GEMSTONE-302: Randomized, Double-Blind, Phase 3 Study of Sugemalimab or Placebo Plus Platinum-Based Chemotherapy as First-Line Treatment for Metastatic NSCLC

Caicun Zhou

Shanghai Pulmonary Hospital, Tongji University, Shanghai/China

Caicun Zhou[1], Ziping Wang[2], Yuping Sun[3], Lejie Cao[4], Zhiyong Ma[5], Rong Wu[6], Yan Yu[7], Wenxiu Yao[8], Jianhua Chang[9], Jianhua Chen[10], Wu Zhuang[11], Jiuwei Cui[12], Xueqin Chen[13], You Lu[14], Hong Shen[15], Jingru Wang[16], Rumei Chen[16], Mengmeng Qin[16], Hao Wang[16], Jason Yang[16]

1.Shanghai Pulmonary Hospital, Tongji University, Shanghai/China, 2.Beijing Cancer Hospital, Beijing/China, 3.Jinan Central Hospital, Jinan/China, 4.Anhui Provincial Hospital, Hefei/China, 5.The Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou/China, 6.Shengjing Hospital of China Medical University, HuaXiang Branch Hospital, Shenyang/China, 7.Harbin Medical University Cancer Hospital, Harbin/China, 8.Sichuan Cancer Hospital & Institute, Chengdu/China, 9.Fudan University Shanghai Cancer Center, Shanghai/China, 10.Hunan Cancer Hospital, Changsha/China, 11.Fujian Provincial Cancer Hospital, Fuzhou/China, 12.The First Hospital of Jilin University, Changchun/China, 13.The Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine, Hangzhou/China, 14.West China Hospital, Sichuan University, Chengdu/China, 15.The Second Affiliated Hospital of Zhejiang University School of Medicine, Zhejiang/China, 16.CStone Pharmaceuticals (Su Zhou) Co., Ltd., Suzhou/China

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Disclosure Information of Prof. Caicun Zhou

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- Advisor: Hengrui Medicine, Innovent Biologics, Qilu Pharmaceutical, TopAlliance Biosciences

Background

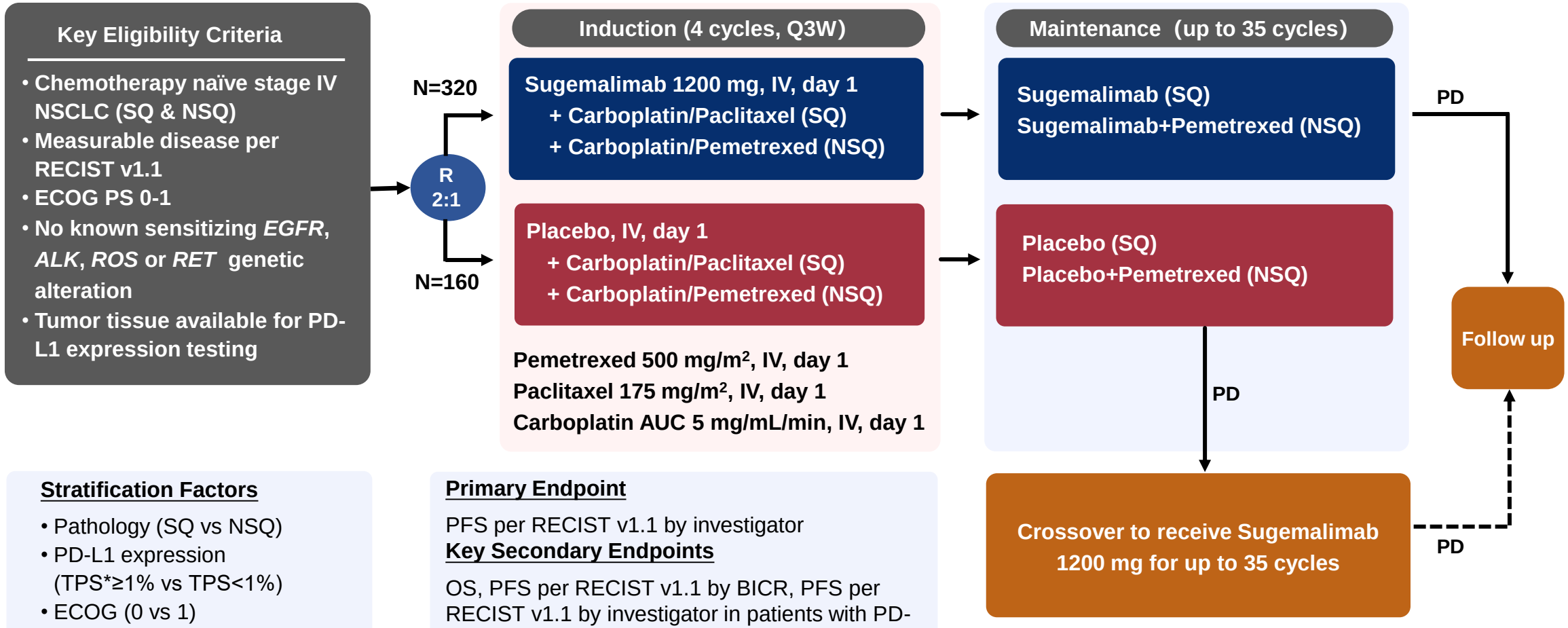
- Sugemalimab is a full-length, fully human programmed death ligand-1 (PD-L1) targeted immunoglobin G4 (IgG4, s228p) monoclonal antibody (mAb)

