First-in-human study of BG-C9074, a B7-H4-targeting ADC in patients with advanced solid tumors: Preliminary results of the dose-escalation phase

3033

Cesar A. Perez,[1] Linda Mileshkin,[2] Saana D'Alonzo,[3] Garry Winkler,[4] Shuai Yuan,[5] Hugh Giovinazzo,[4] Zhaoyin Zhu,[6] Ramil Abdrashitov,[7] Binghe Xu[8]

[1]Sarah Cannon Research Institute at Florida Cancer Specialists, Orlando, FL, USA; [2]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [3]BeOne Medicines Switzerland GmbH, Basel, Switzerland; [4]BeOne Medicines, San Carlos, CA, USA; [5]BeOne Medicines (Shanghai) Co., Ltd, Shanghai, China; [6]BeOne Medicines, Ridgefield Park, NJ, USA; [7]BeOne Medicines, Gaithersburg, MD, USA; [8]Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

CONCLUSIONS

- BG-C9074 showed a manageable safety/tolerability profile in patients with B7-H4 advanced solid tumors
- With limited follow-up, preliminary clinical responses were observed at multiple dose levels across various tumor types without selection for B7-H4 expression in these heavily pretreated patients
- Conjugated and free payload pharmacokinetics were observed to be approximately dose proportional across dose levels
- Dose-escalation and dose-level expansion are ongoing

INTRODUCTION

- B7-H4, a transmembrane glycoprotein in the B7 superfamily, has limited expression in normal tissue but is upregulated in solid tumors, including cholangiocarcinoma, breast, ovarian, and endometrial cancers[1,2]
- BG-C9074 is an investigational topoisomerase I inhibitor antibody–drug conjugate (ADC) that targets B7-H4, with an innovative drug-linker design, a drug-to-antibody ratio of 6 (DAR6), and strong bystander effect (**Figure 1**)
- BG-C9074 is being investigated in a first-in-human phase 1a/1b, open-label, multicenter study alone and in combination with tislelizumab in patients with advanced solid tumors (NCT06233942)
- Here we present the initial results of BG-C9074 monotherapy from the ongoing phase 1a dose-escalation study

Figure 1. BG B7-H4 ADC Molecular Design

METHODS

Study Design

- This phase 1, open-label, multicenter trial consisted of two parts: phase 1a dose escalation and phase 1b dose expansion
- In the monotherapy dose-escalation phase, BG-C9074 was administered intravenously every 3 weeks (Q3W) in sequentially escalating dose cohorts ranging from 1 to 7 mg/kg (**Figure 2**)

Figure 2. Study Design

Key eligibility criteria for the monotherapy dose-escalation phase

- ≥18 years
- Histologically or cytologically confirmed advanced, metastatic, or unresectable solid tumors, irrespective of B7-H4 expression
- ECOG PS ≤1
- Previous standard systemic therapy and cancer that is not amenable to therapy with curative intent or if treatment is not available or not tolerated
  - Prior treatment with B7-H4 targeting ADC not permitted

Endpoints for the dose-escalation phase

- Primary endpoints: safety/tolerability, MTD, MAD, RDFE
- Secondary endpoints: ORR, DOR, DCR, CBR, PK, ADAs
- Exploratory endpoints: PFS, exploratory biomarkers

All antitumor endpoints were assessed by investigator per RECIST v1.1.

Abbreviations: ADA, anti-drug antibody; CBR, clinical benefit rate; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Group Oncology Performance Status; MAD, maximum administered dose; MTD, maximum tolerated dose; ORR, overall response rate; PFS, progression-free survival; PK, pharmacokinetic; RDFE, recommended dose for expansion; RECIST, Response Evaluation Criteria in Solid Tumors.

RESULTS

Study Population

- As of March 16, 2025, 78 patients with advanced solid tumors received BG-C9074 monotherapy in the ongoing dose-escalation phase
- In all, 6 dose levels have been evaluated during dose escalation, with 1 additional dose level evaluated during the safety expansion
- Baseline characteristics are shown in **Table 1**
  - Patients were heavily pretreated: the median (range) number of lines of prior therapy was 4.0 (0–10)
- Median (range) study follow-up was 2.8 (0.2-9.3) months

Table 1. Baseline Demographic and Disease Characteristics

Characteristic	Total (N=78)
Median (range) age, years	59.0 (37.0-79.0)
Sex, n (%)	
Female	69 (88.5)
Race, n (%)	
White	37 (47.4)
Asian	36 (46.2)
Black or African American	1 (1.3)
Other	4 (5.1)
Tumor types	
Cholangiocarcinoma	11 (14.1)
Endometrial cancer	1 (1.3)
HR+/HER2– breast cancer	20 (25.6)
Ovarian cancer	34 (43.6)
Squamous NSCLC	1 (1.3)
TNBC	11 (14.1)
ECOG PS, n (%)	
0	39 (50.0)
1	39 (50.0)
Median (range) prior lines of therapy	4.0 (0-10)

Abbreviations: HR+/HER2–, hormone receptor positive/human epidermal growth factor receptor 2 negative; NSCLC, non-small cell lung cancer; TNBC, triple-negative breast cancer.

