# A Phase Ib Trial of the Anti - PD - L1 Human Monoclonal Antibody, CS1001, in Patients with Advanced Solid Tumors or Lymphomas: Preliminary Efficacy and Safety Results from 4 Cohorts

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# BACKGROUND

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- CS1001 is the first full-length, fully human programmed death ligand-1 (PD-L1) targeted immunoglobin G4 (IgG4, s228p) monoclonal antibody (mAb) developed by the OMT transgenic rat platform. The platform mirrors natural IgG4 human antibody, which may potentially reduce the risk of immunogenicity and toxicity in patients (pts)
- In Phase Ia part of the first-in-human study of CS1001 (NCT03312842), 1200 mg fixed dose every 3 weeks (Q3W) was determined as the recommended Phase 2 dose (RP2D)<sup>1</sup>
- Phase Ib is the dose-expansion phase to further explore the efficacy and safety of CS1001 in multiple cohorts of selected tumor types. Herein, with the cut-off date of 01 Jul 2019, we present the safety data from Phase Ib and efficacy data from 4 cohorts as following:
- CS1001 monotherapy of cholangiocarcinoma or gallbladder carcinoma (CC/GBC);
- CS1001 monotherapy of high-microsatellite instability or mismatch repair deficient phenotype (MSI-H/dMMR) (≥2L);
- CS1001 and chemotherapy combination as first line (1L) treatment in gastric or gastro-esophageal junction carcinoma (GC/GEJ);
- CS1001 and chemotherapy combination as 1L treatment in esophageal squamous cell carcinoma (ESCC)

## METHODS

### **Key Eligibility**

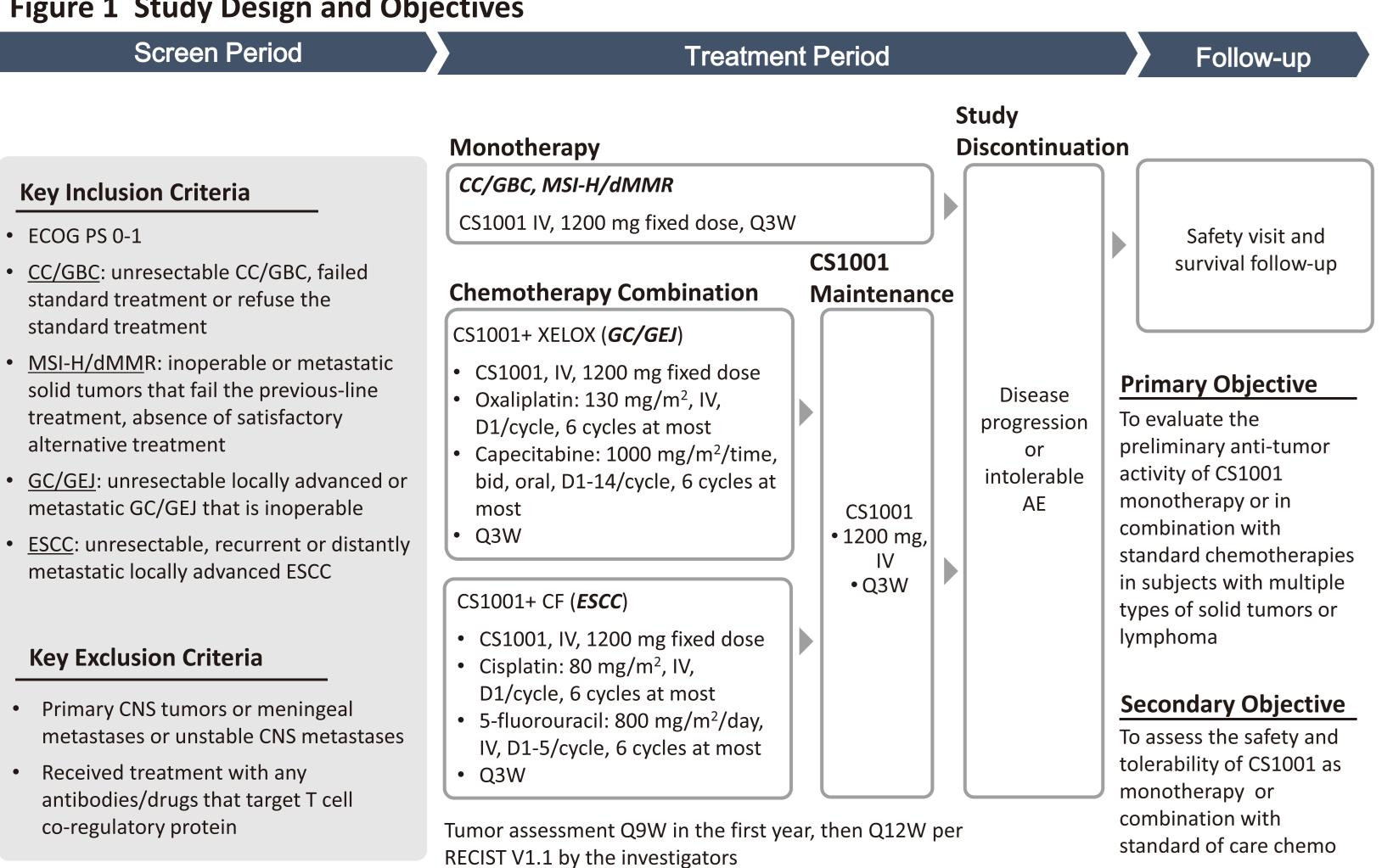
Eastern Cooperative Oncology Group (ECOG) performance status of 0-1