- GEMSTONE-302 is the first phase 3, randomized, double-blind trial to investigate the efficacy and safety of an anti-PD-L1 mAb in combination with platinum-based chemotherapy in patients with squamous or non-squamous NSCLC regardless of PD-L1 expression
  - Primary endpoint of investigator-assessed PFS was met in the pre-planned interim PFS analysis (as of 08 Jun 2020, median follow-up 8.6 months); Sugemalimab plus chemotherapy demonstrated statistically and clinically meaningful benefit in PFS compared to placebo plus chemotherapy[1]
    - Investigator-assessed PFS was 7.8 vs 4.9 months, HR=0.50, P<0.0001
    - ORR was higher (61.4% vs 39.2%) with durable response

- We present the final PFS analysis results, and preliminary OS results with a median follow-up of 18 months

1. Zhou C, et al. Annals of Oncology 2020 31 (suppl_6): S1386-S1406. 10.1016/annonc/annonc367

GEMSTONE-302 Study Design



Stratification Factors

- Pathology (SQ vs NSQ)
- PD-L1 expression (TPS*≥1% vs TPS<1%)
- ECOG (0 vs 1)

Primary Endpoint

PFS per RECIST v1.1 by investigator

Key Secondary Endpoints

OS, PFS per RECIST v1.1 by BICR, PFS per RECIST v1.1 by investigator in patients with PD-L1 expression ≥ 1%, ORR, DoR

