Preliminary Results of a Phase 1/2 Study of BGB-A317, an anti-PD1 mAb in Chinese Patients with Advanced Tumors

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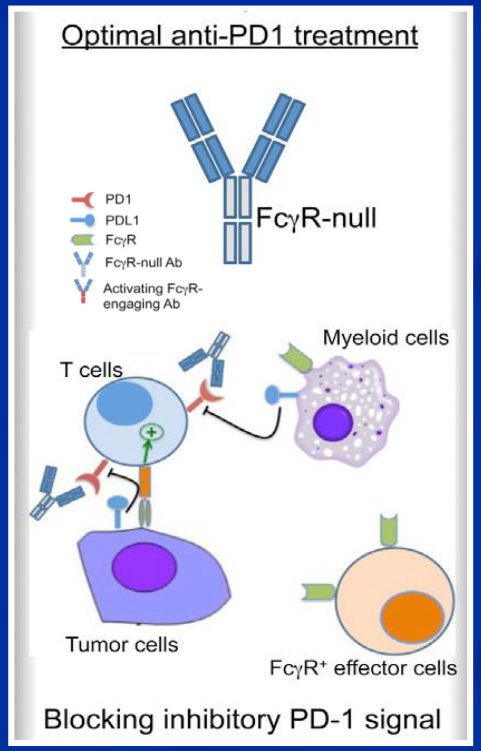
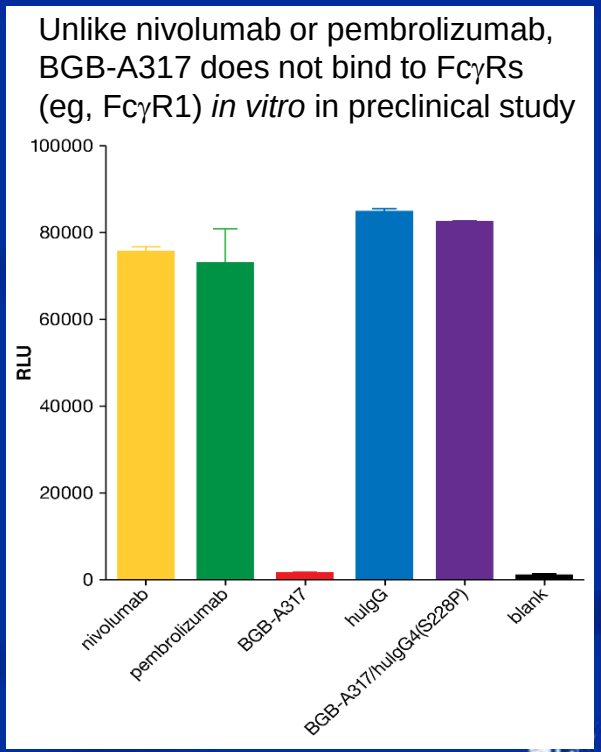
BGB-A317: A Uniquely Engineered Anti-PD-1 Monoclonal Antibody

- **Monoclonal antibodies against the immune checkpoint inhibitory receptor, programmed cell death-1 (PD-1), have demonstrated antitumor activity across multiple malignancies[1]**
- **BGB-A317 is a humanized IgG4 monoclonal antibody with high affinity and binding specificity against PD-1**
  - **Optimal anti-PD-1 mAb does not bind to FcγRs via its Fc fragment (FcγR–null anti-PD-1 mAb)**
  - **Binding of anti-PD-1 to FcγRs (eg, FcγRI or FcγRIIb) attenuates anti-tumor efficacy of Ab in animal models of cancer**





[1]Topalian SL et al. *N Engl J Med.* 2012;366:2443-54.
Figure modified from Dahan R et al. *Cancer Cell* . 2015;28:285–295

Abbreviations: FcγR, Fc region of IgG receptors; IgG, immunoglobulin; PD-1, programmed cell death-1

