Review of Phase 1/2 Study Investigating Safety, Tolerability, Pharmacokinetics and Preliminary Antitumor Activities of Anti-PD-1 Monoclonal Antibody BGB-A317 in Chinese Subjects with Advanced Solid Tumors

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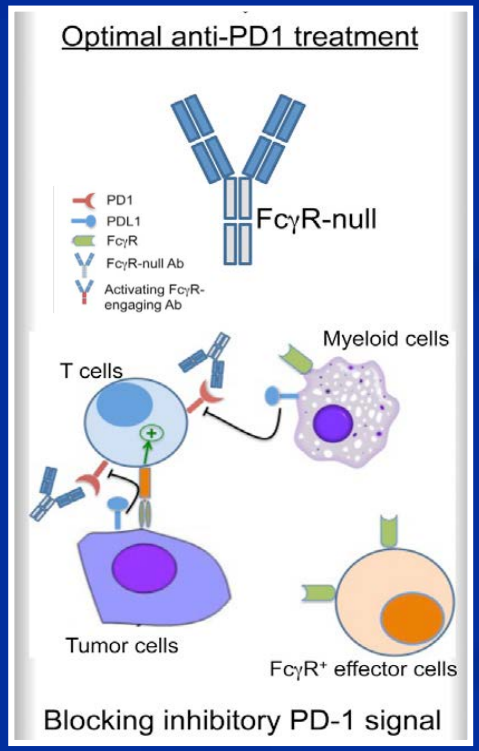
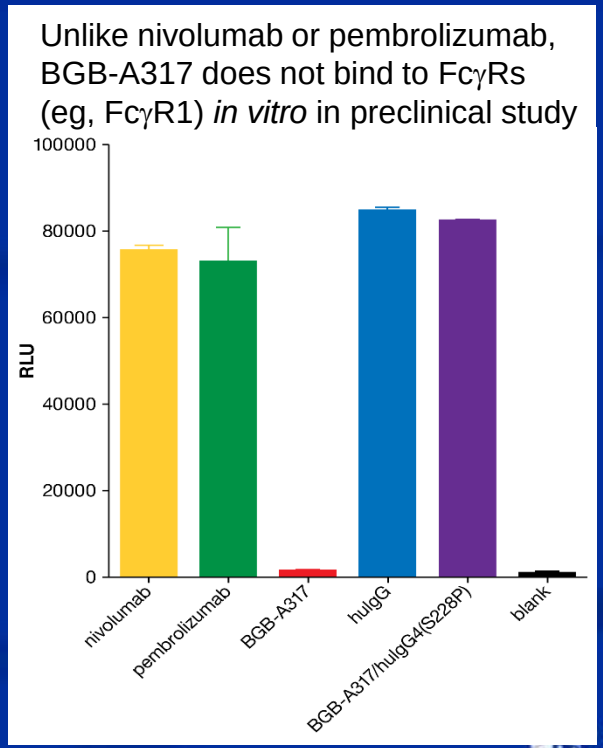
BGB-A317: A Uniquely Engineered Anti-PD-1 Monoclonal Antibody

- 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





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

[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

Ongoing First-in-Human Study of BGB-A317

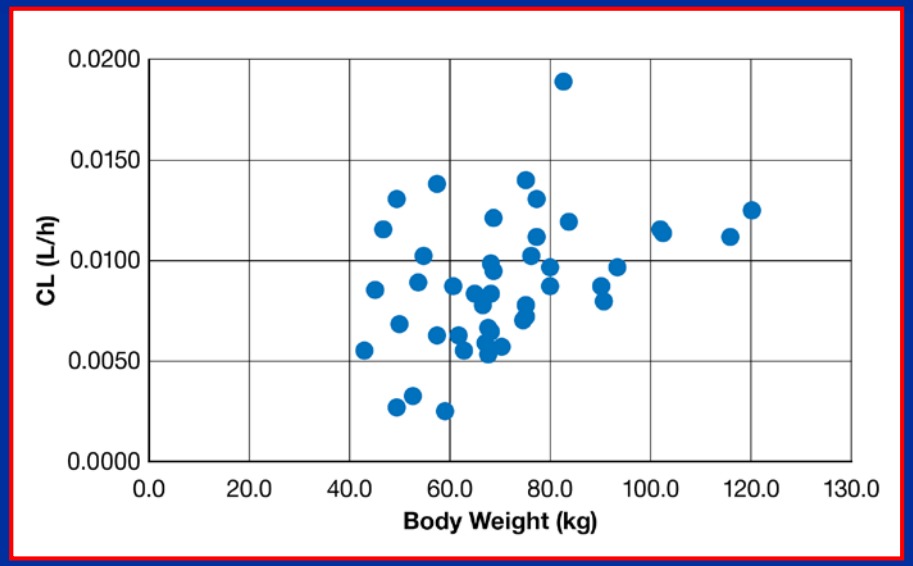
- **A preliminary report from the ongoing first-in-human (FIH) study (NCT02407990) in patients with advanced solid tumors suggest BGB-A317 has antitumor activity, and manageable safety/tolerability profile where adverse events (AEs) were generally of mild/moderate severity and reversible[1]**
  - **Conducted 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

