VIRTUAL 2020 ESMO ASIA

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

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Disclosure Information

Prof. Caicun Zhou

- Honoraria as a speaker: Amoy Diagnositics, Boehringer Ingelheim, CStone Pharmaceuticals, Eli Lily China, Hengrui Medicine, Innovent Biologics, Luye Pharma, MSD, Qilu Pharmaceutical, Roche, Sanofi, TopAlliance Biosciences
- Advisor: Hengrui Medicine, Innovent Biologics, Qilu Pharmaceutical, TopAlliance Biosciences

Background

- Sugemalimab (CS1001) is a full-length, fully human programmed death ligand-1 (PD-L1) targeted immunoglobin G4 (IgG4, s228p) monoclonal antibody (mAb)
  - *In vitro*, sugemalimab specifically binds to PD-L1, competitively blocks the binding of human PD-L1 with PD-1 and CD80, which leads to $CD4^+$ T lymphocyte proliferation and enhances the production of interferon-γ [(1)]
  - Sugemalimab lacks antibody-dependent cellular mediated cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC), but retains antibody-dependent cellular phagocytosis (ADCP), which may further enhance tumor antigen presentation for long-term anti-tumor immunity
- Phase Ib data of sugemalimab plus platinum-based chemotherapy demonstrated promising efficacy and tolerable safety in patients with squamous or non-squamous NSCLC [(2)]
- This is the first phase 3, randomized, double-blind trial of an anti-PD-L1 mAb combined with chemotherapy in patients with squamous or non-squamous NSCLC

1 Zhang J, et al. AACR; Cancer Res 2020; 80:Abstract nr 3260; 2. Shen L, et al. Ann Oncol 31:S841-S873 (P1445), 2020

GEMSTONE-302 Study Design

Key Eligibility Criteria

- Chemotherapy naïve stage IV NSCLC (SQ & NSQ)
- Measurable disease per RECIST v1.1
- ECOG PS 0-1
- No known sensitizing *EGFR*, *ALK*, *ROS* or *RET* genetic alteration
- Tumor tissue available for PD-L1 expression testing

N=320

R 2:1

N=160

Induction (4 cycles, Q3W)

Sugemalimab 1200 mg, IV, day 1
+ Carboplatin/Paclitaxel (SQ)
+ Carboplatin/Pemetrexed (NSQ)

Placebo, IV, day1
+ Carboplatin/Paclitaxel (SQ)
+ Carboplatin/Pemetrexed (NSQ)

Pemetrexed 500 mg/m², IV, day 1
Paclitaxel 175 mg/m², IV, day 1
Carboplatin AUC 5 mg/mL/min, IV, day 1

Maintenance (up to 35 cycles)

Sugemalimab (SQ)
Sugemalimab+Pemetrexed (NSQ)

Placebo (SQ)
Placebo+Pemetrexed (NSQ)

PD

PD

Crossover to receive Sugemalimab 1200 mg for up to 35 cycles

PD

Follow up

Stratification Factors

- Histology (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:

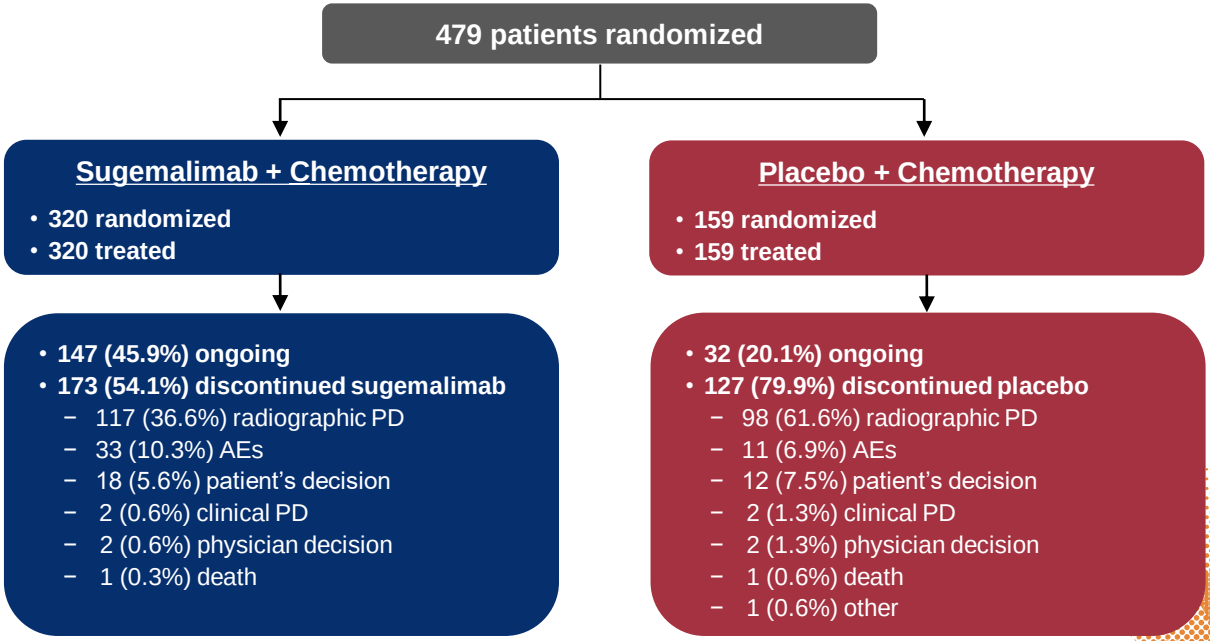
OS, PFS per RECIST v1.1 by BICR, PFS per RECIST v1.1 by investigator in patients with PD-L1 expression ≥ 1%, ORR, DoR

Abbreviations: NSQ=non-squamous; SQ=squamous; PD=progression disease; IV=intravenous injection; BICR=blinded independent central radiologic review
*Percentage of tumor cells with membranous PD-L1 staining assessed using VENTANA PD-L1 (SP263) immunohistochemistry

Statistical Consideration

- **Sample size:**
  - Planned to 480 patients (2:1 ratio) to achieve 360 PFS events
- **Overall alpha for the study**
  - 89% to detect a PFS HR of 0.7 at 2-sided alpha = 0.05.
  - An interim PFS analysis will be performed when 252 PFS events observed. O'Brien-Fleming method will be used to control type I error
- **PFS interim analysis (reviewed by independent data monitoring committee [iDMC])**
  - Data cutoff date: Jun 8, 2020
  - Median follow-up: 8.6 months
  - Observed PFS events: 268 with 2-sided alpha = 0.0188
- **Overall survival will be sequentially tested**
  - Number of events: 252 for OS interim analysis and 360 for final analysis

