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CSTONE PHARMACEUTICALS (2616.HK)

2019 CSCO DATA PRESENTATION

SEPTEMBER 25, 2019

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Agenda

Welcome – *Richard Yeh, CFO*

Business Updates – *Dr. Frank Jiang, Chairman and CEO*

PD-L1 Data Readouts – *Dr. Jason Yang, CMO*

- CS1001 (PD-L1) Overview
- Key data readouts: CS1001-101 PhIb (MSI-H/dMMR Cohort, CC/GBC Cohort, GC/GEJ Cohort, ESCC Cohort)
- Conclusion

PD-1 & CTLA-4 Data Readouts – *Dr. Archie Tse, CTMO*

- CS1002 (CTLA-4 mAb) Ph1a data readouts
- CS1003 (PD-1 mAb) Ph1a data readouts
- CStone combination strategy and near-term development

Research Update – *Dr. Jon Wang, CSO*

Q&A – *Richard Yeh, CFO*

Note: CMO = Chief Medical Officer; CTMO = Chief Translational Medicine Officer; CSO = Chief Scientific Officer

Business Updates in the Last Six Months

Frank Jiang, MD, PhD, Chairman and CEO

Business Updates in the Last Six Months (1/3)

Major regulatory progress, including company's 1st NDA submission

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NDA Submission

Ivosidenib (IDH1)	■ R/R AML, priority review status, Taiwan (May 29, 2019)

IND/CTA Approvals

6 NEW REGISTRATIONAL TRIALS IN CHINA

Ivosidenib (IDH1)	■ R/R IDH1m AML (Jul 17, 2019)
Avapritinib (KIT&PDGFRα)	■ GIST with PDGFRα D842V mutation (Apr 1, 2019) ■ 2L GIST (Aug 28, 2019)
Pralsetinib (RET)	■ NSCLC (Mar 18, 2019) ■ MTC (Mar 18, 2019) ■ 1L NSCLC (Aug 22, 2019)

5 INVESTIGATIONAL TRIALS

CS1001 (PD-L1) + Fisogatinib (FGFR4)	■ HCC, China (May 14, 2019)
CS1003 (PD-1)	■ Advanced solid tumors, New Zealand (May 15, 2019)
CS3002 (HDAC6)	■ Advanced solid tumors, China (Mar 6, 2019), Australia (May 22, 2019)
CS3003 (CDK4/6)	■ Advanced solid tumors, Australia (Aug 14, 2019)

Multiple IND/CTA submissions planned in China and global

Note: AML= Acute Myeloid Leukemia,, cHL= Classical Hodgkin's Lymphoma, GIST = Gastrointestinal Stromal Tumor, HCC = Hepatocellular Carcinoma, NKTL = Natural KILLER/T Cell Lymphoma, NSCLC = Non-small Cell Lung Cancer, MTC = Medullary Thyroid Cancer, R/R = Relapsed or Refractory

Business Updates in the last six months (2/3)

Significant clinical progress, including 4 assets in 9 registrational trials; initiating 4 new registrational trials by year end

CS1001 (PD-L1)	■ **800+** patients dosed across 7 trials in China and the US, including **5 registrational trials in stage III NSCLC, stage IV NSCLC, GC, NKTL and cHL** ■ **Disclosed Ph Ib multiple cohort data at CSCO 2019** ■ Initiating a **China registrational trial for EC** and several exploratory combination trials for large indications by year-end 2019
CS1003 (PD-1)	■ Completed Ph Ia studies in both Australia and China, has extended Ph Ib trial to the US ■ **Disclosed Ph Ia data at CSCO 2019** ■ Initiating a **global registrational trial for HCC** and several exploratory combination trials for large indications by year-end 2019
CS1002 (CTLA-4)	■ Initiated Ph I trial for advanced solid tumors in Australia ■ **Disclosed Ph Ia data at CSCO 2019** ■ Initiating combination trial for solid tumors in Australia and China by year-end 2019
Ivosidenib (IDH1)	■ **2 registrational trials** for 1L IDH1m AML and R/R AML in China
Avapritinib (KIT&PDGFRα)	■ **2 registrational trials** for PDGFRα D842Vm GIST and 3L GIST in China
Pralsetinib (RET)	■ **2 registrational trials** for RETm NSCLC and MTC in China
Fisogatinib (FGFR4)	■ Initiated a Ph I trial for HCC as monotherapy and a Ph I combo trial with PD-L1 in China

Note: AML= Acute Myeloid Leukemia,, cHL= Classical Hodgkin's Lymphoma, GIST = Gastrointestinal Stromal Tumor, HCC = Hepatocellular Carcinoma, NKTL = Natural KILLER/T Cell Lymphoma, NSCLC = Non-small Cell Lung Cancer, EC = Esophagus Cancer, MTC = Medullary Thyroid Cancer, R/R = Relapsed or Refractory

Business Updates in the last six months (3/3)

Value-creating partnerships with MNC pharma and European biotech

Highlight

- Potentially **Best-in-class** PD-L1/HSA/4-1BB tri-specific antibody-based molecule
- Designed to significantly **broaden safety window and higher efficacy** vs current PD-(L)1 therapies
- **Validated dosing and longer half-life** enable convenient dosing schedules vs competing molecules in the same class

Strategic value

- Access to Numab's **novel multi-specific technology platform**
- Complement to CStone's **IO strategy**

Highlight

- **First collaboration with MNC pharma**, one of the very few without PD-(L)1 – a vote of confidence in CStone and CS1001
- **Global collaboration deal** with China focus in large indications such as gastric cancer
- Regorafenib reported **promising data with PD-1 in gastric cancer and colorectal cancer** at ASCO 2019

Strategic value

- Further strengthens our core strategy in **IO combination therapy**
- A big step forward for CStone's **global strategy** in case of positive data

Business Outlook by 2019 year-end

To initiate multiple new trials with strong focus on combo therapies, and release more PD-L1 data at the upcoming ESMO and ASH 2019

Significant Clinical Progress

- **25+ ongoing and/or completed** trials in China and globally by year-end 2019, including:
  - **10+ registrational** trials

Accelerating Combination Therapy Focus

- **10+ combination therapy** trials by year-end of 2019, including several new additions:
  - Ph III registrational trial of CS1001 (PD-L1) combo for EC in China
  - Ph III registrational trial of CS1003 (PD-1) combo for HCC globally
  - Ph Ib trial of CS1001 (PD-L1) + Fisogatinib (FGFR4) for HCC in China
  - Ph Ib trial of CS1001 (PD-L1) + Regorafenib in multiple indications globally
  - Ph Ib trial of CS1001 (PD-L1) + IMP4297 (PARP) for solid tumors globally
  - Ph Ib trial of CS1003 (PD-1) + CS1002 (CTLA4) for solid tumors globally

More PD-L1 Data Disclosure

ESMO, Barcelona Sep 27 to Oct 1, 2019	Ph Ib safety and efficacy data across multiple cohorts
ASH, Orlando Dec 7 to Dec 10, 2019	NKTL registrational trial data

Note: EC = Esophagus Cancer, HCC = Hepatocellular carcinoma, NKTL = Natural Killer T Cell Lymphoma, ESMO = European Society for Medical Oncology, ASH = American Society of Hematology

PD-L1 DATA Readouts

Jason Yang, MD, PhD, Chief Medical Officer

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CS1001 Overview

A Fully Human IgG4 Anti-PD-L1 mAb

Asset overview	■ Generated from OMT transgenic rat platform licensed from an US biotech company ■ Less immunogenic with potentially lower ADA rate ■ Over 800 pts dosed and Phase I data demonstrated that CS1001 was safe, well tolerated and efficacious in multiple tumor types (ESMO 2018, ASCO & CSCO 2019)
Development status	■ **Four Ph III studies** in stage III NSCLC, stage IV NSCLC, 1L gastric (GC) and 1L esophageal cancer (EC) ■ **Two pivotal phase II studies** in natural killer cell/T-cell lymphoma (NKTL) and classical Hodgkin's lymphoma (cHL) ■ **Two phase I studies** in China and US
Strategic value	■ Potentially to be in the **first wave of approval** for several **major indications** in China ■ Serves as an IO backbone for CStone’s combination strategy

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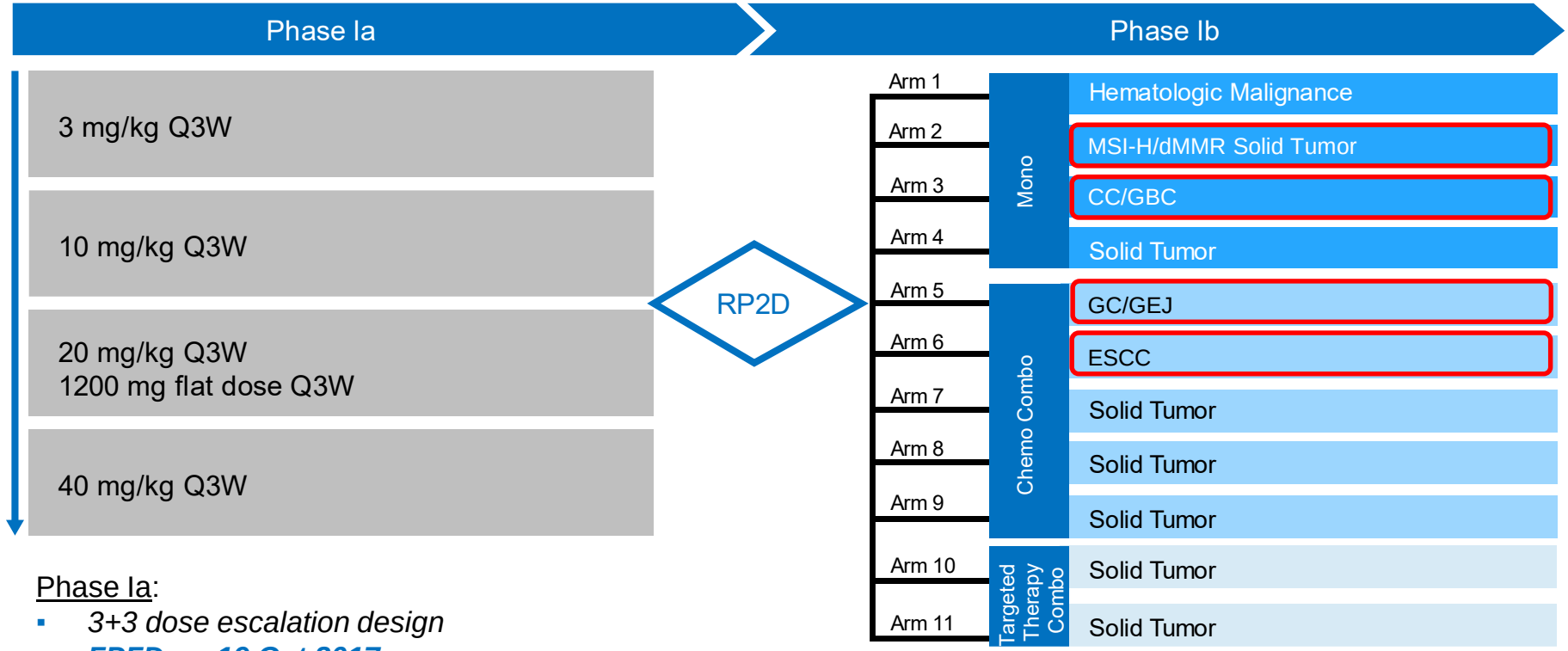
CS1001 Phase Ia / Ib Trial (Gemstone 101)

A Multi-center, Phase Ia/Ib, Open-label, Multi-dose Dose Escalation and Expansion Study Evaluating the Safety, Tolerability, PK and Antitumor Activity of CS1001 in Patients with Advanced Solid Tumor or Lymphoma

CS1001 Phase Ia / Ib Study Design

- **Phase Ia: Dose escalation**
  - Safety, tolerability, PK, and determination of the recommended Phase II dose (RP2D) of CS1001 for future studies
- **Phase Ib: Indication expansion**
  - Preliminary evaluation on the antitumor efficacy in subjects with specific tumors types
  - Further evaluation on the safety, tolerability, PK and immunogenicity



Phase Ia:

- *3+3 dose escalation design*
- ***FPFD on 19 Oct 2017***
- *A total of 29 subjects were enrolled*
- ***ORR 24% (7/29),** 6 of 7 responders still on treatment, data reported in ESMO 2018 and ASCO 2019*

Phase Ib:

- *192 pts dosed as of 1 Jul. 2019*
- *New combinations are being evaluated*

1. CS1001 Chemo Combo in 1L ESCC (1/7)

Study Design

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Screening | **Treatment** | **Follow up**

Key Inclusion Criteria

1. Pts with histologically confirmed unresectable locally advanced or metastatic ESCC who did not receive systemic treatment for it
2. ECOG PS 0 or 1

Key Exclusion Criteria

1. Pts with locally advanced disease suitable for curative concurrent chemo-radiotherapy
2. Pts with primary CNS tumor, meningeal metastasis, unstable CNS metastasis
3. Pts who have received any immune checkpoint inhibitors (including PD-1, PD-L1, etc) for treatment

Chemo Combo

CS1001+ CF

- **CS1001, IV, 1200 mg fixed dose, Q3W**
- **CF Q3W, 6 cycles at most**

CS1001 Maintenance

CS1001
- 1200 mg, IV
- Q3W

Treatment Discontinuation

Until PD or intolerance

Safety and survival follow ups

- Tumor assessment by investigator per RECIST 1.1
- Q9W first year and Q12W thereafter

Primary Objectives

- To assess preliminary efficacy of CS1001 in combination with CF as first line treatment in pts with ESCC

Secondary Objectives

- To assess the safety and tolerance of CS1001 in combination with CF

1. CS1001 Chemo Combo in 1L ESCC (2/7)

Disposition and Baseline Characteristics

Disposition and baseline characteristics（Safety analysis set）	
Subject Enrolled	23
Age（yr）： Median（range）	 61 (45-73)
Sex: Male, n (%) Female, n (%)	 18 (78.3) 5 (21.7)
ECOG Performance Status： 0, n (%) 1, n (%)	 5 (21.7) **18 (78.3)**
Prior anti-cancer treatment: Median（range）	 0（0-2*）
Time since initial diagnosis (yr)： Median（range）	 0.49 (0.01-3.04)
Current cancer stage III, n(%) IV, n(%)	 3 (13) **20 (87)**

- As of 1 July 2019, 23 subjects enrolled into ESCC arm and received study treatment
- 17 subjects are still on study treatment

* prior anti-cancer treatment：8 subjects received neu-adjuvant and/or adjuvant treatment, of which one subject received adjuvant cisplatin and paclitaxel and changed to cisplatin and capecitabine due to allergic to paclitaxel

Data Cut off Date：1 July 2019

1. CS1001 Chemo Combo in 1L ESCC (3/7)

Safety - AE Summary: CS1001 CF Combo was Safe and Tolerable

Description	ESCC (N=23)，n (%)
Number of Subjects with At least one TEAE	23 (100)
At least one Grade 3/4/5 TEAE	18 (78.3)
At least one TEAE Related to Any Drug	23 (100)
At least one Grade 3/4/5 TEAE Related to Any Drug	18 (78.3)
At least one TEAE Leading to CS1001 withdrawn	3 (13)
At least one TEAE Leading to Chemotherapy Withdrawn	3 (13)
At least one TEAE Leading to Treatment Cycle Delay	11 (47.6)
At least one Immune-Related TEAE	16 (69.6)
At least one TEAE Leading to Death	1 (4.3)
At least one infusion-related reaction TEAE	1 (4.3)

