2025 ASCO® ANNUAL MEETING

Phase I study of iza-bren (BL-B01D1), an EGFR x HER3 Bispecific Antibody-drug Conjugate (ADC), in Patients with Locally Advanced or Metastatic Small Cell Lung Cancer (SCLC)

Yan Huang M.D.[1]

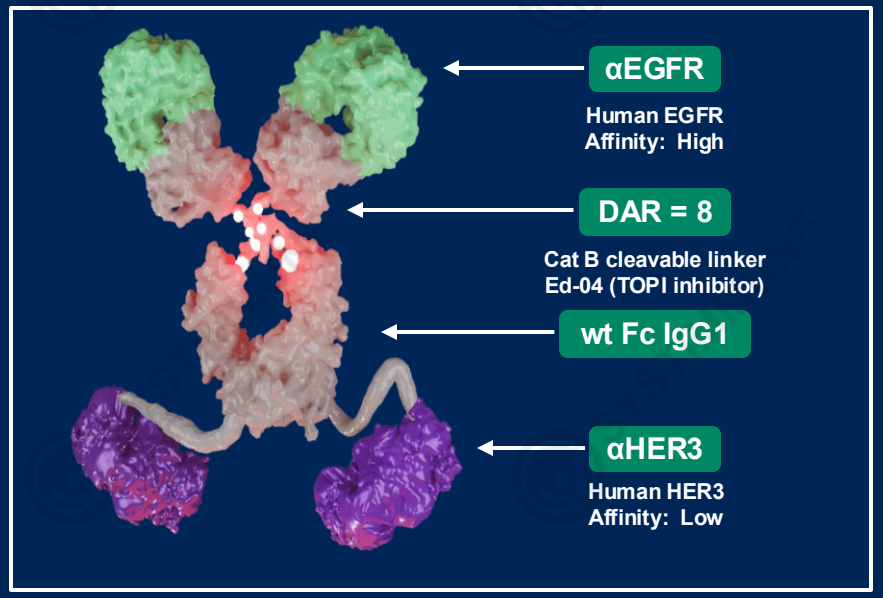
Li Zhang[2], Yuxiang Ma[3], Yuanyuan Zhao[4], Wenfeng Fang[5], Hongyun Zhao[6], Yunpeng Yang[7], Likun Chen[8], Xue Hou[9], Qiming Wang[10], Sa Xiao[11], Hai Zhu[12], Yi Zhu[13]

[1-2, 4-5, 7-8]Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China; [3, 9]Sun Yat-sen University Cancer Center, Guangzhou, China; [6]Department of Clinical Research, Sun Yat-sen University Cancer Center, Guangzhou, China; [10]The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhenzhou, China; [11]Baili-Bio (Chengdu) Pharmaceutical Co., Ltd., Chengdu, China; [12, 13]SystImmune, Inc., Redmond, WA

Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.

Background

iza-bren , an EGFR x HER3 bispecific ADC



wt: wild type; **Cat B:** cathepsin B; **TOPI:** Topoisomerase I

- iza-bren (izalontamab brengitecan) is a potential first-in-class ADC comprised of an EGFR x HER3 bispecific antibody conjugated to a novel topo-I inhibitor payload (Ed-04) via a stable tetrapeptide-based cleavable linker.
- iza-bren uniquely targets EGFR and HER3, which are commonly expressed in SCLC[1-5].
- It has shown promising clinical activity and a manageable safety profile in patients (pts) with advanced or metastatic solid tumors.
- Clinical trial information: NCT05194982

Results for safety, tolerability and preliminary efficacy in patients with locally advanced or metastatic SCLC from phase I study (BL-B01D1-101) are presented

1. K Schmid et al. *Br J Cancer*. 2010 Aug 3;103(5):622–628. **2.** Cerami et al. *Cancer Discovery*. May 2012 2; 401. **3.** Gao et al. *Sci. Signal*. 6, pl1 (2013). **4.** de Bruijn et al. *Cancer Res* (2023).
5. https://www.cbioportal.org/study/summary?id=sclc_clcgp%2Csclc_jhu%2Csclc_ucologne_2015%2Csclc_cancercell_gardner_2017

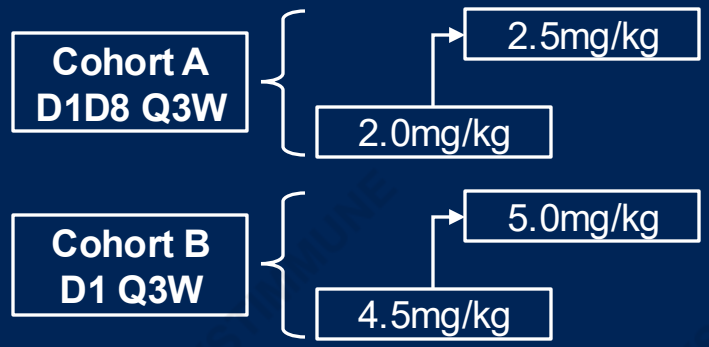
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.

SCLC group overview

Key inclusion criteria

- Locally advanced or metastatic SCLC or other solid tumors
- ECOG PS 0-1
- Measurable disease per RECIST v1.1
- Failed to standard therapy or without feasible treatment

Dose escalation



Dose expansion

Subjects received iza-bren at 2.5mg/kg D1D8 Q3W.

Primary endpoint: DLT, MTD (or MAD), RP2D
Secondary endpoint: PK, ADA, ORR, DCR, DOR
Exploratory endpoint: PFS, OS, Biomarker, Nab

Standard therapy including platinum-based chemotherapy (PBC) or anti-PD(L)-1 + PBC.
ADA: anti-drug antibody; ECOG PS: Eastern Cooperative Oncology Group performance status; **RECIST:** Response Evaluation Criteria in Solid Tumors; **DLT:** Dose Limiting Toxicity; **MTD:** Maximum Tolerated Dose; **MAD:** Maximum Administered Dose; **RP2D:** Recommended Phase 2 Dose; **ORR:** Overall Response Rate; **DCR:** Disease Control Rate; **DOR:** Duration of Response; **PFS:** Progression Free Survival; **OS:** Overall Survival; **Nab:** Neutralizing antibody; PK: pharmacokinetics; SCLC: small-cell lung cancer

Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.