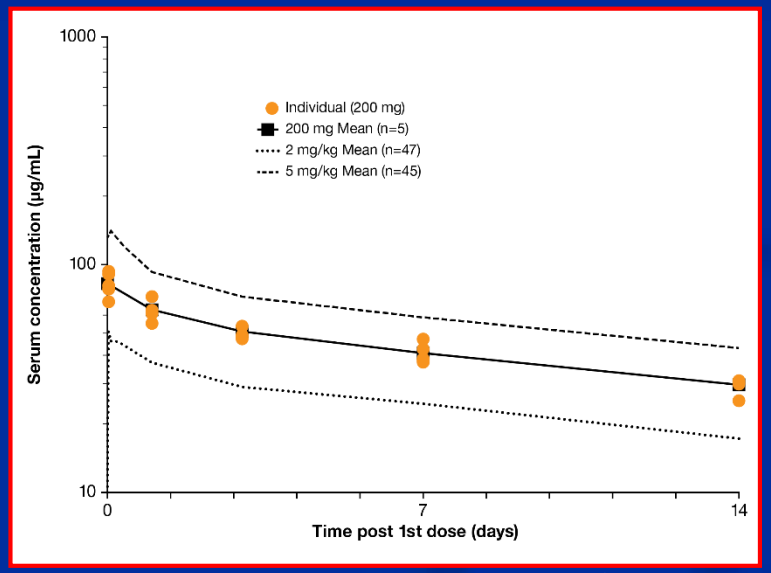
Recommended Dose for Future Pivotal Studies was Established in the FIH Study

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 positive; 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, SCLC or other tumors with MSI-H or dMMR (n=20)
- Arm 10: Nasopharyngeal carcinoma (n=20)
- Arm 11: Child-Pugh A HCC (n=20)

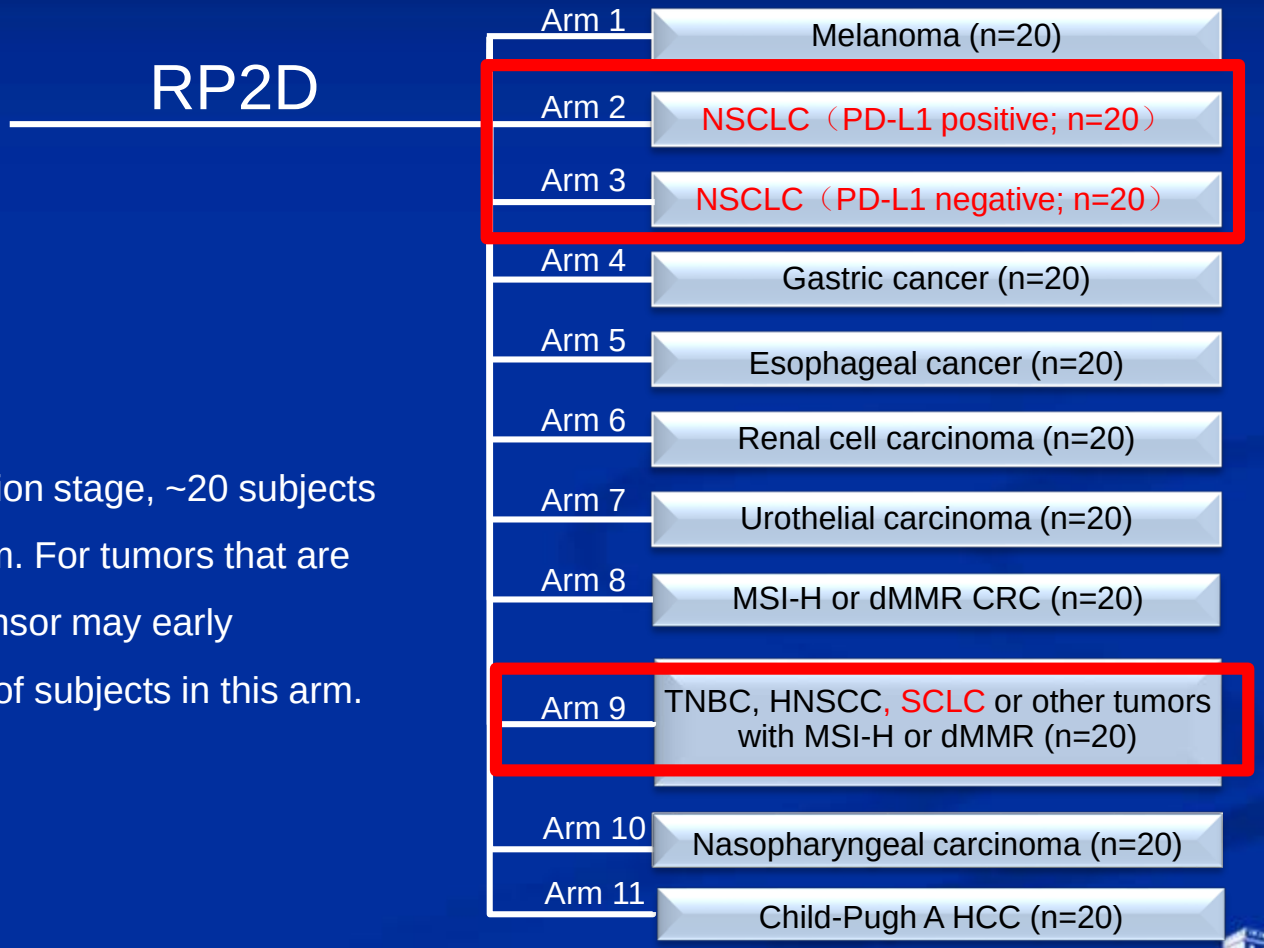
*Three to six subjects were enrolled to assess DLT and RP2D; if no DLT was found, this cohort would be expanded up to 20 subjects