Safety

- Overall, BG-C9074 as monotherapy was generally well tolerated across dose levels (**Table 2**)
- There were 5 dose-limiting toxicities (DLTs) among 3 dose levels, all related to treatment: grade 3 fatigue (n=1); grade 3 febrile neutropenia (n=2); and grade 4 platelet count decreased (n=2)
- The most common treatment-emergent adverse events (TEAEs) were nausea (50.0%; 3 patients grade ≥3), fatigue (39.7%; 3 patients grade ≥3), and neutropenia[a] (38.5%; 11 patients grade ≥3) (**Table 3**)
- The most common grade ≥3 TEAEs were neutropenia[a] (14.1%) and thrombocytopenia[b] (9.0%)
- There were no TEAEs leading to treatment discontinuation or death

[a]Neutropenia was defined by a custom MedDRA basket with neutropenia and neutrophil count decrease preferred terms. [b]Thrombocytopenia was defined by a custom MedDRA basket with thrombocytopenia and platelet count decreased preferred terms.

Table 2. Safety Summary

Event type, n (%)	1 mg/kg Q3W (n=6)	2 mg/kg Q3W (n=4)	4 mg/kg Q3W (n=23)	5 mg/kg Q3W (n=6)	6 mg/kg Q3W (n=24)	6.5 mg/kg Q3W (n=12)	7 mg/kg Q3W (n=5)	Total (N=78)
Any TEAE	4 (100.0)	4 (100.0)	21 (91.3)	5 (83.3)	24 (100.0)	12 (100.0)	5 (100.0)	75 (96.2)
Grade ≥3 TEAEs	1 (25.0)	0 (0.0)	3 (13.0)	0 (0.0)	10 (41.7)	3 (25.0)	4 (80.0)	21 (26.9)
Treatment-related TEAEs	2 (50.0)	4 (100.0)	19 (82.6)	5 (83.3)	24 (100.0)	11 (91.7)	5 (100.0)	70 (89.7)
Grade ≥3 treatment-related TEAEs	0 (0.0)	0 (0.0)	1 (4.3)	0 (0.0)	9 (37.5)	3 (25.0)	4 (80.0)	17 (21.8)
Any TESAEs	2 (50.0)	0 (0.0)	2 (8.7)	0 (0.0)	5 (20.8)	1 (8.3)	2 (40.0)	12 (15.4)
TEAEs leading to study treatment discontinuation	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)[a]	0 (0.0)	1 (1.3)
Infusion-related reaction	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)
DLT, n	0	0	0	0	1	2	2	5

[a]After the data cutoff date, the reason for study drug discontinuation was changed to progressive disease.
Abbreviations: TESAE, treatment-emergent serious adverse event.

Table 3. Most Common TEAEs in >10% of Patients

Event type, n (%)	1 mg/kg Q3W (n=4)	2 mg/kg Q3W (n=4)	4 mg/kg Q3W (n=23)	5 mg/kg Q3W (n=6)	6 mg/kg Q3W (n=24)	6.5 mg/kg Q3W (n=12)	7 mg/kg Q3W (n=5)	Total (N=78)
Nausea	1 (25.0)	3 (75.0)	9 (39.1)	2 (33.3)	14 (58.3)	7 (58.3)	3 (60.0)	39 (50.0)
Fatigue	3 (75.0)	3 (75.0)	8 (34.8)	2 (33.3)	7 (29.2)	5 (41.7)	3 (60.0)	31 (39.7)
Neutropenia[a]	0 (0.0)	0 (0.0)	5 (21.7)	0 (0.0)	15 (62.5)	6 (50.0)	4 (80.0)	30 (38.5)
Vomiting	0 (0.0)	3 (75.0)	5 (21.7)	1 (16.7)	3 (12.5)	4 (33.3)	1 (20.0)	17 (21.8)
Anemia	0 (0.0)	0 (0.0)	3 (13.0)	0 (0.0)	7 (29.2)	4 (33.3)	2 (40.0)	16 (20.5)
Thrombocytopenia[b]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (41.7)	4 (33.3)	3 (60.0)	17 (21.8)
Constipation	0 (0.0)	1 (25.0)	5 (21.7)	0 (0.0)	4 (16.7)	2 (16.7)	1 (20.0)	13 (16.7)
Diarrhea	2 (50.0)	0 (0.0)	2 (8.7)	1 (16.7)	2 (8.3)	2 (16.7)	2 (40.0)	11 (14.1)
ALT increased	0 (0.0)	0 (0.0)	3 (13.0)	0 (0.0)	5 (20.8)	0 (0.0)	0 (0.0)	8 (10.3)

[a]Neutropenia was defined by a custom MedDRA basket with neutropenia and neutrophil count decrease preferred terms. [b]Thrombocytopenia was defined by a custom MedDRA basket with thrombocytopenia and platelet count decreased preferred terms.
Abbreviations: ALT, alanine aminotransferase.