CC/GBC: pts with histologically/cytologically diagnosed unresectable CC/GBC who failed standard treatment or are unable to tolerate or refuse the standard treatment

MSI-H/dMMR (≥2L): pts with inoperable or metastatic MSI-H/dMMR solid tumors who failed the previous-line treatment before enrollment and do not have a satisfactory alternative treatment GC/GEJ (1L): pts with unresectable locally advanced or metastatic GC/GEJ which was histologically confirmed as adenocarcinoma, and who did not receive systemic treatment for advanced or metastatic disease

ESCC (1L): pts with histologically confirmed unresectable, recurrent or distantly metastatic locally advanced ESCC who did not receive systemic treatment

#### Figure 1 Study Design and Objectives



AE: adverse event; bid: twice daily; CNS: central nervous system; D: day; IV: intravenous; ECOG: Eastern Cooperative Oncology Group; PS: performance status; Q3W: once

### **Assessments**

- Tumor assessment was assessed per RECIST V1.1 by investigators every 9 weeks (Q9W) in the first year, then every 12 weeks (Q12W)
- Adverse events (AEs) were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Event (NCI-CTCAE) V4.03

# RESULTS

#### Patients – 4 Cohorts

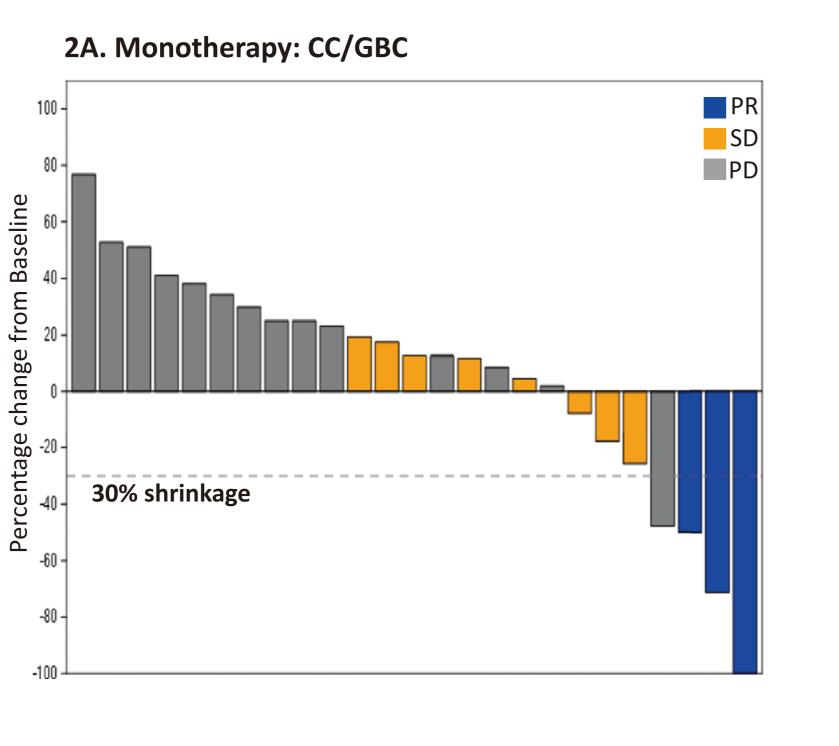
Table 1. Demographics and Baseline Characteristics (Safety Analysis Set)

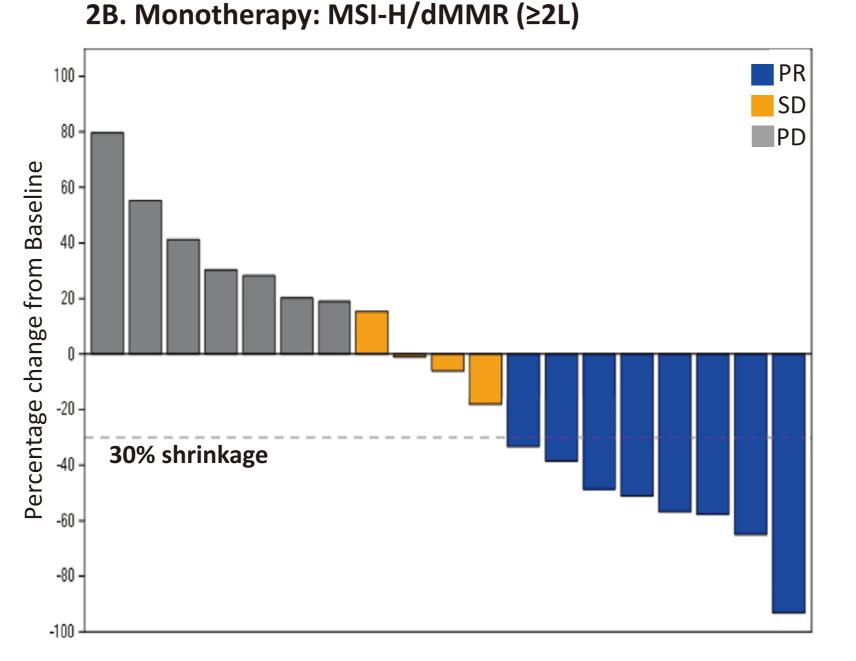
Characteristics		Monotherapy		Chemotherapy Combination	
		CC/GBC	MSI-H/dMMR (≥ 2L)	GC/GEJ (1L)	ESCC (1L)
		N=29	N=21	N=29	N=23
Age (years), Median (range)		55 (39, 72)	53 (25, 71)	60 (40, 73)	61 (45, 73)
Sex, n (%),	Male	9 (31.0)	12 (57.1)	23 (79.3)	18 (78.3)
	Female	20 (69.0)	9 (42.9)	6 (20.7)	5 (21.7)
ECOG PS, n (%)	0	14 (48.3)	0	12 (41.4)	5 (21.7)
	1	13 (44.8)	21 (100)	17 (58.6)	18 (78.3)
	Missing	2 (6.9)	0	0	0
Time since Initial Diagnosis (years)	Median (range)	0.731 (0.03, 1.84)	1.320 (0.36, 19.76)	0.077 (0.01, 6.60)	0.487 (0.01, 3.04)
<b>Prior Anti-Cancer Therapy Regimen</b>	Median (range)	1.0 (0, 6)	2.0 (1, 9)	0.0 (0, 2)*	0.0 (0, 2)**
Current Cancer Stage, n (%)	Stage III	0	0	1 (3.4)	3 (13)
FCOC Factors Commenting Organic PC	Stage IV	29 (100)	21 (100)	28 (96.6)	20 (87)