Patient Disposition



Data cutoff date: Jun 8, 2020

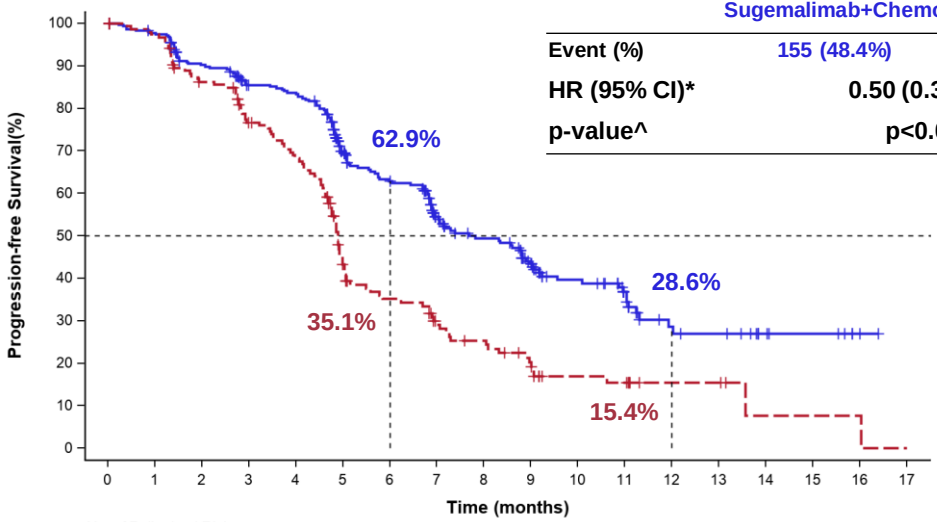
Baseline Characteristics

	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%)
Histology Type, 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%)
Former	197 (61.6%)	103 (64.8%)
Current	35 (10.9%)	16 (10.1%)
Baseline Liver Metastasis, Yes, n(%)	39 (12.2%)	18 (11.3%)
Baseline Brain Metastasis, Yes, n(%)	50 (15.6%)	17 (10.7%)
Prior Adjuvant/Neo-adjuvant/Other, n(%)	16 (5.0%)/0/0	13 (8.2%)/1 (0.6%)/2 (1.3%)

Data cutoff date: Jun 8, 2020

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

	Sugemalimab+Chemo	Placebo+Chemo
Event (%)	155 (48.4%)	113 (71.1%)
HR (95% CI)*	0.50 (0.39, 0.64)	
p-value^	p<0.0001	



No. of Patients at Risk

Sugemalimab + Chemo	320	303	271	246	241	169	143	103	86	66	47	31	17	15	8	6	2	0
Placebo + Chemo	159	150	129	110	97	55	42	31	26	19	11	10	4	4	1	1	1	0

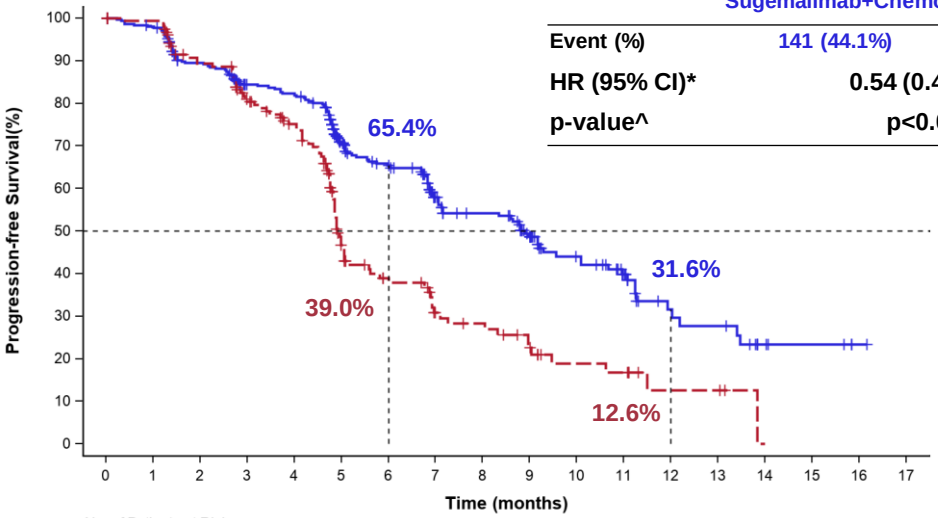
Median (95% CI)
7.82 mo (6.90, 8.97)
4.90 mo (4.70, 5.03)

*stratified cox model
^stratified log-rank test

Data cutoff date: Jun 8, 2020

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

	Sugemalimab+Chemo	Placebo+Chemo
Event (%)	141 (44.1%)	96 (60.4%)
HR (95% CI)*	0.54 (0.41, 0.70)	
p-value^	p<0.0001	



Median (95% CI)

8.90 mo (7.06, 10.09)

4.93 mo (4.83, 5.59)

No. of Patients at Risk

Sugemalimab + Chemo	320	303	266	238	232	162	135	95	82	64	45	31	16	14	6	4	1	0
Placebo + Chemo	159	153	131	113	98	50	36	24	21	15	9	8	3	3	0			