Ongoing First-in-Human Study of BGB-A317

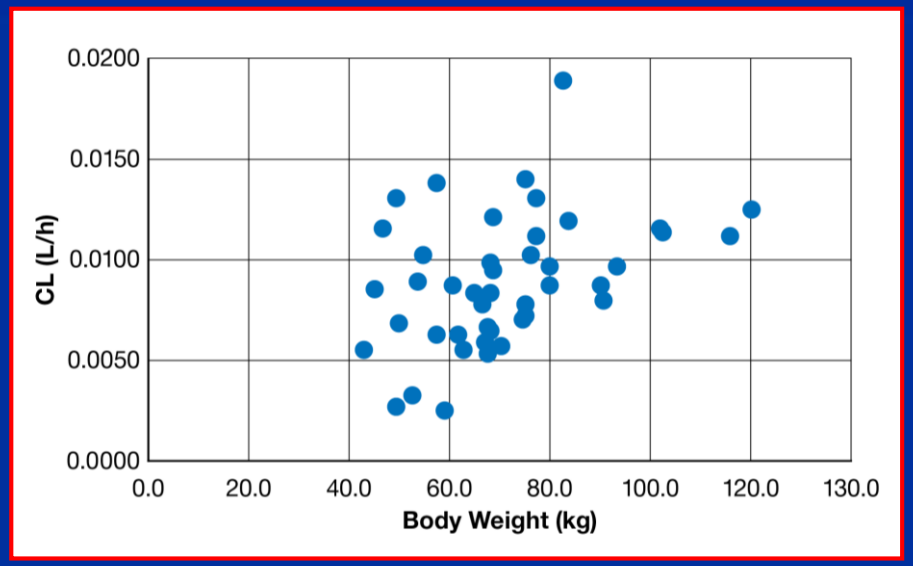
- **A preliminary report from the ongoing first-in-human (FIH) study (NCT02407990) in patients with advanced solid tumors suggest BGB-A317 has antitumor activity, and manageable safety/tolerability profile where adverse events (AEs) were generally of mild/moderate severity and reversible[1]**
  - **Conducted in Australia, Korea, New Zealand, Taiwan, and the United States**
  - **BGB-A317 has been administered IV at doses from 0.5, 2, 5 up to 10 mg/kg Q2W with no MTD identified and only 1 DLT of Grade 3 colitis occurred**

[1]Desai J et al. *J Immunother Cancer.* 2016;4(Suppl 1):P154

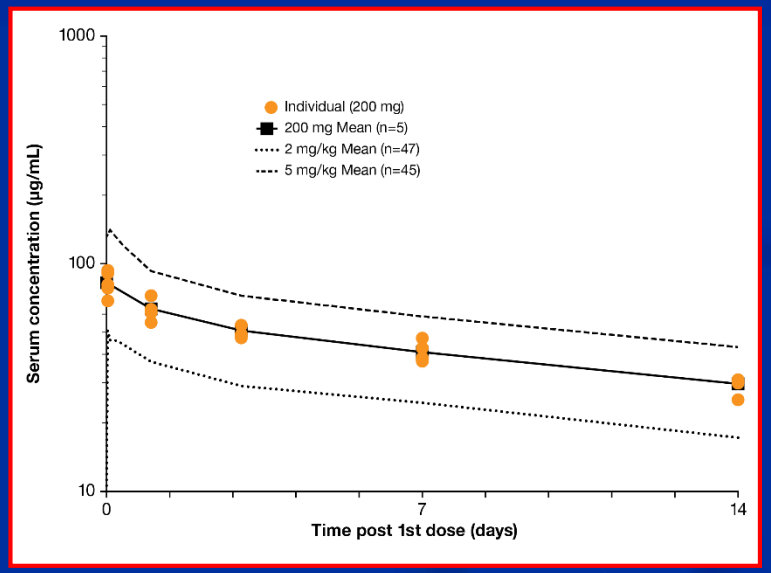
Recommended Dose for future Pivotal Studies was Established in the FIH Study

A fixed dose of 200 mg Q3W was selected as the recommended phase 2 dose (RP2D); factors contributing to this decision included:

1. Lack of correlation between clearance (CL) and body weight



2. Pharmacokinetics of BGB-A317 at 200mg Q3W dose falls in between 2 and 5 mg/kg



cut-off-date: Apr. 18th, 2017

3. There was no significant difference in safety observed between 2 mg/kg and 5mg/kg

4. BGB-A317 (2 and 5 mg/kg Q2-3W) was tolerated and demonstrated preliminary antitumor activity

Design of BGB-A317-102 study: Phase 1/2 Study of BGB-A317 in Chinese Patients

1: Dose verification*

200 mg Q3W → RP2D

2: Indication expansion**

- Arm 1: Melanoma (n=20)
- Arm 2: NSCLC（PD-L1≥10%; n=20）
- Arm 3: NSCLC（PD-L1 negative; n=20）
- Arm 4: Gastric cancer (n=20)
- Arm 5: Esophageal cancer (n=20)
- Arm 6: Renal cell carcinoma (n=20)
- Arm 7: Urothelial carcinoma (n=20)
- Arm 8: MSI-H or dMMR CRC (n=20)
- Arm 9: TNBC, HNSCC, SCNEC or other tumors with MSI-H or dMMR (n=20)
- Arm 10: Nasopharyngeal carcinoma (n=20)
- Arm 11: Child-Pugh A HCC (n=20)

*Three to six subjects were enrolled to assess DLT and RP2D; if no DLT was found, this cohort would be expanded up to 20 subjects

**In the indication-extension stage, ~20 subjects are enrolled into each arm. For tumors that are difficult to enroll, the Sponsor may early terminate the enrollment of subjects in this arm.