MedDRA Preferred Term，n (%)	All Grades (N=23)，n (%)	≥Grade 3 (N=23)，n (%)
Number of Subjects with At least one TRAE	23 (100)	18 (78.3)
Anaemia	16 (69.6)	7 (30.4)
Neutrophils count decreased	15 (65.2)	7 (30.4)
WBC count decreased	12 (52.2)	5 (21.7)
Nausea	11 (47.8)	3 (13.0)
Decreased appetite	10 (43.5)	1 (4.3)
Blood corticotrophin increased	9 (39.1)	0 (0.0)
Platelet count decreased	7 (30.4)	2 (8.7)
Hyponatremia	6 (26.1)	2 (8.7)
Vomiting	6 (26.1)	3 (13.0)
Amylase increased	6 (26.1)	2 (8.7)
Asthenia	5 (21.7)	1 (4.3)
Bone marrow failure	2 (8.7)	2 (8.7)

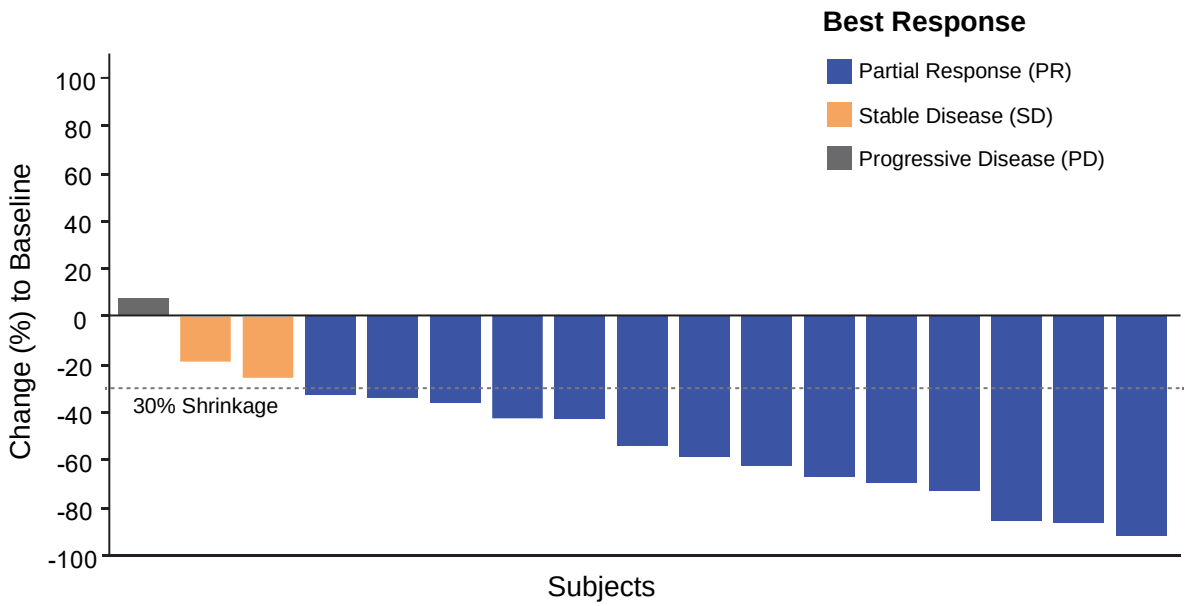
Data Cut off Date：1 July 2019

1. CS1001 Chemo Combo in 1L ESCC (4/7)

Promising Antitumor Activity: ORR= 77.8% (14/18), DCR=88.9% (16/18)

- Among 23 treated subjects, 18 were included in efficacy analysis set, 14 subjects (77.8%) were evaluated as PR according to RECIST (v1.1)

Target Lesion Shrinkage from Baseline (Efficacy Analysis Set)



Best Response	Total (N=18) n (%)
Partial Response (PR)	14 (77.8)
Stable Disease (SD)	2 (11.1)
Progressive Disease (PD)	1 (5.6)
Not Applicable (NA)	1 (5.6)
Overall Response Rate ORR=CR+PR	**14 (77.8)**
Disease Control Rate DCR=CR+PR+SD	**16 (88.9)**

* 5 ongoing subjects who had not reached the 1st post-baseline tumor assessment were excluded in efficacy analysis set. Efficacy analysis set includes patients who received study drug and had measurable disease at baseline

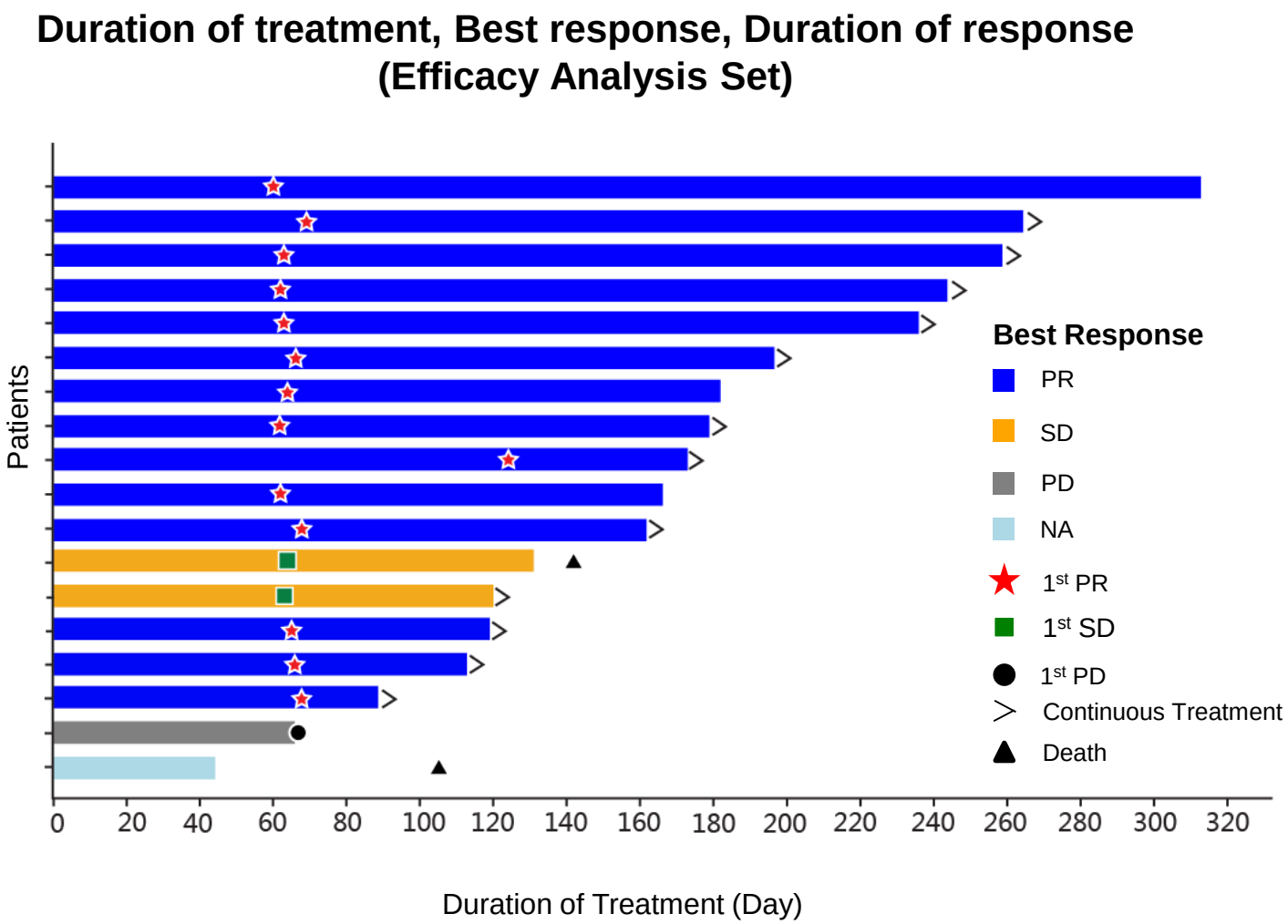
** 1 subjects were not shown in the figure due to no post-baseline target lesion evaluation; the subject was treated as Not Applicable for best response assessment in efficacy analysis

*** 12 subjects with confirmed PRs; The 2 subjects with unfirmed PR were still on treatment and didn't reach the following assessment schedule

Data Cut off Date : 1 July 2019

1. CS1001 Chemo Combo in 1L ESCC (5/7)

Durable Response

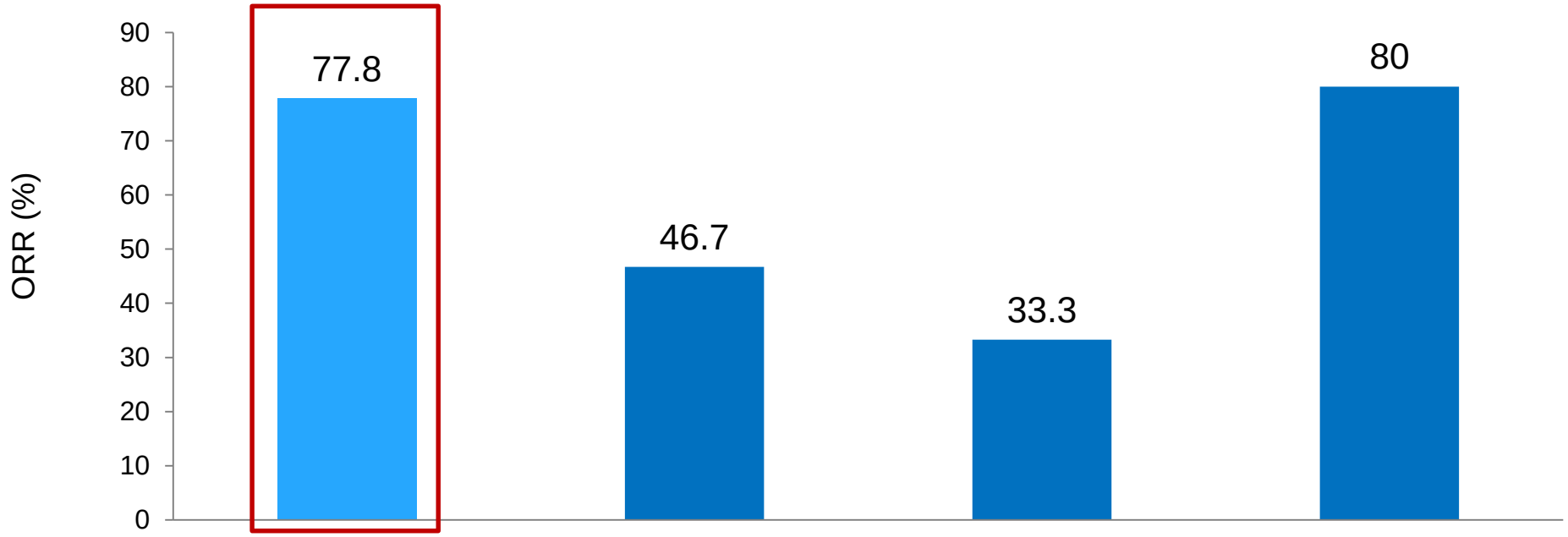


- 13 (92.9%) of 14 PR achieved at 1st post-baseline assessment (week 9)
- 11 (78.6%) of 14 responders (PR) still on treatment
- Median DOR not reached, range (0.03+ ~ 8.4+) months

Data Cut off Date : 1 July 2019

1. CS1001 Chemo Combo in 1L ESCC (6/7)

Comparison with Other PD-(L)1s



	CS1001	Tislelizumab	Durvalumab+ Tremelimumab	Camrelizumab+ Apatinib
Class	PD-L1	PD-1	PD-L1	PD-1
n	23	15	6	30
ECOG	0: 21.3% 1: 78.3%	0: 26.7% 1: 73.3%	0: 0% 1: 100%	**0: 83.3%** 1: 16.7%
Chemo Regimen	CF	CF	CF	liposomal paclitaxel+ nedaplatin
DOR (m)	NR (0.03+~8.4+)	12.8	Not reported	Not reported
Source	CSCO 2019	CSCO 2019	ASCO GI 2019	ASCO 2019

1. CS1001 Chemo Combo in 1L ESCC (7/7)

Summary

- CS1001 combo with CF demonstrated promising antitumor activities in ESCC patients. The observed ORR was 77.8%
- Response is durable, median DOR not reached, all 14 partial responses are continuing as of data cutoff
- CS1001 combo with CF was safe and tolerable
- Current data support further development of CS1001+CF for 1L treatment of advanced ESCC patients

Data Cut off Date： 1 July 2019

2. CS1001 Chemo Combo in GC/GEJ (1/7)

Study Design

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Screening | **Treatment** | **Follow up**

Key Inclusion Criteria

1. Pts with histologically confirmed unresectable locally advanced or metastatic GC/GEJ who did not receive systemic treatment
2. ECOG PS 0 or 1

Key Exclusion Criteria

1. Known Her2 positive disease*
2. Pts with primary CNS tumor, meningeal metastasis, unstable CNS metastasis
3. Pts who have received any immune checkpoint inhibitors (including PD-1, PD-L1, etc) for treatment

*Her 2 positive: IHC 3+ or IHC 2+/ISH +

Chemo Combo

CS1001+ XELOX

- **CS1001, IV, 1200 mg fixed dose, Q3W**
- **XELOX Q3W, 6 cycles max**

CS1001 Maintenance

CS1001
- 1200 mg, IV
- Q3W

Treatment Discontinuation

Until PD or intolerance → Safety and survival follow ups

- Tumor assessment by investigator per RECIST 1.1
- Q9W first year and Q12W thereafter

Primary Objectives

- To assess preliminary efficacy of CS1001 in combination with XELOX as first line treatment in pts with GC/GEJ

Secondary Objectives

- To assess the safety and tolerance of CS1001 in combo with XELOX

2. CS1001 Chemo Combo in GC/GEJ (2/7)

Disposition and Baseline Characteristics

Disposition and baseline characteristics （Safety analysis set)	
Subject Enrolled	29
Age （yr）： Median （range)	 60 (40-73)
Sex： Male, n (%) Female, n (%)	 23 (79.3) 6 (20.7)
ECOG Performance Status： 0, n (%) 1, n (%)	 5 (21.7) **18 (78.3)**
Prior anti-cancer treatment： Median （range)	 0 （0-2*)
Time since initial diagnosis (yrs) ： Median （range)	 0.077 (0.01，61.60)
Initial diagnosis, n (%) GC GEJ	 **26 (89.7)** 3 (10.3)
Current cancer stage III, n(%) IV, n(%)	 1 (3.4) **28 (96.6)**

- As of 1 July 2019, 29 subjects enrolled into GC/GEJ arm and received study treatment
- 15 subjects still on study treatment

* prior anti-cancer treatment：10 subjects received neu-adjuvant and/or adjuvant treatment, of which one subject received both neu-adjuvant and adjuvant treatment

Data Cut off Date：1 July 2019

2. CS1001 Chemo Combo in GC/GEJ (3/7)

Safety - AE Summary: CS1001 XELOX Combo was Safe and Tolerated

Description	GC/GEJ (N=29)，n (%)
Number of Subjects with At least one TEAE	29 (100)
At least one Grade 3/4/5 TEAE	19 (65.5)
At least one TEAE Related to Any Drug	29 (100)
At least one Grade 3/4/5 TEAE Related to Any Drug	16 (55.2)
At least one TEAE Leading to CS1001 withdrawn	3 (10.3)
At least one TEAE Leading to Chemotherapy Withdrawn	8 (27.6)
At least one TEAE Leading to Treatment Cycle Delay	16 (55.2)
At least one Immune-related TEAE	18 (62.1)
At least one TEAE Leading to Death	0 (0)
At least one infusion-related reaction TEAE	2 (6.9)

MedDRA Preferred Term，n (%)	All Grades (N=29)，n (%)	≥Grade 3 (N=29)，n (%)
Number of Subjects with At least one TEAE related to any drug	**29 (100)**	**16(55.2)**
Platelet count decreased	20 (69.0)	5(17.2)
Anaemia	20 (69.0)	4(13.8)
White blood cell count decreased	18 (62.1)	3 (10.3)
Neutrophil count decreased	11 (37.9)	5(17.2)
Aspartate aminotransferase increased	9 (31.0)	0(0.0)
Proteinuria	9 (31.0)	0(0.0)
Alanine aminotransferase increased	8 (27.6)	0(0.0)
Rash	7 (24.1)	0(0.0)
Decreased appetite	6 (20.7)	0(0.0)
Hypoaesthesia	6 (20.7)	0(0.0)
Neutropenia	4 (13.8)	2(6.9)
Blood alkaline phosphatase increased	3 (10.3)	1(3.4)
Thrombocytopenia	3 (10.3)	1(3.4)
Hypothyroidism	2 (6.9)	1(3.4)
Fatigue	2 (6.9)	2(6.9)
Hepatic function abnormal	2 (6.9)	1(3.4)
Bilirubin increased	2(6.9)	1(3.4)
Blood creatinine increased	2 (6.9)	1(3.4)

