Abstract
#P-140

PRELIMINARY RESULTS OF A PHASE 1A/1B STUDY OF BGB-A317, AN ANTI-PD-1 MONOCLONAL ANTIBODY (mAb), IN PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA (HCC)

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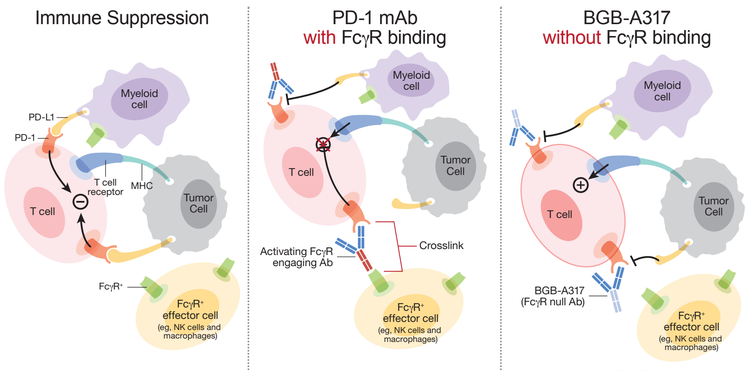
INTRODUCTION

- Hepatocellular carcinoma (HCC) is a leading cause of death due to malignancy, and sorafenib is the only approved first-line treatment, with modest efficacy and considerable toxicity[1]
- Monoclonal antibodies against the immune checkpoint inhibitory receptor, programmed cell death-1 (PD-1), have demonstrated antitumor activity across multiple malignancies[2], including HCC[3]
- BGB-A317 is a uniquely engineered humanized IgG4 monoclonal antibody with high affinity and binding specificity against PD-1
  - BGB-A317 was specifically engineered to minimize FcγR binding on macrophages to abrogate antibody-dependent phagocytosis, a potential mechanism of T-cell clearance (**Figure 1**)
- Previous reports from an ongoing phase 1A/1B study (NCT02407990) of BGB-A317 in patients with advanced solid tumors suggested that BGB-A317 is tolerable; in addition, its toxicity profile demonstrates that adverse events (AEs) are generally of low severity, manageable, and reversible[4]
- Here, we present the preliminary results as of April 28, 2017, of the pooled subset of patients with refractory/relapsed HCC enrolled in this phase 1A/1B study
  - Data presented here are early and immature

Figure 1: Lack of FcγR Binding Prevents Macrophage-Mediated T-Cell Clearance

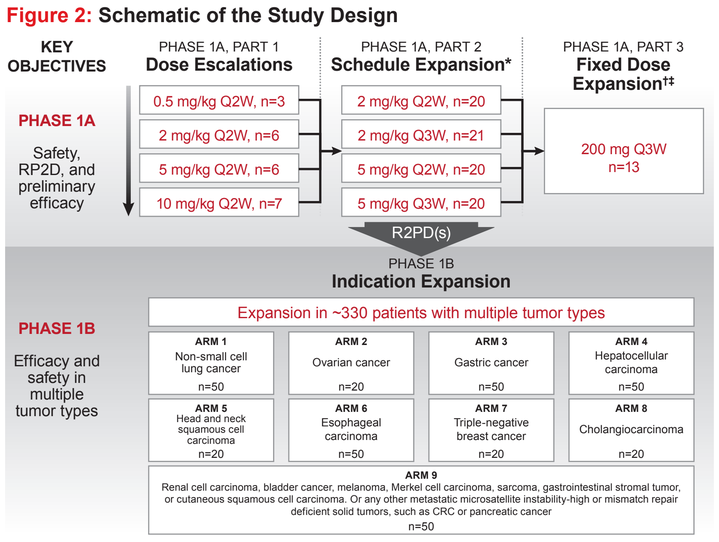


Adapted from Dahan et al, *Cancer Cell.* 2015;28:285–295.

