
- Duration of immunotherapy was 6 months in both arms
- Nivo arm compared to historical control of CCRT alone, Nivo/Ipi arm compared to historical control of CCRT -> Durvalumab



	Nivolumab Alone (N=54)	Nivo/Ipi (N=51)
Median Age, yrs (range)	65 (44-82)	63 (41-83)
Gender, n (%)		
Male	24 (44.4)	29 (56.9)
Race, n (%)		
White	2 (77.8)	30 (58.8)
Black/African-American	10 (18.5)	16 (31.4)
Other/Unknown	2 (3.7)	5 (9.8)
ECOG PS, n (%)		
0	18 (33.3)	27 (52.9)
Stage, n (%)		
ША	30 (55.6)	29 (56.9)
Histology, n (%)		
Non-Squamous	31 (57.4)	28 (54.9)
Chemotherapy Regimen, n (%)		
Carboplatin/Paclitaxel	36 (66.7)	37 (72.5)
Cisplatin/Pemetrexed	8 (14.8)	3 (5.9)
Cisplatin/Etoposide	7 (13)	7 (13.7)
Carboplatin/Pemetrexed	3 (5.6)	4 (7.8)
Completed 100% of Planned Tx	38 (70.4)	23 (45.1)



Unresectable Stage IIIA/IIIB
NSCLC

Concurrent Chemoradiation
Plt Doublet + 59.4-66.6 Gy XRT

/

1:1 Randomization

Nivolumab 480mg IV q4 weeks Nivolumab 240mg
IV q2 weeks
+
Ipilimumab
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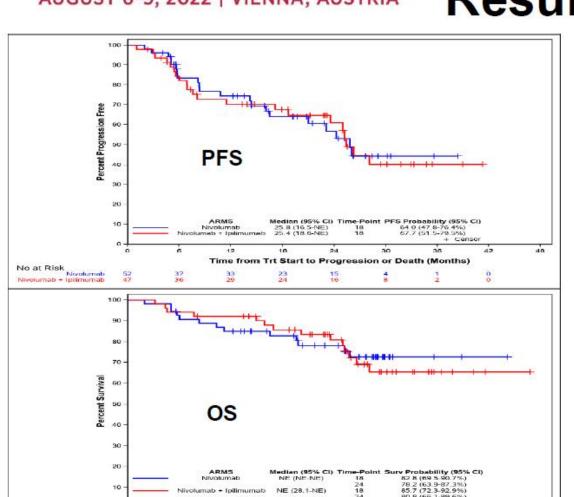


No at Risk Nivolumab Nivolumab + Ipilimumab

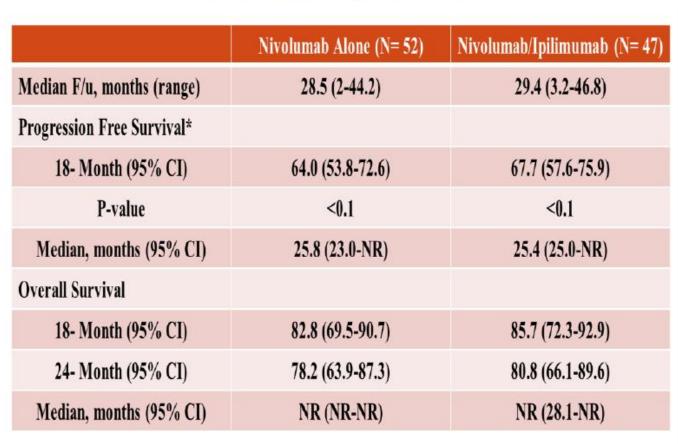
2022 World Conference on Lung Cancer

AUGUST 6-9, 2022 | VIENNA, AUSTRIA

Results



Time from Trt Start to Death (Months)