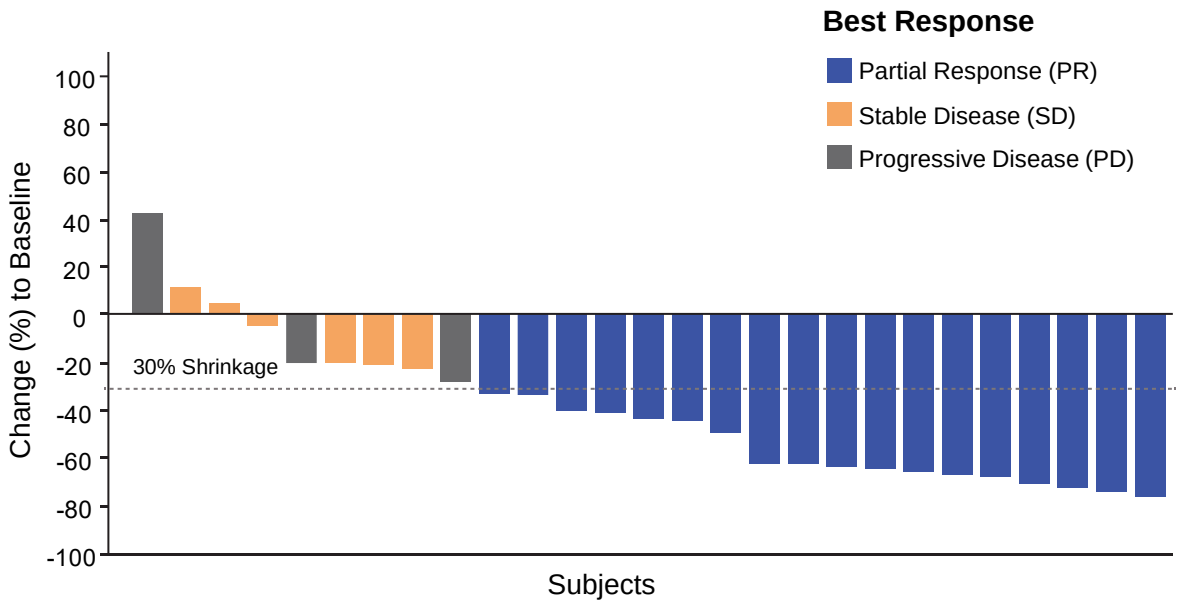
Data Cut off Date： 1 July 2019

2. CS1001 Chemo Combo in GC/GEJ (4/7)

Promising Antitumor Activity: ORR=62.1% (18/29), DCR=82.8%(24/29)

- 29 treated subjects were included in efficacy analysis set, 18 subjects (62.1%) were evaluated as PR according to RECIST (v1.1)

Target Lesion Shrinkage from Baseline (Efficacy Analysis Set)



Best Response	Total (N=29) n (%)
Partial Response (PR)	18 (62.1)
Stable Disease (SD)	6 (20.7)
Progressive Disease (PD)	3 (10.3)
Not Applicable (NA)	2 (6.9)
Overall Response Rate ORR=CR+PR	**18 (62.1)**
Disease Control Rate DCR=CR+PR+SD	**24 (82.8)**

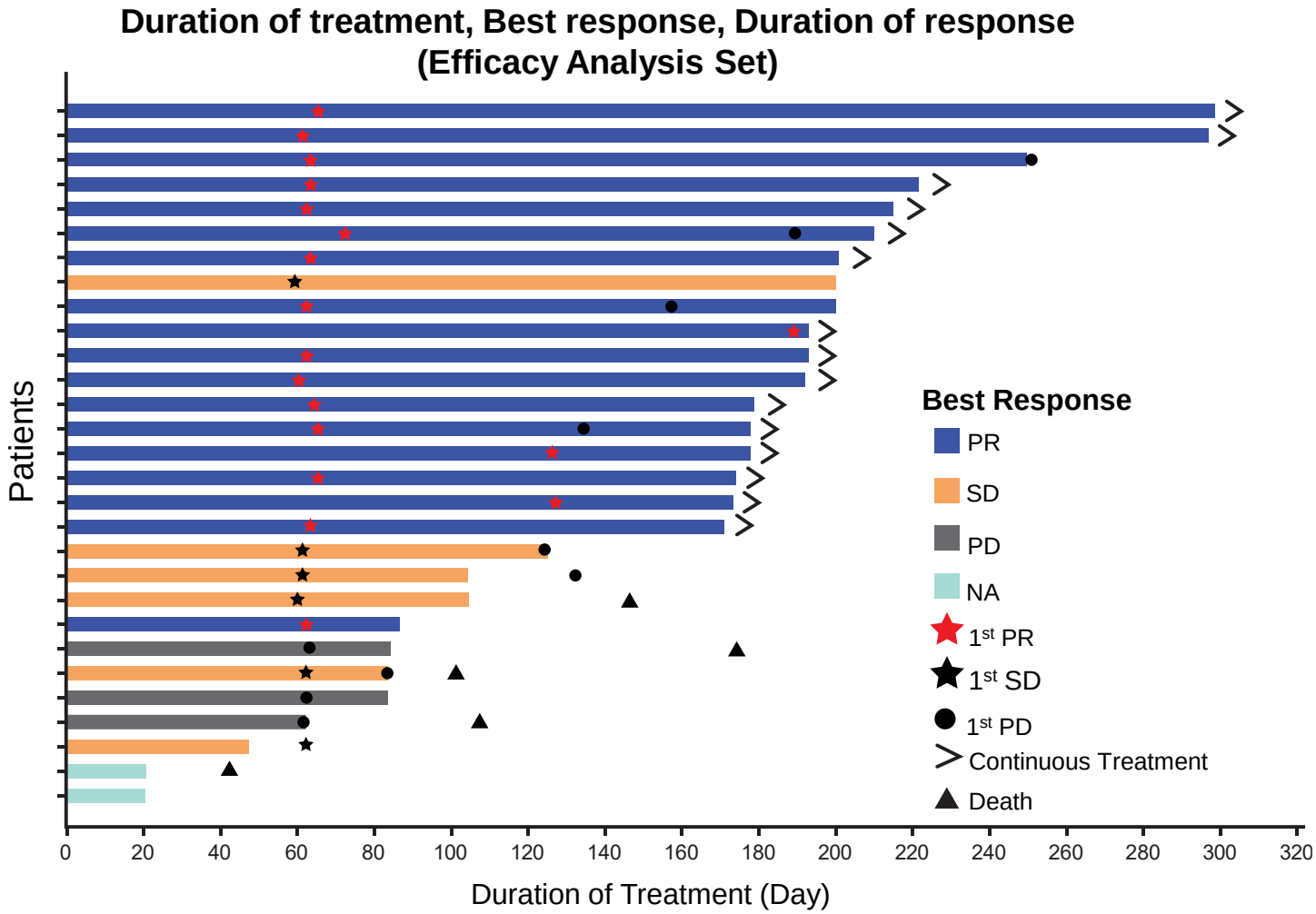
a. 2 subjects were not shown in the figure due to no post-baseline target lesion evaluation; they were assessed as Not Applicable for best response assessment

b. 15 PR confirmed as of cutoff date

Data Cut off Date : 1 July 2019

2. CS1001 Chemo Combo in GC/GEJ (5/7)

Durable Response

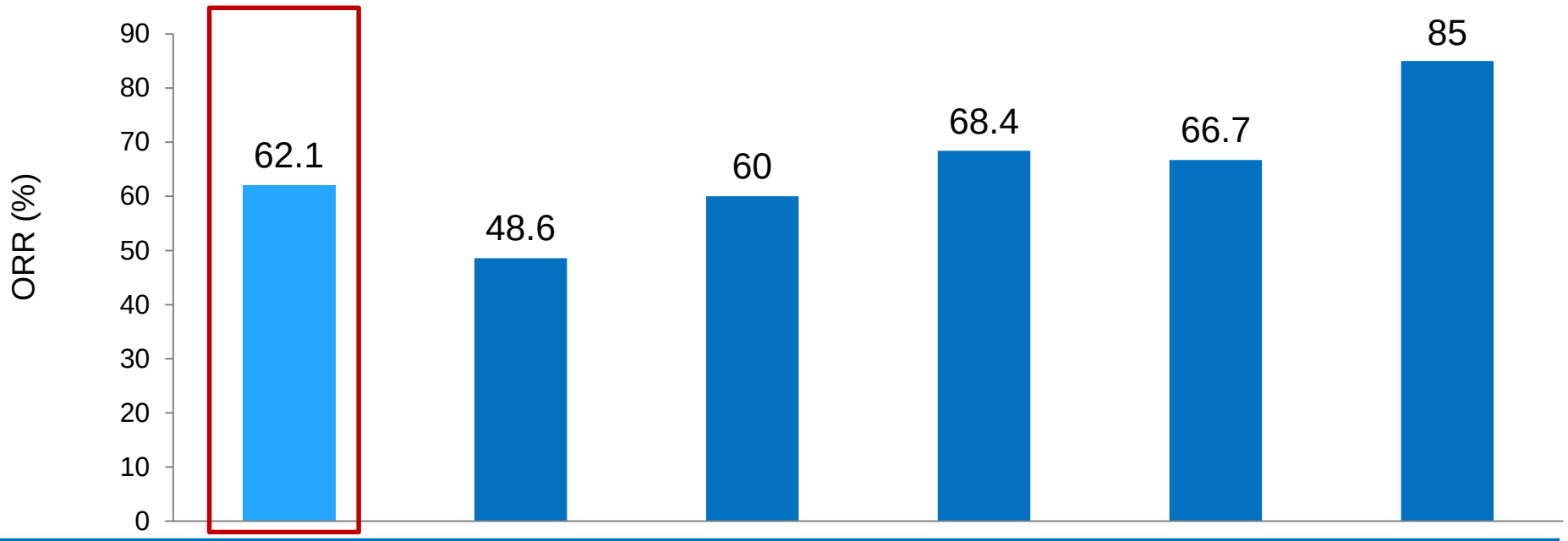


- 15 (83.3%) of 18 PR achieved at 1st post baseline tumor assessment (week 9)
- 14 (77.8%) of 18 responders (PR) still on treatment
- Median DOR: 6.21 months, range (0.03+ ~ 6.21+)
- 6-month DOR rate: 72.7%

Data Cut off Date : 1 July 2019

2. CS1001 Chemo Combo in GC/GEJ (6/7)

Comparison with Other PD-(L)1s



	CS1001	Keytruda (062)	Keytruda (059)	Opdivo	Camrelizumab	Sintilimab
Class	PD-L1	PD-1	PD-1	PD-1	PD-1	PD-1
n	21	257 vs 250*	25	38	48	20
ECOG	0: 41.4% 1: 58.6%	0: 46.0% 1: 54.0%	0: 60.0% 1: 40.0%	0: 50.0% 1: 50.0%	0: 41.7% 1: 58.3%	0: 45.0% 1: 55.0%
Chemo Regimen	XELOX	Cisplatin + 5-FU or Capecitabine	Cisplatin + 5-FU or Capecitabine	SOX or XELOX	XELOX	XELOX
DOR (m)	6.2 (0.03+ ~ 6.21+)	6.8	4.6 (2.6 ~ 20.3+)	9.9 (5.8, NR)	NR	5.3 (4.8~7.2)
Source	CSCO 2019	ASCO 2019	ESMO 2017	Ann Oncol. 2019 Feb 1;30(2):250-258	ASCO 2019	ASCO 2019

* ORR of Cisplatin + 5-FU or Capecitabie was 37.3%

2. CS1001 Chemo Combo in GC/GEJ (7/7)

Conclusions

- CS1001 combo with XELOX demonstrated promising antitumor activities in GC/GEJ patients. The observed ORR was 62.1%
- Response is durable, 14 of 18 partial responses are continuing as of data cutoff
- CS1001 combo with XELOX was safe and tolerable
- Current data support further development of CS1001+XELOX for the 1L treatment of advanced GC/GEJ patients

Data Cut off Date： 1 July 2019

3. CS1001 Monotherapy in CC/GBC (1/7)

Study Design

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Screening → **Treatment** → **Follow up**

Key Inclusion Criteria

1. Pts with unresectable CC/GBC, failed standard treatment or refuse the standard treatment
2. ECOG PS 0 or 1

Key Exclusion Criteria

1. Pts with primary CNS tumor, meningeal metastasis, unstable CNS metastasis
2. Pts who have received any immune checkpoint inhibitors (including PD-1, PD-L1, etc) for treatment

Study Treatment

CS1001 Dosing:

- **IV**
- **1200 mg**
- **Q3W**

Treatment Discontinuation

Until PD or intolerance → Safety and survival follow ups

- Tumor assessment by investigator per RECIST 1.1
- Q9W first year and Q12W thereafter

Primary Objectives

- To assess preliminary efficacy of CS1001 as monotherapy in pts with CC/GBC cancer

Secondary Objectives

- To further assess the safety and tolerance

3. CS1001 Monotherapy in CC/GBC (2/7)

Disposition and Baseline Characteristics

Disposition and baseline characteristics (Safety analysis set)	
Subject Enrolled	29
Age (yr) :	
Median (range)	55 (39-72-73)
Sex:	
Male, n (%)	9 (31.0)
Female, n (%)	20 (69.0)
ECOG Performance Status :	
0, n (%)	14 (48.3)
1, n (%)	13 (44.8)
unknown, n (%)	2 (6.9)
Prior anti-cancer treatment:	
Median (range)	1 (0-6)
Treatment duration (day) :	
Median (range)	137 (21-377)
Time since initial diagnosis (yr) :	
Median (range)	0.731 (0.03, 1.84)
Initial Diagnosis	
CC	**27 (93.1)**
GBC	2 (6.9)
Current cancer stage	
IV, n (%)	**29 (100)**

- As of 1 July 2019, 29 subjects enrolled into CC/GBC arm and received study treatment
- 3 subjects are still receiving study treatment

Data Cut off Date : 1 July 2019

3. CS1001 Monotherapy in CC/GBC (3/7)

Safety - AE Summary: CS1001 was Safe and well Tolerated

Description	CC/GBC (N=29)，n (%)
Number of Subjects with At least one TEAE	28 (96.6)
At least one Grade 3/4/5 TEAE	16 (55.2)
At least one TEAE Related to CS1001	22 (75.9)
At least one Grade 3/4/5 TEAE Related to CS1001	7 (24.1)
At least one Serious TEAE	9 (31.0)
At least one Serious TEAE Related to CS1001	5 (17.2)
At least one Immune-related TEAE	11 (37.9)
At least one TEAE Leading to Treatment Cycle Delayed	9 (31.0)
At least one TEAE Leading to Study Drug Withdrawn	3 (10.3)
At least one TEAE Leading to Death	0 (0)
At least one infusion-related reaction TEAE	1 (3.4)