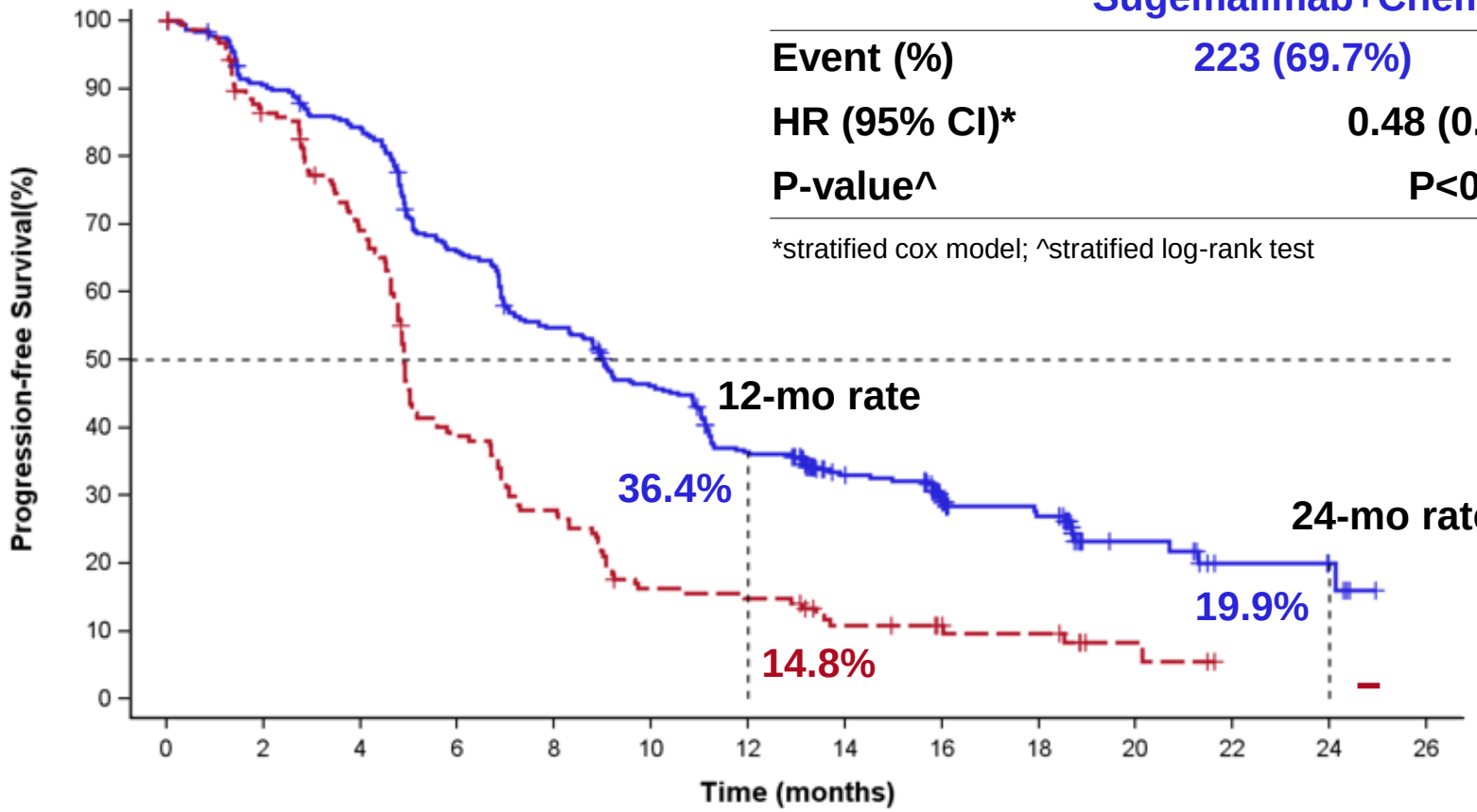
Abbreviations: BICR=blinded independent central radiologic review; IV=intravenous injection; NSQ=non-squamous; PD=progression of disease; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; Q3W=once every three weeks; SQ=squamous
*Percentage of tumor cells with membranous PD-L1 staining assessed using VENTANA PD-L1 (SP263) immunohistochemistry

Baseline Characteristics

	Sugemalimab+Chemo N=320	Placebo+Chemo N=159
Age, Median (range), Years	62.0 (29, 75)	64.0 (36, 75)
Sex, Male, n(%)	254 (79.4%)	129 (81.1%)
Baseline ECOG Performance Status, n(%)		
0	59 (18.4%)	25 (15.7%)
1	261 (81.6%)	134 (84.3%)
Pathologic Subtype, n(%)		
Squamous Cell Carcinoma	129 (40.3%)	63 (39.6%)
Non-Squamous Cell Carcinoma	191 (59.7%)	96 (60.4%)
PD-L1 Expression, n(%)		
<1%	124 (38.8%)	64 (40.3%)
≥1%	196 (61.3%)	95 (59.7%)
Tobacco Use, n(%)		
Never	88 (27.5%)	40 (25.2%)
Current/Former	232 (72.5%)	119 (74.8%)
Baseline Liver Metastasis, Yes, n(%)	39 (12.2%)	18 (11.3%)
Baseline Brain Metastasis, Yes, n(%)	50 (15.6%)	17 (10.7%)

Data cutoff date: 15 Mar 2021

Investigator-Assessed PFS (RECIST v1.1, ITT)



