Preliminary Safety, Pharmacokinetics and Efficacy Results from a Phase I Study of CS1001, a Fully Human Anti-PD-L1 Monoclonal Antibody in Patients With Advanced Tumors (GEMSTONE 101)

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CS1001: The First Full-Length, Fully Human Anti-PD-L1 Monoclonal Antibody in China

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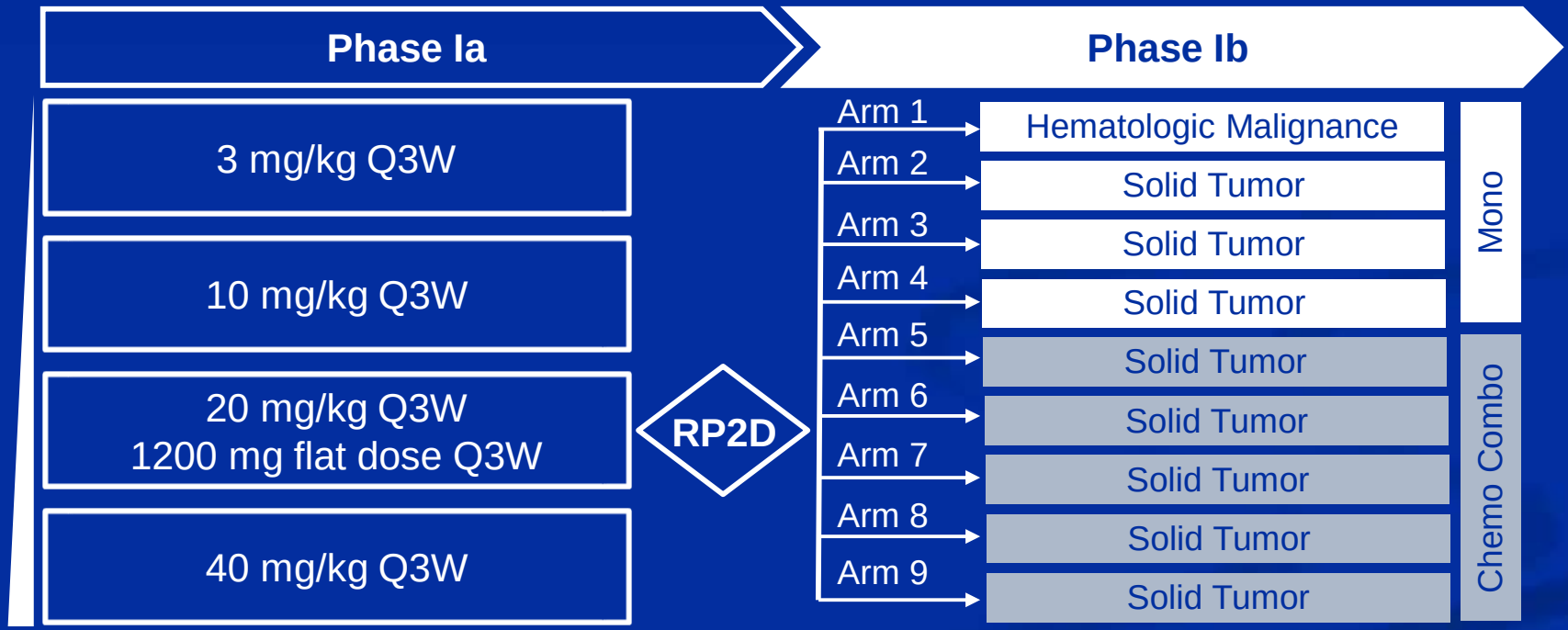
- **Innovative molecule – wholly owned by CStone**
- **One-step all-human antibody discovered using OMT's OmniRat platform**
  - Potentially less immunogenic
  - Industry's first fully human monoclonal antibody platform using transgenic rat
- **IgG4 subtype**
  - Classical IgG4 PK profile
  - No ADCC to PD-L1 expressing immune cells