MedDRA Preferred Term，n (%)	All Grades (N=29), n(%)	≥3 grade 3 (N=29) , n(%)
Number of Subjects with at least one TEAE related to CS1001	22 (75.9)	7 (24.1)
ALT increased	8 (27.6)	1 (3.4)
Anaemia	7 (24.1)	1 (3.4)
AST increased	6 (20.7)	0
Proteinuria	6 (20.7)	0
Pyrexia	4 (13.8)	0
Hypothyroidism	4 (13.8)	0
Blood creatinine phosphokinase increased	3 (10.3)	0
Hyperthyroidism	3 (10.3)	1 (3.4)
Amylase increased	2 (6.9)	0
Blood bilirubin increased	2 (6.9)	0
Bilirubin conjugated increased	2 (6.9)	0
Liver function abnormal	2 (6.9)	1 (3.4)
Pancytopenia	1 (3.4)	1 (3.4)
Vomiting	1 (3.4)	1 (3.4)
Hyponatremia	1 (3.4)	1 (3.4)
Hypocalcemia	1 (3.4)	1 (3.4)
Lung infection	1 (3.4)	1 (3.4)

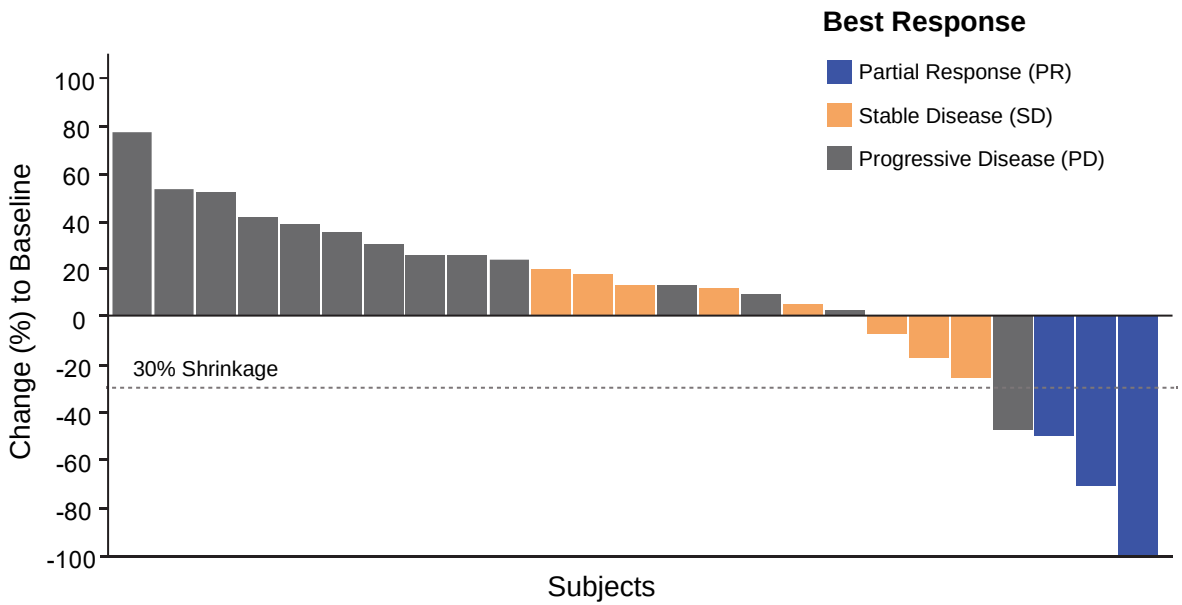
Data Cut off Date： 1 July 2019

3. CS1001 Monotherapy in CC/GBC (4/7)

Preliminary Antitumor Activity Data - ORR=10.3% (3/29), DCR=37.9%(11/29)

- All 29 treated subjects included in efficacy analysis set, 3 subjects (10.3%) were evaluated as PR according to RECIST (v1.1)

Target Lesion Shrinkage from Baseline (Efficacy Analysis Set)



Best Response	Total (N=29) n (%)
Partial Response (PR)	3 (10.3)
Stable Disease (SD)	8 (27.6)
Progressive Disease (PD)	14 (48.3)
Not Applicable (NA)	4 (13.8)
Overall Response Rate ORR=CR+PR	**3 (10.3)**
Disease Control Rate DCR=CR+PR+SD	**11 (37.9)**

a. Four subjects were not shown in the figure due to no post-baseline target lesion evaluation; they were assessed as Not Applicable for best response assessment in efficacy analysis

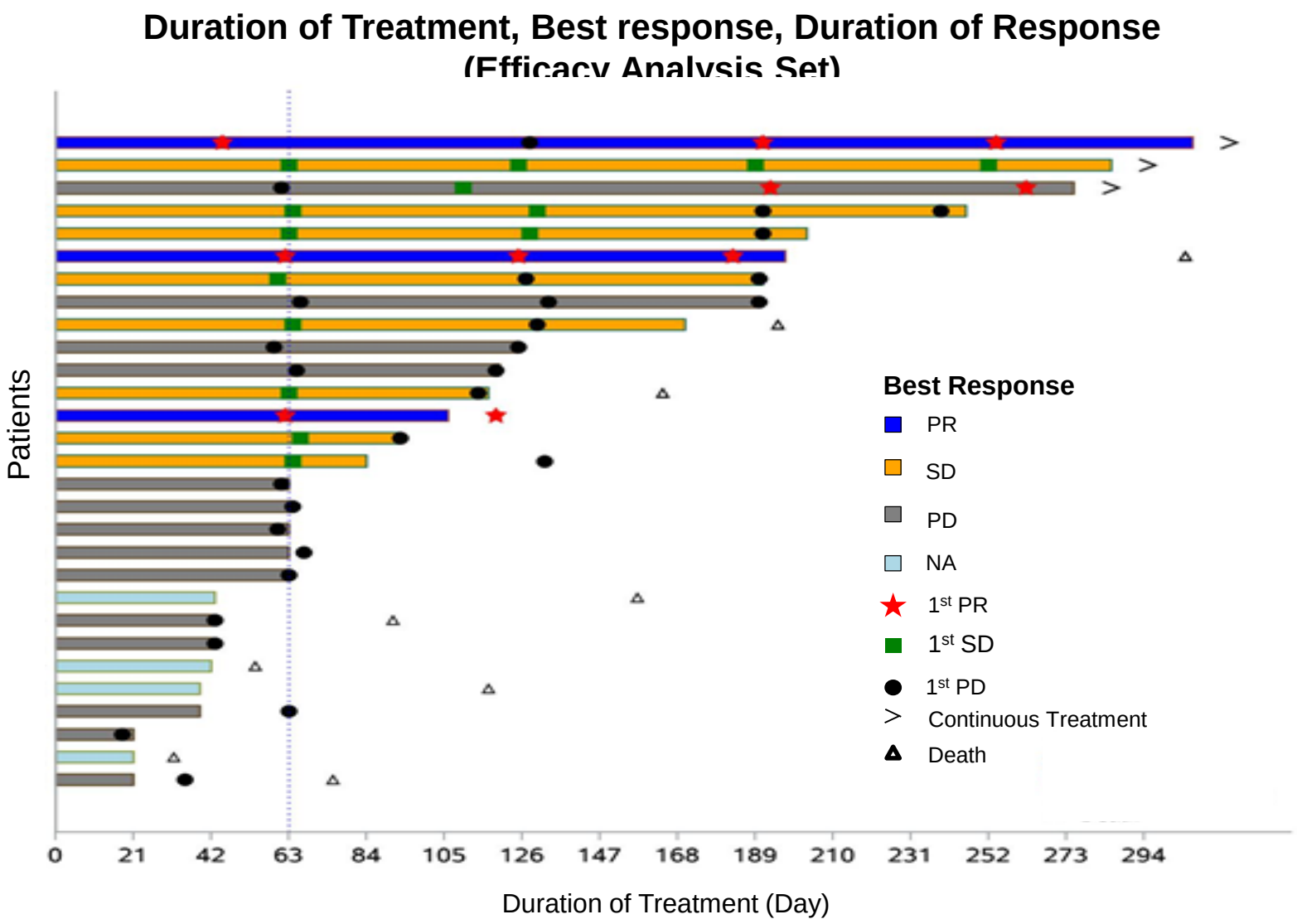
b. 2 PRs were confirmed. 1 responder was not counted as confirmed even though the response were assessed as PR in two consecutive imaging assessment following a pseudo-progression

c. One PR was excluded in ORR calculation since the PR was demonstrated following an initial PD assessment (new lesion)

Data Cut off Date : 1 July 2019

3. CS1001 Monotherapy in CC/GBC (5/7)

Time to and Duration of Response

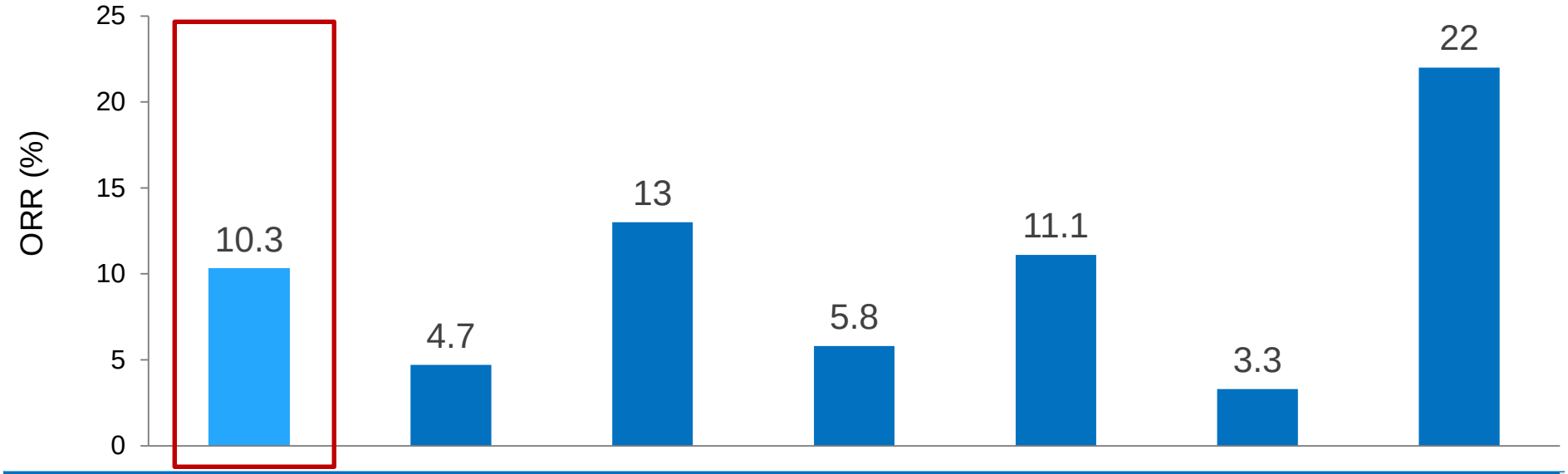


- All 3 PR achieved in 1st post-baseline assessment (week 9)
- Median DOR: 5.39 months, range (1.91+ ~ 8.02+)

Data Cut off Date : 1 July 2019

3. CS1001 Monotherapy in CC/GBC (6/7)

Data Comparison with Other PD-(L)1 as Monotherapy



	CS1001	Imfinzi Asia	Keytruda (PD-L1>=1%)	Keytruda (global)	Keytruda (PD-L1>=1%) Korean	Opdivo Japan	Opdivo US
Class	PD-L1	PD-L1	PD-1	PD-1	PD-1	PD-1	PD-1
n	29	42	24	104	39	30	54
ECOG	0: 14(48.3) 1: 13(44.8) NA: 2 (6.9)	0: 27(64) 1: 15(36)	0: 9(37.5) 1: 15(62.5)	0: 42(40.4) 1: 62(59.6)	Not reported	Not reported	Not reported
Regimen	1200mg IV Q3W	10 mg/kg Q2W	10mg/kg IV Q2W	200mg IV Q3W	200mg IV Q3W	Mono: nivolumab 240mg Q2W	240mg Q2W for 16 weeks then 480mg Q4W
DOR (m)	5.39 (1.91+,8.02)	9.7	NR (21.5 -29.4+)	NR (6.2-23.2+)	Not reported	Not reported	Not reported
Source	CSCO 2019	JCO 2019	ASCO 2019	ASCO 2019	JCO 2019	Lancet 2019	JCO 2019

3. CS1001 monotherapy in CC/GBC (7/7)

Conclusions

- CS1001 monotherapy demonstrated preliminary antitumor activities in CC/GBC patients, comparable to other PD-(L)1. The observed ORR was 10.3%
- CS1001 was safe and well tolerated
- Current data support further development of CS1001 for the treatment of pts with unresectable CC/GBC cancer

Data Cut off Date： 1 July 2019

4. CS1001 Monotherapy in MSI-H/dMMR Cancer (1/7)

Study Design

Screening → **Treatment** → **Follow up**

Key Inclusion Criteria

1. 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
2. ECOG PS 0 or 1

Key Exclusion Criteria

1. Pts with primary CNS tumor, meningeal metastasis, unstable CNS metastasis
2. Pts who have received any immune checkpoint inhibitors (including PD-1, PD-L1, etc)

Study Treatment

CS1001 Dosing:

- **IV**
- **1200 mg**
- **Q3W**

Treatment Discontinuation

Until PD or intolerance → Safety and survival follow ups

- Tumor assessment by investigator per RECIST 1.1
- Q9W first year and Q12W thereafter

Primary Objectives

- To assess preliminary efficacy of CS1001 as monotherapy in pts with MSI-H/dMMR cancer

Secondary Objectives

- To further assess the safety and tolerance

4. CS1001 Monotherapy in MSI-H/dMMR Cancer (2/7)

Disposition and Baseline Characteristics

- As of 1 July 2019, 21 subjects enrolled and received study treatment
- 9 subjects still on study treatment

Tumor Type	
Subject Enrolled	**21**
CRC	18
Pancreatic Cancer	2
Small intestine cancer	1

Disposition and baseline characteristics (Safety analysis set)	
Subject Enrolled	21
Age（yr）：	
Median（range）	53 (25-71)
Sex：	
Male, n (%)	12 (57.1)
Female, n (%)	9 (42.9)
ECOG Performance Status：	
0, n (%)	0 (0)
1, n (%)	**21 (100)**
Prior anti-cancer treatment：	
Median（range）	**2 (1-9)**
Treatment duration（day）：	
Median（range）	137 (21-377)
Time since initial diagnosis (yr)：	
Median（range）	1.32 (0.36-19.76)
Current cancer stage	
IV, n (%)	**21 (100)**

Data Cut off Date：1 July 2019

4. CS1001 Monotherapy in MSI-H/dMMR Cancer (3/7)

Safety - AE Summary: CS1001 was Safe and Well Tolerated

Description	MSI-H/dMMR (N=21)，n (%)
Number of Subjects with at least one TEAE	20 (95.9)
At least one grade 3/4/5 TEAE	5 (23.8)
At least one TEAE related to CS1001	18 (85.7)
At least one Grade 3/4/5 TEAE related to CS1001	1 (4.8)
At least one Serious TEAE	2 (9.5)
At least one Serous TEAE related to CS1001	0 (0)
At least one Immune-related TEAE	9 (42.9)
At least TEAE leading to Treatment Cycle Delayed	3 (14.3)
At Least one TEAE leading to CA1001 withdrawn	0 (0)
At Least one TEAE Leading to Death	0 (0)
At Least one infusion-related reaction TEAE	0 (0)

MedDRA Preferred Term	All Grades (N=21), n(%)	≥3 grade 3 (N=21) , n(%)
Number of Subjects with at least one TEAE related to CS1001	**18 (85.7)**	**1 (4.8)**
Anaemia	5 (23.8)	1 (4.8)
ALT increased	4 (19.0)	0
AST increased	4 (19.0)	0
WBC count decreased	4 (19.0)	0
Lipase increased	2 (9.5)	0
Platelet count decreased	2 (9.5)	0
Conjugated bilirubin increased	2 (9.5)	0
Neutrophils count decreased	2 (9.5)	0
ECG QT prolonged	2 (9.5)	0
Constipation	2 (9.5)	0
Hyperthyroidism	2 (9.5)	0
Cough	2 (9.5)	0