Abbrevations: NSCLC: non small cell lung cancer; TNBC: triple negative breast carcinoma; HNSCC: head and neck squamous cell carcinoma; SCNEC: small cell neuroendocrine carcinoma; HCC; hepatocellular carcinoma

Design of BGB-A317-102 study: Phase 1/2 Study of BGB-A317 in Chinese Patients

1: Dose verification*

200 mg Q3W

RP2D

2: Indication expansion**

Arm 1

Arm 2

Arm 3

Arm 4

Arm 5

Arm 6

Arm 7

Arm 8

Arm 9

Arm 1

Arm 1

Child-Pugh A HCC (n=20)

*Three to six subjects were enrolled to assess DLT and RP2D; if no DLT was found, this cohort would be expanded up to 20 subjects

**In the indication-extension stage, ~20 subjects are enrolled into each arm. For tumors that are difficult to enroll, the Sponsor may early terminate the enrollment of subjects in this arm.

Here, we report the preliminary results from Phase 1 (Dose verification) of this multi-center clinical study of BGB-A317 at 200 mg Q3W in Chinese patients with advanced solid tumors

Patient Demographics and Baseline Disease Characteristics

- As of 16 June 2017, 20 patients were dosed at least once in Phase 1
  - Study population was primarily male; median age of the population was 49.5 years and more than half (n=11/20) of the patients had received ≥2 prior anticancer treatment regimens for progressive disease

Patient demographics and baseline disease characteristics	Total Population (N=20)
Median age, years (range)	**49.5 (22–73)**
Sex, n	
Male	16
Female	4
Ethnicity	
Han	19
Dai	1
Prior anticancer therapy regimens, median (range)	**2.0 (0 –5)**
Number of prior anticancer therapy regimens	
0	2
1	7
2	4
≥3	7

Data cut-off date: 16 June 2017

Study Participant Tumor Types

- **Of the 20 patients who received at least one dose of BGB-A317 in Phase 1, one-quarter (n=5/20) of the population were patients with MSI–H colorectal cancer**

Tumor Types	Total Population (N=20)
Colorectal carcinoma (MSI-H)	**5**
Liver cancer	**3**
Hepatocellular carcinoma	*2*
Mixed hepatocellular-cholangiocarcinoma	*1*
Urothelial carcinoma	**3**
Esophageal carcinoma	**2**
Gastric carcinoma	**2**
Melanoma	**2**
Small cell lung cancer	**1**
Malignant fibrous histiocytoma	**1**
Gastrointestinal stromal tumor	**1**

Data cut-off date: 16 June 2017

Safety and Tolerability Profiles of BGB-A317 in Chinese Patients

- As of 16 June 2017, of the 19 patients with ≥21 days follow up, no DLT has been observed
- The most common TRAEs were related to changes in clinical laboratory value, most of which were grade ≤2 severity
- In addition to AEs related to clinical laboratory abnormalities, grade ≥3 TRAEs are neutropenia and leukopenia
- One patient with advanced urothelial carcinoma was assessed as PD per local CT scanning 5 weeks post initial treatment and died two weeks later
  - Cause of death was PD
  - Causality to treatment was possibly treatment unrelated at the discretion of investigator

Treatment-Related Adverse Events Occurring in ≥2 Subjects

	All Grades, n	Grade ≥3*, n
Subjects who experienced ≥1 TRAE	**19**	**4**
Increased blood bilirubin	8	**0**
Increased AST	5	**1**
Bilirubin conjugated increased	5	**1**
Blood bilirubin unconjugated increased	5	**1**
Increased ALT	4	0
Anemia	4	0
Protein urine present	4	0
Pyrexia	4	0
Hemoglobin decreased	3	0
Proteinuria	3	0
Vomiting	3	0
Hyperthyroidism	2	0
Leukopenia	2	**1**
Nausea	2	0
Decreased neutrophil count	2	0
Pruritus	2	0
Thrombocytopenia	2	0
Decreased white blood cell count	2	0
White blood cells urine positive	2	0

Abbreviations: AST, aspartate aminotransferase; ALT, Alanine aminotransferase; TRAE, treatment-related adverse event

Data cut-off date: 16 June 2017

Immune-Related Adverse Events

- As of June 16, 2017, increased AST and ALT were the most commonly reported immune-related adverse events; only one report of increased AST was of grade ≥3 in severity

Immune-Related Adverse Events Occurring in ≥2 Subjects		
	All Grades, n	Grade ≥3, n
Increased AST	5	1*
Increased ALT	4	0
Hyperthyroidism	2	0
Pruritus	2	0
Arthralgia	1	0
Increased blood thyroid stimulating hormone	1	0
Diabetes mellitus	1	0
Diarrhea	1	0
Drug eruption	1	0
Hyperglycemia	1	0
Hypothyroidism	1	0
Pain in extremity	1	0
Decreased free tri-iodothyronine	1	0