*stratified cox model

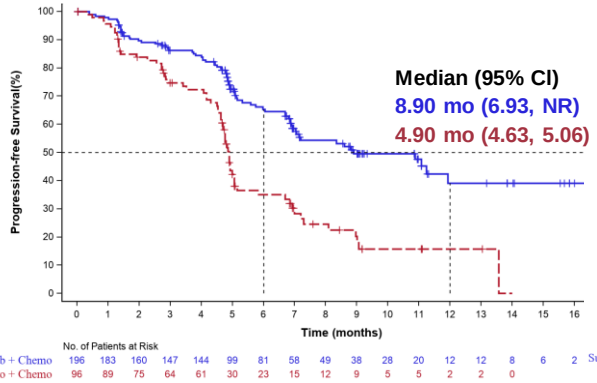
^stratified log-rank test

Data cutoff date: Jun 8, 2020

Investigator-Assessed PFS by PD-L1 Expression

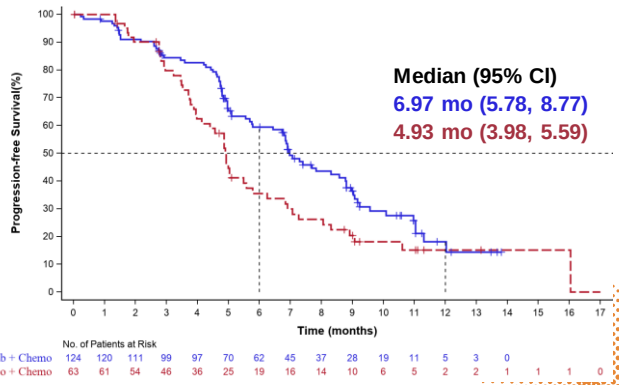
PD-L1 TPS≥1%

	Sugemalimab+Chemo	Placebo+Chemo
Event (%)	76 (38.8%)	65 (67.7%)
HR (95% CI)	0.42 (0.30, 0.59)	



PD-L1 TPS<1%

	Sugemalimab+Chemo	Placebo+Chemo
Event (%)	79 (63.7%)	48 (76.2%)
HR (95% CI)	0.66 (0.46, 0.94)	



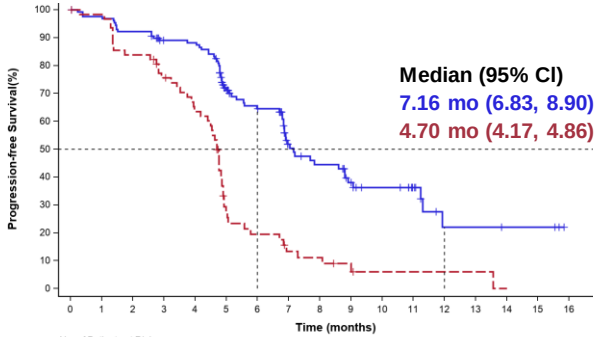
Subgroup was not powered for formal statistical testing.

Data cutoff date: Jun 8, 2020

Investigator-Assessed PFS by Histology

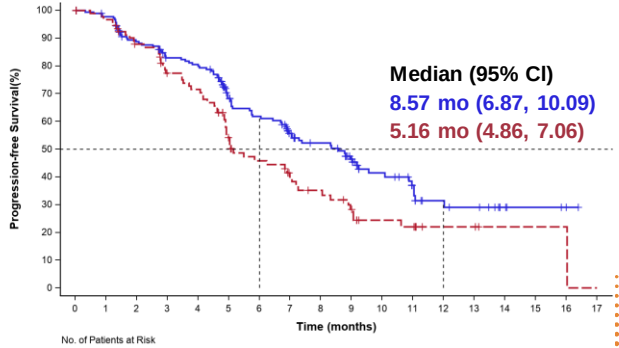
Squamous NSCLC

	Sugemalimab+Chemo	Placebo+Chemo
Event (%)	64 (49.6%)	53 (84.1%)
HR (95% CI)	0.33 (0.22,0.47)	



Non-squamous NSCLC

	Sugemalimab+Chemo	Placebo+Chemo
Event (%)	91 (47.6%)	60 (62.5%)
HR (95% CI)	0.66 (0.48,0.92)	

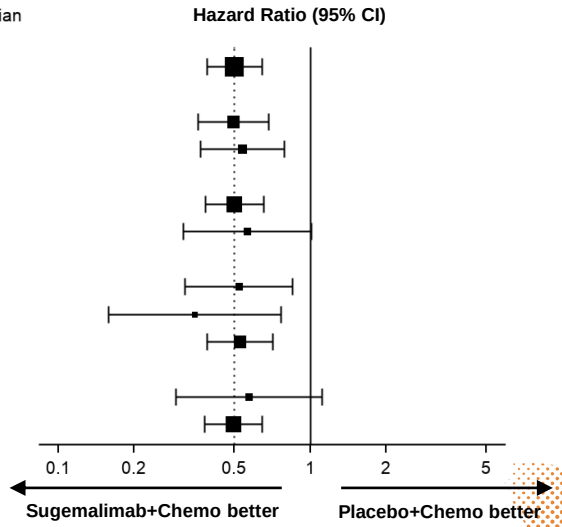


Subgroup was not powered for formal statistical testing.