Patient disposition

	Total (N = 58)	2.0mg/kg D1D8Q3W (N = 1)	2.5mg/kg D1D8Q3W (N = 52)	4.5mg/kg D1Q3W (N = 4)	5.0mg/kg D1Q3W (N = 1)
Enrolled, n	58	1	52	4	1
Treatment discontinued, n (%)	51 (87.9)	1 (100)	45 (86.5)	4 (100)	1 (100)
Reasons of discontinuation, n (%)					
PD	40 (69.0)	1 (100)	35 (67.3)	4 (100)	0
AE	7 (12.1)	0	7 (13.5)	0	0
Death	1 (1.7)	0	0	0	1 (100)
Withdraw voluntarily	2 (3.4)	0	2 (3.8)	0	0
Other	1 (1.7)	0	1 (1.9)	0	0

Data cutoff: Dec 05, 2024

Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.

Baseline characteristics

	Total (N = 58)	2.0mg/kg D1D8Q3W (N = 1)	2.5mg/kg D1D8Q3W (N = 52)	4.5mg/kg D1Q3W (N = 4)	5.0mg/kg D1Q3W (N = 1)
Median (Q1, Q3) age, years	60.5 (56.0, 65.0)	63.0 (63.0, 63.0)	60.5 (56.0, 65.0)	54.0 (47.0, 60.5)	66.0 (66.0, 66.0)
Male, n (%)	46 (79.3)	1 (100)	42 (80.8)	2 (50.0)	1 (100)
Smoking history, n (%)					
Never	15 (25.9)	0	12 (23.1)	2 (50.0)	1 (100)
Ever (current)	43 (74.1)	1 (100)	40 (76.9)	2 (50.0)	0
Median (range) baseline SOD, mm	66.8 (11.0, 195.0)	90.0 (90.0, 90.0)	60.6 (11.0, 195.0)	89.5 (34.8, 146.0)	112.0 (112.0, 112.0)
Median (range) number of metastasis organs	2 (0, 7)	3 (3, 3)	2 (0, 7)	3 (1, 6)	3 (3, 3)
Baseline brain metastasis, n (%)	17 (29.3)	0	14 (26.9)	2 (50.0)	1 (100)
ECOG-PS score, n (%)					
0	2 (3.4)	0	1 (1.9)	1 (25.0)	0
1	56 (96.6)	1 (100)	51 (98.1)	3 (75.0)	1 (100)
Prior lines of therapy, n (%)					
1L	25 (43.1)	0	22 (42.3)	2 (50.0)	1 (100)
2L	14 (24.1)	1 (100)	11 (21.2)	2 (50.0)	0
3L and above	19 (32.8)	0	19 (36.5)	0	0
Prior lines of chemotherapy, n (%)					
1L	26 (44.8)	0	23 (44.2)	2 (50.0)	1 (100)
2L	22 (37.9)	1 (100)	19 (36.5)	2 (50.0)	0
3L and above	10 (17.2)	0	10 (19.2)	0	0
Prior platinum-based chemotherapy, n (%)	58 (100)	1 (100)	52 (100)	4 (100)	1 (100)
Prior anti-PD(L)-1, n (%)	49 (84.5)	1 (100)	44 (84.6)	3 (75.0)	1 (100)
Prior irinotecan, n (%)	21 (36.2)	0	19 (36.5)	2 (50.0)	0

Data cutoff: Dec 05, 2024

Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.

Preliminary efficacy

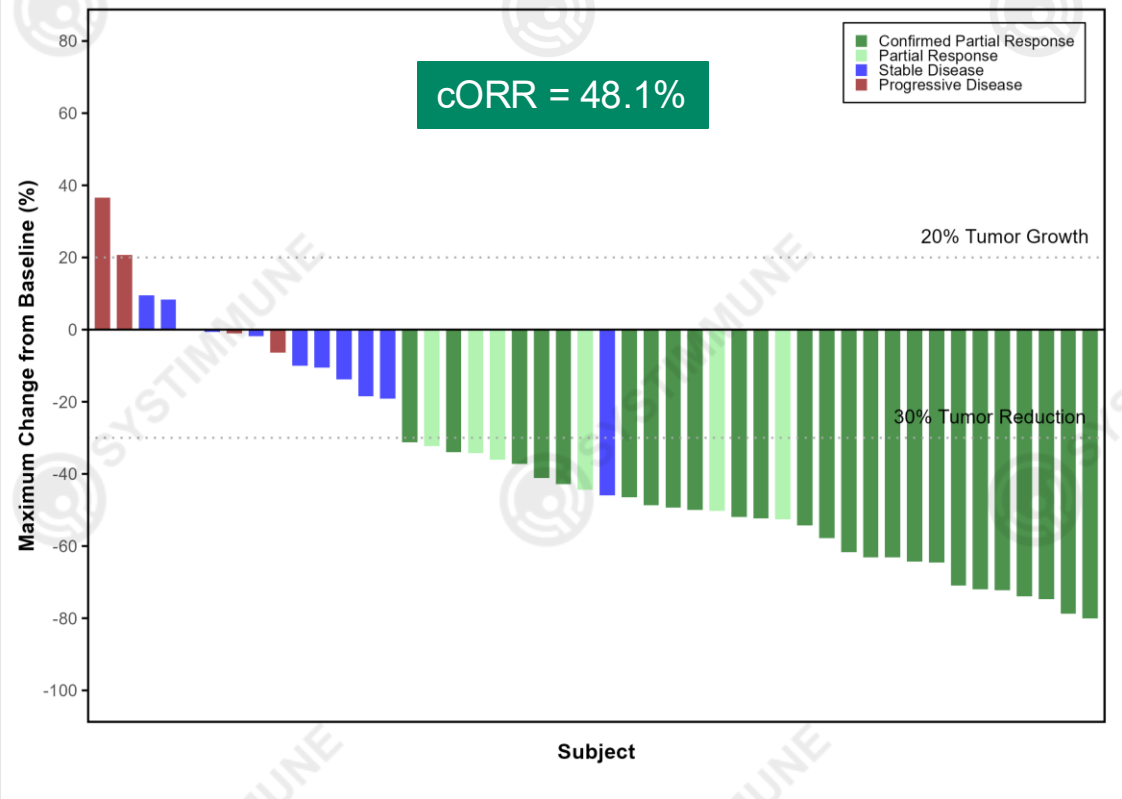
	Total (N = 58)	2.5mg/kg D1D8 Q3W		
		Total (N = 52)	1 prior line† (N = 22)	2L+ prior line (N = 30)
Median (range) LoT	2 (1-7)	2 (1-7)	1 (1-1)	3 (2-7)
BOR, n				
PR	32	31	17	14
Confirmed PR	26	25	16	9
SD	15	11	3	8
PD	5	4	1	3
NE*	6	6	1	5
ORR, % (95% CI)	55.2 (41.5, 68.3)	59.6 (45.1, 73.0)	77.3 (54.6, 92.2)	46.7 (28.3, 65.7)
cORR, % (95% CI)	44.8 (31.7, 58.5)	48.1 (34.0, 62.4)	72.7 (49.8, 89.3)	30.0 (14.7, 49.4)
DCR, % (95% CI)	81.0 (68.6, 90.1)	80.8 (67.5, 90.4)	90.9 (70.8, 98.9)	73.3 (54.1, 87.7)
Median DOR, mo (95%CI)	4.6 (4.2, 6.0)	4.9 (4.2, 6.7)	4.9 (3.1, 6.7)	4.4 (3.0, 7.0)
Median PFS , mo (95% CI)	4.0 (3.0, 5.5)	4.1 (3.0, 5.5)	6.2 (3.7, 8.2)	3.0 (2.6, 4.4)
Median OS, mo (95% CI)	12.0 (9.1, 13.2)	12.2 (9.1, 13.2)	15.0 (8.7, NR)	10.3 (7.9, 12.4)