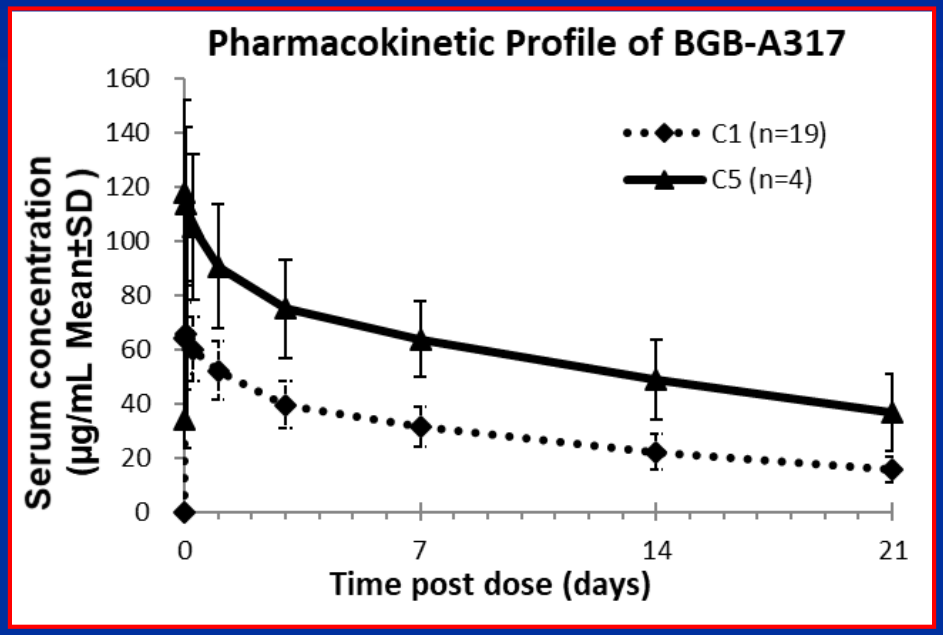
Abbreviations: ALT, Alanine aminotransferase AST, aspartate aminotransferase; TRAE, treatment-related adverse event

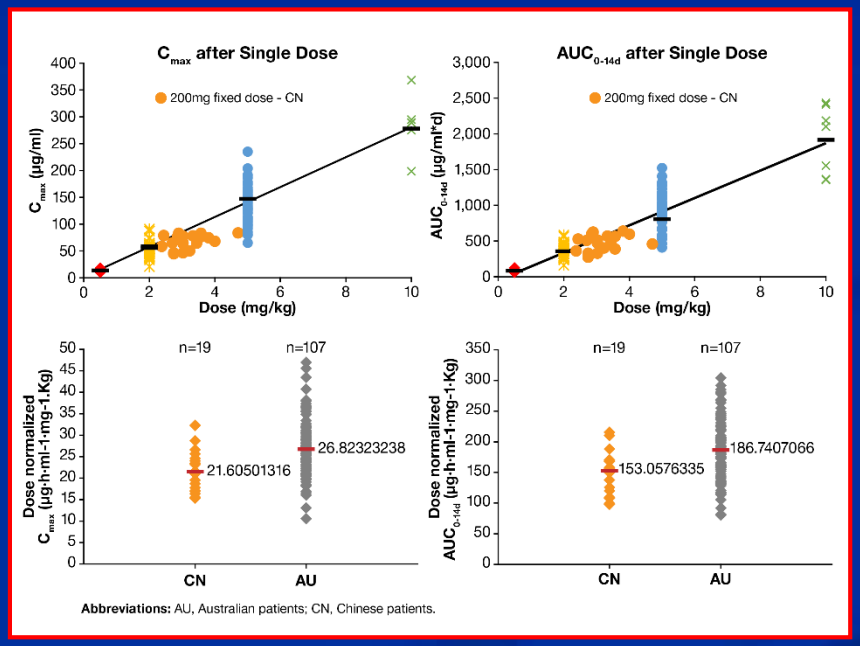
*** Increased AST was assessed possibly unrelated to drug treatment by investigator**

Data cut-off date: 16 June 2017

Pharmacokinetic Profile of BGB-A317

- In this study, the BGB-A317 single-dose (Cycle 1) PK profiles were obtained from 19 patients and multi-dose PK (Cycle 5) from 4 patients
- Preliminary BGB-A317 single-dose PK profiles were consistent between this Chinese study and the global FIH study