METHODS

Study Design

Figure 2: Schematic of the Study Design



*In select tumors for RP2D determination and preliminary differentiation.
†In select tumors at fixed doses that do not exceed the exposure of MTD.
‡Conducted in parallel with phase 1B.
Abbreviations: MTD, maximum tolerated dose; RP2D, recommended phase 2 dose.

- The study design is detailed in **Figure 2**
  - In phase 1A, 10 mg/kg Q2W was the maximum administered dose; MTD was not reached
  - All patients in phase 1B received BGB-A317 as a 5 mg/kg IV infusion Q3W
  - Radiographic assessment was every 9 weeks
  - Results presented here include patients with advanced HCC treated with 5 mg/kg Q3W

Key Eligibility of the Pooled HCC Population Subset

- Adult patients (aged ≥18 years) with histologically or cytologically confirmed advanced/metastatic HCC who had not received prior PD-1 or PD-L1 treatment were enrolled
  - Specific inclusion criteria included Barcelona Clinic Liver Cancer stage C or stage B refractory/not amenable to loco-regional therapy, and not amenable to a curative treatment approach, and Child–Pugh A without encephalopathy of any grade
  - Eligible patients must have a hepatitis B virus (HBV) viral load <200 IU/mL (~1000 cps/mL) and subjects with active HBV infection need to be on anti-HBV suppression for ≥3 months throughout treatment and for 6 months after
  - Patients with active hepatitis C virus (HCV) infection who are untreated are not allowed on study

RESULTS

Table 1: Patient Demographics and Disease Characteristics

		HCC Population (N=40)
Median age, years (min, max)		55.5 (28, 76)
Sex	Male/female	32/8
Race	Asian/White/other	35/3/2
Median treatment duration, days (min, max)		64 (1, 471)
Median number of prior anti-cancer treatment regimens (min, max)		2 (0, 6)
Prior anti-cancer therapy regimens, n*	0	2†
	1	16
	2	12
	≥3	10
Infection status, n	HBV	28
	HCV	2
	HBV/HCV co-infection	6
	No infection	4

*Only 1 patient was sorafenib naïve; †Both patients had received sorafenib as adjuvant therapy.
Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus.

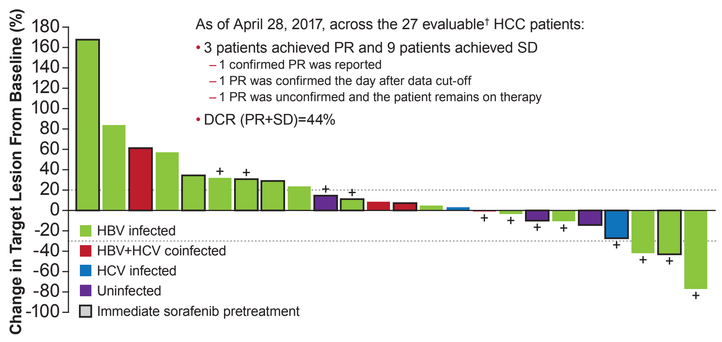
Patient Disposition

- As of April 28, 2017, 40 patients with advanced HCC, the majority of whom were HBV positive (n=34/40), had enrolled in this study (**Table 1**)
  - A total of 24 patients remain on treatment

Preliminary Antitumor Activity

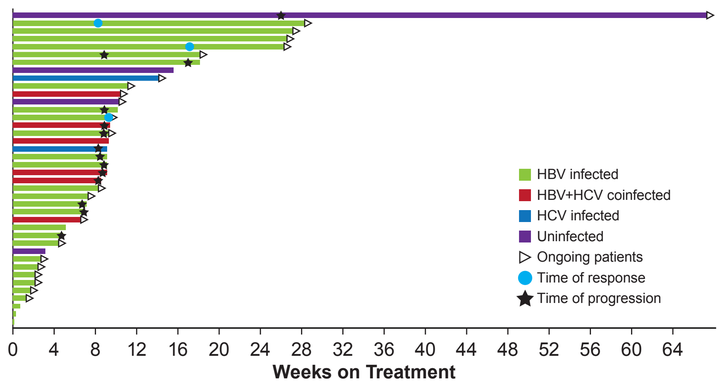
- A total of 27 patients were evaluable; 25 had measurable disease and at least 1 evaluable post-baseline tumor assessment; 2 died prior to the 1st scheduled date of tumor assessment
- Antitumor activity of BGB-A317 is presented in **Figures 3–7**