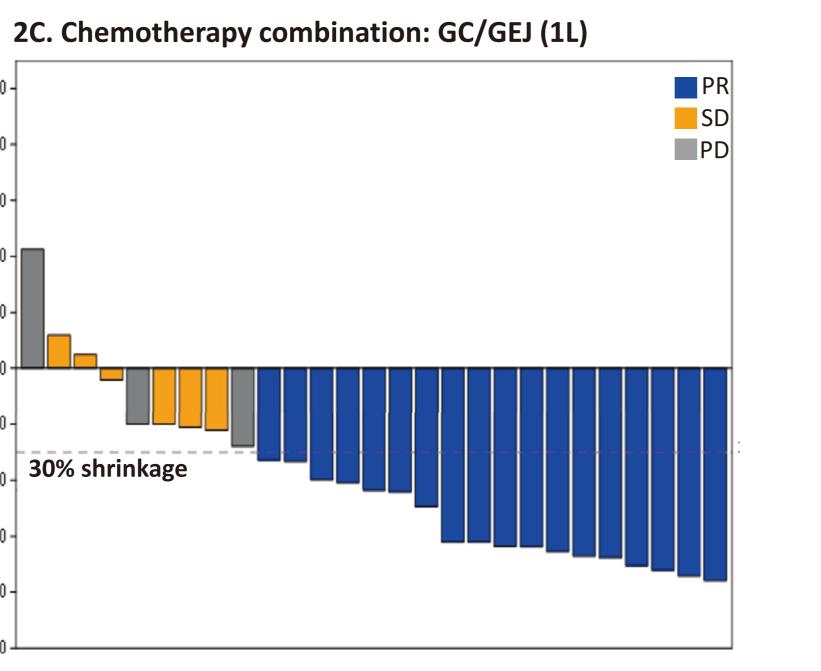
ECOG: Eastern Cooperative Oncology Group; PS: performance status \*A total of 10 patients received neoadjuvant and/or adjuvant therapy. 1 patient received both neo-adjuvant and adjuvant therapies around curative surgery. \*\*A total of 8 patients received adjuvant and/or neoadjuvant drug therapy, among which 1 patient received cisplatin + paclitaxel after radical surgery, and subsequently changed to cisplatin + capecitabine due to taxol allergy.