GEMSTONE 101 Study Design

- **Phase Ia: Dose escalation**
  - Safety and tolerability & Recommended phase II dose (RP2D)
- **Phase Ib: Indication expansion**
  - Exploring activity in various tumor types
  - Safety and efficacy data to support pivotal studies



Phase 1a:
- *3+3 dose escalation*
- *RP2D was further confirmed in 12 patients*
- *29 patients have been enrolled*

Phase 1b:
- *35 patients have been enrolled as of Sep 7th, 2018*

Cut-off date: July 20th , 2018

Demographics and Baseline Characteristics in Phase Ia

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Characteristics	Safety analysis set (N=29)
Median age, years (range)	53 (23-75)
Sex, n (%)	
Male	19 (65.5)
Female	10 (34.5)
Baseline ECOG, n (%)	
0	4 (13.8)
1	25 (86.2)
Prior anti-cancer therapy lines, median (range)	2.0 (0-7)

Cut-off date: July 20th , 2018

Tumor Types Enrolled in Phase Ia

Tumor types	n (N=29)	Tumor types	n (N=29)
Classical Hodgkin lymphoma (cHL)	5	Middle and low differentiated adenocarcinoma of ampulla	1
Colorectal cancer (CRC)	4	Mixed histology of esophagus cancer and malignant melanoma	1
Gastric cancer (GC)	3	Salivary gland carcinoma	1
Gastrointestinal stromal tumors (GIST)	2	Ovarian mucinous cystadenoma	1
Cholangiocarcinoma	1	Primary malignant neuroectodermal tumor of the Ileum	1
Cervical cancer	1	Intrahepatic bile duct cancer recurrent	1
Non-small cell lung cancer (NSCLC)	1	Jejunum adenocarcinoma	1
Nasopharyngeal cancer	1	Abdominal wall sarcoma	1
Melanoma	1	Appendix mucinous adenocarcinoma	1
Breast cancer	1		

Cut-off date: July 20th , 2018

Treatment-Emergent Adverse Events (TEAE) in Phase Ia (all grades ≥10% or any grade ≥3)

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Event, n (%)	3 mg/kg (N=3)	10 mg/kg (N=4)	20 mg/kg (N=3)	1200 mg (N=16)	40 mg/kg (N=3)	Total	
						All grades (N=29)	Grade ≥3 (N=29)
Anaemia	3 (100)	1 (25.0)	1 (33.3)	7 (43.8)	0	12 (41.4)	1 (3.5)
Proteinuria	1 (33.3)	2 (50.0)	1 (33.3)	3 (18.8)	1 (33.3)	8 (27.6)	0
Blood bilirubin increased	2 (66.7)	0	1 (33.3)	2 (12.5)	1 (33.3)	6 (20.7)	0
White blood cell count decreased	1 (33.3)	0	1 (33.3)	2 (12.5)	1 (33.3)	5 (17.2)	0
Aspartate aminotransferase increased	2 (66.7)	0	1 (33.3)	2 (12.5)	0	5 (17.2)	0
Decreased appetite	2 (66.7)	0	2 (66.7)	1 (6.3)	0	5 (17.2)	0
Nausea	2 (66.7)	1 (25.0)	1 (33.3)	0	0	4 (13.8)	0
Bilirubin conjugated increased	2 (66.7)	0	1 (33.3)	0	1 (33.3)	4 (13.8)	1 (3.5)
Alanine aminotransferase increased	1 (33.3)	0	1 (33.3)	2 (12.5)	0	4 (13.8)	0
Cough	1 (33.3)	0	0	3 (18.8)	0	4 (13.8)	0
Blood creatine phosphokinase increased	0	1 (25.0)	0	2 (12.5)	0	3 (10.3)	1 (3.5)
Vomiting	0	2 (50.0)	1 (33.3)	0	0	3 (10.3)	0
Rash	1 (33.3)	0	1 (33.3)	0	1 (33.3)	3 (10.3)	0
Platelet count decreased	0	0	1 (33.3)	0	0	1 (3.5)	1 (3.5)
Bone pain	0	1 (25.0)	0	0	0	1 (3.5)	1 (3.5)
Hepatic function abnormal	0	0	0	1 (6.3)	0	1 (3.5)	1 (3.5)
Pulmonary tuberculosis	0	0	0	1 (6.3)	0	1 (3.5)	1 (3.5)
Ascites	0	1 (25.0)	0	0	0	1 (3.5)	1 (3.5)
Gastric haemorrhage	0	1 (25.0)	0	0	0	1 (3.5)	1 (3.5)