Data cutoff date: Jun 8, 2020

Investigator-Assessed PFS in Subgroups (1/2)

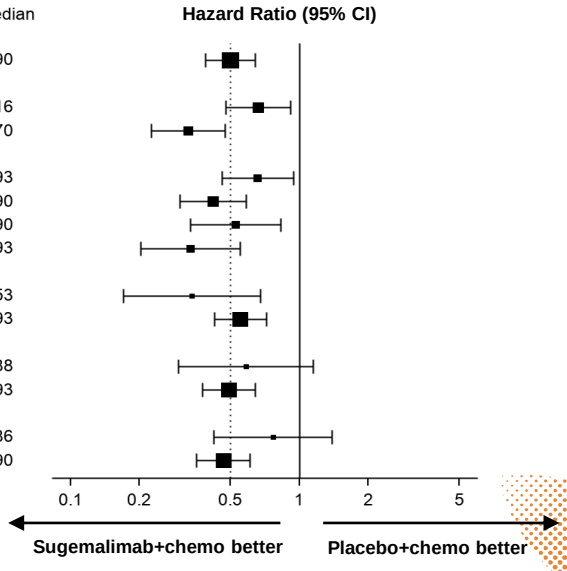
Subgroup	Sugemalimab+Chemo Event/n	Sugemalimab+Chemo Median	Placebo+Chemo Event/n	Placebo+Chemo Median
All Patients	155/320	7.82	113/159	4.90
Age(yrs)				
< 65	95/202	8.80	64/91	4.90
>= 65	60/118	7.06	49/68	4.90
Sex				
Male	125/254	7.82	95/129	4.90
Female	30/66	7.06	18/30	5.17
Smoking Status				
Never	42/88	7.69	26/40	4.93
Current	13/35	12.02	13/16	4.60
Former	100/197	7.39	74/103	4.90
ECOG				
0	23/59	-	14/25	4.90
1	132/261	7.69	99/134	4.90



Data cutoff date: Jun 8, 2020

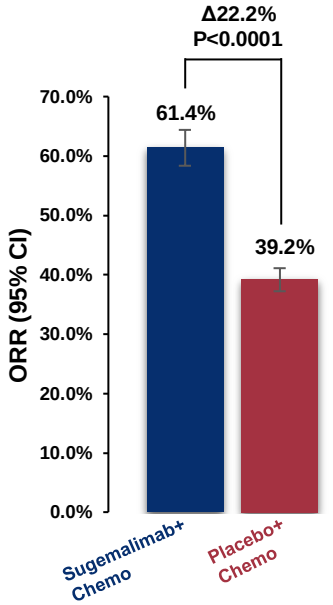
Investigator-Assessed PFS in Subgroups (2/2)

Subgroup	Sugemalimab+Chemo Event/n	Sugemalimab+Chemo Median	Placebo+Chemo Event/n	Placebo+Chemo Median
All Patients	155/320	7.82	113/159	4.90
Histology Type				
Non-squamous	91/191	8.57	60/96	5.16
Squamous	64/129	7.16	53/63	4.70
PD-L1				
<1%	79/124	6.97	48/64	4.93
>=1%	76/196	8.90	65/95	4.90
1-49%	45/92	7.06	33/48	4.90
>=50%	31/104	-	32/47	4.93
Brain Metastasis				
Yes	22/50	10.09	15/17	4.53
No	133/270	7.39	96/140	4.93
Liver Metastasis				
Yes	24/39	5.98	14/18	3.88
No	131/281	8.61	99/141	4.93
Prior Caner Therapy				
Yes	28/50	7.03	18/28	4.86
No	127/270	8.57	95/131	4.90



