Poster #89

Phase 2 Trial of Mecbotamab Vedotin (BA3011), a CAB-AXL-ADC, Alone or in Combination With Nivolumab in Patients With Non-Squamous NSCLC

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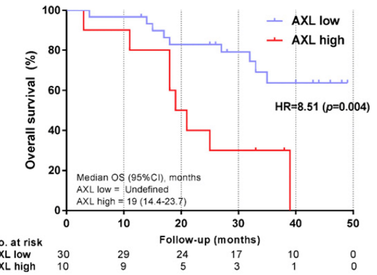
Background

- Mecbotamab vedotin is a Conditionally Active Biologic[1] anti-AXL antibody-drug conjugate (CAB-AXL-ADC) with a monomethyl auristatin E (MMAE) payload for patients with advanced solid tumors[2]
  - BA3011 is engineered to conditionally and reversibly bind AXL under tumor-specific, low-pH conditions (pH 5.8-6.7)[1]
  - pH selectivity reduces on- and off-tumor toxicity without increasing immunogenicity, avoids target-mediated drug disposition, and improves pharmacokinetics
- AXL is a cell-surface receptor tyrosine kinase highly expressed in several solid tumor types[3] and is a documented poor prognostic indicator for patient survival[4,5] (**Figure 1**)
- Increased AXL expression has been associated with worse clinical outcomes and tumor resistance to chemotherapy, favoring invasion, metastasis, and disease recurrence[5]

Figure 1. Lower overall survival in patients with early-stage, surgically resected lung adenocarcinoma with high levels of tissue AXL[4]



Reproduced from de Miguel-Pérez D, et al. *Cancers (Basel)*. 2019;11(11):1750[4].
Abbreviation: HR, hazard ratio; OS, overall survival.

Conclusions

- **BA3011 was associated with promising antitumor activity among patients with extensively pretreated, post–anti-PD-1/L1 therapy, non-squamous NSCLC whose tumors expressed AXL, an established poor prognostic factor[4,5]**
- **Treatment with BA3011 was well tolerated with a manageable safety profile**
- **These observations of multiple responses among such heavily pretreated patients, including those with AXL TmPS of only 1%, support further evaluation of BA3011 in an AXL-agnostic population**

References

1. Chang HW, Frey G, Liu H, et al. Generating tumor-selective conditionally active biologic anti-CTLA4 antibodies via protein-associated chemical switches. *Proc Natl Acad Sci USA*. 2021;118(9):e2020606118. doi:10.1073/pnas.2020606118
2. Sharp LL, Chang C, Frey G, et al. Anti-tumor efficacy of BA3011: a novel conditionally active biologic (CAB) anti-AXL-ADC. Poster presented at: American Association for Cancer Research Annual Meeting; April 14-18, 2018; Chicago, IL.
3. Gay CM, Balaji K, Byers LA. Giving AXL the axe: targeting AXL in human malignancy. *Br J Cancer*. 2017;116(4):415-423. doi:10.1038/bjc.2016.428
4. de Miguel-Pérez D, Bayarri-Lara CI, Ortega FG, et al. Post-surgery circulating tumor cells and AXL overexpression as new poor prognostic biomarkers in resected lung adenocarcinoma. *Cancers (Basel)*. 2019;11(11):1750. doi:10.3390/cancers11111750
5. Zhang G, Wang M, Zhao H, Cui W. Function of Axl receptor tyrosine kinase in non-small cell lung cancer. *Oncol Lett*. 2018;15(3):2726-2734. doi:10.3892/ol.2017.7694

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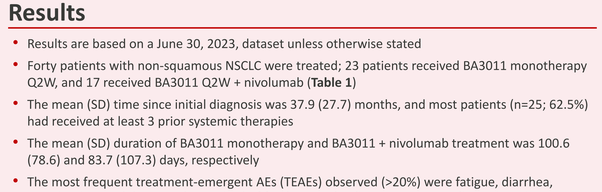
Methods

Figure 2. Multicenter, Phase 2, open-label trial evaluating the efficacy and safety of BA3011 alone and in combination with nivolumab



*Coded by MedDRA and graded according to NCI CTCAE v5
Abbreviations: 2Q3W, twice every 3 weeks (1.8 mg/kg dosed on Days 1 and 8 in a 3-week cycle); 3Q4W, 1.8 mg/kg three times every 4 weeks (1.8 mg/kg dosed on Day 1, then 1.2mg/kg dosed on Days 8 and 15, followed by 1.2mg/kg dosed on Days 1, 8, and 15 in a 4-week cycle); AE, adverse event; ALK, anaplastic lymphoma kinase; BOR, best overall response; CTCAE, Common Terminology Criteria for Adverse Events; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; MedDRA, Medical Dictionary for Regulatory Activities; NCI, National Cancer Institute; NSCLC, non–small cell lung cancer; ORR, objective response rate; PD-1/L1, programmed cell death protein 1/ligand 1; PFS, progression-free survival; Q2W, once every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TmPS, tumor membrane percent score; TTR, time to response.