Cut-off date: July 20th , 2018

Treatment-Related Adverse Events (TRAE) in Phase Ia

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- As of July 20th, 2018, a total of 29 patients in Phase Ia were treated with CS1001 across 5 dose cohorts
- No dose-limiting toxicity (DLT) was observed, and the maximum tolerated dose (MTD) was not reached
- No drug-related pneumonia
- No drug-related SAE
- No drug-related death

Event, n (%)	All grades (N=29)	Grade ≥3 (N=29)
Anaemia	12 (41.4)	1 (3.5)
Proteinuria	7 (24.1)	0
Blood bilirubin increased	6 (20.7)	0
Aspartate aminotransferase increased	5 (17.2)	0
Decreased appetite	5 (17.2)	0
Alanine aminotransferase increased	4 (13.8)	0
Bilirubin conjugated increased	4 (13.8)	0
White blood cell count decreased	4 (13.8)	0
Nausea	4 (13.8)	0
Rash	3 (10.3)	0
Platelet count decreased	1 (3.5)	1 (3.5)

Cut-off date: July 20th , 2018

Immune-Related Adverse Events (irAE) in Phase Ia

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- As of July 20th, 2018, irAEs were reported in 4 patients, including endocrine disorders (10.3%), skin and subcutaneous tissue disorders (6.9%), and investigations (3.4%)

System organ class Preferred term, n (%)	Total (N=29)
Endocrine disorders	3 (10.3)
Hypothyroidism	2 (6.9)
Adrenal insufficiency	1 (3.4)
Hyperthyroidism	1 (3.4)
Skin and subcutaneous tissue disorders	2 (6.9)
Rash	1 (3.4)
Rash pruritic	1 (3.4)
Investigations	1 (3.4)
Blood thyroid stimulating hormone decreased	1 (3.4)
Thyroxine free increased	1 (3.4)
Tri-iodothyronine free increased	1 (3.4)