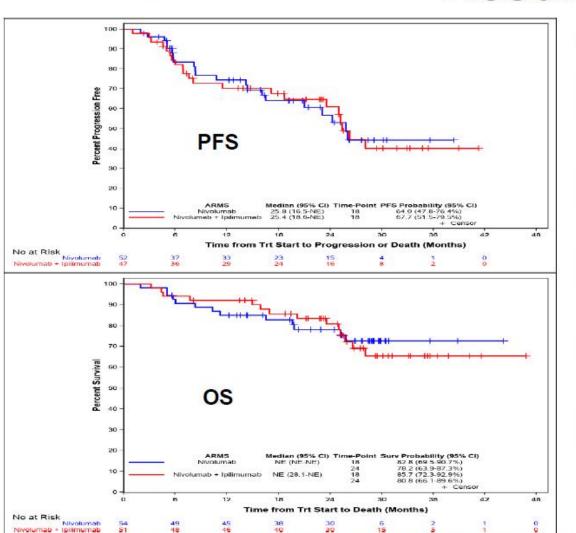


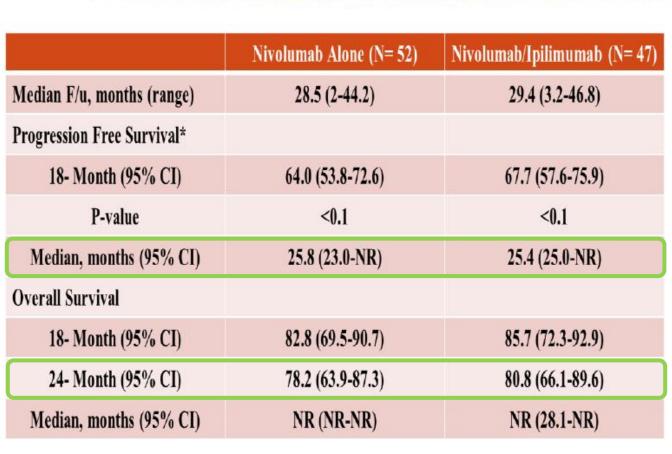


2022 World Conference on Lung Cancer

AUGUST 6-9, 2022 | VIENNA, AUSTRIA

Results







Adverse Events

	Nivolumab Alone (N=54)	Nivolumab/Ipilimumab (N=51)
Any Treatment-Related AE (TRAE), n (%)	39 (72.2)	41 (80.4)
Any Grade ≥3 AE, n (%)*	21 (38.9)	27 (52.9)
Any Grade ≥3 TRAE, n (%)	10 (18.5)	14 (27.5)
TRAE Occurring in ≥ 10% Pts, n (%)		
Fatigue	17 (31.5)	16 (31.4)
Dyspnea	8 (14.8)	10 (19.6)
Rash	9 (16.7)	8 (15.7)
Hypothyroidism	7 (13)	8 (15.7)
Diarrhea	4 (7.4)	10 (19.6)
Pruritus	5 (9.3)	9 (17.7)
Arthralgia	2 (3.7)	6 (11.8)
Nausea	2 (3.7)	6 (11.8)
Pneumonitis		
Grade ≥2	12 (22.2)	16 (31.4)
Grade 3 (no Gr 4/5 pneumonitis)	5 (9.3)	9 (17.6)
Median time to Gr ≥2 Pneum, mo. (range)	11.9 (4.1-36.6)	7.3 (1.3-36.9)

- AE profile was in line with previous trials of Nivo and Ipi
- Pneumonitis rates were increased in the Ipi arm
- Most patients with pneumonitis recovered quickly with steroids
- No grade 4/5 pneumonitis
- There were two grade 5 events (Covid 19 and Cardiac Arrest)





Phase II Study of Durvalumab Plus Concurrent Radiotherapy in Unresectable Locally Advanced NSCLC DOLPHIN Study (WJOG11619L)

Motoko Tachihara¹, Kayoko Tsujino², Mototsugu Shimokawa³,Takeaki Ishihara⁴, Hidetoshi Hayashi⁵, Yuki Sato⁶, Takayasu Kurata⁷, Shunichi Sugawara⁸, Yoshimasa Shiraishi⁹, Shunsuke Teraoka¹⁰, Koichi Azuma¹¹, Haruko Daga¹², Masafumi Yamaguchi¹³, Takeshi Kodaira¹⁴, Miyako Satouchi¹⁵, Nobuyuki Yamamoto¹⁰, Kazuhiko Nakagawa⁵

¹Division of Respiratory Medicine, Kobe University Graduate School of Medicine, Kobe, Japan. ²Department of Radiation Oncology, Hyogo Cancer Center, Akashi, Japan.³Department of Biostatistics, Yamaguchi University Graduate School of Medicine Yamaguchi, Ube, Japan. ⁴Division of Radiation Oncology, Kobe University Graduate School of Medicine, Kobe, Japan. ⁵Department of Medical Oncology, Kindai University, Osakasayama, Japan. ⁵Department of Respiratory Medicine, Kobe City Medical Center General Hospital, Kobe, Japan. ⁵Department of Thoracic Oncology, Kansai Medical University Hospital, Hirakata, Japan. ⁵Department of Pulmonary Medicine, Sendai Kousei Hospital, Sendai, Japan. ⁵Research Institute for Diseases of the Chest, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan.¹¹Internal Medicine, Medicine, Kurume University School of Medicine, Fukuoka, Japan.¹¹Department of Medical Oncology, Osaka City General Hospital, Osaka, Japan.¹¹Department of Thoracic Oncology, National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan.¹¹Departments of Radiation Oncology, Aichi Cancer Center Hospital, Nagoya, Aichi.¹⁵Department of Thoracic Oncology, Hyogo Cancer Center, Akashi, Japan.