Table 1. Demographics and baseline characteristics

	BA3011 monotherapy (N=23)	BA3011 + nivolumab (N=17)	Total (N=40)
Age, y, mean (SD)	68.3 (8.0)	68.9 (8.2)	68.6 (8.0)
Gender, n (%)			
Male	11 (47.8)	7 (41.2)	18 (45.0)
Female	12 (52.2)	10 (58.8)	22 (55.0)
Race, n (%)			
White	15 (65.2)	14 (82.4)	29 (72.5)
Asian	4 (17.4)	2 (11.8)	6 (15.0)
Black or African American	3 (13.0)	0	3 (7.5)
Other	1 (4.3)	0	1 (2.5)
Number of prior systemic therapies, n (%)			
1	4 (17.4)	2 (11.8)	6 (15.0)
2	6 (26.1)	3 (17.6)	9 (22.5)
3	9 (39.1)	2 (11.8)	11 (27.5)
≥4	4 (17.4)	10 (58.8)	14 (35.0)
Received prior anti-PD-1/L1 treatment, n (%)			
Yes	21 (91.3)	15 (88.2)	36 (90.0)
No	2 (8.7)	2 (11.8)	4 (10.0)
EGFR mutation status, n (%)			
Wild-type	16 (69.6)	14 (82.4)	30 (75.0)
Mutant	4 (17.4)	2 (11.8)	6 (15.0)
Unknown or missing	3 (13.0)	1 (5.9)	4 (10.0)

Results

- Results are based on a June 30, 2023, dataset unless otherwise stated
- Forty patients with non-squamous NSCLC were treated; 23 patients received BA3011 monotherapy Q2W, and 17 received BA3011 Q2W + nivolumab (**Table 1**)
- The mean (SD) time since initial diagnosis was 37.9 (27.7) months, and most patients (n=25; 62.5%) had received at least 3 prior systemic therapies
- The mean (SD) duration of BA3011 monotherapy and BA3011 + nivolumab treatment was 100.6 (78.6) and 83.7 (107.3) days, respectively
- The most frequent treatment-emergent AEs (TEAEs) observed (>20%) were fatigue, diarrhea, constipation, and decreased appetite (**Table 3**). TEAEs leading to treatment discontinuation occurred in 1 patient who received monotherapy due to an infusion-related reaction and 1 patient who received combination therapy due to acute kidney injury
- Monotherapy (n=18):
  - Patients who previously experienced PD-1/L1 treatment failure and were evaluable for efficacy at 12 weeks; response rate was 27.8%, and DCR was 55.6% (**Table 4**)
  - Five of 15 (33.3%) evaluable patients with EGFR wild-type NSCLC who previously experienced PD-1/L1 treatment failure responded to BA3011 monotherapy (**Figure 3**)
    - Among these 5 responders, 2 patients with AXL TmPS of 1% experienced partial response (PR)
    - Median duration of response was estimated to be 4.8 months with a range of 2.3-12.1+ months as of November 20, 2023
- Combination therapy (n=17)*:
  - Evaluable patients (majority with 4+ prior lines of therapy) received BA3011 + nivolumab
  - One patient experienced an ongoing complete response (CR), 2 patients experienced PR, and 8 patients experienced stable disease (SD)
- BOR in higher frequency dosing regimens (BA3011 2Q3W and 3Q4W)*: 6 patients were response evaluable with 1 EGFR mutant. 3 SD and 3 progressive disease (PD)

*As of November 8, 2023

Safety

Table 2. Summary of TEAEs in the study population

Number of patients who experienced any, n (%)	BA3011 monotherapy (N=23)	BA3011 + nivolumab (N=17)	Total (N=40)
TEAE	23 (100)	16 (94.1)	39 (97.5)
Related TEAE	21 (91.3)	15 (88.2)	36 (90.0)
≥Grade 3 TEAE	15 (65.2)	8 (47.1)	23 (57.5)
Related ≥grade 3 TEAE	8 (34.8)	3 (17.6)	11 (27.5)
Serious TEAE	9 (39.1)	5 (29.4)	14 (35.0)
Related serious TEAE	3 (13.0)	1 (5.9)	4 (10.0)
TEAE leading to treatment discontinuation	1 (4.3)	1 (5.9)	2 (5.0)
Discontinuation due to related TEAE	1 (4.3)	1 (5.9)	2 (5.0)
TEAE leading to death	0	1 (5.9)	1 (2.5)
Related TEAE leading to death	0	0	0

Table 3. All TEAEs of any grade (≥15% of patients) OR grade ≥3* (≥3% of patients) in the study population

Preferred term	TEAEs of any grade, n (%)	TEAEs of grade 3, n (%)
Fatigue	14 (35.0)	1 (2.5)
Diarrhea	10 (25.0)	1 (2.5)
Constipation	9 (22.5)	0
Decreased appetite	9 (22.5)	1 (2.5)
Anemia	8 (20.0)	2 (5.0)
Nausea	8 (20.0)	0
Peripheral neuropathy	7 (17.5)	1 (2.5)
Increased AST	7 (17.5)	3 (7.5)
Dyspnea	6 (15.0)	2 (5.0)
Neutropenia	6 (15.0)	2 (5.0)
Increased ALT	5 (12.5)	3 (7.5)