Cut-off date: July 20th , 2018

Best Objective Responses (BOR) in Phase Ia

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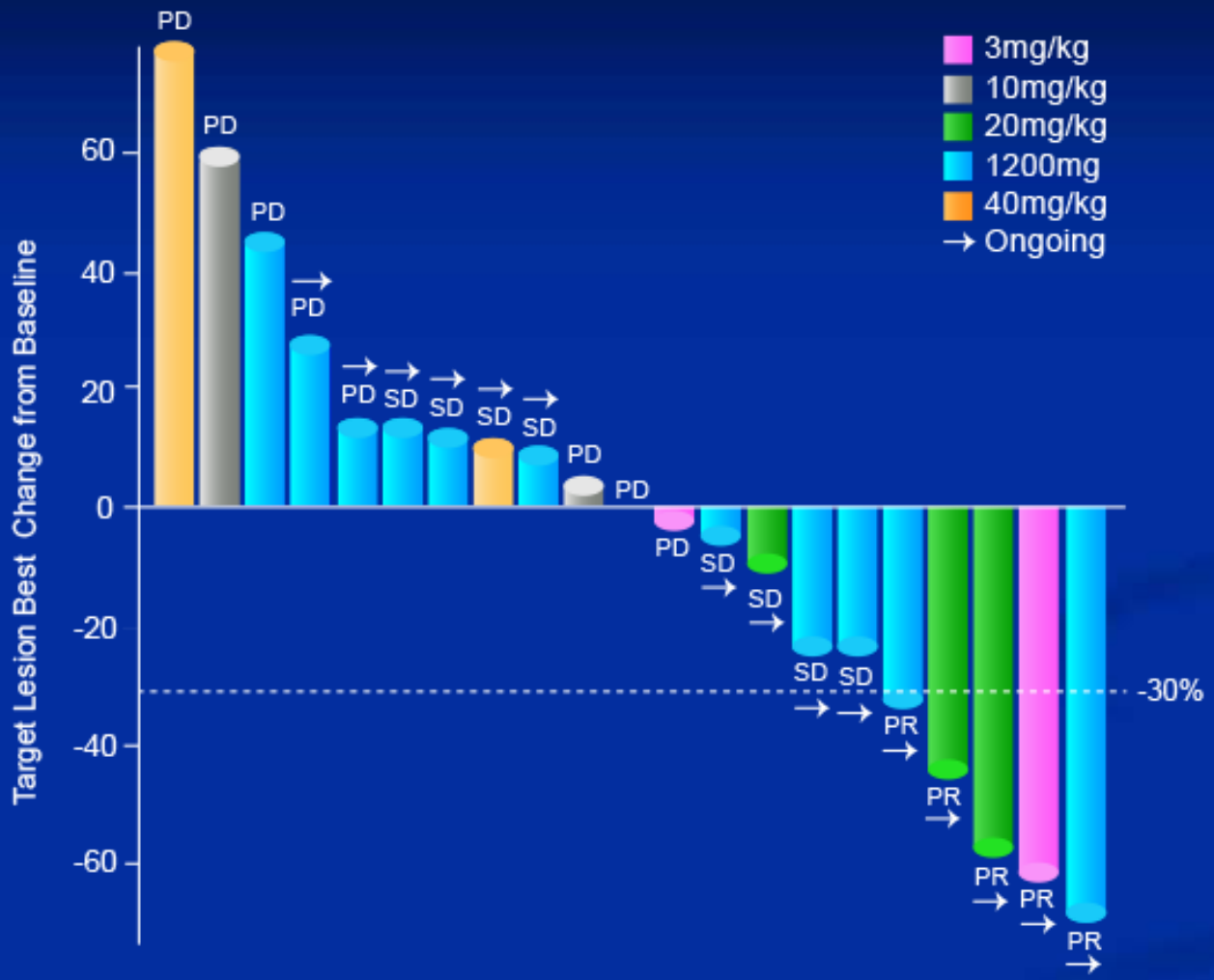

Response, n (%)	Total (N=25*)
Partial response (PR)	5 (20.0)
Stable disease (SD)	8 (32.0)
Progressive disease (PD)	9 (36.0)
Objective response (CR+PR)	5** (20.0)
Disease control (CR+PR+SD)	13 (52.0)

- Patients with PR: ampullary carcinoma with MSI-H, cholangiocarcinoma, NSCLC, cervical cancer, mixed histology of esophagus cancer and melanoma

* 25 patients were included in the efficacy analysis set, which is defined as patients who received study drug and had measurable disease at baseline (4 ongoing patients who had not reached the 1st post-baseline tumor assessment were excluded). Of the 25 patients, 4 were not shown on the plot due to no post-baseline target lesion evaluation: 3 patients had the BOR of not evaluable, and 1 had PD