Data cutoff date: Jun 8, 2020

Objective Response Rate (ORR) and Duration



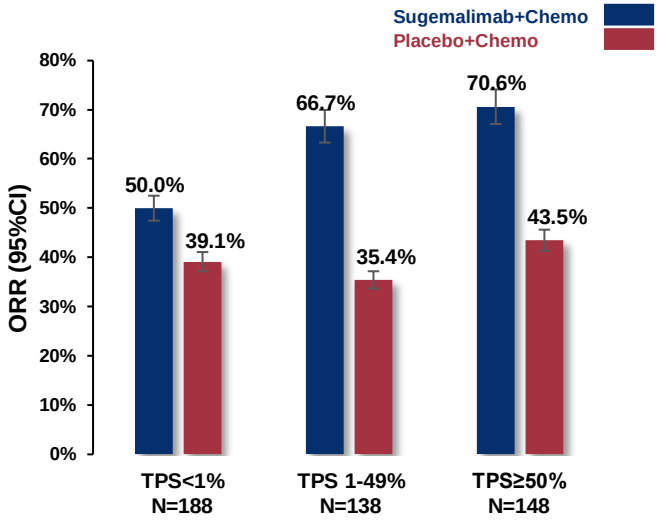
	Sugemalimab + Chemo (n=316)	Placebo + Chemo (n=158)
ORR, % (95% CI)	**61.4% (55.8%, 66.8%)**	**39.2% (31.6%, 47.3%)**
Best overall response, n (%)		
CR	0	0
PR	194 (61.4%)	62 (39.2%)
SD	85 (26.9%)	73 (46.2%)
PD	22 (7.0%)	15 (9.5%)
NE	2 (0.6%)	1 (0.6%)
NA	13 (4.1%)	7 (4.4%)
Median DoR (95% CI), months	**9.69 (7.43, NR)**	**3.68 (3.48, 5.72)**

CI=confidence interval; CR=complete response; DoR=duration of response; NA=not applicable; NE=not evaluable; NR=not reached; PD=progressive disease; PR=partial response; SD=stable disease.
Note: 5 patients who were on treatment but didn't reach the first tumor assessment time at data cut off date were not included in the ORR analysis.