Figure 3: Maximum Tumor Reduction by Hepatitis Infection Status*



+ Indicates patient still on treatment; *Includes 24 of 25 evaluable patients; 1 patient, who progressed due to a new lesion, had no post-baseline target lesion measurement; †Evaluable is defined as a patient who had at least 1 tumor assessment after enrollment on study or had progressed or died prior to the initial tumor assessment.
Abbreviations: DCR, disease control rate; PR, partial response; SD, stable disease.

Figure 4: Duration of Treatment and Response



Each line represents an individual patient.

Figure 5: Baseline and Most Recent CT Assessment in the Three Patients with Partial Response

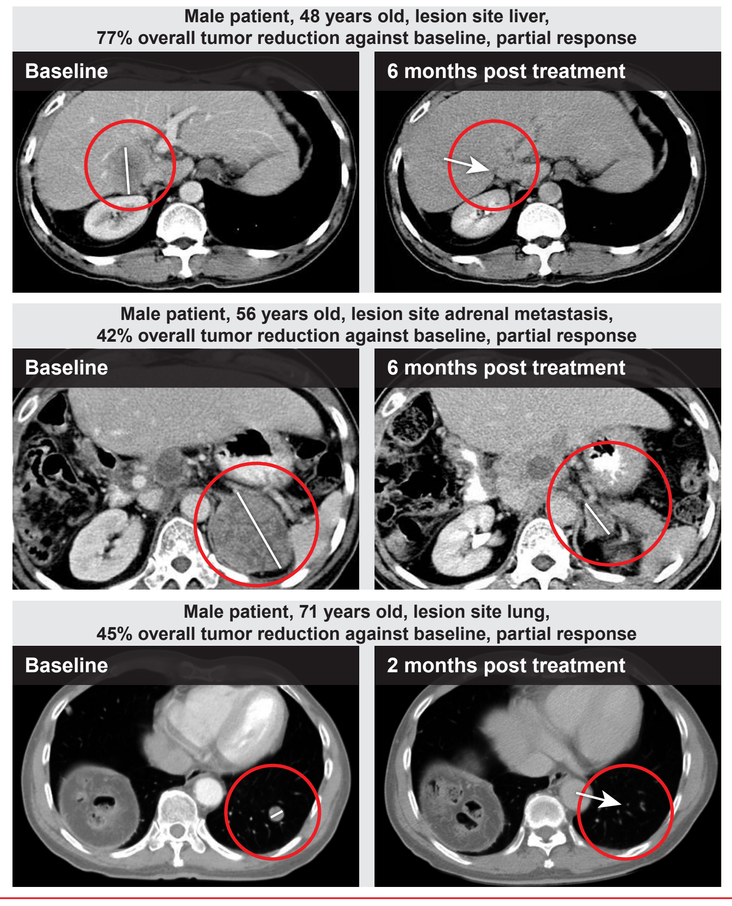


Figure 6: Change in Tumor Burden over Time

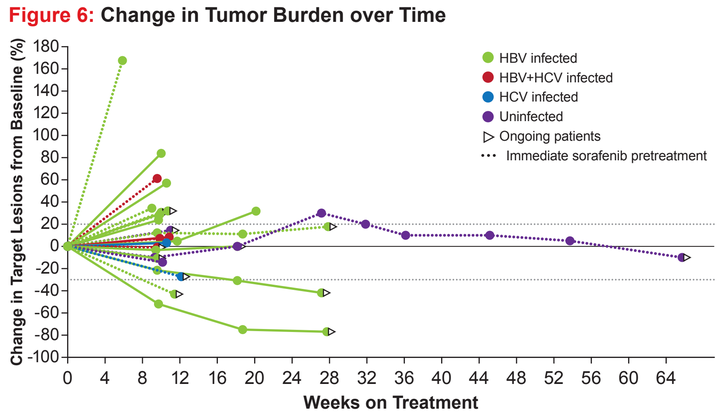
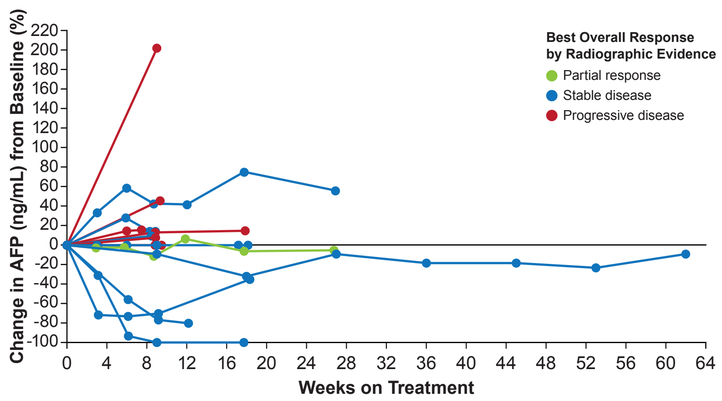


Figure 7: Change in Alpha-Fetoprotein (AFP) from Baseline



CONCLUSIONS

- Treatment with BGB-A317 was generally well tolerated in pretreated patients with advanced HCC
  - As of April 28, 2017, in this early report more than half of patients remain on study (n=24/40); median treatment duration is 64 days (range: 1–471 days)
  - Rate of treatment discontinuation due to a treatment-related AE was low (n=1/40)
- Adverse events reported in this cohort were consistent with the overall safety profile observed in the study and were generally of low severity, manageable, and reversible
- Most patients had underlying viral infection (HBV+, n=28; HCV+/HBV+, n=6; HCV+, n=2)
- Tumor reductions meeting the definition of "partial response" were observed in 3 patients (**Figure 3**); all were HBV+ which is associated with poor prognosis
- Nine patients achieved stable disease, some of whom also had significant reductions in AFP (**Figure 7**)