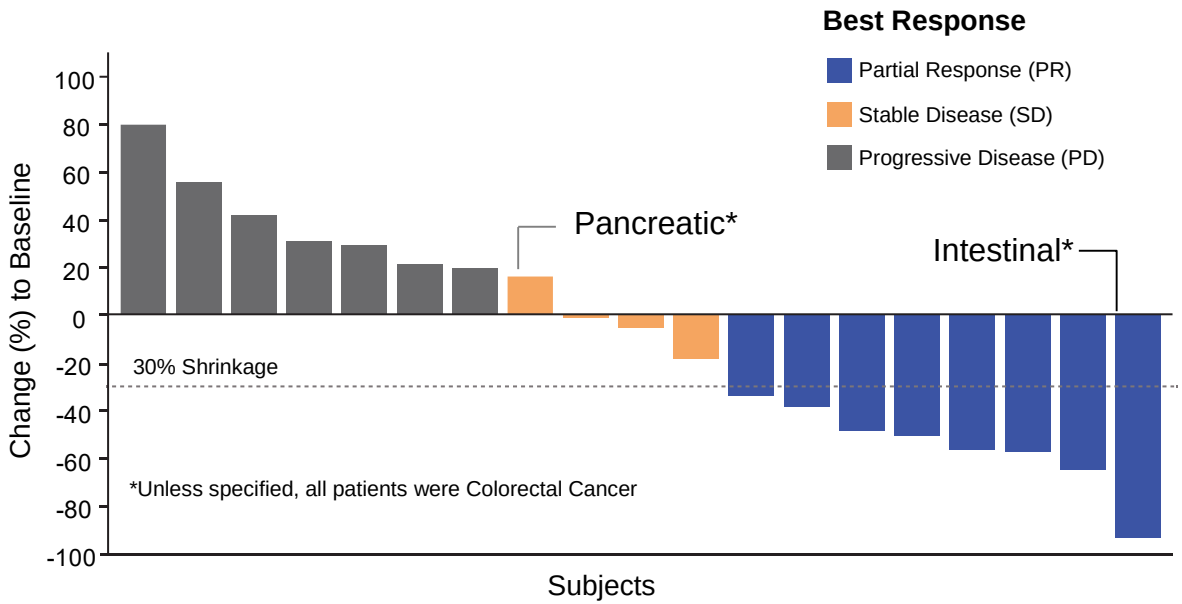
Data Cut off Date： 1 July 2019

4. CS1001 Monotherapy in MSI-H/dMMR Cancer (4/7)

Promising Antitumor Activity: ORR = 38.1% (8/21), DCR=57.1% (12/21)

- All 21 subjects were included in efficacy analysis, 8 subjects (38.1%) were assessed as PR according to RECIST (v1.1)

Target Lesion Shrinkage from Baseline (Efficacy Analysis Set)



Best Response	Total (N=21) n (%)
Partial Response (PR)	8 (38.1)
Stable Disease (SD)	4 (19.0)
Progressive Disease (PD)	7 (33.3)
Not Applicable (NA)	2 (9.5)
Overall Response Rate ORR=CR+PR	**8 (38.1)**
Disease Control Rate DCR=CR+PR+SD	**12 (57.1)**

- 2 subjects were not shown in the plot due to no post-baseline target lesion evaluation; they were assessed as Not Applicable for best response assessment in efficacy analysis
- Among 8 PR patients:
  - 7 subjects with colorectal cancer and 1 subject with small intestine cancer
  - 6 subjects with confirmed PRs as of cutoff date

Data Cut off Date : 1 July 2019

4. CS1001 Monotherapy in MSI-H/dMMR Cancer (5/7)

Rapid and Durable Response

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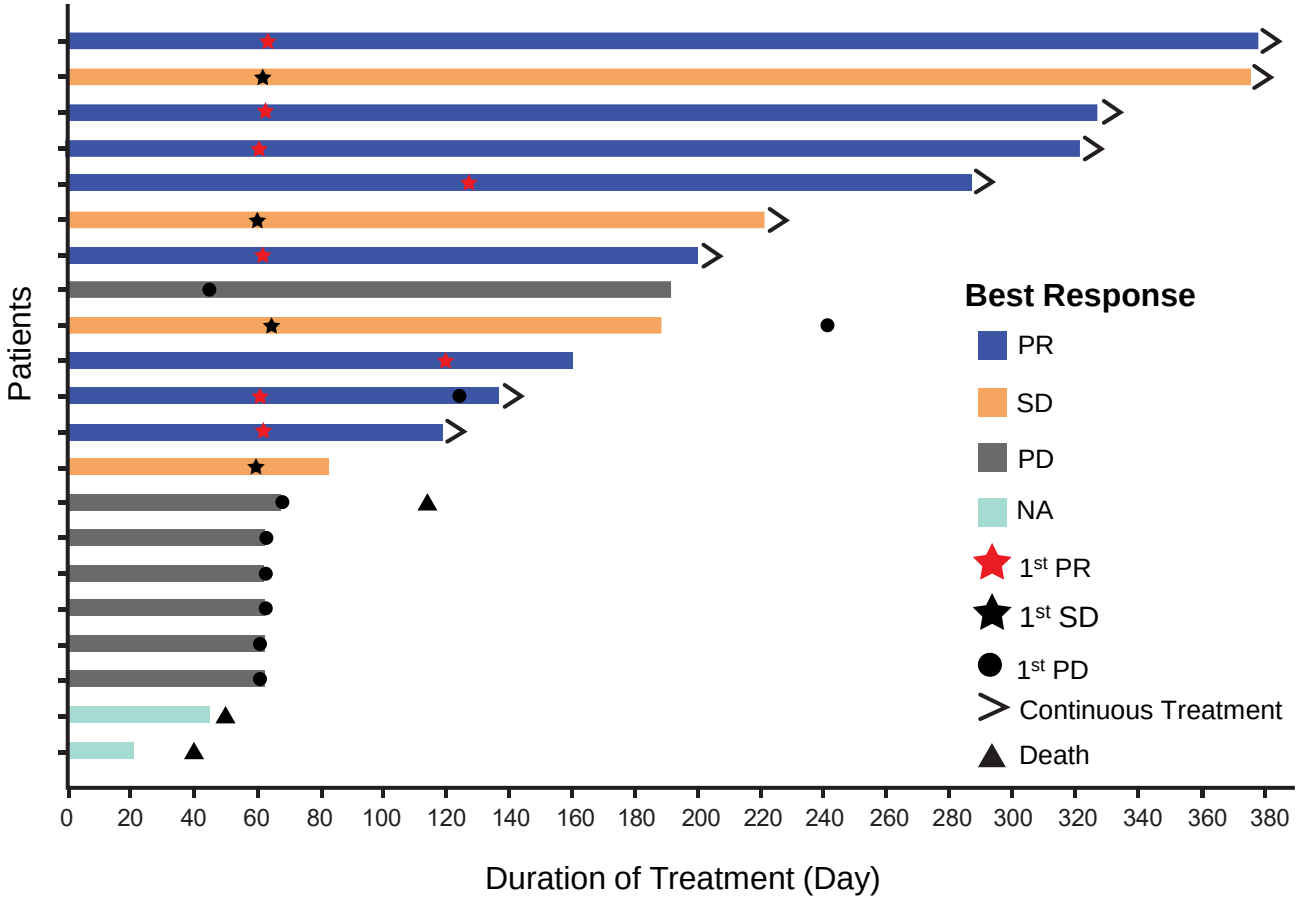
Duration of treatment, best response, duration of response (Efficacy Analysis Set)

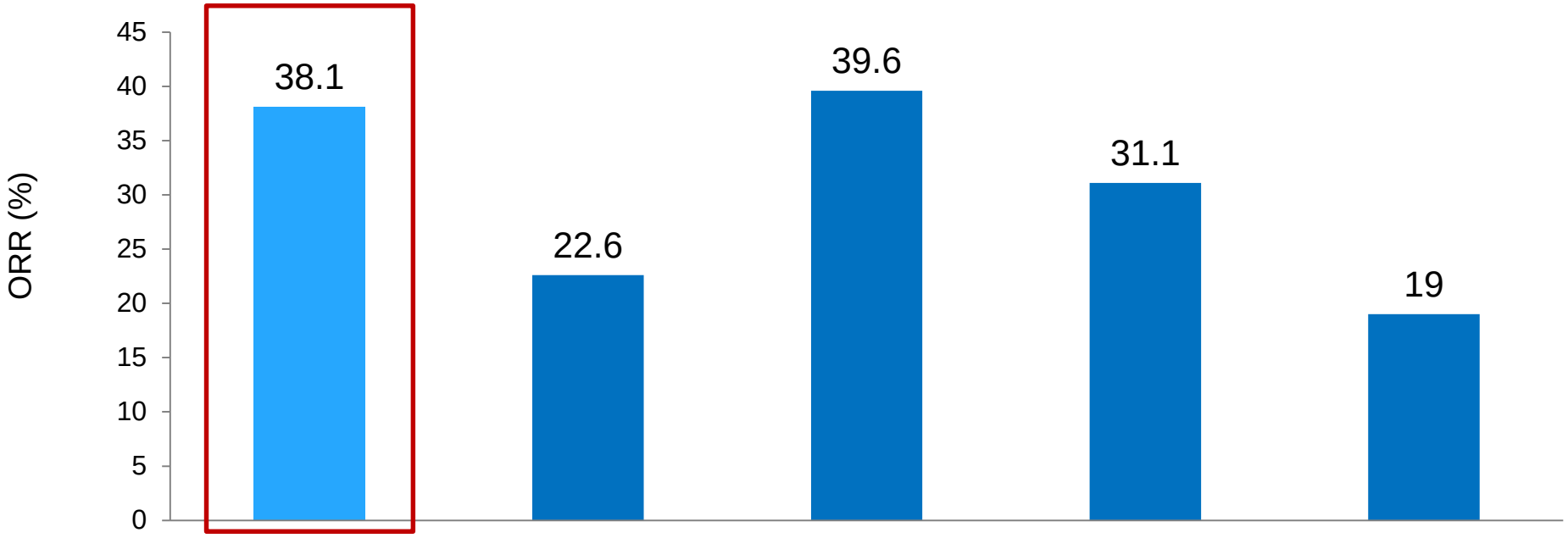


- 6 of 8 (75%) PR achieved at 1st post-baseline tumor assessment (week 9)
- 7 (87.5%) of 8 responders still on treatment
- Median DOR not reached, range (0.03+ ~ 8.6+) months

Data Cut off Date : 1 July 2019

4. CS1001 Monotherapy in MSI-H/dMMR Cancer (6/7)

Comparison with Other PD-(L)1s



	CS1001	Imfinzi	Keytruda	Opdivo	Tislelizumab
Class	PD-L1	PD-L1	PD-1	PD-1	PD-1
n	21	62	149	74	16
ECOG	0: 0 1: 100%	Not reported	0:36% 1:64%	0:43% 1:57%	Not reported
Regimen	1200mg iv q3w	10mg/kg q2w	200mg q3w /10mg/kg q2w	3mg/kg q2w	200mg q3w
DOR (m)	NR (0.03+, 8.6+)	Not reported	NR (1.6+, 22.7+)	NR	NR
Source	CSCO 2019	ASCO GI 2019	PI, 05/2017	Lancet Oncol 2017	CSCO 2019

4. CS1001 monotherapy in MSI-H/dMMR Cancer (7/7)

Conclusions

- CS1001 demonstrated promising antitumor activities in MSI-H/dMMR tumors with an ORR of 38.1%, data comparable to other PD-(L)1s
- The response is durable, median DOR not reached, 6 of 8 partial responses were continuing as of data cutoff
- CS1001 was safe and well tolerated
- Current data support further development of CS1001 for the treatment of pts with unresectable or metastatic MSI-H/dMMR cancer

Data Cut off Date： 1 July 2019

5.1 CS1001-301: Ph3 Trial in Stage III NSCLC

Trial in Progress Reported at CSCO 2019

- The is 1st PD-(L)1 study designed to investigate the efficacy of CS1001 as consolidation monotherapy in Chinese patients with stage III NSCLC
- The study explores its efficacy in a broader population, including pts after receiving either concurrent and sequential chemoradiotherapy

- Patients with stage III, locally advanced, unresectable NSCLC who have not progressed following definitive platinum-based chemoradiation therapy (≥ 2 cycles)
- ≥ 18 years old
- ECOG score 0 or 1
- Without EGFR mutation, ALK rearrangement and ROS1 rearrangement
- Tissues was required

R 2:1
N=402

CS1001 1200mg q3w
for up to 24 months

Placebo 1200mg q3w
for up to 24 months

Stratification Factors:

- **ECOG** (0 vs 1)
- **Radiation**
  (<60 Gy vs => 60 Gy)
- **Chemoradiation**
  (sequential vs concurrent)

Primary endpoints

- PFS (Inv)

Secondary endpoints

- OS
- PFS (BICR)
- ORR
- DoR
- TTDM
- Safety & tolerability
- PK

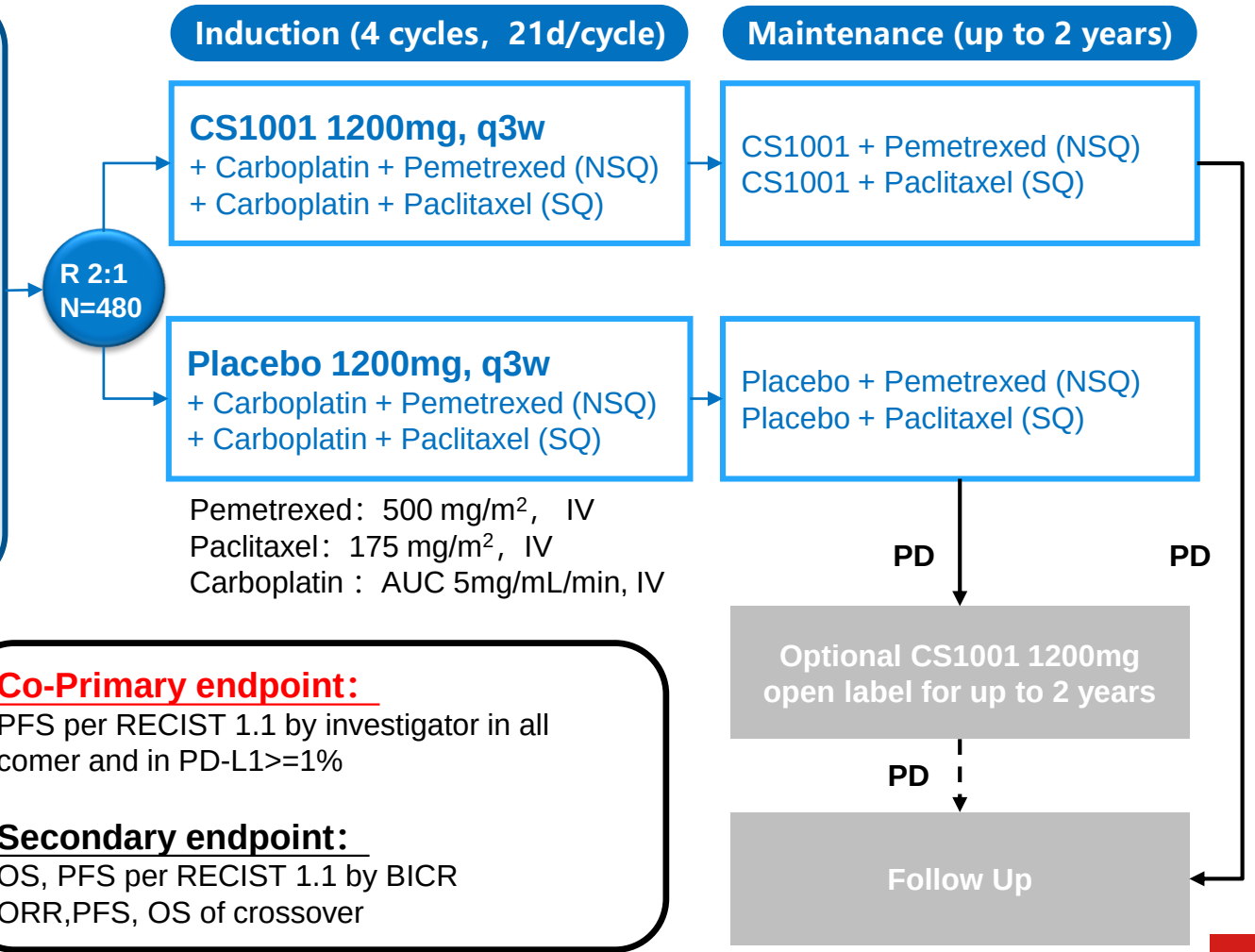
5.2 CS1001-302: Ph3 Trial for Stage IV NSCLC