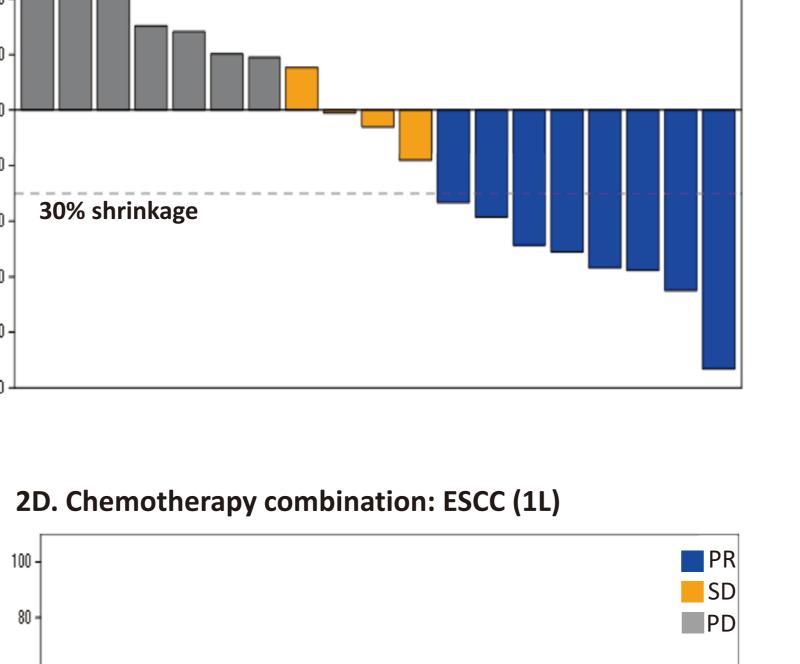
#### Efficacy – 4 Cohorts

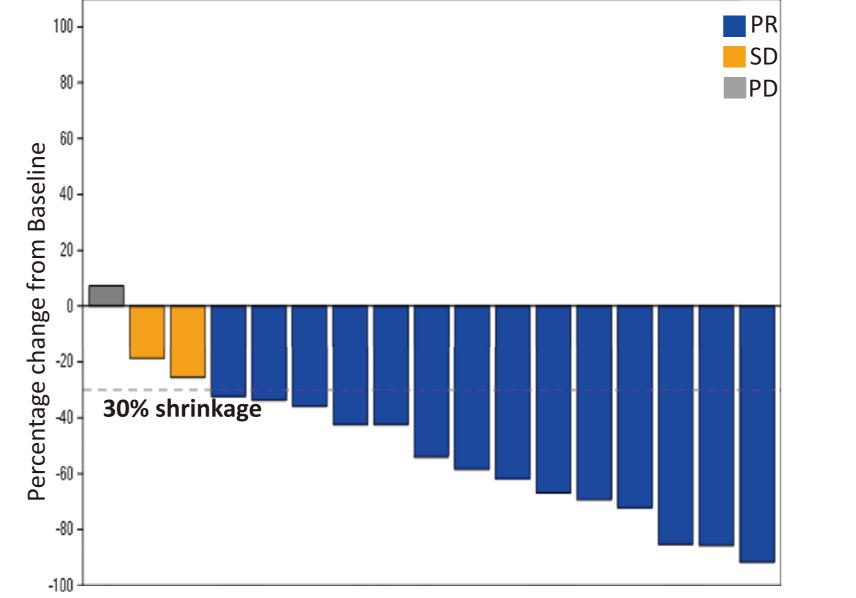
#### Figure 2 Waterfall Plot of Maximum Target Lesion Shrinkage by RECIST V1.1 (Efficacy Analysis Set)











#### **Table 2. Summary of Objective Response** (Efficacy Analysis Set)- Monotherapy

Response	CC/GBC (N=29) n (%)	MSI-H/dMMR (≥ 2L) (N=21) n (%)
artial response (PR)	3 (10.3)	8 (38.1)*
table disease (SD)	8 (27.6)	4 (19.0)
rogression (PD)	14 (48.3)	7 (33.3)
IA	4 (13.8)	2 (9.5)
)RR	3 (10.3)	8 (38.1)
onfirmed ORR	2 (6.9)**	6 (28.6)
isease control rate (DCR)	11 (37.9)	12 (57.1)
Ouration of response (DoR,	5.39 (1.91+,	NR (0.03+,
Months), Median (Range)	8 02)	8 61+)

our (4) patients and 2 patients in CC/GBC and MSI-H/dMMR cohorts, respectively (NA in this table), therefore, were not shown in two figures (Figures 2A and 2B). \*Of the 8 responders in MSI-H/dMMR cohort, 7 patients were colorectal cancer,

Figure 3 Percentage Change from Baseline in Sum of Diameters (Efficacy Analysis Set)

→ PR → SD → PD

New lesion

Figure 4 Duration of Treatment and Tumor Assessment by RECIST V1.1 (Efficacy Analysis Set)

\*\*Of the 3 responders in CC/GBC cohort, 1 achieved first PR after PD and was not counted in confirmed ORR.

♦ This patient experienced PD after initial PR, but achieved 2 consecutive PRs afterwards.