- The preliminary safety profile and antitumor activity support continued development of BGB-A317 in patients with advanced HCC

Table 2: Treatment-Related Adverse Events

	HCC Population (N=40)	
	All grades	Grade ≥3
Any treatment-related AE	21	1
Rash	8	0
Pruritus	5	0
AST increased	3	0
Fatigue	2	0
Hypothyroidism	2	0
Decreased appetite	2	0
Acute hepatitis*	1	1
ALT increased	1	0
Blood creatine increased	1	0
Blood creatinine increased	1	0
QT prolongation	1	0
Skin reaction	1	0
Chills	1	0
Feeling hot	1	0
Nausea	1	0
Vomiting	1	0
Arthralgia	1	0
Proteinuria	1	0
Cough	1	0
Hypertension	1	0

Data presented as n.
Bold font indicates events that are possibly immune related.
*Acute hepatitis was fatal (grade 5).

- Treatment-related AEs occurred in 21 of the 40 patients with HCC (**Table 2**)
  - All but one of these events were grade ≤2
  - The most common events were rash (n=8) and pruritus (n=5)
- Two patients discontinued treatment due to any treatment-emergent AE, one of which was a grade 5 AE considered related to treatment by the investigator
  - A 49-year-old Asian male with HBV and HCC widely metastatic to brain, liver and lung, developed evidence of progression (disturbed consciousness, abdominal pain, and changes on chest x-ray) shortly following the first and only dose of BGB-A317. The patient died approximately 5 weeks after entering the study, despite treatment with methylprednisolone and entecavir. Viral serology was negative; no autopsy was performed. The cause of death was attributed to acute hepatitis and confounded by rapid disease progression

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ACKNOWLEDGMENTS

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 SuccinctChoice Medical Communications, Chicago, IL.