Trial in Progress Reported at CSCO 2019

- The trial was designed to evaluate efficacy of CS1001 in combo with chemo as 1L treatment of both Sq and non-Sq stage IV NSCLC
- 1st domestic PD-L1 in a chemo comb Ph3 trial for 1L treatment of stage IV NSCLC

Key Eligibility Criteria:

- Untreated stage IV NSCLC
- Squamous and non-squamous
- Baseline measurable disease per RECIST v1.1
- All comer
- ECOG PS 0-1
- No sensitizing EGFR, ALK, ROS and RET
- No symptomatic brain metastases



Stratification Factors:

- SQ vs NSQ
- **PD-L1≥1% vs PD-L1<1%**
- **ECOG: 0 vs 1**

Co-Primary endpoint:

PFS per RECIST 1.1 by investigator in all comer and in PD-L1>=1%

Secondary endpoint:

OS, PFS per RECIST 1.1 by BICR
ORR,PFS, OS of crossover

Conclusion

- CS1001 monotherapy or combo with chemotherapy were safe and well tolerated in the reported cohorts.
- CS1001 monotherapy or combo with chemotherapy has demonstrated promising antitumor activity in multiple tumor types and the response is durable
  - CS1001 monotherapy demonstrated promising antitumor activities in MSI-H/dMMR solid tumor patients with an observed ORR of 38.1%.
  - CS1001 monotherapy demonstrated preliminary antitumor activities in CC/GBC patients with an observed ORR of 10.3%.
  - CS1001 combo with XELOX demonstrated promising antitumor activities in GC/GEJ patients, with an observed ORR of 62.1%
  - CS1001 combo with CF demonstrated promising antitumor activities in ESCC patients with an observed ORR of 77.8%
- These data together with reported phase Ia and undisclosed data support full development of CS1001 as mono/combo therapy for multiple indications in ongoing and planned clinical trials including GC, EC, and NSCLC
- Our Phase III trials in stage III and IV NSCLC is progressing according to or ahead of schedule.

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CTLA-4 & PD-1 DATA ANALYSIS

Archie Tse, MD, PhD, Chief Translational Medicine Officer

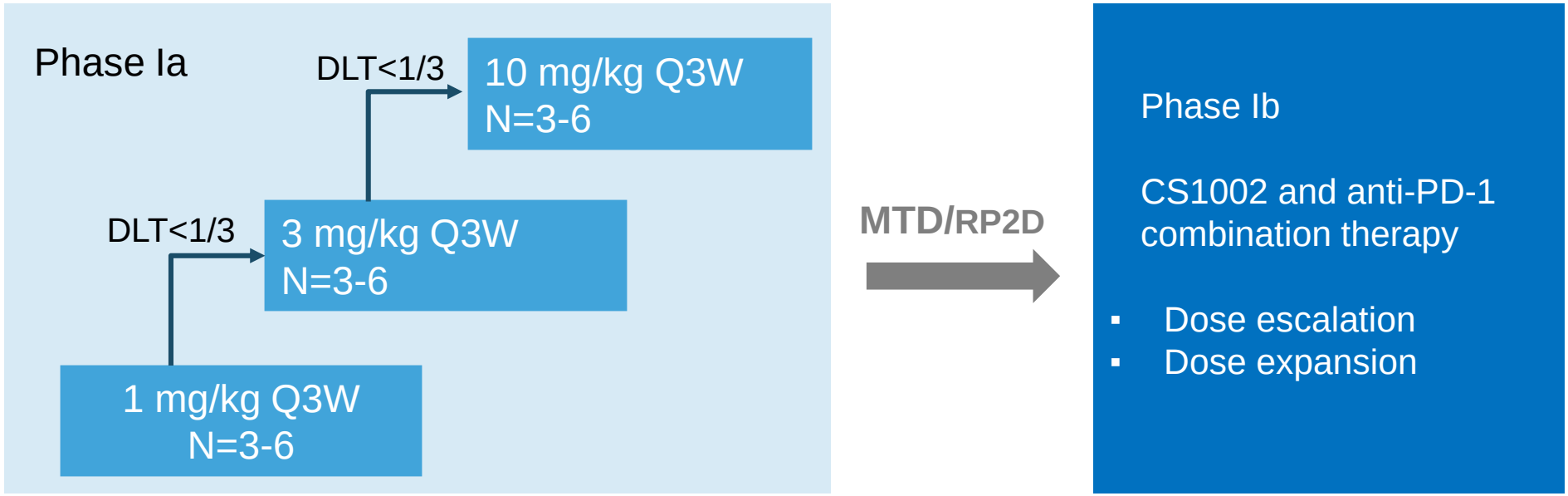
Table of Contents

CS1002 (anti-CTLA-4 mAb) Phase I Preliminary Safety and Pharmacokinetics (PK) Results in Advanced Solid Tumors

CS1002 Phase I Study Design

- **Objectives (Phase Ia)**
  - Safety and tolerability
  - MTD and Recommended phase II dose (RP2D) / Recommended combination dose

- **Study Design**



  - *3+3 dose escalation design*
  - *Dosage: induction Q3W, up to 4 doses; maintenance Q12W, up to 2 years*
  - *DLT evaluation conducted during the first cycle (21 day)*

DLT： dose-limiting toxicity； MTD: maximum tolerated dose; Q3W： once every 3 weeks; Q12W: once every 12 weeks

Demographics and Baseline Characteristics in Phase Ia

Characteristics	Safety Analysis Set (N=13)
Age (years), median (range)	58 (48-75)
Sex, n (%)	
Male	4 (30.8)
Female	9 (69.2)
Baseline ECOG, n (%)	
0	7 (53.8)
1	6 (46.2)
Prior anti-cancer therapy lines, median (range)	3.0 (1-6)

Colorectal cancer was the major cancer type enrolled in Ph Ia (n = 4); other enrolled cancer types included adenocarcinoma (n = 2); oesophageal adenocarcinoma, pleural mesothelioma, cholangiocarcinoma, pancreatic adenocarcinoma, prostate cancer, hepatocellular carcinoma, and gastrointestinal stromal tumor (n = 1 each)

Cut-off date: Apr 25th , 2019

Summary of Safety Data in Phase Ia

- No DLTs; MTD not reached
- Treatment-related treat-emergent adverse events (TEAEs) reported in 4 patients, including diarrhoea (15.4%), fatigue (15.4%), and alanine aminotransferase increased and aspartate aminotransferase increased (7.7%)
- Treatment-related Grade 3-5 TEAEs reported in 2 patients, diarrhoea (7.7%, Grade 3), and alanine aminotransferase increase (7.7%, Grade 3)
- irAEs reported in 2 patients, diarrhoea (7.7%), and fatigue (7.7%)
- No treatment-related SAE
- No treatment-related death
- No treatment-related AE leading to drug discontinuation

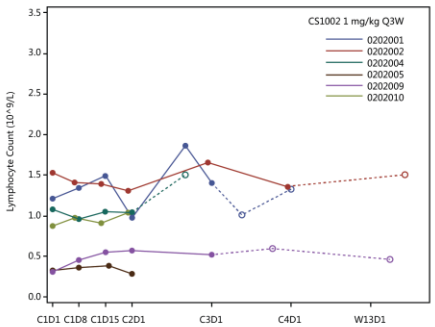
Cut-off date: Apr 25th , 2019

Pharmacodynamics and Efficacy of CS1002 in Phase Ia

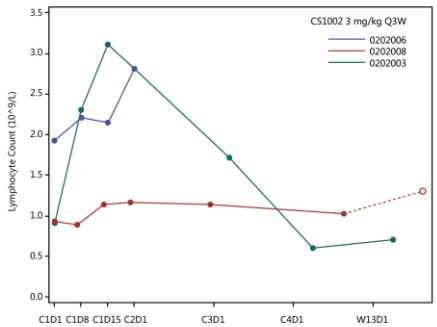
- **CS1002 induced an early increase in absolute lymphocyte count (ALC) during treatment (similarly to Ipilimumab)**
  - Early increase of ALC across all dose groups, indicating CS1002 functions similar to ipilimumab

CS1002

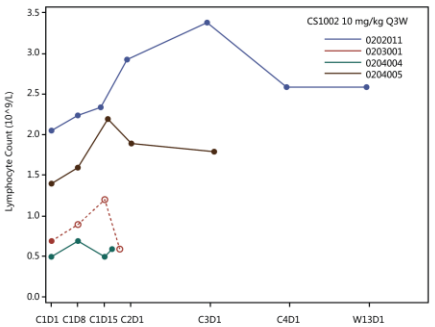
1 mg/kg (N=6)



3 mg/kg (N=3)

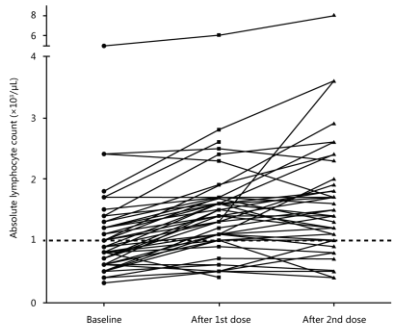


10 mg/kg (N=4)



Ipilimumab

10 mg/kg



- **9 patients were included for the tumor assessment in Phase Ia**
  - No complete response (CR) or partial response (PR), 2 stable disease
  - One cholangiocarcinoma patient is still on treatment with SD for 11 months since Oct., 2018

Martens A, *et al*. Clin Cancer Res. 2016, 22(19): 4848
Bjoern J, *et al*. OncoImmunology. 2016
Ku GY, *et al*. Cancer. 2010(116):1767

Cut-off date: Apr 25th , 2019

Conclusions

- CS1002 was well tolerated across dosage levels from 1 mg/kg to 10 mg/kg Q3W, with no reported DLT and treatment-related SAE
- MTD was not reached
- No clinical response was observed based on current data (not unexpected from anti-CTLA4 monotherapy and tumor types treated)
- CS1002 demonstrated dose-proportional PK profile with $T_{1/2}$ of 12~15 days
- Overall clinical profile is consistent with that of ipilimumab
- Future development will focus on combination with CS1003 (anti-PD-1 antibody) in subjects with solid tumors (Phase Ib)

CS1003 (anti-PD-1 mAb) Phase I Preliminary Safety, Pharmacokinetics, and Efficacy Results in Advanced Solid Tumors and Lymphoma in China

Phase I Development Plan of CS1003

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CS1003 Highlight

- Humanized IgG4 anti-PD-1 monoclonal antibody
- Recognize both human and murine PD-1, providing a unique advantage to evaluate efficacy in syngeneic mouse models, esp. for testing combo therapies

Objectives

Phase Ia: Dose Escalation

- Safety and tolerability
- Recommended Phase II Dose (RP2D)

Phase Ib: Indication Expansion

- Preliminary anti-tumor activity in selected tumor types
- Safety and efficacy data to support pivotal studies

First-in-Human Study

First patient enrolled in Australia in May 2018

CS1003-101

- 1 mg/kg Q3W
- 3 mg/kg Q3W
- 200 mg Q3W (Fixed Dose)
- 10 mg/kg Q3W

→

- Expand in patients with selected types of solid tumor at **200 mg Q3W**
- CS1003 monotherapy

China Phase I Bridging Study

First patient enrolled in China in Nov 2018

CS1003-102

- 60 mg Q3W (Fixed Dose)
- 200 mg Q3W (Fixed Dose)

→

- Expand in patients with selected types of solid tumor and lymphoma at **200 mg Q3W**
- CS1003 monotherapy or in combination with SoC

Q3W – Once every 3 weeks; SoC – Standard of Care

Demographics and Baseline Characteristics in CS1003-102 Phase Ia

Parameter, unit	60 mg (n=7)	200 mg (n=12)	Total (N=19)
Sex, n(%)			
Male	3 (42.9%)	6 (50.0%)	9 (47.4%)
Female	4 (57.1%)	6 (50.0%)	10 (52.6%)
Age, Years			
Mean (SD)	56.3 (9.62)	46.2 (15.50)	49.9 (14.24)
Median (range)	53.0 (41, 68)	50.5 (22, 66)	53.0 (22, 68)
ECOG Performance Status			
0	4 (57.1%)	1 (8.3%)	5 (26.3%)
1	3 (42.9%)	11 (91.7%)	14 (73.7%)
Prior systemic therapy, regimens			
1	4 (57.1%)	5 (41.7%)	9 (47.4%)
2	1 (14.3%)	2 (16.7%)	3 (15.8%)
>=3	2 (28.6%)	5 (41.7%)	7 (36.8%)

Data cut-off date： Jun 15, 2019

Treatment-Related Adverse Events (TRAEs) in CS1003-102 Phase Ia (≥10% or Grade ≥3)

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- DLT not observed at either dose level; MTD not reached; Median duration of treatment in 60 mg cohort was 9.1 weeks (range: 3-29.3) and in 200 mg cohort was 9 weeks (range: 4.9-21.7)

Event, n (%) MedDRA Preferred Term	60 mg (n=7)		200 mg (n=12)		Total (N=19)	
	All	Grade ≥3	All	Grade ≥3	All	Grade ≥3
Number of patients with at least one event	6 (85.7%)	1 (14.3%)	12 (100.0%)	2 (16.7%)	18 (94.7%)	3 (15.8%)
Asthenia	2 (28.6%)	0	3 (25.0%)	0	5 (26.3%)	0
Blood bilirubin increased *	1 (14.3%)	0	2 (16.7%)	1 (8.3%)	3 (15.8%)	1 (5.3%)
Hypothyroidism	2 (28.6%)	0	1 (8.3%)	0	3 (15.8%)	0
Anaemia	1 (14.3%)	0	2 (16.7%)	0	3 (15.8%)	0
Alanine aminotransferase increased	0	0	2 (16.7%)	0	2 (10.5%)	0
Aspartate aminotransferase increased *	0	0	2 (16.7%)	1 (8.3%)	2 (10.5%)	1 (5.3%)
Bilirubin conjugated increased	2 (28.6%)	0	0	0	2 (10.5%)	0
Blood lactate dehydrogenase increased	0	0	2 (16.7%)	0	2 (10.5%)	0
Hyperthyroidism	1 (14.3%)	0	1 (8.3%)	0	2 (10.5%)	0
Rash	2 (28.6%)	0	0	0	2 (10.5%)	0
Blood alkaline phosphatase increased *	0	0	1 (8.3%)	1 (8.3%)	1 (5.3%)	1 (5.3%)
Gamma-glutamyltransferase increased *	0	0	1 (8.3%)	1 (8.3%)	1 (5.3%)	1 (5.3%)
White blood cell count increased #	1 (14.3%)	1 (14.3%)	0	0	1 (5.3%)	1 (5.3%)
Diarrhoea ※	0	0	1 (8.3%)	1 (8.3%)	1 (5.3%)	1 (5.3%)
Hyponatraemia *	0	0	1 (8.3%)	1 (8.3%)	1 (5.3%)	1 (5.3%)

1 patient experienced one grade 4 white blood cell count increased#, reported as SAE; 1 patient had one grade 3 diarrhoea※, reported as SAE; 1 patient experienced grade 3 ALP increased*, grade 3 AST increased*, grade 3 GGT increased*, grade 3 blood bilirubin increased*, and grade 3 hyponatraemia (n=1 each); Other TRAEs were CTCAE grade 1-2

Data cut-off date: Jun 15, 2019; MedDRA version 22.0; CTCAE version 4.03

Immune-Related Adverse Events (irAEs) in CS1003-102 Phase Ia (≥10% or Grade ≥3)