At the time of data cutoff, 3 patients were still undergoing study treatment, 2 patients had

confirmed PR. The median treatment (CS1001) duration was 84 days

3C. Chemotherapy combination: GC/GEJ (1L)

IA: not applicable: NR: not reached

3A. Monotherapy: CC/GBC

### Table 3. Summary of Objective Response (Efficacy **Analysis Set)- Chemotherapy Combination**

Response	GC/GEJ (1L) (N=29) n (%)	ESCC (1L) (N=18) n (%)
Partial response (PR)	18 (62.1)	14 (77.8)
Stable disease (SD)	6 (20.7)	2 (11.1)
Progression (PD)	3 (10.3)	1 (5.6)
NA	2 (6.9)	1 (5.6)
ORR	18 (62.1)	14 (77.8)
Confirmed ORR	15 (51.7)	12 (66.7)*
Disease control rate (DCR)	24 (82.8)	16 (88.9)
Duration of response (DoR,	6.21 (0.03+,	NR (0.03+,
Months), Median (Range)	6.21+)	8.41+)
NA: not applicable: NR: not reached		

have any tumor assessment post baseline and were regarded as non-responders (NA in this table), therefore, were not shown in two figures (Figures 2C and 2D). \*Of the 14 responders in ESCC cohort, 2 did not reach the second tumor assessment point by data cut off day and was not counted in confirmed ORR

3B. Monotherapy: MSI-H/dMMR (≥2L)

3D. Chemotherapy combination: ESCC (1L)

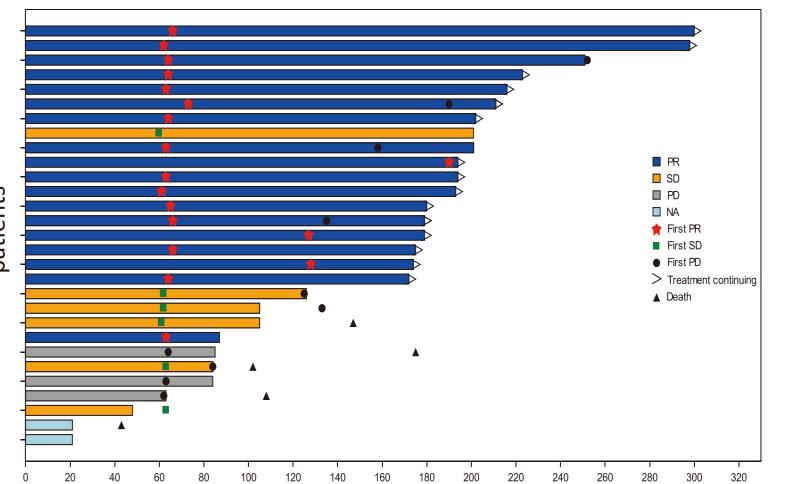
4B. Monotherapy: MSI-H/dMMR (≥2L)

At the time of data cutoff, 9 patients were still undergoing study treatment, 6

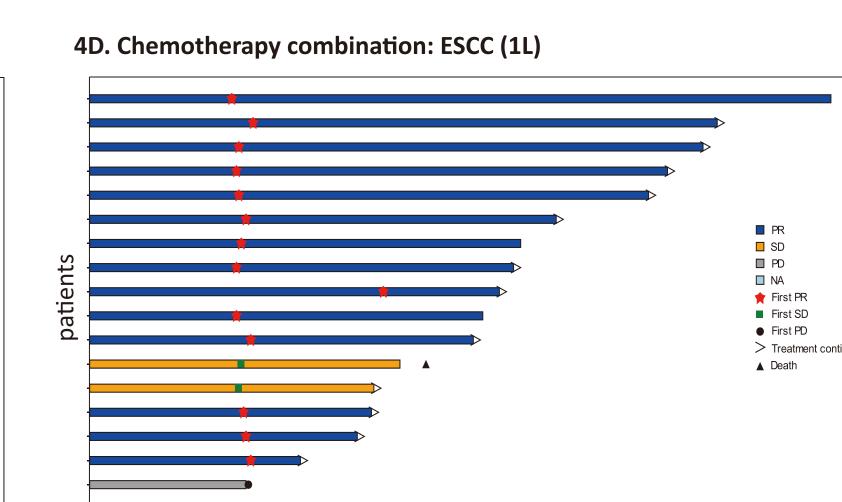
patients had confirmed PR. The median treatment (CS1001) duration was 137