** Response include 4 confirmed and 1 unconfirmed response, but subsequently confirmed after the data cut-off date

Cut-off date: July 20th , 2018

Durable Clinical Benefit in Phase Ia

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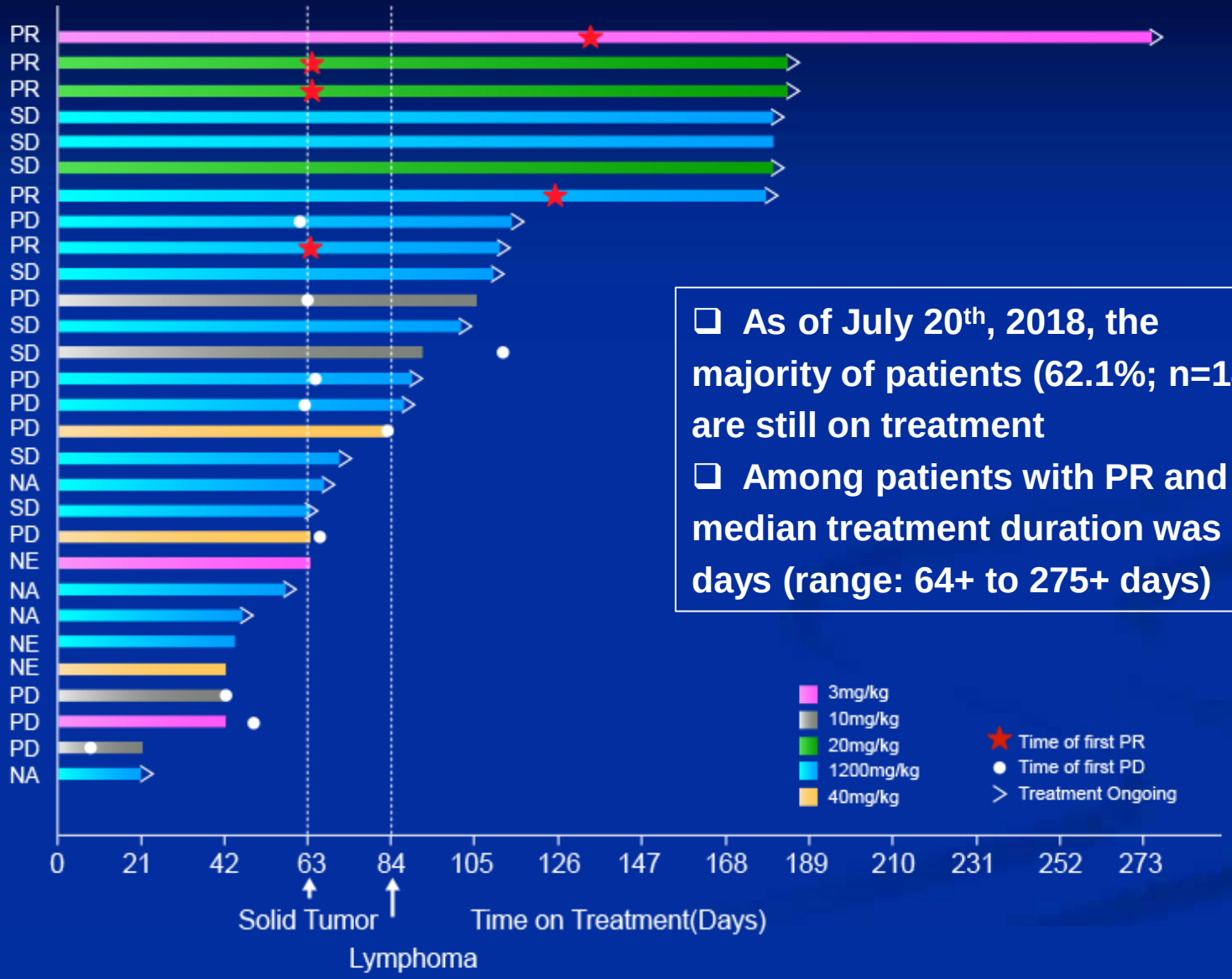