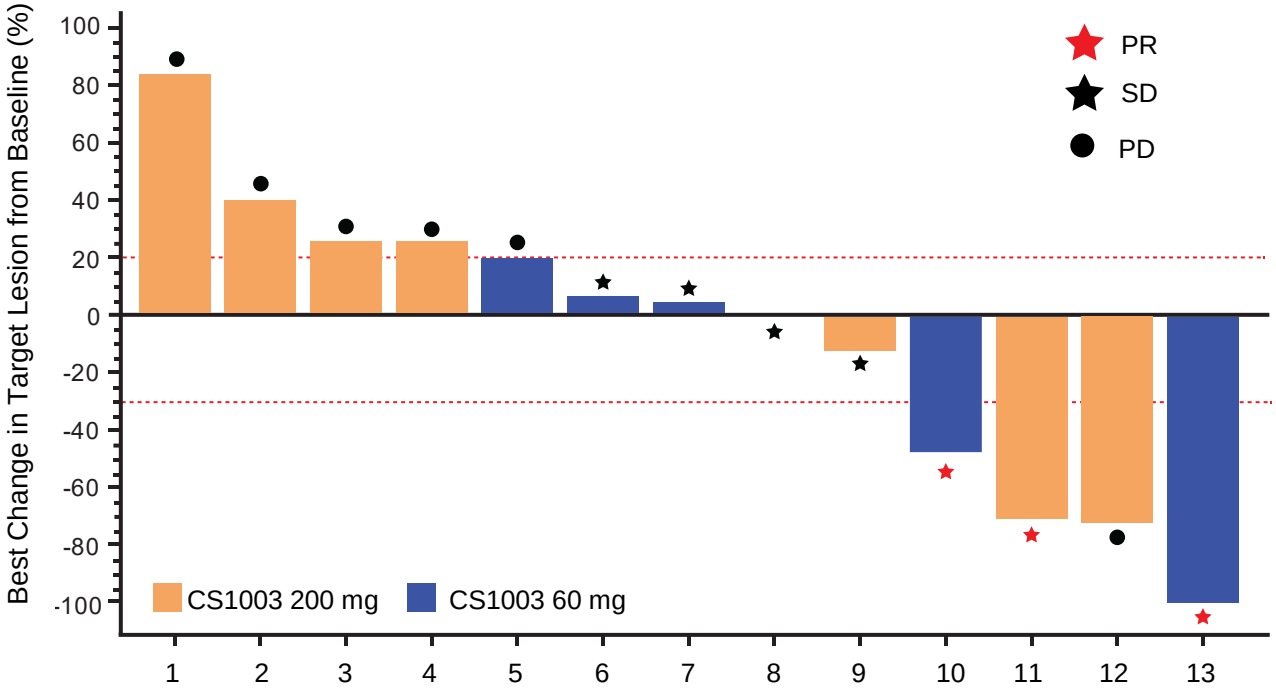
Event, n (%) MedDRA Preferred Term	Total (N=19)	
	All	Grade ≥3
Number of patients with at least one irAE	9 (47.4%)	3 (15.8%)
Asthenia	3 (15.8%)	0
Hypothyroidism#	3 (15.8%)	0
Hyperthyroidism#	2 (10.5%)	0
Rash	2 (10.5%)	0
Aspartate aminotransferase increased*	1 (5.3%)	1 (5.3%)
Gamma-glutamyltransferase increased*	1 (5.3%)	1 (5.3%)
Blood bilirubin increased*	1 (5.3%)	1 (5.3%)
White blood cell count increased	1 (5.3%)	1 (5.3%)
Diarrhoea	1 (5.3%)	1 (5.3%)

Out of 19 subjects who received CS1003 treatment, 9 subjects experienced at least one irAE; The most frequent irAEs included: asthenia (n=3), hypothyroidism (n=3), hyperthyroidism (n=2), rash (n=2)

1 subject with oesophageal squamous cell carcinoma experienced a grade 1 hyperthyroidism#, followed by a grade 2 hypothyroidism#; 1 subject with small intestine carcinoma experienced grade 3 AST increased*, grade 3 GGT increased*, and grade 3 blood bilirubin increased* (n=1 each)

Data cut-off date: Jun 15, 2019; MedDRA version 22.0; CTCAE version 4.03

Preliminary Efficacy Data in CS1003-102 Phase Ia



1=Squamous cell carcinoma of the cervix ; 2=Synovial sarcoma ; 3=Hepatocellular carcinoma ; 4=Gastric adenocarcinoma; 5=Leiomyosarcoma; 6=Malignant melanoma; 7= Leiomyosarcoma; 8= Fibromatosis; 9= Follicular dendritic cell sarcoma; 10=Uterine Leiomyosarcoma; 11= Laryngeal squamous cell carcinoma; 12= Oesophageal squamous cell carcinoma; 13= Oesophageal squamous cell carcinoma.

Best Overall Response (BOR), n (%)	Total (N=16*)
Partial Response (PR)†	3 (18.8%)
Stable Disease (SD)	4 (25.0%)
Progressive Disease (PD)‡	6 (37.5%)
Not Evaluable §	3 (18.8%)

* Among 19 patients enrolled in Phase Ia study, 16 patients were included in the efficacy analysis set while 3 patients were excluded due to absence of measurable disease at baseline (n=1) or because patients remained on treatment as of data cut off date but had not reached 1st post-baseline tumor assessment (n=2)

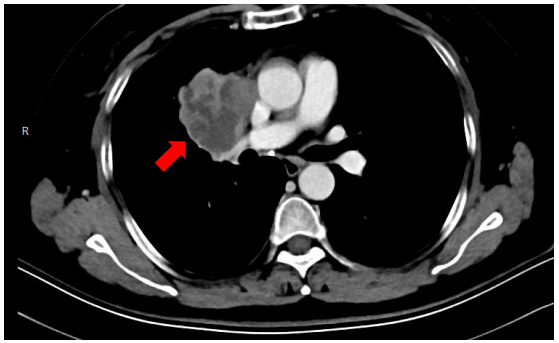
† Per RECIST v1.1, two patients from 60 mg cohort were evaluated as confirmed PR (No. 13 oesophageal squamous cell carcinoma and No. 10 uterine leiomyosarcoma in above waterfall plot); one patient from 200 mg cohort was evaluated as PR awaiting confirmation (No. 11 laryngeal squamous cell carcinoma in above waterfall plot)

‡ One patient with oesophageal squamous cell carcinoma from 200 mg cohort (No. 12 in above waterfall plot) was evaluated as PD in 1st post-baseline tumor assessment and continuously received CS1003 beyond progression; tumor reduction compared to baseline was observed in the following tumor assessment, and the patient remained on treatment as of data cut off date; however, according to RECIST v1.1, BOR was still PD

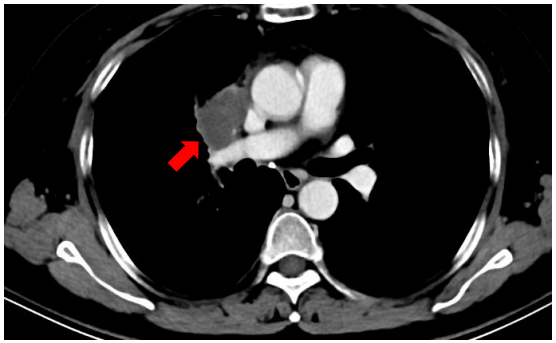
§ Three patients were discontinued from CS1003 treatment without evaluable post-baseline tumor assessment results, hence BOR was "not evaluable"

Data cut-off date： Jun 15, 2019

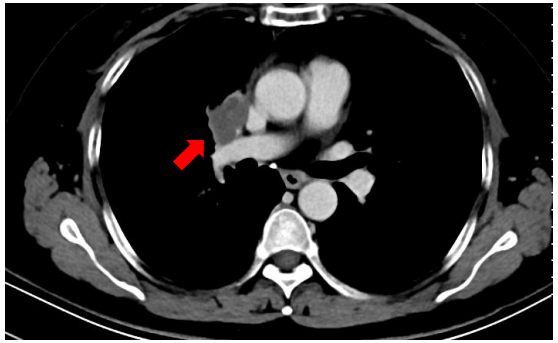
Representative CT Scan Images of Responders



Baseline

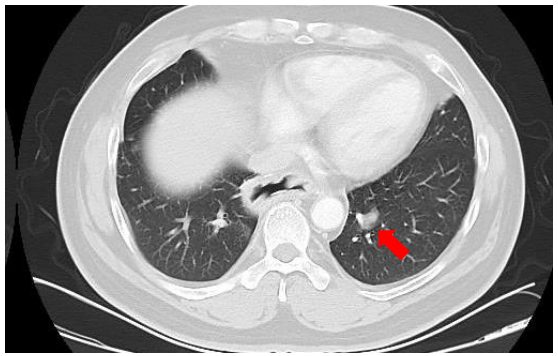


9 weeks - PR

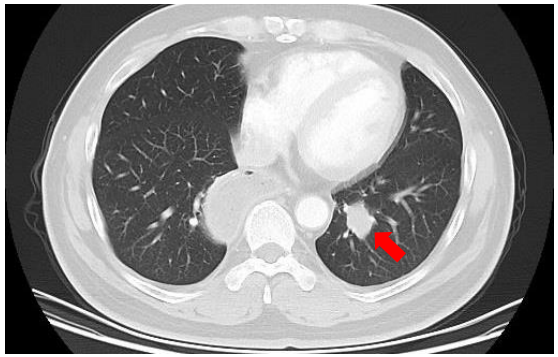


18 weeks - PR

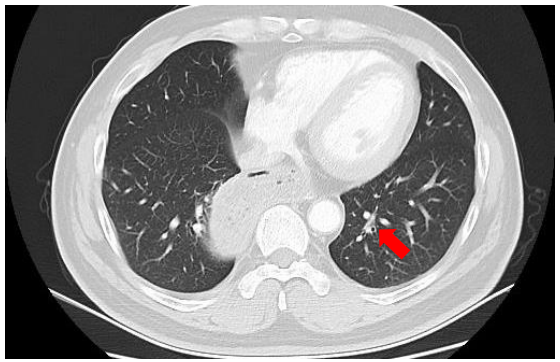
Female, 53 years old, uterine leiomyosarcoma with right mediastinal metastasis, stage IV; 60 mg Q3W cohort; As of data cut off date, 9 cycles of CS1003 treatment have been completed, and the patient remained on treatment



Baseline



10 weeks - PD



19 weeks - Tumor Reduction

Male, 52 years old, oesophageal squamous cell carcinoma with lung metastasis, stage IV; 200 mg Q3W cohort; According to RECIST v1.1, patient was evaluated as PD in 1st post-baseline tumor assessment and continuously received CS1003 beyond progression; tumor reduction was observed in the following tumor assessment; As of data cut off date, 8 cycles of CS1003 treatment have been completed, and the patient remained on treatment

Data cut-off date: Jun 15, 2019

Conclusions

- CS1003 cross-reactivity with mouse PD-1 could facilitate proof-of-concept evaluation of combination therapies in syngeneic mouse models, enabling, e.g. upcoming clinical studies of CS1003 in combination with CDK4/6 inhibitor or TKI
- CS1003 appeared tolerable and safe; no DLT or MTD was observed
- Preliminary anti-tumor activity of CS1003 has been observed in multiple tumor types
- Dose proportional increase in systemic exposure to CS1003 was observed in China Phase I clinical study, and the PK profile of CS1003 was comparable between patients in China and in Australia
- Preliminary ADA data suggested low immunogenicity of CS1003, treatment-induced/-enhanced ADA positivity was not observed after CS1003 administration
- Current safety and efficacy data support further clinical development of CS1003

CStone combination strategy and near-term development

Global Collaboration Deal with Bayer to Evaluate PD-L1 in Combination with Regorafenib in Key Indications e.g. GC

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BAYER

PD-L1 + Stivarga (regorafenib) tablets

Highlights

- First collaboration with a MNC pharma, one of the very few without PD-(L)1 – a vote of confidence in CStone and CS1001
- Global collaboration deal with China focus in key indications such as gastric cancer

Strategic Value

- Further strengthens our core strategy in IO combination therapy
- A big step forward for CStone's global strategy in case of positive data

Regorafenib reported promising data with PD-1 in gastric cancer and colorectal cancer at 2019 ASCO

Indication	Mono/Combo	ORR
Advanced GC	Pembro	13%[1]
	Rego + Nivo	**44%[2]**
pMMR/MSS CRC (95% of mCRC)	Pembro	0%[3]
	Rego	2%[4]
	Atezo	2%[4]
	Atezo + MEK	3%[4]
	Rego + Nivo	**33%[2]**

Note: 1. KEYNOTE059; 2. 2019 ASCO data, All respondents were Microsatellite stable (MSS); 3. 2015 ASCO data; 4. IMBlaze370
pMMR = mismatch repair proficient

Sizable Portfolio Anchored Around 3 IO Backbone Agents to Drive Differentiated Combo Strategy

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3 IO backbone agents

- Only company in China owns clinical stage ***PD-L1, PD-1 and CTLA-4***

15 assets in the pipeline

- ***10*** in-house developed de-risked assets plus ***5*** in-licensed FIC/BIC assets

1 potential 2nd generation of PD-(L)1

- ***PD-L1x4-1BB*** *provides more flexible* combo and potential better efficacy

De-risked Combo

- PD-(L)1 + Regorafenib
- PD-1 + CS1002 (CTLA-4)
- PD-L1 + IMP4297
- PD-(L)1 + Donafenib

Novel Combo Unique to CStone

- PD-L1 + Fisogatinib (FGFR4)
- PD-L1 + CS3002 (CDK4/6)*
- PD-1 + Ivosidenib (IDH1)*
- Potentially more…

Multi-specific

- NM21-1480 (PD-L1 x 4-1BB)
- Potentially more…

8 combo programs with **10+** combo studies cross multiple indications by **2019 year-end**

** FPFD 4Q2020 or 1Q2021*

RESEARCH UPDATE

Jon Wang, PhD, Chief Scientific Officer

Pipeline 2.0 for Sustained Growth of CStone

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Pipeline 1.0 → **GAP Analysis** → **Pipeline 2.0**

Balanced Portfolio

- De-risked I/O Backbone & Assets
- Precision Medicine
- Validated & Novel I/O Combination

New Targets

- "Practice changing" potential?
- Convincing combo activity with PD-(L)1 or pipeline 1.0 candidates?
- "Disruptive" biology?

Advanced Portfolio

- Novel pathway with potentially disruptive biology
- FIC/FW or BIC multispecific mAbs/scaffolds
- Cancer vaccines

Dual Sources of Innovation

Internal Development

External Partnerships

- KOL Connections
- Database
- R&D / Partnership Meetings
- Literature
- Academia Network

Note: FIC = first in class; FW = first wave; BIC = best in class; TME = tumor microenvironment.