**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.

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

Lung Cancer Treatment Arms of BGB-A317-102 Study Phase 2

2: Indication expansion**



**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.

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

Endpoints of Study BGB-A317-102

- **Phase I**
  - Primary Endpoints:
    BGB-A317 safety and tolerability
    MTD (if any) and/or RP2D (s)

  - Second Endpoints:
    PK evaluations
    Efficacy evaluations: ORR, CR rate, PR rate, SD rate, PFS, DOR, and duration of SD and OS
    Immunogenic responses to BGB-A317

- **Phase II**
  - Primary Endpoints:
    ORR

  - Second Endpoints:
    Efficacy evaluations: CR rate, PR rate, SD rate, PFS, DOR, and duration of SD and OS
    BGB-A317 safety and tolerability
    PK evaluations
    Immunogenic responses to BGB-A317

Target Population Profile of BGB-A317-102 Study

- Subjects with advanced or metastatic solid tumors (unresectable) progressed since last anti-tumor treatment, have no standard treatment or have refused standard therapy
- For NSCLC Arms - Arm 2 (PD-L1 positive) and Arm 3 (PD-L1 negative)
  - Subjects must be EGFR wild type and without known ALK gene rearrangements
  - PD-L1 expression must be tested prospectively at the central laboratory (using Ventana PD-L1 protocol [SP263 antibody])

    PD-L1 positive: ≥10%

    PD-L1 negative: <10%

Study BGB-A317-102 Site List

Site No.	Site Name	PI Name
01	**Guangdong General Hospital**	**Yi-Long Wu***
02	**Beijing Cancer Hospital**	**Lin Shen****
03	**Beijing Cancer Hospital**	**Jun Guo****
06	Harbin Medical University Cancer Hospital	Yuxian Bai
07	Harbin Medical University Cancer Hospital	Qingyuan Zhang
08	Zhongshan Hospital of Fudan University	Tianshu Liu
10	The Second Affiliated Hospital Zhejiang University School of Medicine	Ying Yuan
11	Beijing Cancer Hospital	Jun Zhao
12	Cancer Institute and Hospital, Chinese Academy of Medical Sciences	Aiping Zhou
13	The People's Hospital of Jiangsu Province	Yongqian Shu

Site No.	Site Name	PI Name
14	Hospital, Zhejiang Univesity, School of Medicine	Hongming Pan
15	Fudan University Shanghai Cancer center	Dingwei Ye
16	Cancer Institute and Hospital, Chinese Academy of Medical Sciences	Jie Wang
17	The fifth Affiliated Hospital Sun Yat-Sen University	Siyang Wang
18	Sun Yat-sen Memorial hospital, Sun Yat-sen University	Xiaoming Huang
19	Cancer Center of Guangzhou Medical University	Chuan Jin
20	Fudan University Shanghai Cancer center	Ye Xu
21	The First Affiliated Hospital of Nanchang University	Ting Sun
22	Henan Provincial Tumor Hospital	Quanli Gao

* Principle Investigator
** Coordinating Investigator

Summary of Current Study Status

- As of Jun. 16 2017, 20 patients were enrolled into Phase 1 study
  - No DLT has been observed among 19 evaluable patients in Phase I that experienced ≥21 days follow up
  - 200 mg Q3W was confirmed as RP2D in Chinese patients
- Patients are currently enrolled into Arm 2, 3 and 9 of Phase 2 study and dosed with BGB-A317 200 mg Q3W

Acknowledgement and Support Disclosure

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