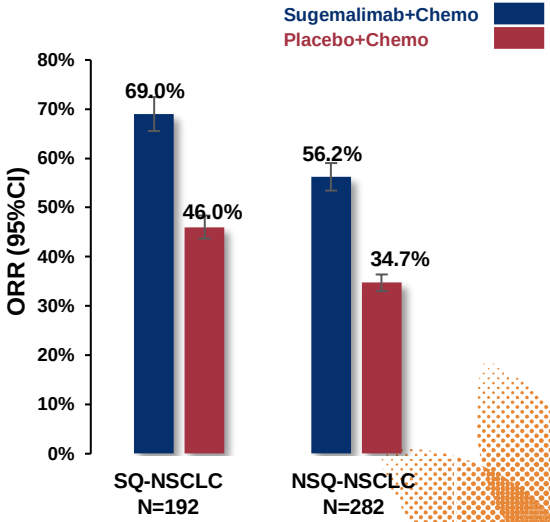
Data cutoff date: Jun 8, 2020

ORR by PD-L1 Expression and Histology

ORR by tumor PD-L1 expression



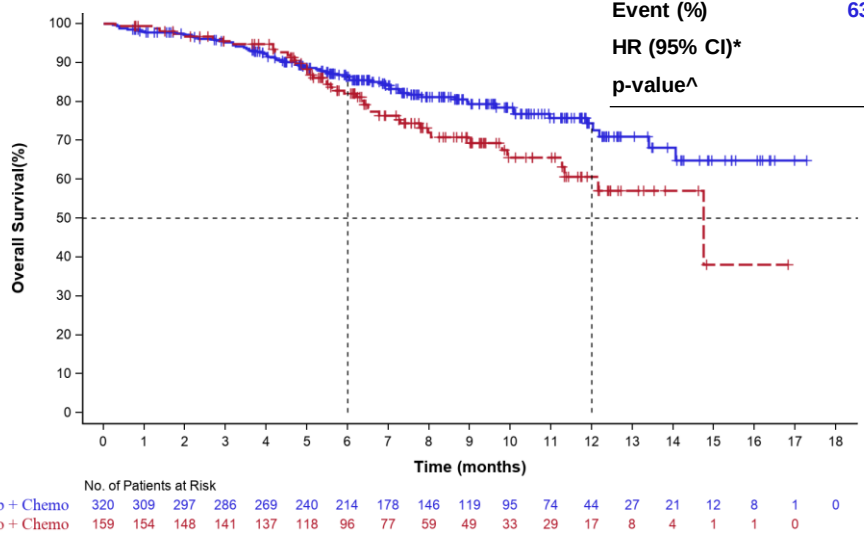
ORR by histology



Data cutoff date: Jun 8, 2020

Preliminary Overall Survival Analysis

	Sugemalimab+Chemo	Placebo+Chemo
Event (%)	63 (19.7%)	43 (27.0%)
HR (95% CI)*	0.66 (0.44, 0.97)	
p-value^	0.0338	



Median (95% CI)

NR (NR, NR)

14.75 mo (11.33, NR)

The OS data were not yet mature; no formal analysis was performed.