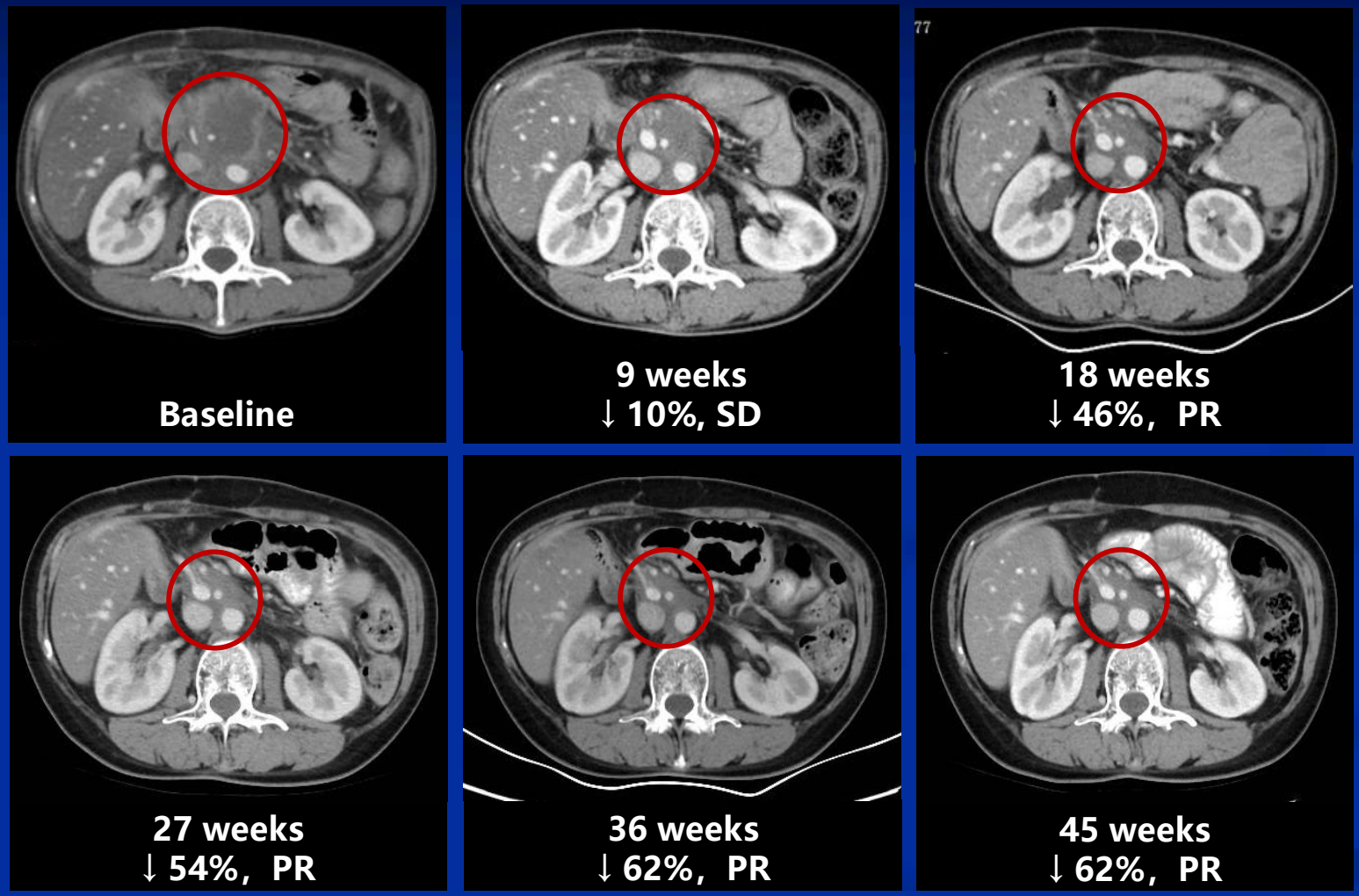
- As of July 20th, 2018, the majority of patients (62.1%; n=18/29) are still on treatment
- Among patients with PR and SD, median treatment duration was 178 days (range: 64+ to 275+ days)

*Tumor assessment performed every 9 weeks for solid tumor and every 12 weeks for lymphoma

**PR: Partial response; PD: Progressive disease; SD: Stable disease; NE: Not evaluable; NA: Not assessed

Cut-off date: July 20th , 2018

Representative CT Scan Images in Patient with Response to CS1001 (1/2)



Female patient, 37 years old, ampullary carcinoma with abdominal lymph node metastases, MSI-H, stage IV; 3 mg/kg Q3W cohort; ongoing response at the time of cutoff.