Current Pre-clinical Pipeline

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Drug Candidate	Target	Project Initiation / Lead Identification / Lead Optimization / Lead Nomination / PCC / Preclinical	IND/CTN
CS3002	CDK4/6		2019 (AUS)
CS3005	To be disclosed		Dec 2019
ND021	PD-L1/4-1BB/HSA		Q1 2020
CS1009	To be disclosed		Q2 2021
	Target 1		TBD
	Target 2		TBD
	Target 3		2022
	Target 4		2022
	Target 5		2022
	And more…	At various stages	2022

Challenges and Unmet Needs of Immunotherapy

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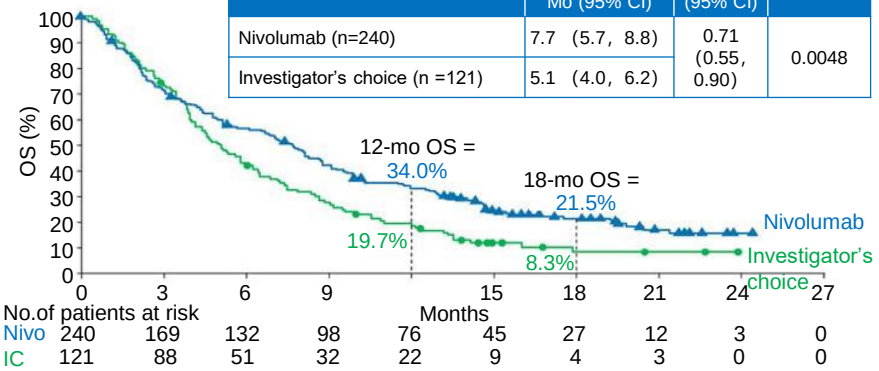
Low ORR in unselected populations

Agent	NSCLC Histology	PD-L1 positivity	ORR
Ipilimumab (phased with carboplatin/paclitaxel)	Any	N/A	32% vs. 18%
Nivolumab	Any	50%	18%
BMS-936559	Any	NA	10%
Nivolumab	Squamous	29%	15%
Nivolumab	Squamous	assessed at 1, 5 and 10% cutoffs	20% (vs. 9% docetaxel)
Nivolumab	Nonsquamous	assessed with no clear association with response	17%
Pembrolizumab	Any	23.2% positive with 22C3 PD-L1 >50% staining	19.4% overall; 45.2% in PD-L1+
Atezolizumab	Any	26% positive with SP142 >5% staining	23% (83% in PD-L1 IC3 patients)

Low overall survival rate

CheckMate 141: Nivolumab in R/M Head and Neck Squamous Cell Carcinoma after Platinum Therapy

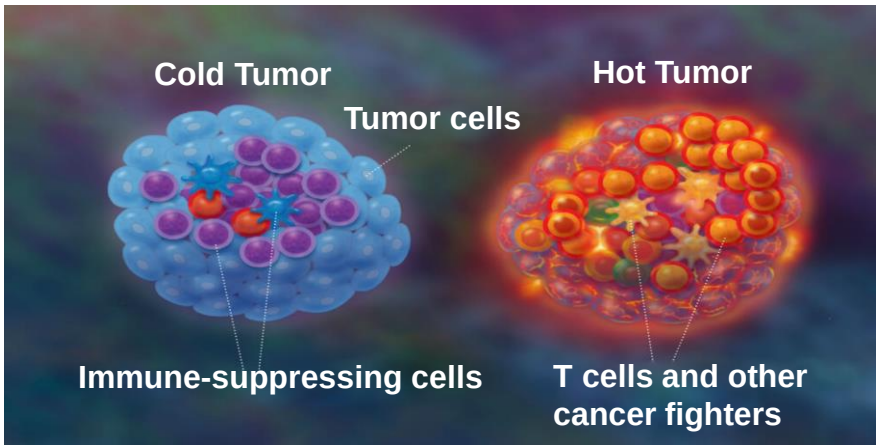
	Median OS, Mo (95% CI)	HR (95% CI)	*P* value
Nivolumab (n=240)	7.7 (5.7, 8.8)	0.71 (0.55, 0.90)	0.0048
Investigator's choice (n =121)	5.1 (4.0, 6.2)		



Failed in 2L HCC, TNBC, 1L GC

PD-1/PD-L1 failed pivotal studies			
Indication	**Keytruda**	**Opdivo**	**Tecentriq**
NSCLC		CM-026 (1L)	IMpower131 (1L)
SCLC		CM-451 (1L) CM-331 (2L)	
HCC	KN-240 (2L)	CM-459 (1L)	
GC	KN-061 (2L) KN-062 (1L)		
TNBC	KN-119 (2L)		
CRC			Imblaze370 (3L)

Cold tumor remains a challenge for I/O



[1] *Patel SP. Immune checkpoint blockade for lung cancer: state of the art. Transl Cancer Res 2015;4(4)*
[2] *ESMO 2017: Nivolumab Demonstrates Antitumour Activity Post-progression in Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma.*
[2] *https://mp.weixin.qq.com/s/-2EPxsoRh6AB3xIhtR9oGQ*
4 https://blog.dana-farber.org/insight/2018/06/enhancing-immunotherapy-race-make-cold-tumors-hot/

Strategies to Combat Resistance to Immunotherapy

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1) New MoA & Modality

- ICI + novel target
- Multi-specific biologics
  (PD-L1 x 4-1BB x HSA)

ND021
Target #5 &
Early Eval.

2) Modulate TME

- ICI + cytokines
- ICI + NK cell activators
- ICI + MDSC inhibitors
- ICI + anti-angiogenic agents

CS3005
Target #1, #2

3) Improve Immune cell activity

- ICI + immune stimulatory
- (4-1BB, OX40, ICOS)
- ICI + adaptive cell transfer
- ICI + Macrophage activators
- ICI + epigenetic modulation

CS1009
Target #3, #4

4) Enhance antigenicity

- ICI + chemotherapy
- ICI + radiation
- ICI + target therapies
- ICI + cancer vaccines
- ICI + oncolytic viruses

Targets #6-8
Early Eval.

2019 ASCO Annual Meeting, Pradnya, The Next Frontier: Understanding and Overcoming Resistance to Targeted Therapy and Immunotherapy

Focus Areas – Cancer Vaccine and Novel Biology

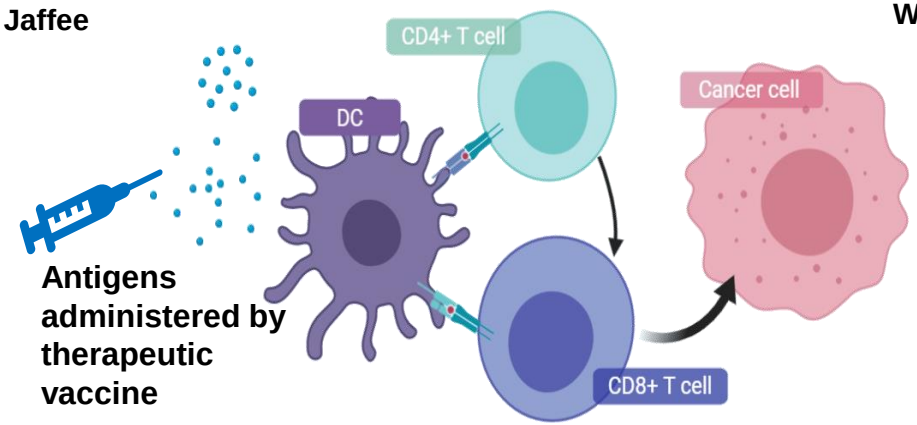
- **GAP Analysis**
  - Identify new targets with novel biology
  - Deeply understand the pathway
- **CStone Project Nomination**
  - Work with academic lab/industrial partners on their promising technology/platform
- **BD Effort**
  - Seek opportunities with FIC/FW potential

Cancer Vaccines

Elizabeth Jaffee MD

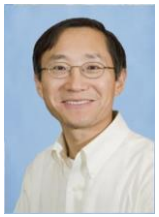
Internal Development

External Partnerships

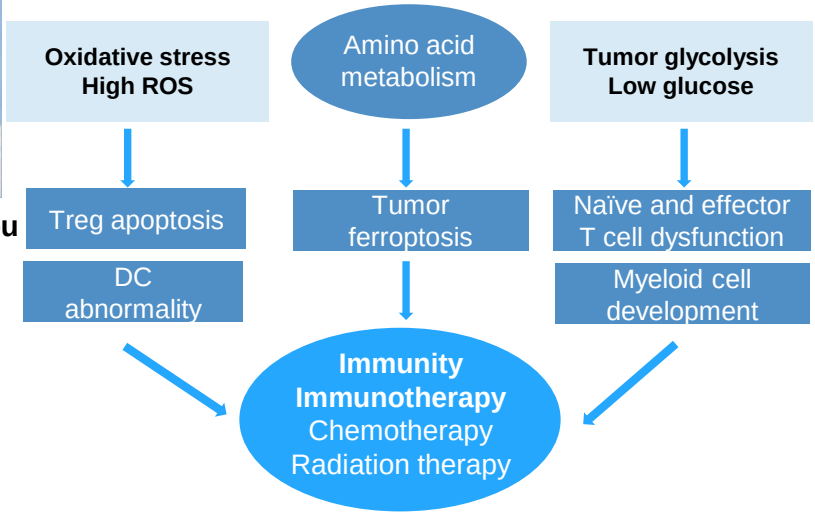


Antigens administered by therapeutic vaccine

Novel Biology



Weiping Zou MD, PhD



Targeting **ferroptosis pathway** may sensitize and improve immunotherapy efficacy

L Jiang et al. Ferroptosis as a p53-mediated activity during tumour suppression Nature 2015, 520: 57–62

ND021 (PD-L1x4-1BBxHSA) Has the Potential to be the BIC Molecule as the Next Generation PD-(L)1 Inhibitors

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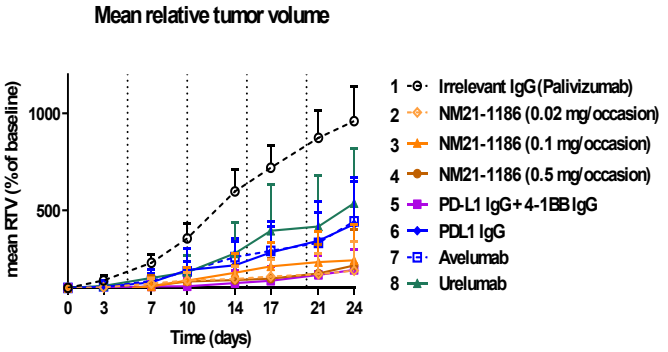
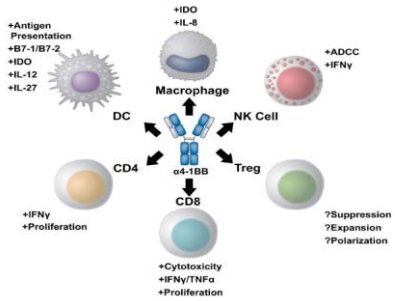
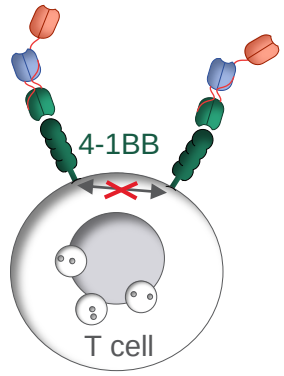
- Bridge new biology
- Improve therapeutic index & reduce unwanted toxic effects
- Expand combo options & improve administration convenience

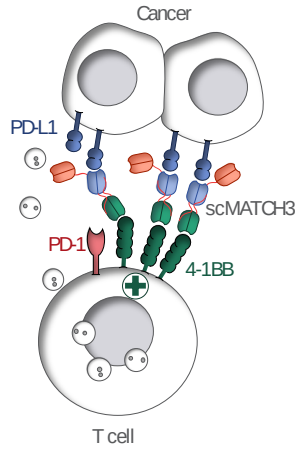
Six key features of ND021

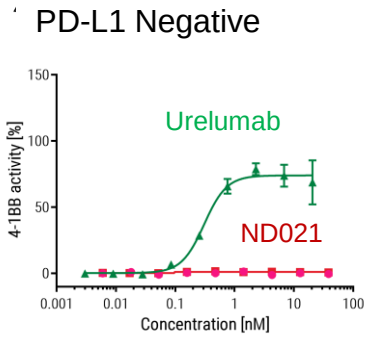
- Combination therapy in one molecule
  →expands combo options with SoC and other ICIs
- Monovalent 4-1BB binding remains inactive until PD-L1 engagement
  →maximizes safety
- Ultra-high affinity (pM) to PD-L1
  →broadens PD-L1+ tumor types
- Standard affinity to 4-1BB (nM)
  →ensures effective activation
- HSA extends T1/2 & 100% effector null
  →enables convenient dosing & eliminated undesirable FcgR-mediated activation
- MW ~70kDa, only half of conventional mAb
  →leads to better tumor penetration & efficacy

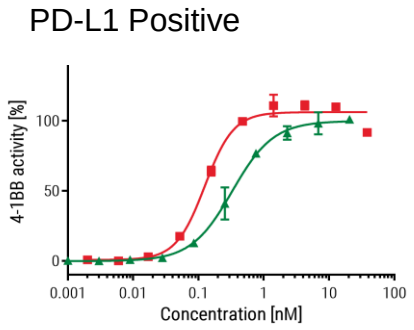












Leverage the Ecosystem Centered around Our Suzhou Translational Medicine Research Center (TMRC)

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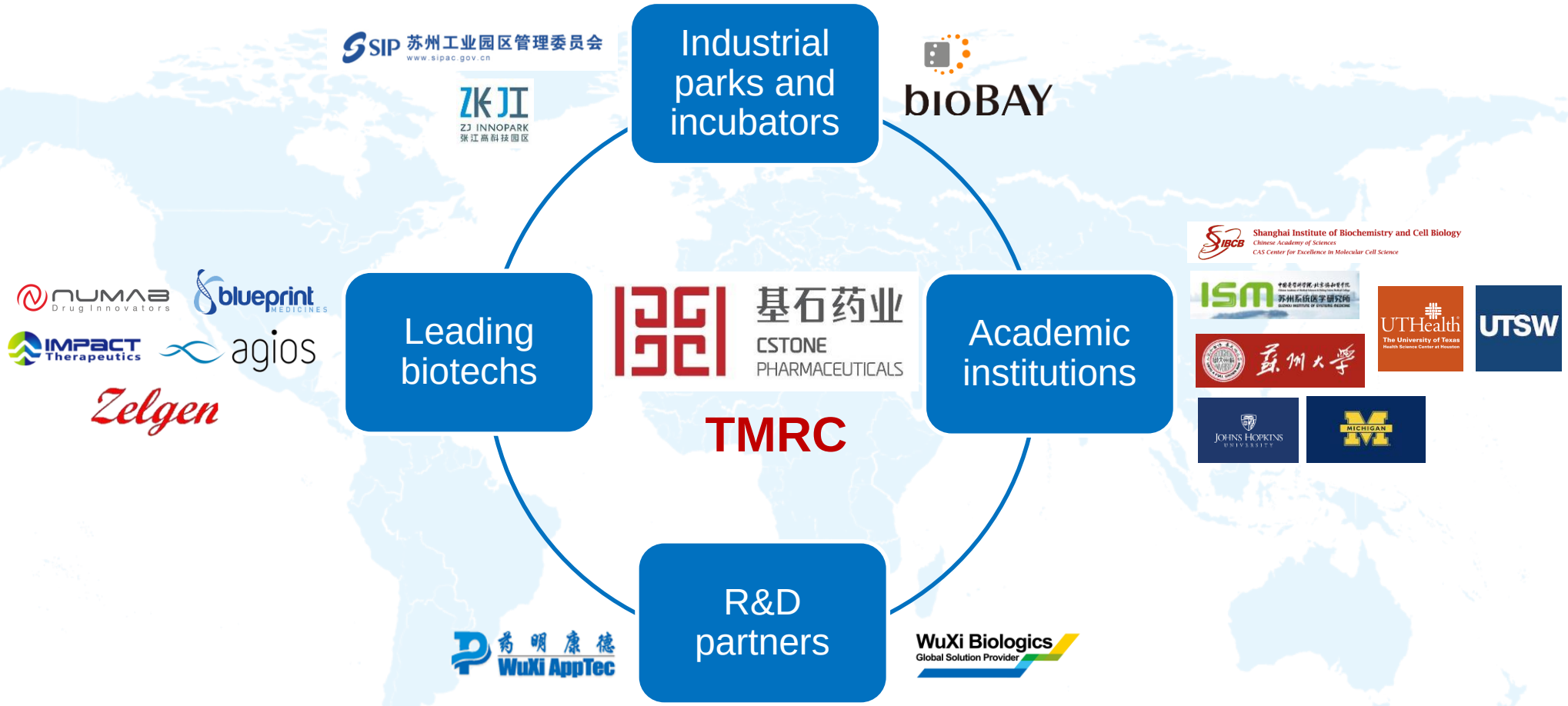

Target to deliver 1-2 new molecules INDs per year!

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Thank you!

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Q & A