	Sugemalimab+Chemo	Placebo+Chemo
Event (%)	223 (69.7%)	135 (84.9%)
HR (95% CI)*	0.48 (0.39, 0.60)	
P-value^	P<0.0001	

*stratified cox model; ^stratified log-rank test

Median (95% CI)

9.0 mo (7.4, 10.8)

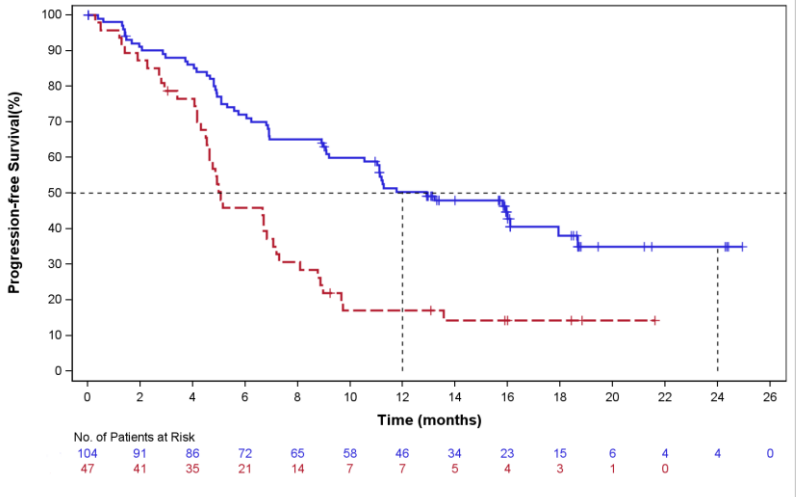
4.9 mo (4.8, 5.1)

Data cutoff date: 15 Mar 2021

Investigator-Assessed PFS by PD-L1 Expression

PD-L1 TPS ≥50%

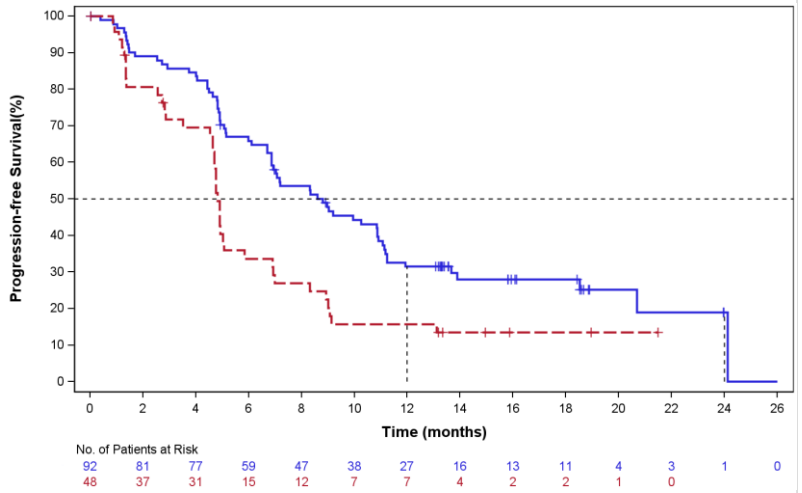
HR (95% CI): 0.41 (0.27, 0.62)
Median PFS (95% CI): 12.9 (9.2, 17.9) vs 5.1 (4.5, 7.1)



PFS Rate	Sugemalimab+ Chemo	Placebo +Chemo
12 months	50.3%	17.0%
24 months	34.9%	–