Representative CT Scan Images in Patient with Response to CS1001 (2/2)

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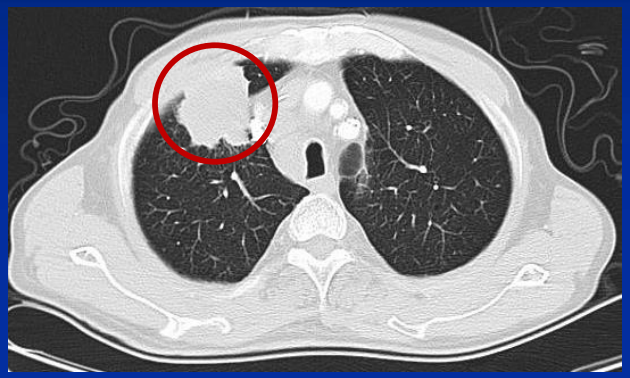
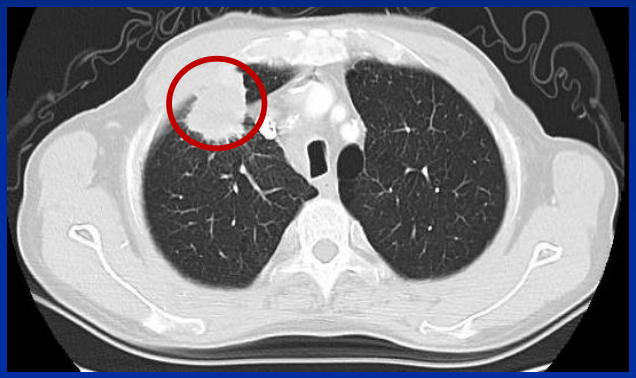
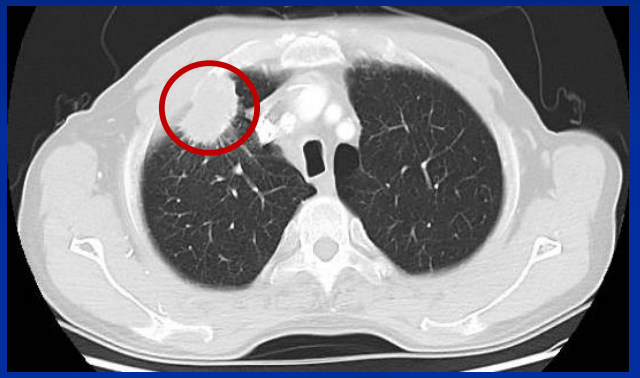