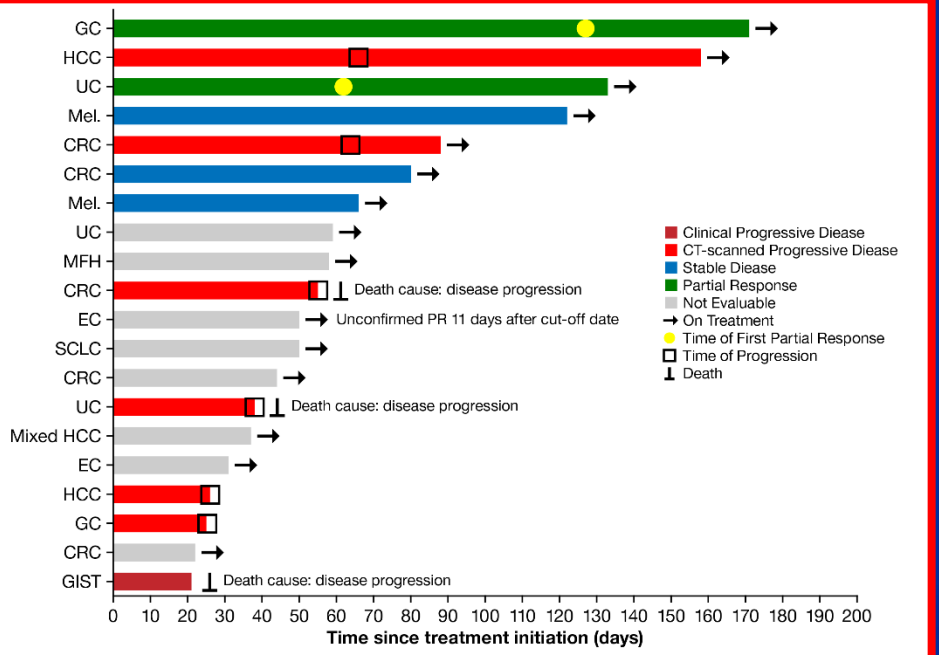


BGB-A317 single-dose PK in the global FIH study were from 107 patients who received doses of 0.5, 2.0, 5.0 and 10 mg/kg single dose

Data cut-off date: 16 June 2017

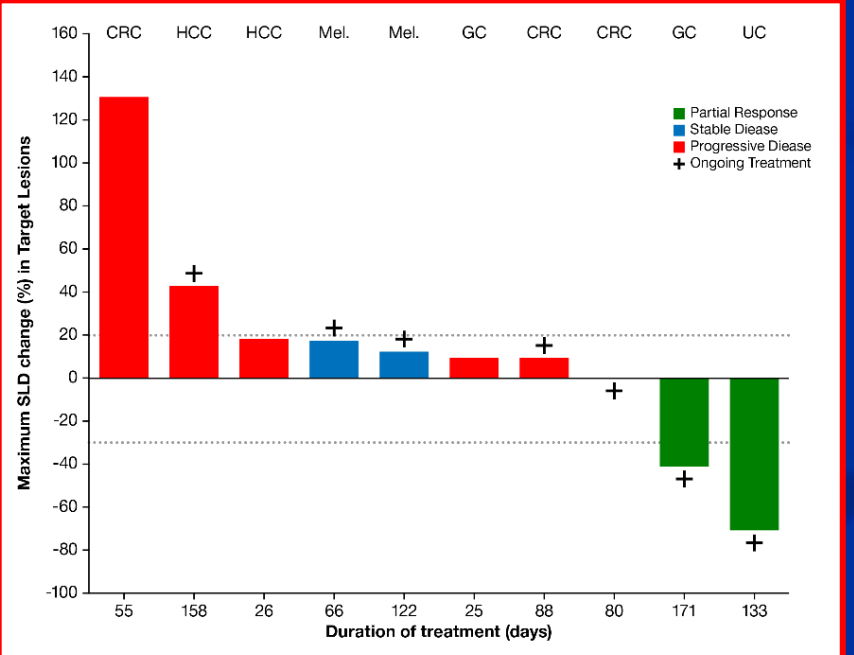
Preliminary Antitumor Activity

- **BGB-A317 median treatment duration was 52.5 days (range: 21–171 days)**
- **As of June 16, 2017, among 12 evaluable patients, two patients achieved partial response (one confirmed) and three patients achieved stable disease; in addition to these 12 patients, a third PR was observed in a patient with esophageal carcinoma 11 days after the cut-off date**
- **The majority of patients (75%; n=15/20) are still on study**



Abbreviations: CRC: Colorectal carcinoma; EC: Esophageal carcinoma; GC: Gastric cancer; GIST: gastrointestinal stromal tumor; HCC: Hepatocellular carcinoma; Mel.: Melanoma; MFH: Malignant fibrous histiocytoma; Mixed HCC: Mixed hepatocellular-cholangiocarcinoma; SCLC: small cell lung cancer; UC: Urothelial carcinoma

Cut-off date: June 16, 2017



Two patients that having no assessment of target lesions are not included in the above waterfall plot of Maximum SLD changes: 02005 with GISC had clinical PD; 03003 with UC had CT scanning from local hospital suggesting new lesions but no available CT scanning of target lesion.