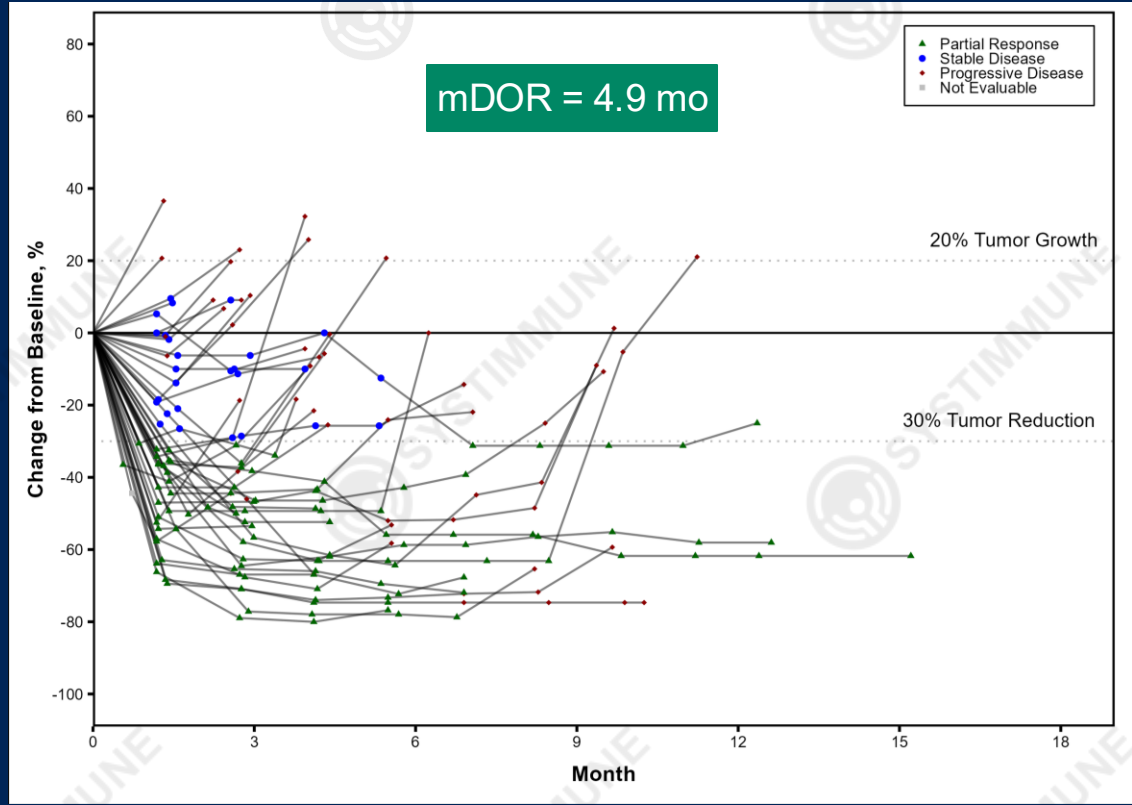
Patients received at least one study drug were included in the analysis. The median follow-up time is 16.4 months.
†: all patients received platinum-based chemotherapy: 2 patients did not receive prior anti-PD(L)-1 treatment; 20 patients with prior anti-PD(L)-1 treatment.
*: Including patients without post-baseline tumor assessment.
CI: confidence interval; **cORR:** confirmed objective response rate; **PR:** partial response; **SD:** stable disease; **PD:** progressive disease; **NE:** not evaluable

Data cutoff: Dec 05, 2024

Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.