*stratified cox model;
^stratified log-rank test

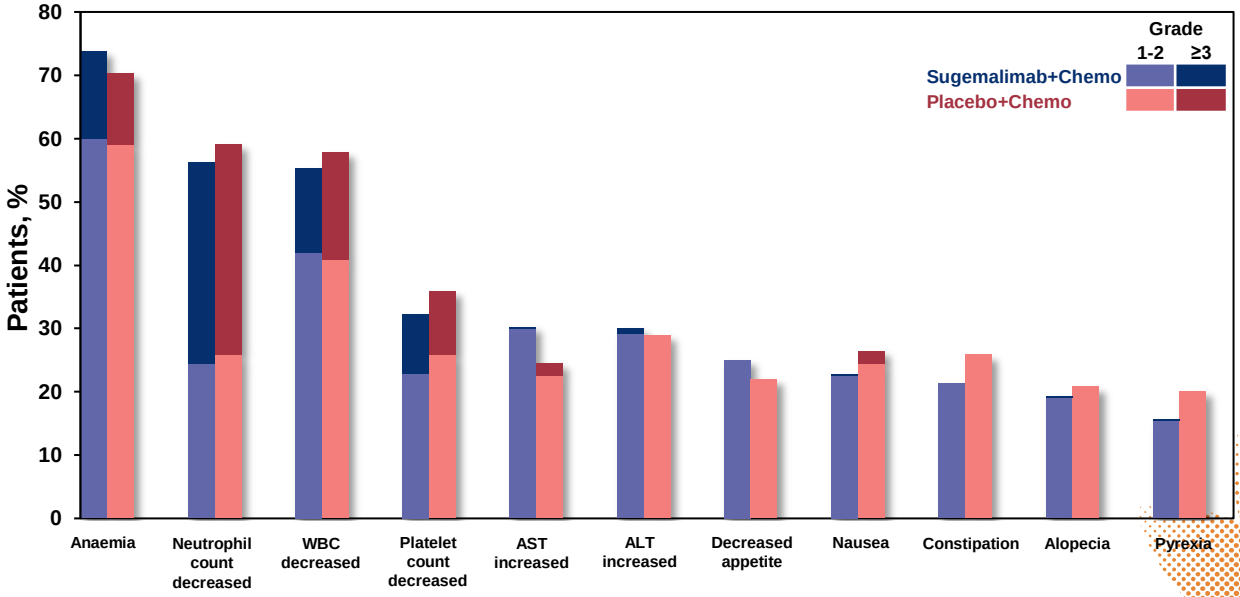
Data cutoff date: Jun 8, 2020

Summary of Adverse Events

	Sugemalimab+Chemo N=320	Placebo+Chemo N=159
Number of Patients with at Least One TEAE	318 (99.4%)	157 (98.7%)
Any Drug Related TEAE	315 (98.4%)	153 (96.2%)
Sugemalimab/Placebo Related TEAE	247 (77.2%)	101 (63.5%)
TEAE of Grade ≥3	198 (61.9%)	98 (61.6%)
Any Drug Related TEAE of Grade ≥3	176 (55.0%)	91 (57.2%)
Sugemalimab/Placebo Related TEAE of Grade ≥3	83 (25.9%)	36 (22.6%)
TEAE of Special Interest	58 (18.1%)	4 (2.5%)
TEAE of Special Interest of Grade ≥3	11 (3.4%)	0
TEAE Leading to Death	18 (5.6%)	9 (5.7%)
TEAE Leading to Sugemalimab/Placebo Permanently Discontinuation	33 (10.3%)	12 (7.5%)

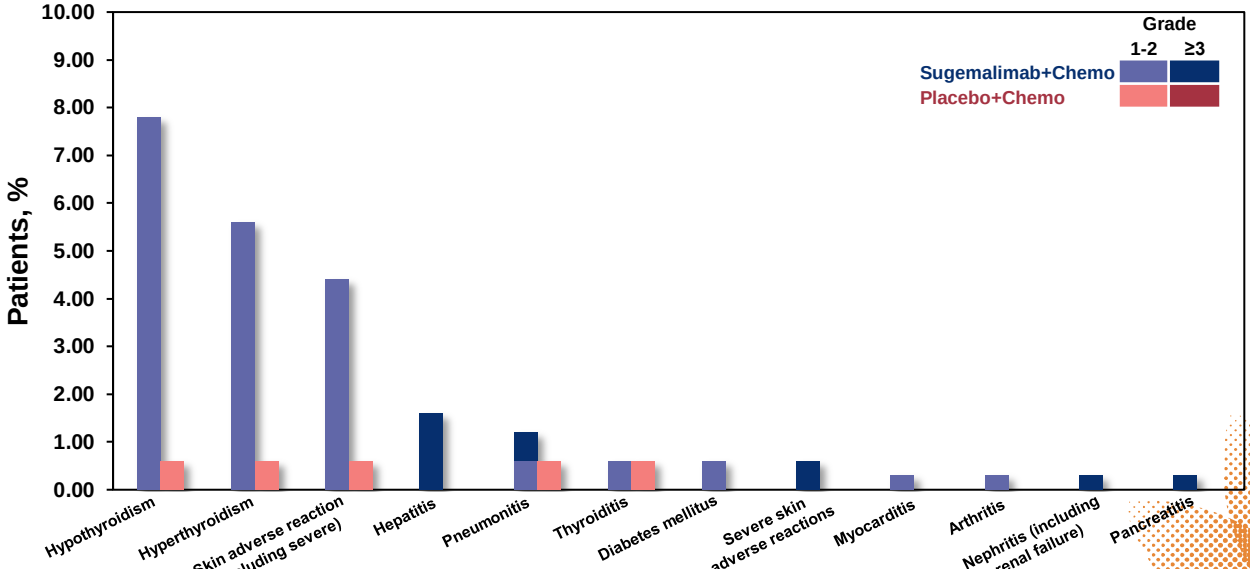
Data cutoff date: Jun 8, 2020

Adverse Events (All Cause) in ≥ 20% Patients



Data cutoff date: Jun 8, 2020

Adverse Events of Special Interest



Data cutoff date: Jun 8, 2020

Conclusions

- GEMSTONE-302 study is the first phase 3, randomized, double-blind trial of an anti-PD-L1 mAb combined with chemotherapy in patients with squamous or non-squamous NSCLC
- Sugemalimab plus chemotherapy demonstrated statistically significant and clinically meaningful benefit in PFS compared to placebo plus chemotherapy
  - Investigator-assessed PFS: 7.8 vs 4.9 months, HR=0.50
  - BICR-assessed PFS: 8.9 vs 4.9 months, HR=0.54
- ORR was higher (61.4% vs 39.2%) with durable response
- OS data was immature, but showed the clinical improvement in sugemalimab plus chemotherapy (HR=0.66)
- The combination had a manageable safety profile and no new safety signals were identified
- Sugemalimab plus chemotherapy provides a new treatment option for metastatic NSCLC patients

Acknowledgements

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