Abbreviations: CRC: Colorectal carcinoma; GC: Gastric cancer; HCC: Hepatocellularcarcinoma; Mel.: Melanoma; UC: Urothelial carcinoma

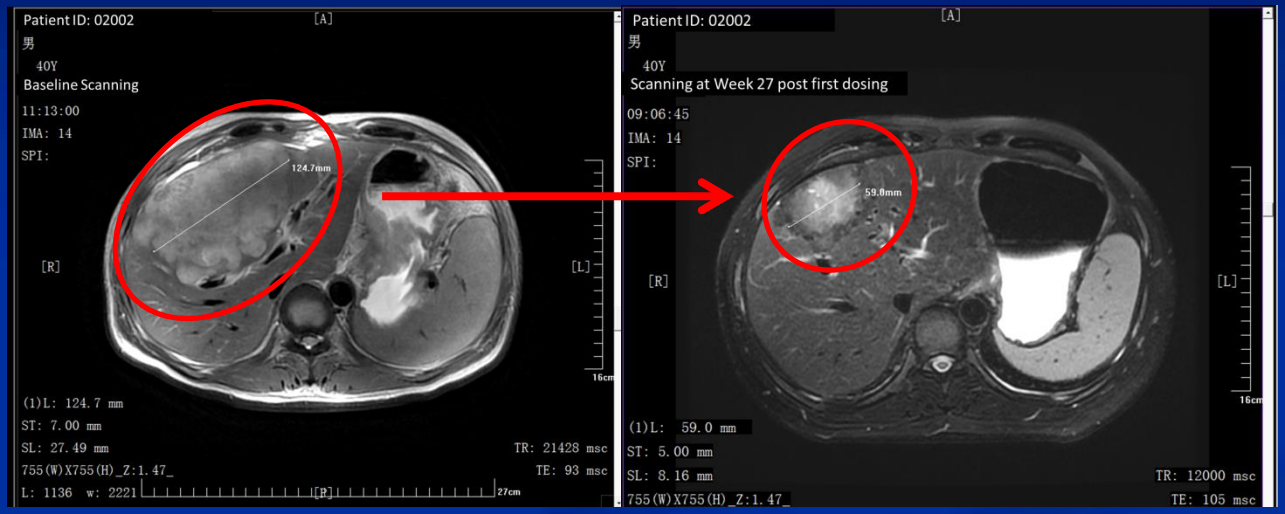
Cut-off date: June 16, 2017

Preliminary Antitumor Activity – Case of 02002

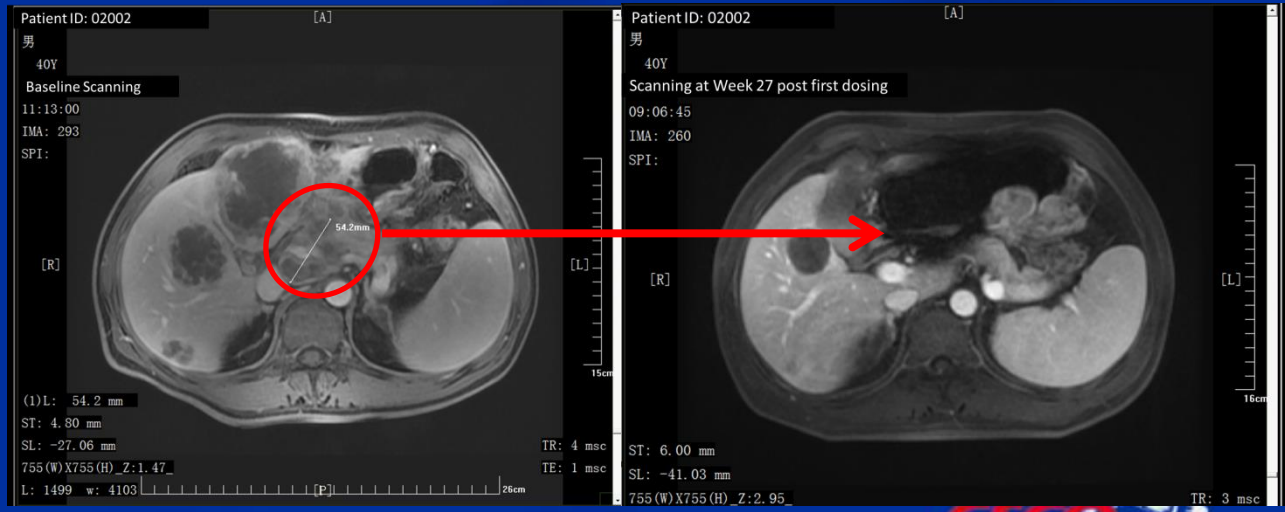
- **Gender:** Male
- **Age:** 40 years
- **Disease:** Gastric carcinoma
- **Metastases:** Lymph nodes, liver
- **Prior line treatments**: 3
- **Best overall response**: PR