*No grade 4+ TEAEs among most frequent.
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Efficacy

Table 4. Treatment response in patients receiving BA3011 monotherapy

	Prior PD-1/L1 treatment EGFR wild-type (N=15)	Prior PD-1/L1 treatment (N=18)
Best Overall Response, n (%)		
Confirmed PR	3 (20.0)	3 (16.7)
Unconfirmed PR	2 (13.3)	2 (11.1)
SD	7 (46.7)	10 (55.6)
PD	2 (13.3)	2 (11.1)
NA (early discontinuation due to AE)	1 (6.7)	1 (5.6)
Response Rate		
n (%)	5 (33.3)	5 (27.8)
Exact 95% CI	11.8, 61.6	9.7, 53.5
Disease Control Rate		
n (%)	8 (53.3)	10 (55.6)
Exact 95% CI	26.6, 78.7	30.8, 78.5

The response-evaluable population includes all patients who were dosed at least 12 weeks prior to the data cutoff and have at least 1 post-baseline disease assessment and/or discontinued treatment or the study due to death or disease progression.
Abbreviations: NA, not available.

Figure 4. Percent change from baseline in sum of target lesions in patients receiving BA3011 monotherapy with EGFR wild-type NSCLC who received prior anti–PD-1/L1 treatment

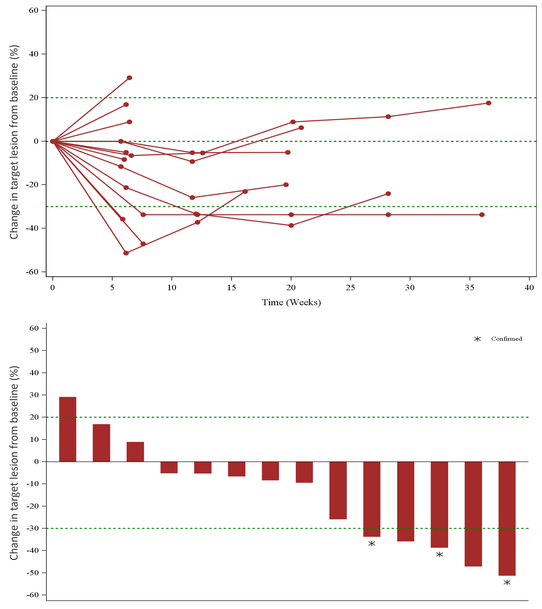


Figure 3. Treatment response in patients receiving BA3011 monotherapy with EGFR wild-type NSCLC who received prior anti–PD-1/L1 treatment

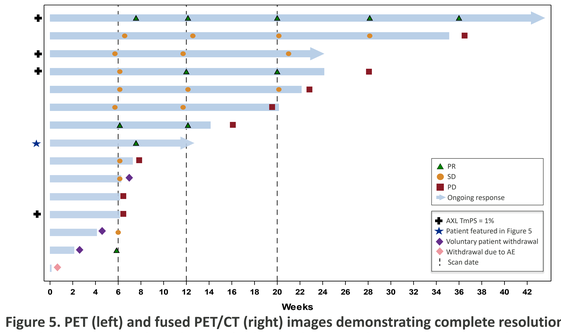
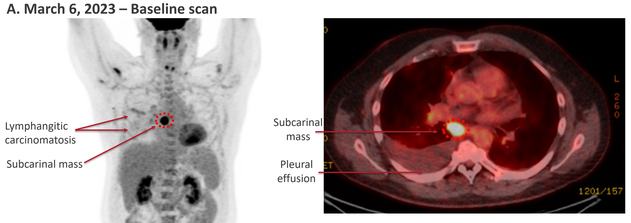
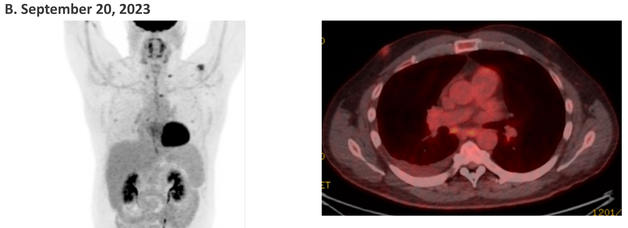


Figure 5. PET (left) and fused PET/CT (right) images demonstrating complete resolution of metabolic activity and resolution of subcarinal mass with improvement in malignant pleural effusion on BA3011 monotherapy.

A. March 6, 2023 – Baseline scan



B. September 20, 2023



53-year-old patient status post 3 lines of therapy (including prior anti-PD1/L1 treatment) with TP53 mutated, PD-L1 TPS <1%
RECIST v1.1 showed 47% tumor reduction of subcarinal mass
Abbreviations: CT, computed tomography; PET, positron emission tomography; TPS, tumor proportion score.

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