→ SD

★ New Lesion



At the time of data cutoff, 15 patients were still undergoing study treatment, 1 patients had confirmed PR. The median treatment (CS1001) duration was 179



At the time of data cutoff, 17 patients were still undergoing study treatment ( patients were not included in efficacy analysis set, so as were not shown in this figure), 12 patients had confirmed PR. The median treatment (CS1001) duration

#### **Exposure and Safety - Phase Ib**

- As of 01 Jul 2019, 192 patients were enrolled in Phase Ib across multiple cohorts of various tumor types
- Median duration of CS1001 treatment was 112 (Range: 3 377) days
- The majority of patients reported treatment-emergent AEs (TEAEs) (monotherapy: 95.9% vs chemotherapy combination: 99.0%). 38.4% of the patients from monotherapy cohorts reported Grade (G) 3-5 TEAEs, and 70.1% of the patients from chemotherapy combination cohorts reported G3-5 TEAEs
- The incidence of serious AEs (SAEs) nearly doubled in the chemo combo cohorts compared to the monotherapy cohorts (40.2% vs 20.5%)

#### Table 4. Summary of Adverse Events (Safety Analysis Set)

Events	Monotherapy (N=73) n(%)	Chemotherapy Combination (N=97) n(%)
TEAE	70 (95.9)	96 (99.0)
TEAE Related to CS1001	59 (80.8)	87 (89.7)
Grade 3-5 TEAE	28 (38.4)	68 (70.1)
Grade 3-5 TEAE Related to CS1001	11 (15.1)	36 (37.1)
Serious TEAE	15 (20.5)	39 (40.2)
Serious TEAE Related to CS1001	7 (9.6)	22 (22.7)
TEAE Leading to CS1001 Discontinuation	5 (6.8)	8 (8.2)
TEAE Leading to any Combination Chemotherapeutics Withdrawn	NA	20 (20.6)
Immune-related TEAE	34 (46.6)	43 (44.3)
TEAE Leading to Death	0	3 (3.1)
Infusion-related reaction TEAE	1 (1.4)	4 (4.1)



- CS1001 monotherapy or combination with standard-of-care chemotherapies demonstrated promising anti-tumor activity and a tolerable safety profile
- Data support further exploration to ongoing development of CS1001 in combination with chemotherapy in GC and ESCC:
- Phase III trial (GEMSTONE-303, NCT03802591) investigating CS1001 in combination with XELOX in patients with GC/GEJ
- Phase III trial investigating CS1001 in combination with CF in patients with ESCC
- Data support further exploration and development of CS1001 in CC/GBC and MSI-H/dMMR

1. Shen, L., et al. Presented at: European Society for Medical Oncology (ESMO), October 19-23, 2018; Munich, Germany, 1165P

We thank the patients who participated in the study, their families, participating study investigators and clinical sites. This study is sponsored by CStone Pharmaceuticals (Su Zhou) Co., Ltd. Medical writing assistance was provided by Mengxin Chen

#### **DISCLOSURES**

All authors have declared no conflicts of interest

NA: not applicable; TEAE: treatment emergent adverse event

Poster presented at: European Society for Medical Oncology (EMSO) - Barcelona, Spain; 27 Sep - 01 Oct 2019. Contact corresponding author: ClinicalDevelopment@cstonepharma.com ClinicalTrials.gov identifier: NCT03312842

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4A. Monotherapy: CC/GBC