Depth & duration of response at 2.5mg/kg D1D8 Q3W



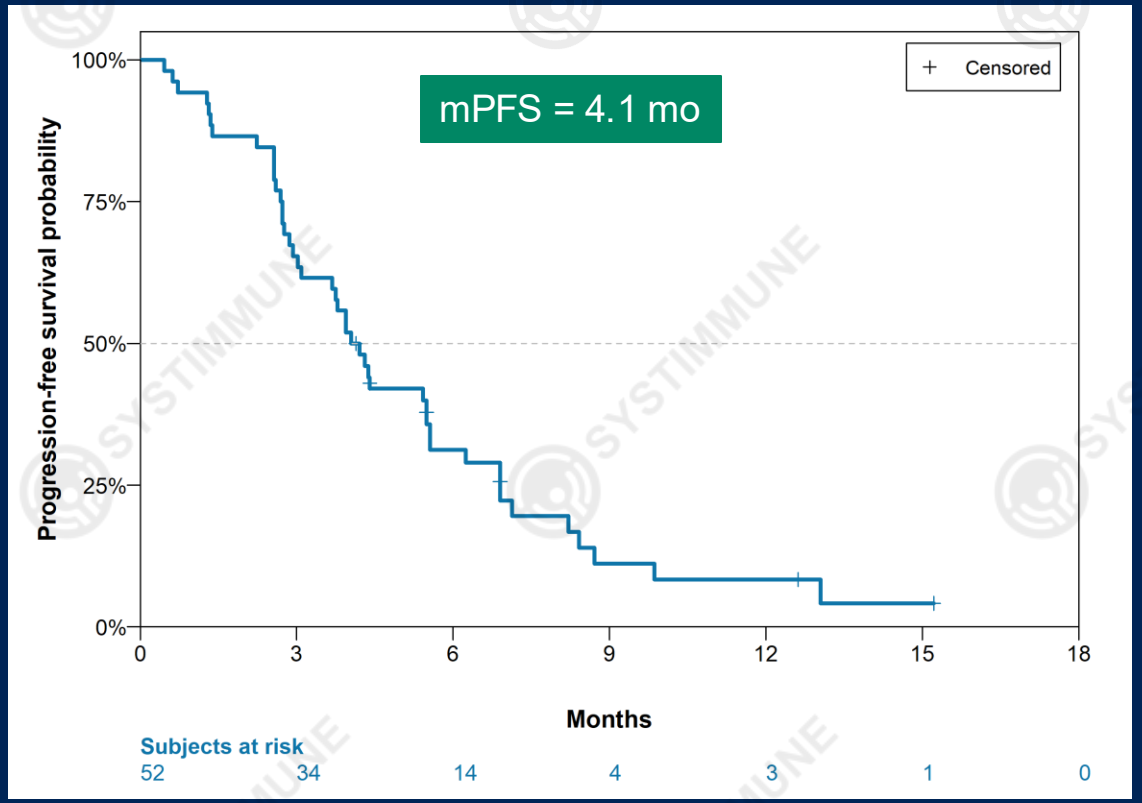


Data cutoff: Dec 05, 2024

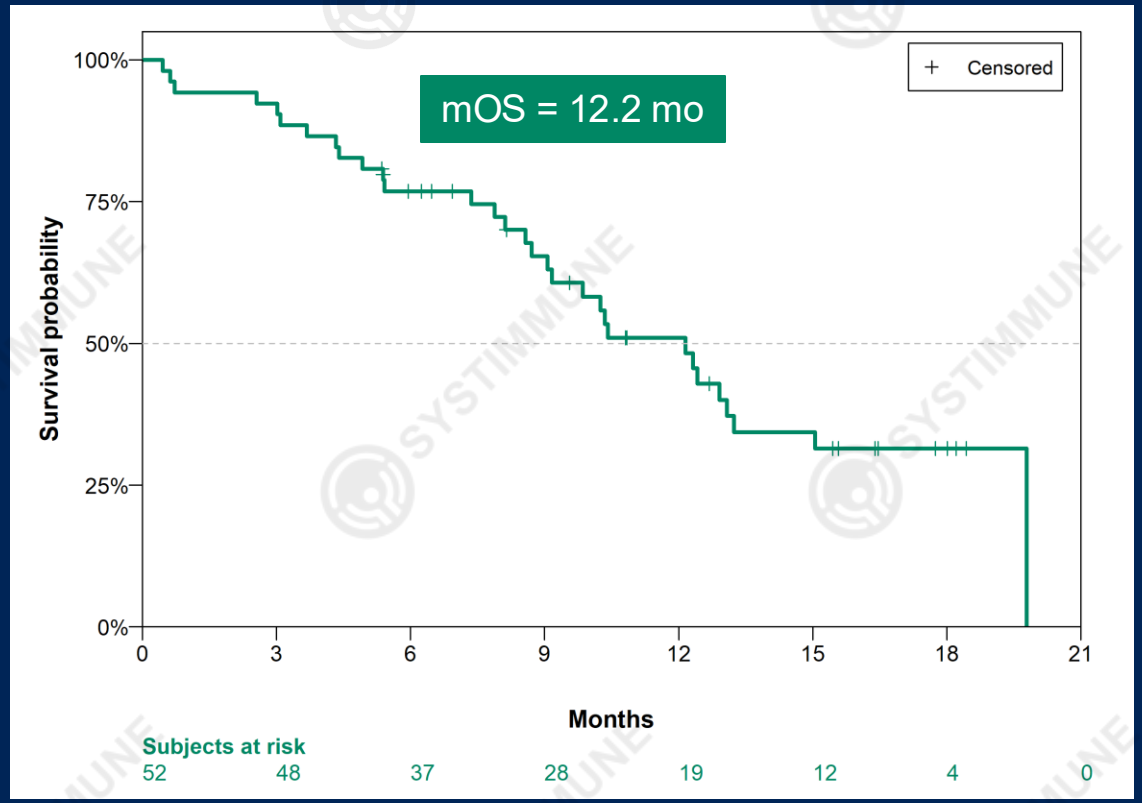
PRESENTED BY: Yan Huang, Department of Medical Oncology, Sun Yat-sen University Cancer Center
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

PFS and OS at 2.5mg/kg D1D8 Q3W

PFS KM curve



OS KM curve



Data cutoff: Dec 05, 2024

PRESENTED BY: Yan Huang, Department of Medical Oncology, Sun Yat-sen University Cancer Center
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

Preliminary efficacy - 1 prior line of PBC + anti-PD(L)-1

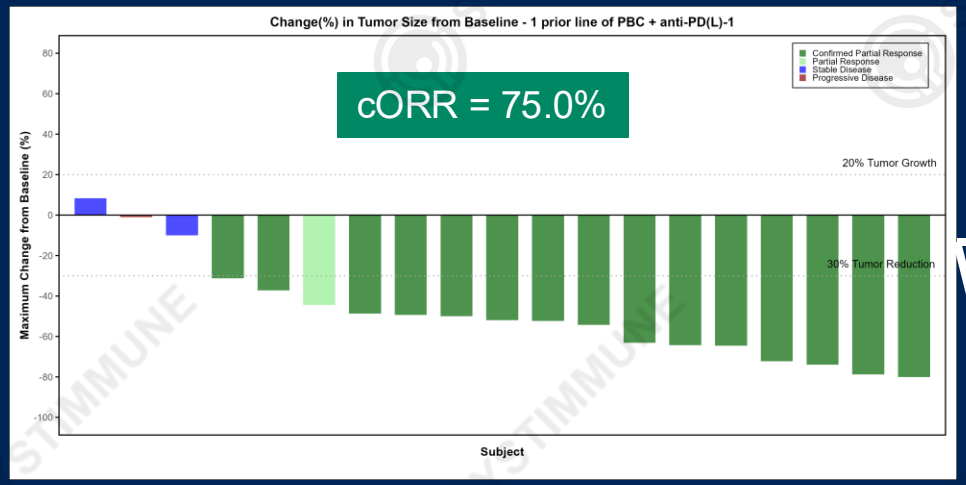
	2.5mg/kg D1D8Q3W & 1 prior line of PBC + anti-PD(L)-1		
	Total (N = 20)	≤6 Months† (N = 8)	> 6 Months† (N = 12)
Median (range) LoT	1 (1-1)	1 (1-1)	1 (1-1)
BOR, n			
PR	16	7	9
Confirmed PR	15	6	9
SD	2	1	1
PD	1	0	1
NE*	1	0	1
ORR, % (95% CI)	80.0 (56.3, 94.3)	87.5 (47.3, 99.7)	75.0 (42.8, 94.5)
cORR, % (95% CI)	75.0 (50.9, 91.3)	75.0 (34.9, 96.8)	75.0 (42.8, 94.5)
DCR, % (95% CI)	90.0 (68.3, 98.8)	100 (63.1, 100.0)	83.3 (51.6, 97.9)
Median DOR, mo (95%CI)	5.6 (3.1, 8.6)	4.9 (2.6, NR)	6.0 (2.5, NR)
Median PFS , mo (95% CI)	6.9 (3.7, 8.7)	5.4 (2.6, NR)	7.1 (3.1, 9.9)
Median OS, mo (95% CI)	15.0 (8.7, NR)	NR (5.4, NR)	15.0 (3.7, NR)