Study Design

Multi-center, Single arm, Investigator Initiated, phase II trial (JapicCTI- 194840)

Primary registration

Key Eligibility Criteria

- Suspected

 unresectable stage III or postoperative recurrent

 NSCLC
- ECOG PS 0 or 1
 - Sep 2019- Nov 2020
 - 12 institutions in Japan

Secondary registration

Key Eligibility Criteria

- Confirmed
 unresectable stage III or
 postoperative recurrent
 NSCLC
- Can be treated according to radiation protocol
- PD-L1≥1% (SP263)

n = 35

Treatment

Radiation therapy (60Gy) plus durvalumab (10 mg/kg, Q2w)

for up to 1 year until PD or unacceptable toxicity

Tumor evaluation by CT scan Q8W

Sample size calculated

threshold of the 12-month PFS rate; 28% expected rate: 50%

α=0.05(one-sided) and power 0.8

Primary endpoint:12-month PFS rate (assessed by independent central review) **Secondary endpoints**:PFS, OS, objective response rate, disease control rate, treatment completion rate, time to death or distant metastasis, and safety



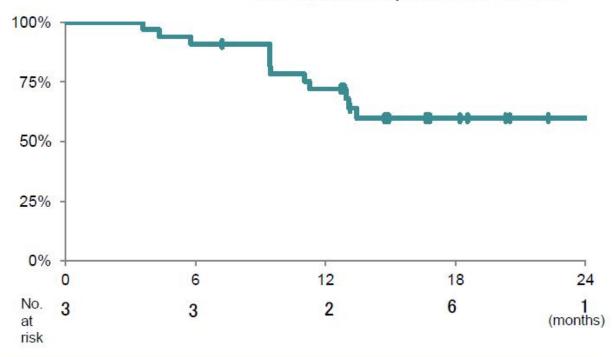
Baseline Characteristics

Characteristics, n	nedian(range), n(%)	n=35
Age		72(44-83)
Sex	male(%)	31 (88.6)
Smoking history	never	1 (2.9)
14 - 14	former	16 (45.7)
	current	18 (51.4)
Pathology	adenocarcinoma	19 (54.3)
0°0,747	Squamous cell carcinoma	15 (42.9)
	NOS	1 (2.9)
Stage	post-operative recurrence	9 (25.7)
	IIIA	16 (45.7)
	IIIB	7 (20.0)
	IIIC	3 (8.6)
ECOG PS	0/1	19/16 (54.3/45.7)
TPS (SP263)		60(1-100)
Radiation	3D-CRT	24 (70.6)



12-month PFS rate by ICR

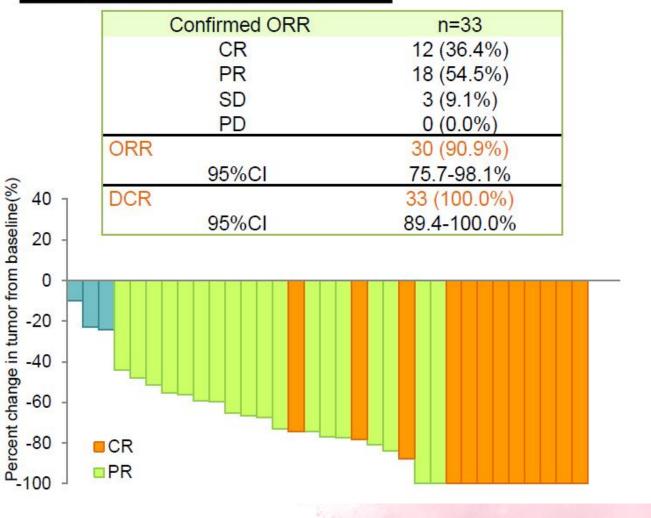
Median follow-up time; 18.7 months



12-month PFS rate	90%CI (%)	95%CI(%)
72.1%	59.1-85.1	56.1-87.6



Response rate by ICR





Safety

	n(%)
Any grade AEs	34 (100)
Grade 3/4	16 (47.1)
Grade 5	2 (5.9)
Leading to discontinuation of durvalumab	6 (17.6)
Leading to discontinuation of RT	0 (0.0)
Any grade treatment-related AEs	30 (88.2)
SAEs	13 (38.2)
Severe immune-mediated AEs	10 (29.4)

Pneumonitis or Radiation Pneumonitis	n(%)
Any grade	21 (61.8)
Grade 3/4	4 (11.8)
Grade 5	0 (0.0)
Leading to discontinuation of durvalumab	2 (5.9)
Leading to discontinuation of RT	0 (0.0)



Response rate by ICR

		C	Confirmed ORR	n=33	
	CR		CR	12 (36.4%)	
			PR	18 (54.5%)	
			SD	3 (9.1%)	
(9			PD	0 (0.0%)	
		ORR		30 (90.9%)	
			95%CI	75.7-98.1%	
(%)	40 -	DCR		33 (100.0%)	
elin	20		95%CI	89.4-100.0%	
pas	20 -				
mo	0 -				
or fr	20 -				
tum	-20				
<u>=</u> .	-40 -				
Percent change in tumor from baseline(%)	60				
	-00 -				
cent	-80 -	■CR			
Per	100 -	■PR			



Safety

	n(%)
Any grade AEs	34 (100)
Grade 3/4	16 (47.1)
Grade 5	2 (5.9)
Leading to discontinuation of durvalumab	6 (17.6)
Leading to discontinuation of RT	0 (0.0)
Any grade treatment-related AEs	30 (88.2)
SAEs	13 (38.2)
Severe immune-mediated AEs	10 (29.4)

Pneumonitis or Radiation Pneumonitis	n(%)
Any grade	21 (61.8)
Grade 3/4	4 (11.8)
Grade 5	0 (0.0)
Leading to discontinuation of durvalumab	2 (5.9)
Leading to discontinuation of RT	0 (0.0)