Baseline **27 weeks**

Liver S4-S8



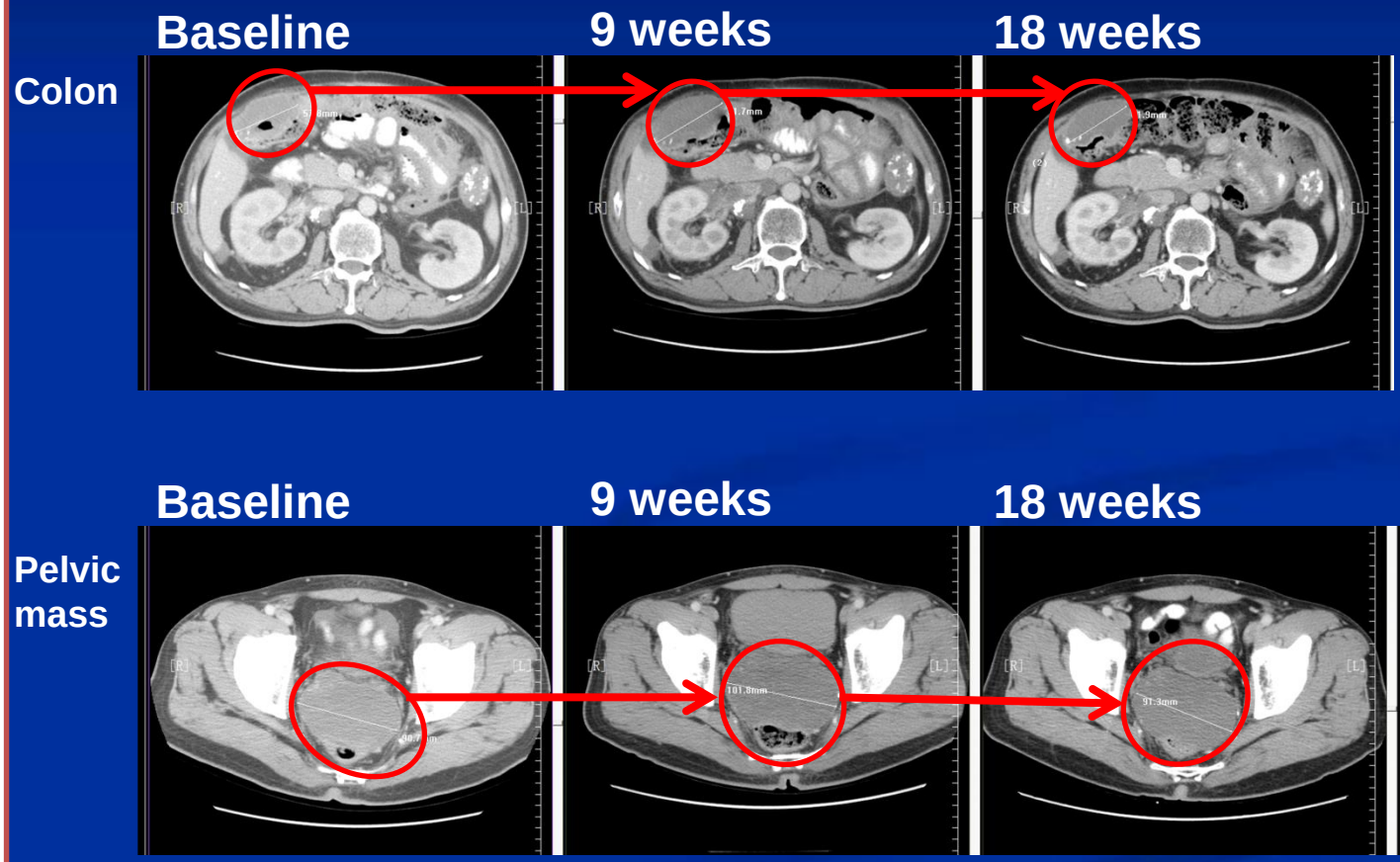
Liver S5



Data cut-off date: 16 June 2017

Preliminary Antitumor Activity - Case of 02008

- **Gender:** Male
- **Age:** 44 years
- **Disease:** Colorectal carcinoma
- **Metastases:** Lymph nodes, liver, pelvic cavity, colonic anastomosis
- **Prior line treatments**: 5
- **Best overall response**: PD
  - Suspected pseudo PD