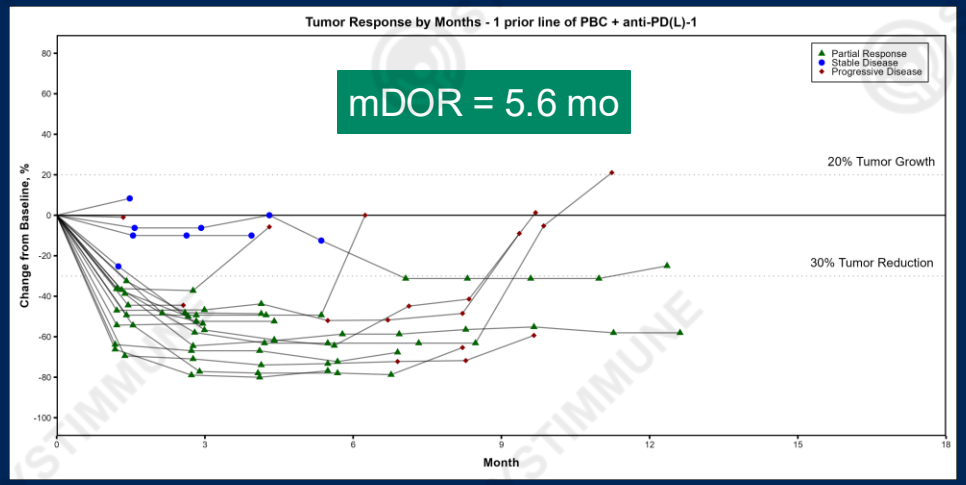
Patients received at least one study drug were included in the analysis.
†: refers to the duration from last platinum-based chemotherapy to disease progression.
*: Including patients without post-baseline tumor assessment.
CI: confidence interval; **cORR:** confirmed objective response rate; **PR:** partial response; **SD:** stable disease; **PD:** progressive disease; **NE:** not evaluable

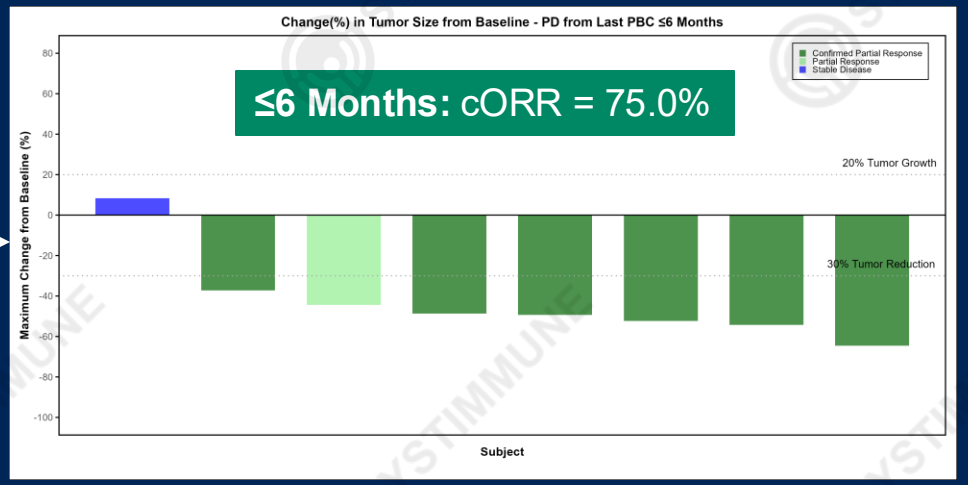
Data cutoff: Dec 05, 2024

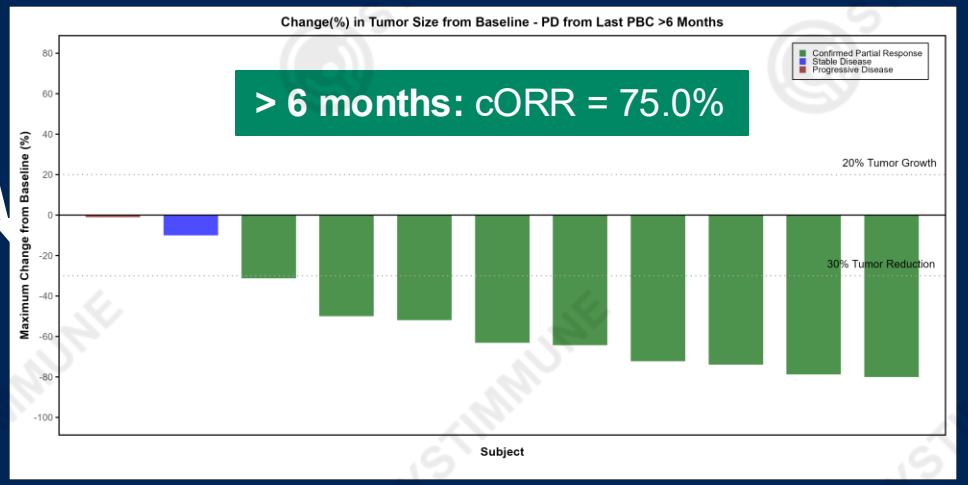
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.