Baseline



9 weeks, ↓ 51%, PR

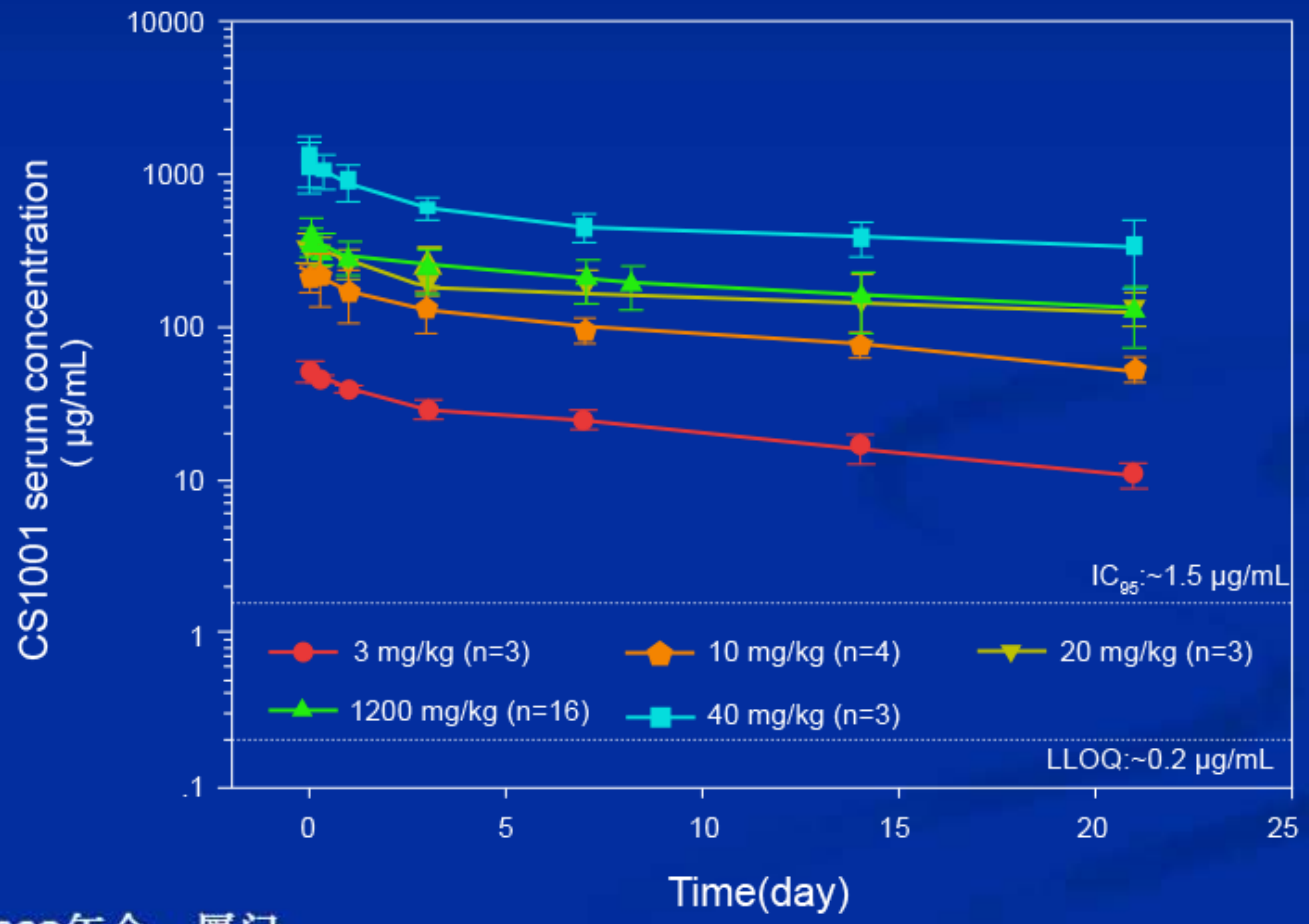


18 weeks, ↓ 51%, PR

Male patient, 70 years old, NSCLC with distant lymph nodes and pelvic cavity metastases, stage IV; **20 mg/kg Q3W cohort**; ongoing response at the time of cutoff.

Pharmacokinetic Profile of CS1001 in Phase Ia

- CS1001 demonstrated dose-proportional PK profile across 5 dose levels
- $T_{1/2}$ is 11~16 days



CS1001 Cycle 1 PK profile

Cut-off date: July 20th , 2018

Conclusions

- CS1001 was well tolerated with no reported DLT and drug-related SAE
- Early anti-tumor activity observed among 25 patients, including 5 PRs (all remain on treatment)
- CS1001 demonstrated dose-proportional PK profile with $T_{1/2}$ of 11~16 days
- 1200 mg Q3W flat dose determined as RP2D based on safety, PK, and preclinical pharmacology data
- The preliminary safety profile and antitumor activity support continued development of CS1001 in patients with advanced tumors

Acknowledgement

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