PD-L1 TPS 1-49%

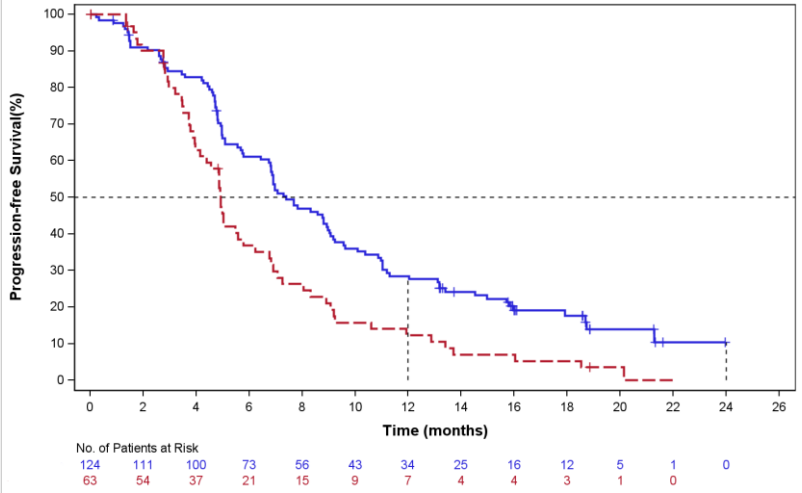
HR (95% CI): 0.53 (0.35, 0.79)
Median PFS (95% CI): 8.8 (6.9, 10.9) vs 4.8 (4.6, 5.1)



PFS Rate	Sugemalimab+ Chemo	Placebo +Chemo
12 months	31.5%	15.7%
24 months	18.9%	–

PD-L1 TPS<1%

HR (95% CI): 0.55 (0.40, 0.77)
Median PFS (95% CI): 7.4 (6.8, 9.0) vs 4.9 (4.0, 5.8)



PFS Rate	Sugemalimab+ Chemo	Placebo +Chemo
12 months	28.5%	12.3%
24 months	–	0%

Subgroup was not powered for formal statistical testing.

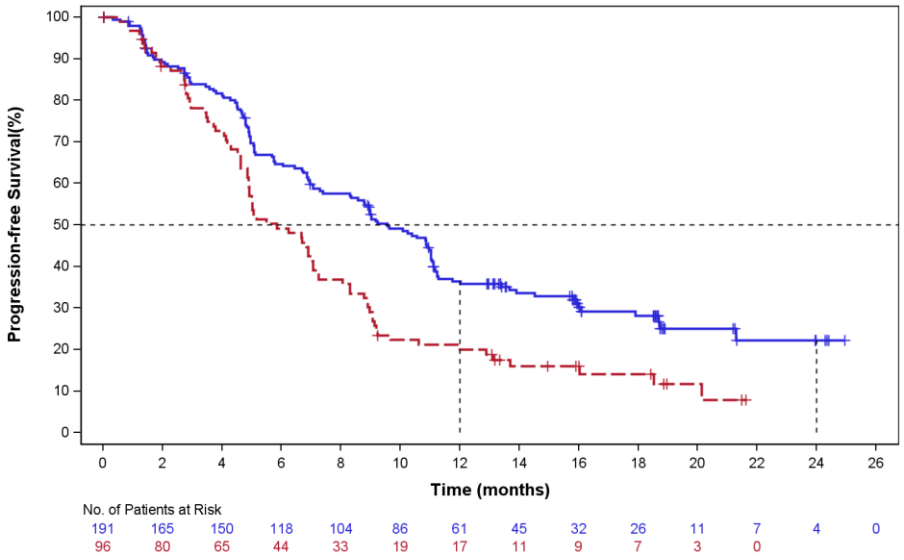
Data cutoff date: 15 Mar 2021

Investigator-Assessed PFS by Pathology

Non-squamous

HR (95% CI): 0.59 (0.45, 0.79)

Median PFS (95% CI): 9.6 (8.3, 11.0) vs 5.9 (4.9, 7.1)