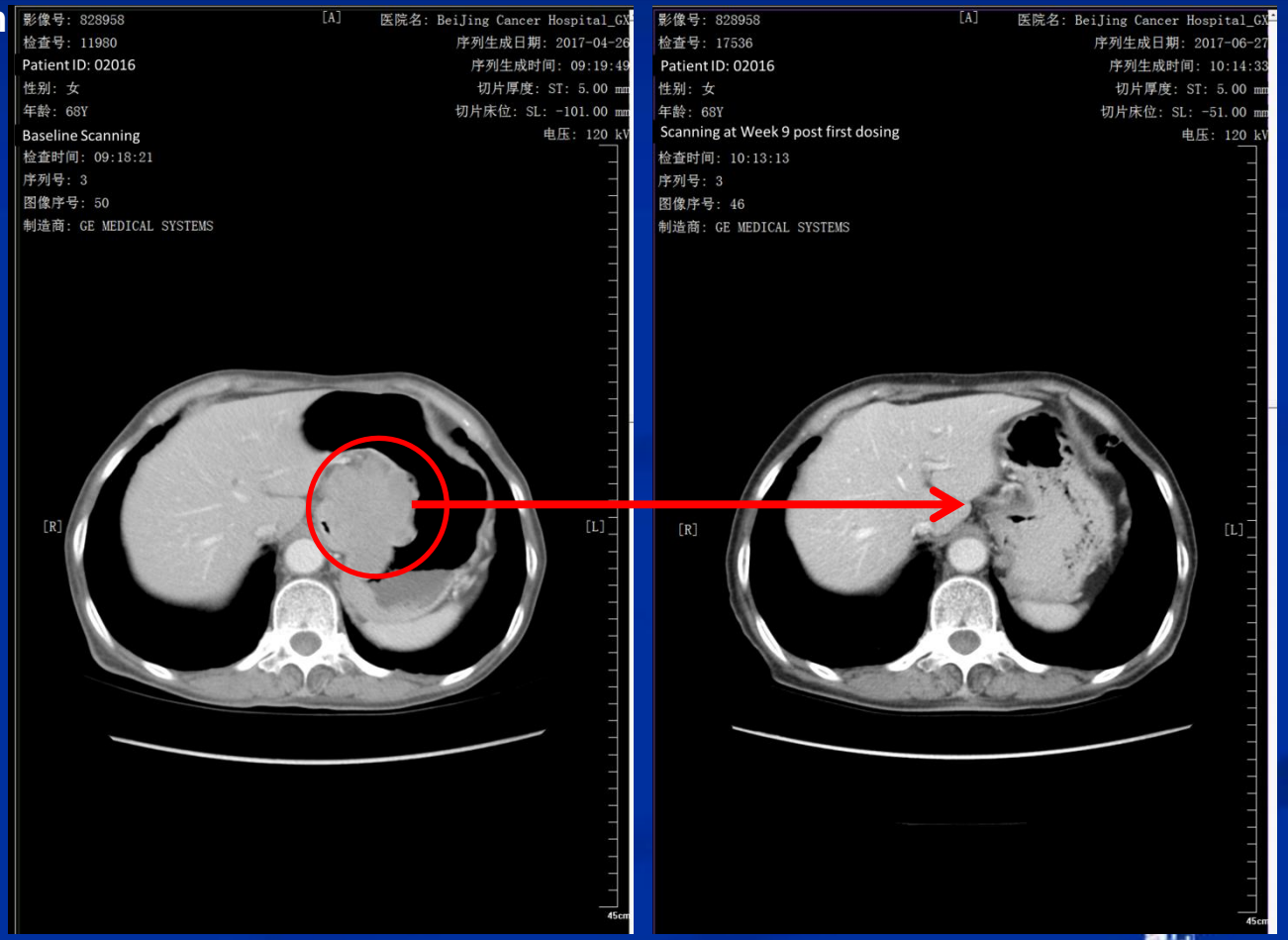
Data cut-off date: 16 June 2017

Preliminary Antitumor Activity - Case of 02016

- **Gender:** Female
- **Age:** 68 years
- **Disease:** Esophageal carcinoma
- **Metastases:** Lymph nodes
- **Prior line treatment**: 0
- **Best overall response**: PR (11 days after cut-off date)

Baseline **9 weeks**

Lymph nodes



Data cut-off date: 16 June 2017

Conclusions

- These preliminary results suggest BGB-A317 treatment was generally well tolerated in a heavily pretreated study population with advanced solid tumors
  - Immune-related AEs reported in this study were consistent with those reported in other studies of BGB-A317
- BGB-A317 PK profile in Chinese patients was consistent with other populations
- As of June 16, 2017, among 12 evaluable patients, two patients had PRs including one patient with gastric carcinoma; in addition to these 12 patients, a third PR was observed in a patient with esophageal carcinoma 11 days after the cut-off date
- The preliminary safety profile and antitumor activity support continued development of BGB-A317 in Chinese patients with advanced solid tumors
- The recruitment of phase 2 trial in select tumor types is ongoing

The authors wish to acknowledge the investigative center study staff and study patients, as well as recognize those from BeiGene who have substantially contributed to the development of this presentation.

BeiGene, Ltd., provided financial support for this presentation, including writing and editorial assistance by Drs Aarati Rai and Regina Switzer of SuccinctChoice Medical Communications, Chicago, IL.