Depth & duration of response - 1 prior line of PBC + anti-PD(L)-1







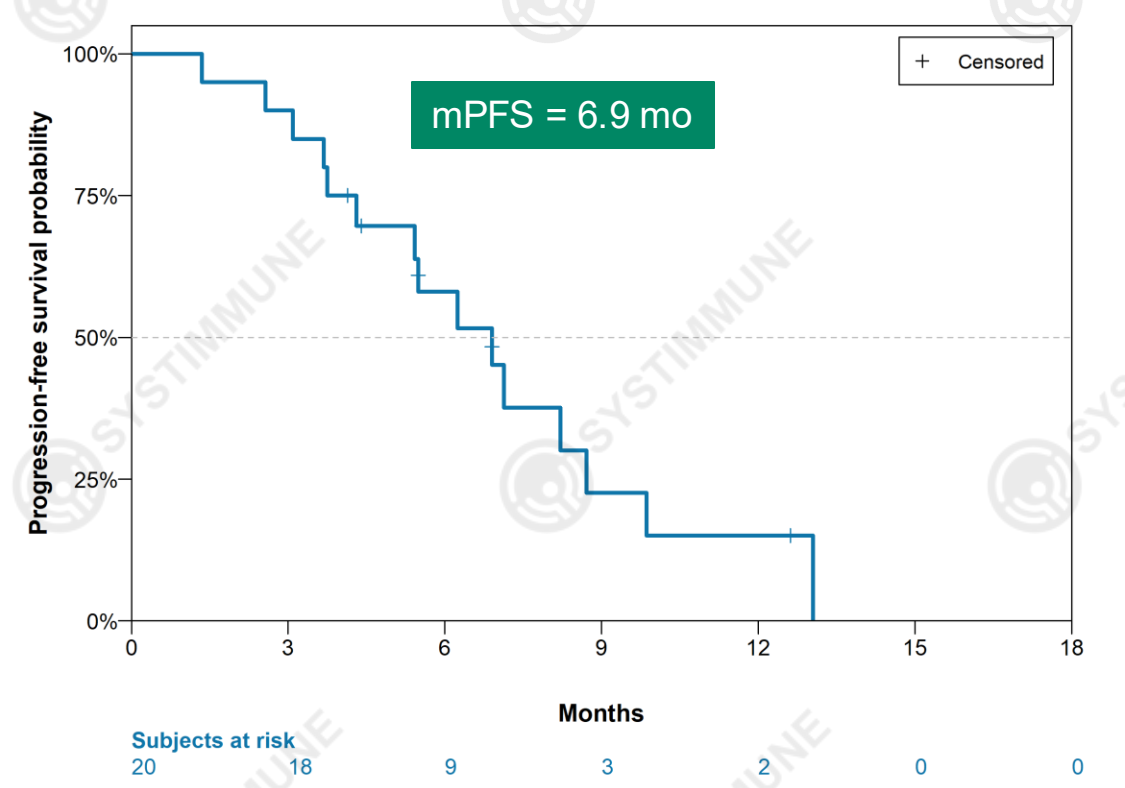


Data cutoff: Dec 05, 2024

PRESENTED BY: Yan Huang, Department of Medical Oncology, Sun Yat-sen University Cancer Center
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

PFS and OS - 1 prior line of PBC + anti-PD(L)-1

PFS KM curve



OS KM curve

Data cutoff: Dec 05, 2024

PRESENTED BY: Yan Huang, Department of Medical Oncology, Sun Yat-sen University Cancer Center
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

Preliminary efficacy by prior irinotecan treatment

	2.5mg/kg D1D8Q3W	
	Prior irinotecan† (N = 19)	Without prior irinotecan (N = 33)
Median (range) LoT	3 (2-7)	1 (1-6)
BOR, n		
PR	8	23
Confirmed PR	6	19
SD	5	6
PD	3	1
NE*	3	3
ORR, % (95% CI)	42.1 (20.3, 66.5)	69.7 (51.3, 84.4)
cORR, % (95% CI)	31.6 (12.6, 56.6)	57.6 (39.2, 74.5)
DCR, % (95% CI)	68.4 (43.4, 87.4)	87.9 (71.8, 96.6)
Median DOR, mo (95%CI)	5.7 (3.0, NR)	4.9 (3.2, 6.0)
Median PFS , mo (95% CI)	2.9 (1.4, 4.4)	5.4 (3.7, 6.9)
Median OS, mo (95% CI)	10.3 (4.9, 12.4)	12.9 (9.1, NR)

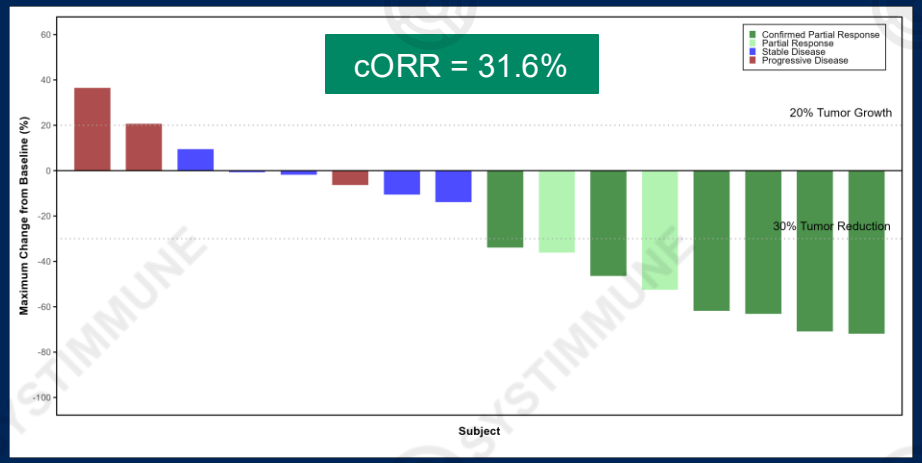
Patients received at least one study drug were included in the analysis.
†: refers to patients who have received prior irinotecan.
*: Including patients without post-baseline tumor assessment.
CI: confidence interval; **cORR:** confirmed objective response rate; **PR:** partial response; **SD:** stable disease; **PD:** progressive disease; **NE:** not evaluable

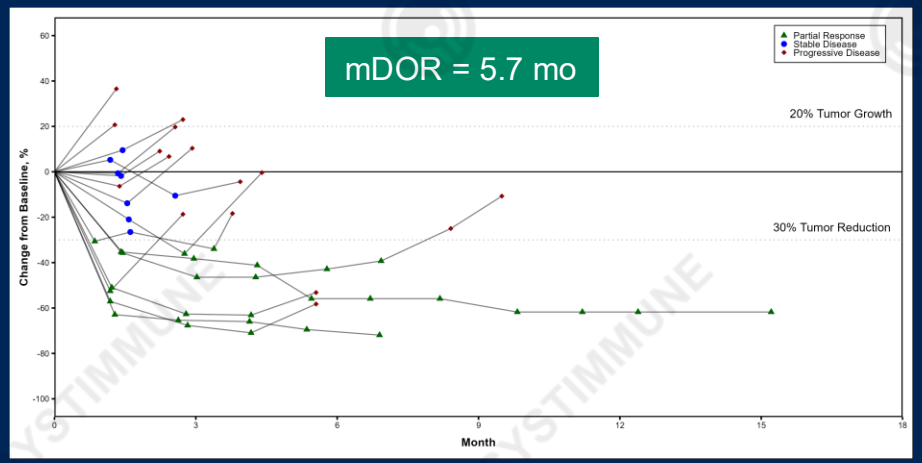
Data cutoff: Dec 05, 2024

PRESENTED BY: Yan Huang, Department of Medical Oncology, Sun Yat-sen University Cancer Center
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.