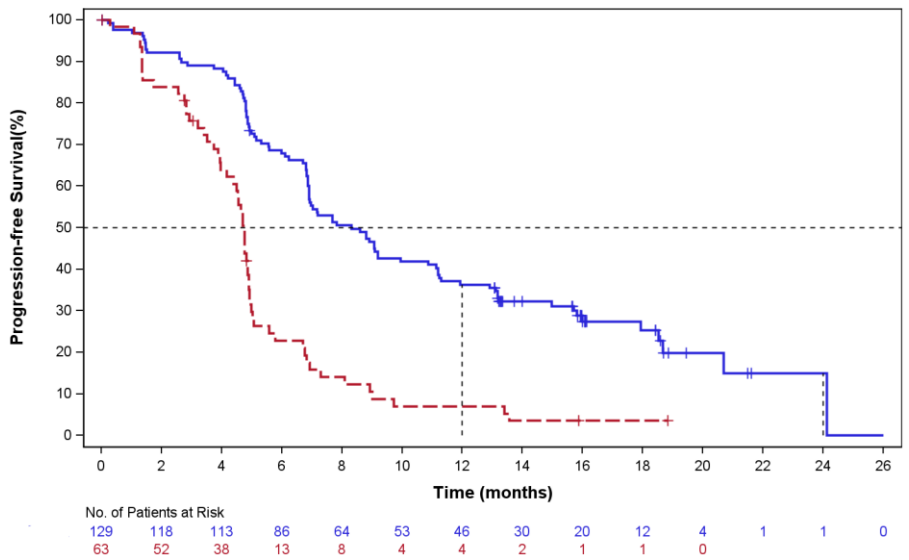


PFS Rate	Sugemalimab +Chemo	Placebo +Chemo
12 months	36.3%	19.9%
24 months	22.3%	–

Squamous

HR (95% CI): 0.34 (0.24, 0.48)

Median PFS (95% CI): 8.3 (6.9, 10.9) vs 4.8 (4.2, 4.9)



PFS Rate	Sugemalimab +Chemo	Placebo +Chemo
12 months	36.3%	7.0%
24 months	14.9%	–

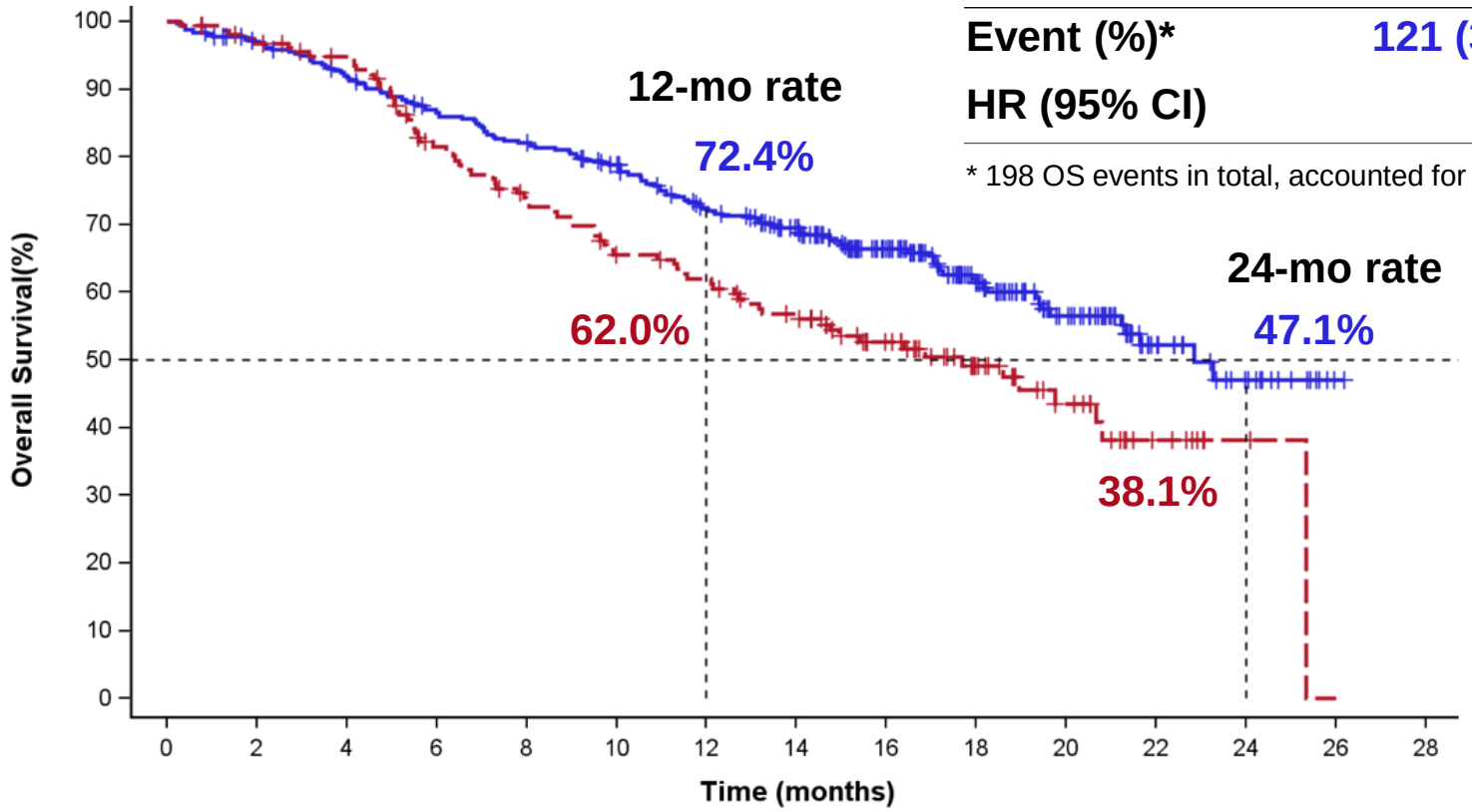
Subgroup was not powered for formal statistical testing.