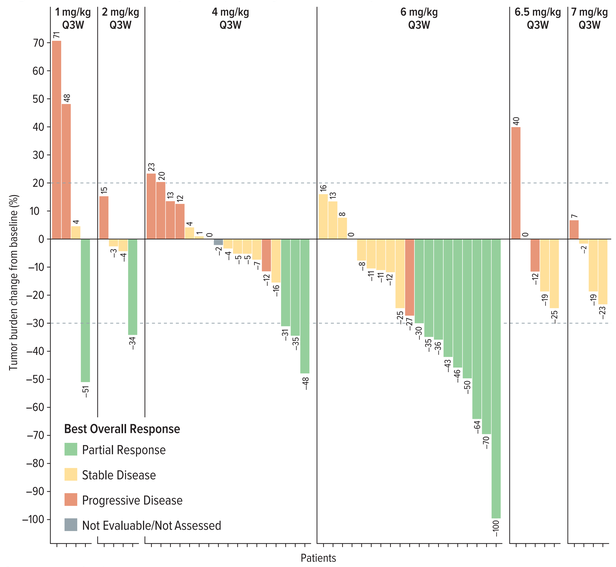
Antitumor Activity

- Antitumor activity data are summarized in **Figures 3 and 4**
- Dose-response relationship was observed at the dose levels tested (**Figure 3**)
- With limited follow-up among the 56 efficacy-evaluable patients, confirmed overall response rate (ORR) (95% confidence interval) was 16.1% (9/56; 7.6%-28.3%), with 9 confirmed partial responses; unconfirmed ORR was 25.0% (14/56; 14.4%-38.4%) (n=14 partial responses)
- Confirmed disease control rate (DCR) was 73.2% (59.7%-84.2%) and confirmed clinical benefit rate (CBR) was 17.9% (8.9%-30.4%)

Pharmacokinetics

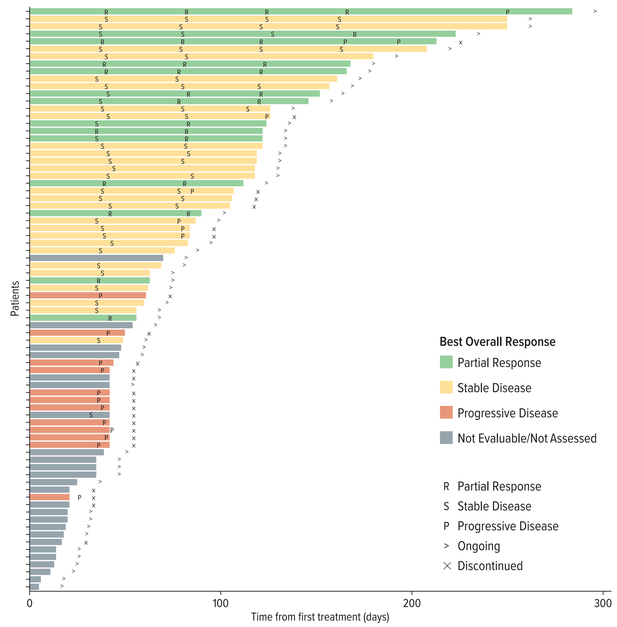
- Serum concentrations of BG-C9074 conjugated and free payload decreased in a biexponential manner (**Figure 5**)
- Maximum concentrations (C_{max}) after end of infusion observed 15 min to 4 hours for conjugated payload and 2-6 hours for free payload
- Exposure of conjugated and free payload increased approximately dose-proportionally across dose levels

Figure 3. Best Overall Response (Efficacy Evaluable Population)



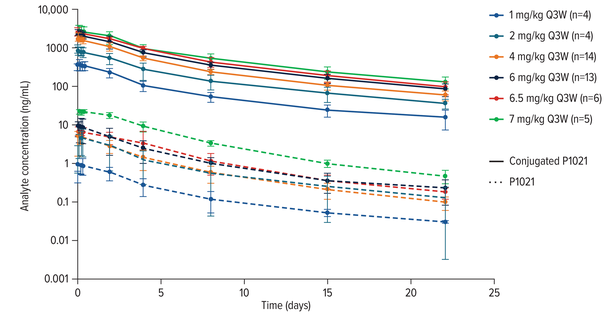
Responses are unconfirmed.

Figure 4. Duration of Treatment and Response (Safety Analysis Set)



Responses are unconfirmed.

Figure 5. Single-Dose Pharmacokinetics of BG-C9074



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DISCLOSURES

CAP reports consulting or advisory roles for BeOne Medicines and research funding from BeOne Medicines.

ACKNOWLEDGMENTS

The authors thank the patients and their families, investigators, co-investigators, and the study teams at each of the participating centers. This study was sponsored by BeOne Medicines, Ltd (formerly BeiGene, Ltd.). Medical writing support was provided by Tricia Gallagher, MS, MBA, of AMICULUM, and supported by BeOne Medicines.

CORRESPONDENCE: Dr Cesar A. Perez: Cesar.PerezBatista@flcancer.com

Presented at ASCO Annual Meeting; May 30-June 3, 2025; Chicago, IL, USA