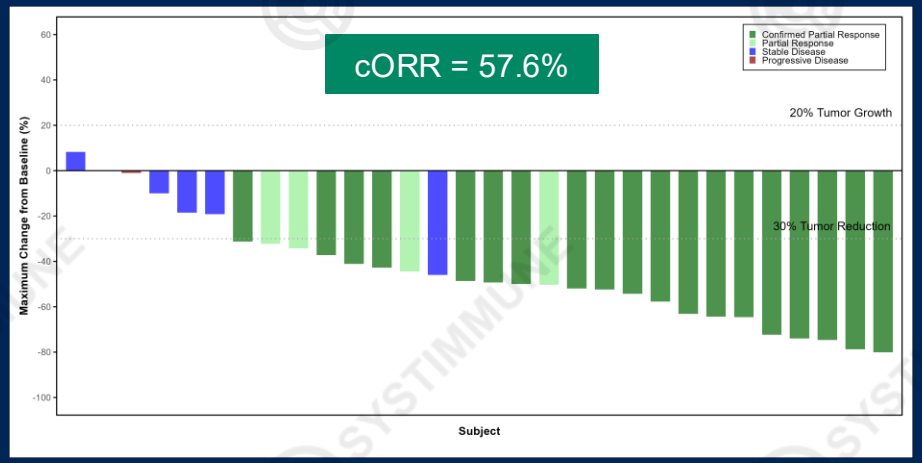
Depth & duration of response by prior irinotecan treatment

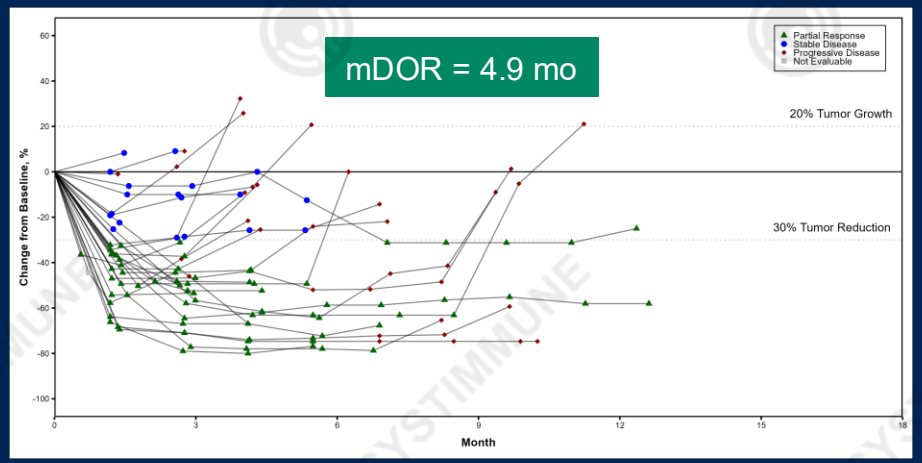
With prior irinotecan





Without prior irinotecan

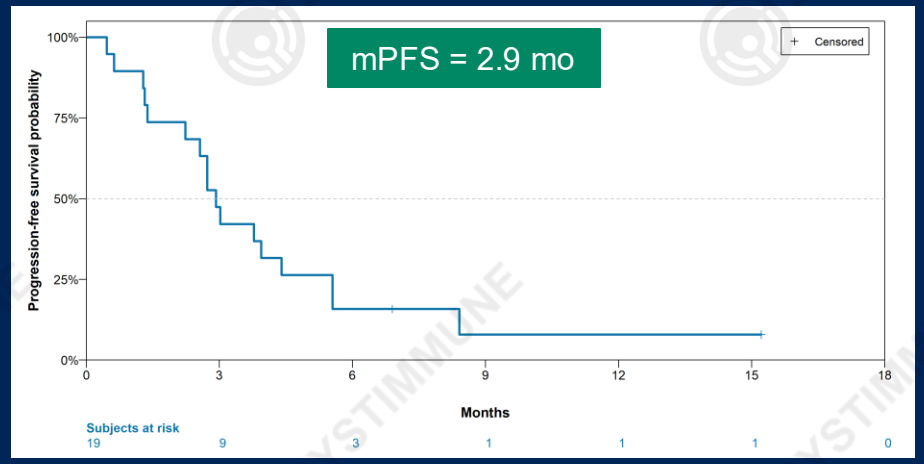
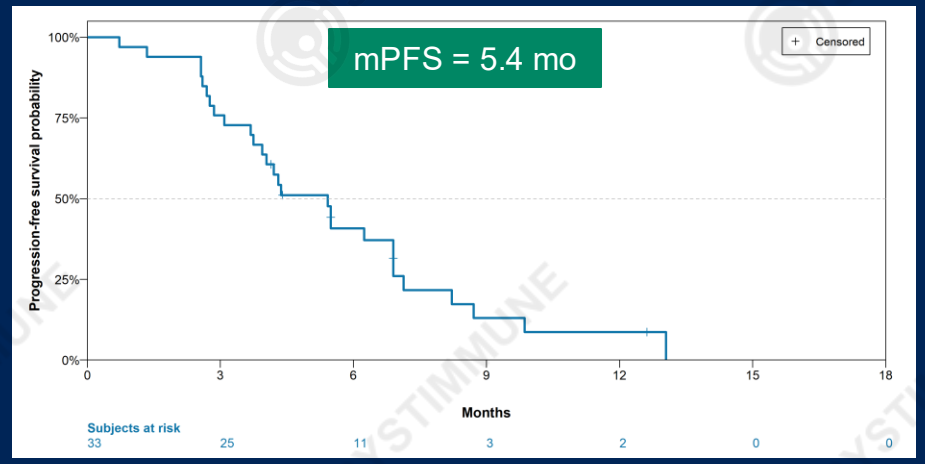
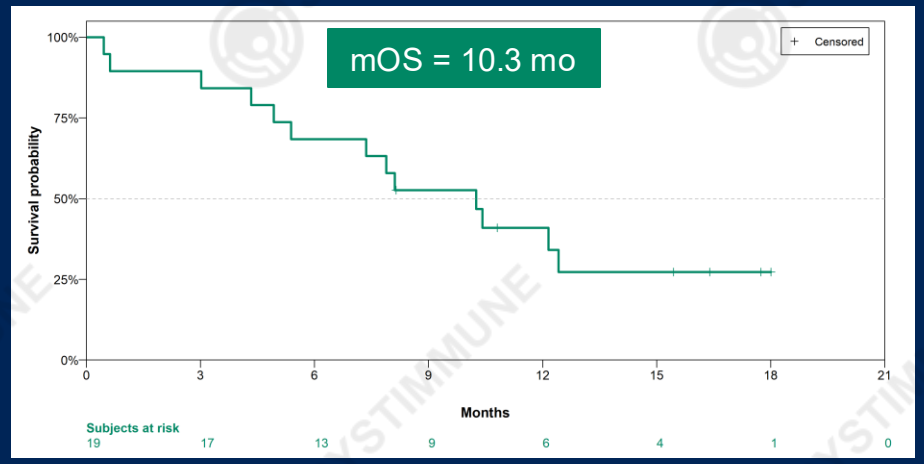
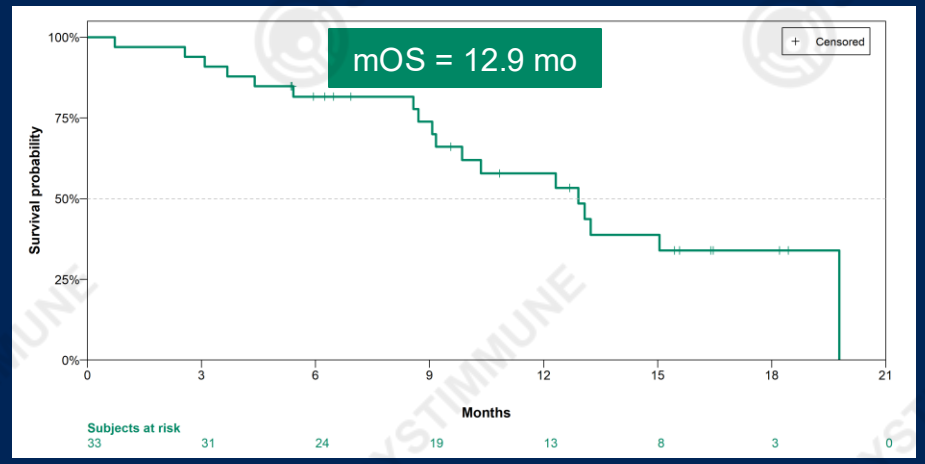