Data cutoff date: 15 Mar 2021

Overall Survival

	Sugemalimab+Chemo	Placebo+Chemo
Event (%)*	121 (37.8%)	77 (48.4%)
HR (95% CI)	0.67 (0.50, 0.90)	

* 198 OS events in total, accounted for 55% of the final OS events



Median (95% CI)

22.8 mo (19.7, NR)

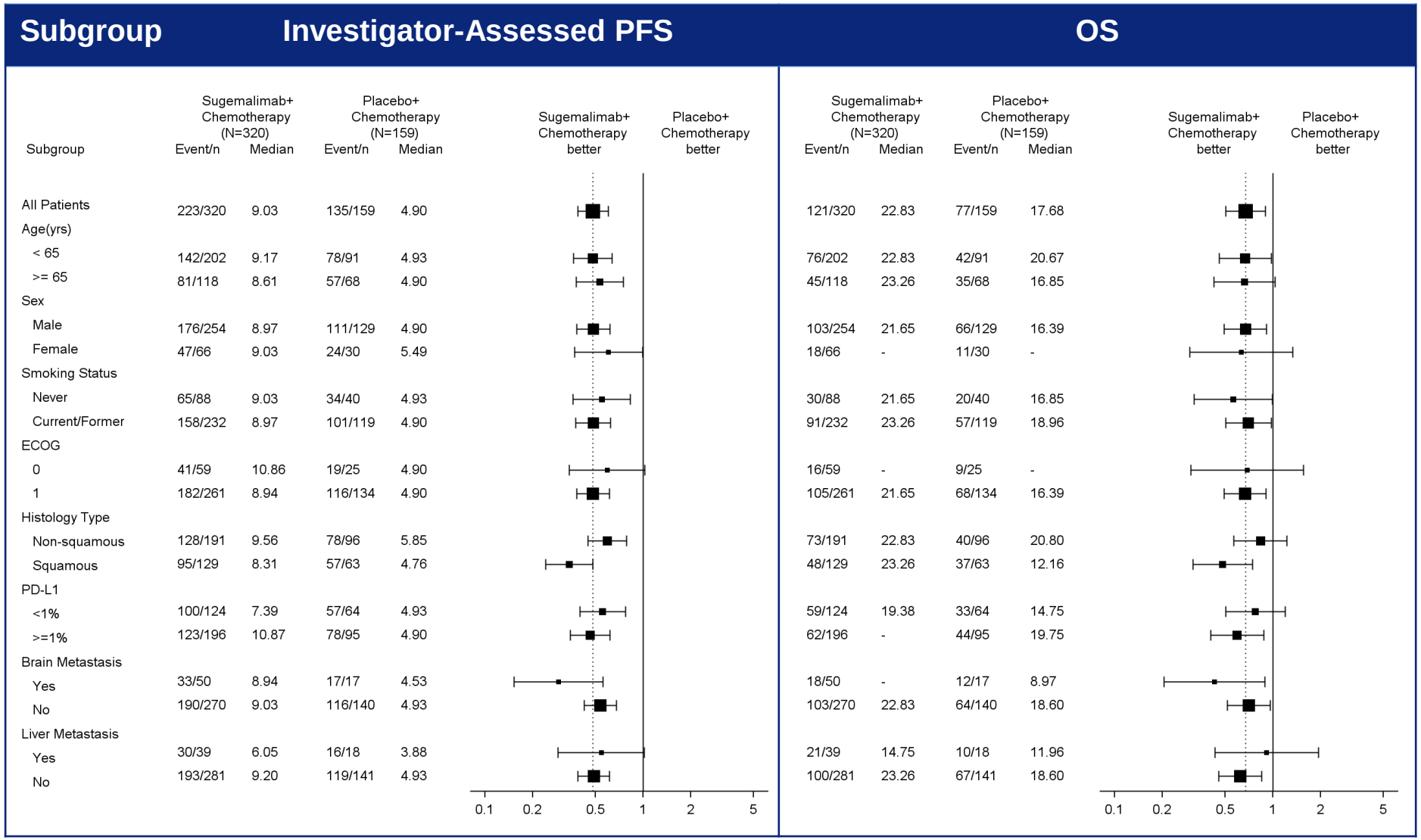
17.7 mo (12.8, 20.8)