Data cutoff: Dec 05, 2024

PRESENTED BY: Yan Huang, Department of Medical Oncology, Sun Yat-sen University Cancer Center
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

PFS and OS by prior irinotecan treatment

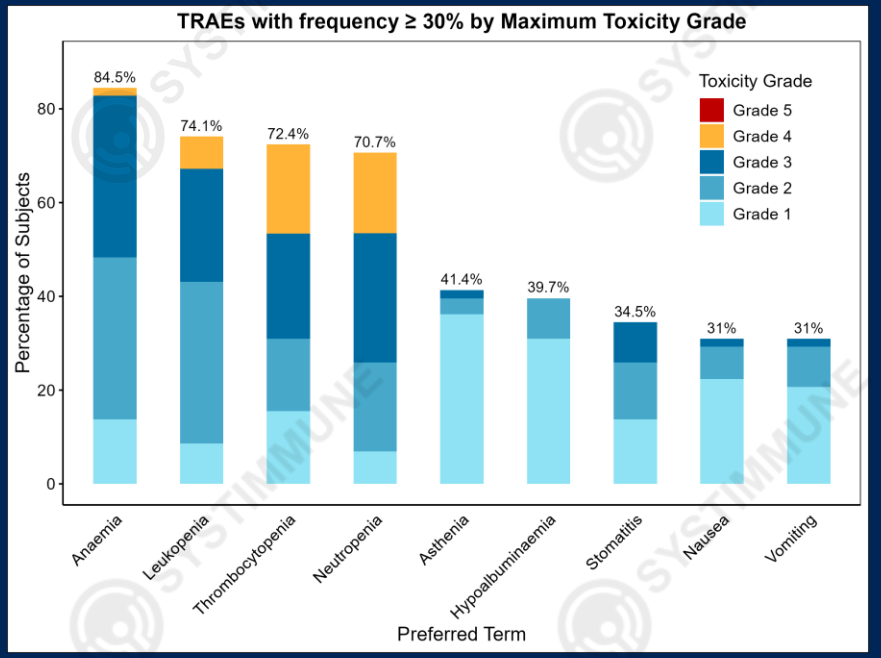
	With prior irinotecan	Without prior irinotecan
PFS		
OS		

Data cutoff: Dec 05, 2024

PRESENTED BY: Yan Huang, Department of Medical Oncology, Sun Yat-sen University Cancer Center
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

Safety of iza-bren in SCLC

Overall Safety Summary	Total (N=58)	2.5mg/kg D1D8Q3W (N = 52)
TRAEs, n (%)	58 (100)	52 (100)
Treatment-related SAEs, n (%)	27 (46.6)	26 (50.0)
≥Grade 3 TRAEs, n (%)	43 (74.1)	39 (75.0)
TRAEs leading to death, n (%)	2 (3.4)	2 (3.8)
TRAEs leading to discontinuation of study drug, n (%)	7 (12.1)	7 (13.5)
TRAEs leading to dose reduction, n (%)	24 (41.4)	24 (46.2)
TRAEs leading to drug delay, n (%)	35 (60.3)	33 (63.5)



Grade 3 and above TRAEs which were predominantly hematologic in nature, were able to be effectively managed with standard supportive measure including dose reductions and growth factor support.

Two infection-related deaths (1 respiratory failure, 1 gastrointestinal infection) associated with iza-bren were reported.

No ILD was observed.

No new safety signals were identified.

SAE: serious adverse event; TRAE: treatment related adverse event;

Data cutoff: Dec 05, 2024

PRESENTED BY: Yan Huang, Department of Medical Oncology, Sun Yat-sen University Cancer Center
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.

Conclusions

- iza-bren demonstrated a promising efficacy in previously treated ES-SCLC pts, especially in pts prior treated with 1 prior line of PBC and anti-PD(L)-1 with cORR of 75.0%, mPFS of 6.9 months, and mOS of 15.0 months.
- iza-bren also showed an encouraging efficacy in SCLC pts regardless of platinum-resistance or platinum-sensitive relapse.
- Pts with prior irinotecan treatment could also benefit from iza-bren.
- iza-bren demonstrated manageable safety profile and no new safety signal was observed in SCLC pts.
- The phase III study of iza-bren in SCLC pts who received 1 prior line of PBC and anti-PD(L)-1 combination treatment is ongoing in China (NCT06500026).

Data cutoff: Dec 05, 2024

Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.

Acknowledgments

- Thanks to all the patients and their families for their participation.
- Thanks to the investigators, study nurses, and other staffs for their contributions to this study.

PRESENTED BY: Yan Huang, Department of Medical Oncology, Sun Yat-sen University Cancer Center

Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.