Note：OS data has not reached the pre-defined interim analysis time, so no statistical conclusion can be made

NR: not reached

Data cutoff date: 15 Mar 2021

Subgroup Analysis



Subgroup was not powered for formal statistical testing.

OS data has not reached the pre-defined interim analysis time, so no statistical conclusion can be made.

Data cutoff date: 15 Mar 2021

Summary of Adverse Events

	Sugemalimab+Chemo N=320	Placebo+Chemo N=159
Number of Patients with at Least One TEAE	319 (99.7%)	157 (98.7%)
Any Drug Related TEAE	317 (99.1%)	153 (96.2%)
TEAE of Grade ≥3	205 (64.1%)	98 (61.6%)
Any Drug Related TEAE of Grade ≥3	182 (56.9%)	91 (57.2%)
Immune-related TEAE*	80 (25.0%)	5 (3.1%)
Immune-related TEAE of Grade ≥3	13 (4.1%)	0
TEAE Leading to Death	19 (5.9%)	9 (5.7%)
TEAE Leading to Sugemalimab/Placebo Permanently Discontinuation	42 (13.1%)	12 (7.5%)

* Immune-related AEs were defined based on a list of preferred terms specified by the sponsor and included in the analysis regardless of whether they were attributed to treatment by the investigator

Data cutoff date: 15 Mar 2021

Conclusions

- Sugemalimab plus chemotherapy provided prolonged PFS and encouraging OS as first-line treatment for patients with metastatic NSCLC
  - Investigator-assessed PFS: **9.0** vs **4.9** months, HR=0.48, P<0.0001
  - Preliminary OS: **22.8** vs **17.7** months, HR=0.67
- The improvements were observed across different subgroups, including PD-L1 expression levels, pathology, and patients with CNS or liver metastases
- The combination was well-tolerated and no new safety signals were identified with longer follow-up
- Sugemalimab plus chemotherapy provides a new treatment option as the first-line treatment of patients with metastatic NSCLC

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GEMSTONE-302 Study Investigators

Caicun Zhou
Ziping Wang
Yuping Sun
Meili Sun
Lejie Cao
Zhiyong Ma
Rong Wu
Yan Yu
Wenxiu Yao
Jianhua Chang

Huijie Wang
Jianhua Chen
Wu Zhuang
Jiuwei Cui
Xueqin Chen
You Lu
Hong Shen
Chunhong Hu
Jiwei Liu
Yunpeng Liu

Mengzhao Wang
Xingya Li
Ping Sun
Yongqian Shu
Jianying Zhou
Bingqiang Ni
Jingzhang Li
Kangsheng Gu
Changli Wang
Hui Zhao

Yiping Zhang
Chunling Liu
Jun Qian
Hui Yang
Xiaochun Zhang
Rui Ma
Lin Li
Li Liang
Yang Zhang
Man Li