Poster #
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Botensilimab (BOT) plus balstilimab (BAL) in microsatellite stable metastatic colorectal cancer: Assessing efficacy in non-liver metastatic sites

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BACKGROUND

- Botensilimab (BOT) is an Fc-enhanced, multifunctional anti-CTLA-4 antibody with differentiated mechanisms of action, designed to extend therapy to cold/poorly immunogenic solid tumors including microsatellite stable metastatic colorectal cancer (MSS mCRC; Figure 1)[1,2]
- Responses to novel immunotherapy (I-O) combinations in MSS mCRC have typically been restricted to non-liver metastatic (NLM) populations. Within this subgroup, responses outside of metastatic sites such as the lungs and lymph nodes are rare[3,4]
- We sought to determine whether BOT and balstilimab (BAL; anti–PD-1) could confer responses in NLM sites outside of the lungs and lymph nodes

Botensilimab Mechanism of Action

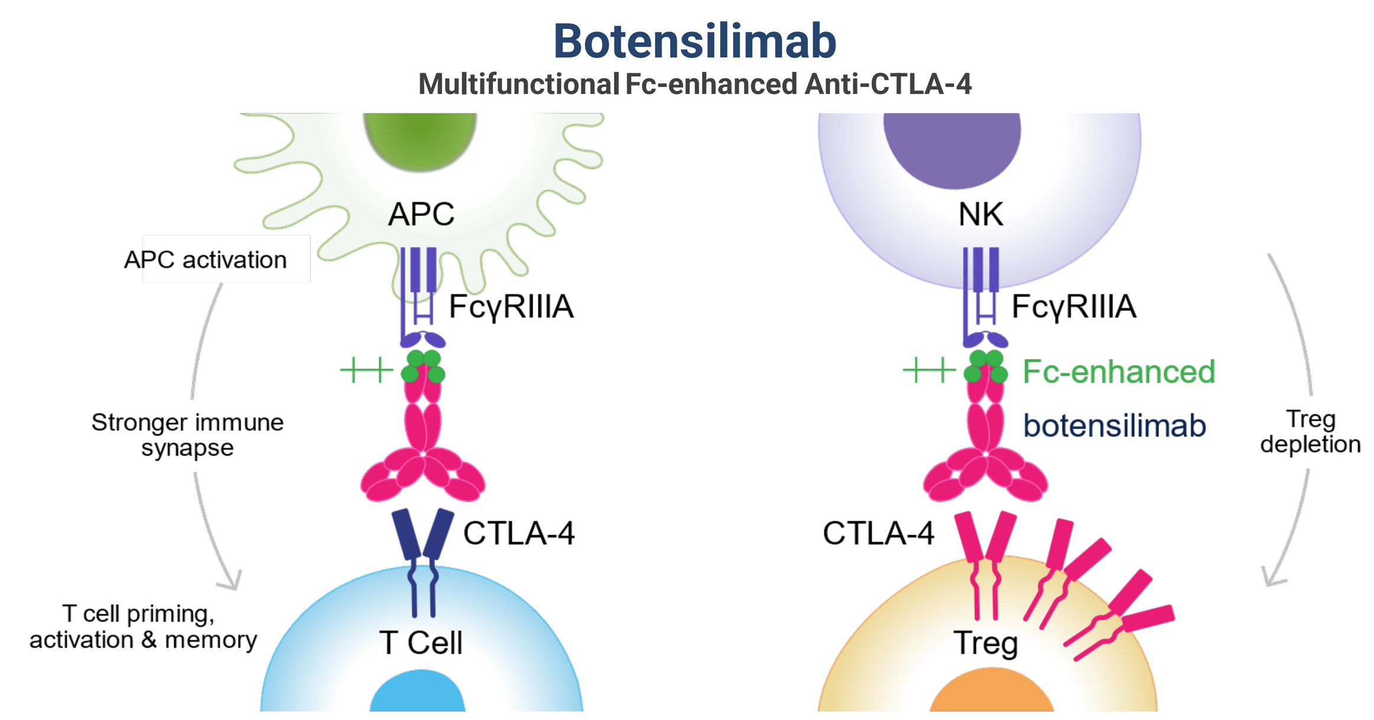


Figure 1. A novel innate and adaptive immune activator. BOT promotes enhanced T cell priming and expansion, T cell activation and memory formation, activation of antigen presenting cells, and reduction of intratumoral regulatory T cells, while improving safety through a reduction in complement-mediated toxicities[1,2]

C-800-01 Study Design: NLM MSS mCRC Cohort (N=77)

NCT0386027: First-in-human trial of **BOT ± BAL** in patients with advanced cancer[5]

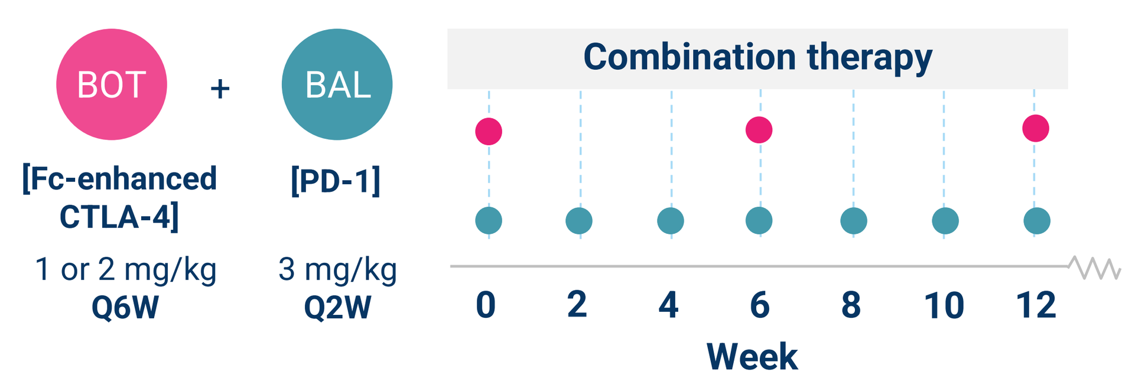
Key Eligibility

- Relapsed/refractory mCRC
- MSS by local assessment
- Prior I-O allowed

Study Endpoints

- Efficacy: ORR, DCR, DOR, PFS, OS
- Safety: AEs

Treatment *(up to 2 years)*



Patient Population

- *Safety Analysis Population* – **77** patients with NLM MSS mCRC treated with 1 or 2 mg/kg BOT Q6W plus 3 mg/kg BAL Q2W
- *Efficacy Evaluable Population* – **70** of these patients with ≥1 post-baseline 6-week imaging scan

References: 1. Chand et al. Submitted manuscript. 2. Bullock A et al. *Ann Oncol* 2023;34:S178–9. 3. Fakih M et al. *EClinicalMedicine* 2023; 58:101917. 4. Fakih M et al. *JAMA Oncol* 2023; 9: 627-634. 5. https://clinicaltrials.gov/ct2/show/NCT03860272.

Abbreviations: AE, adverse event; APC, antigen presenting cell; bal, balstilimab; bot, botensilimab; CR, complete response; CT, computed tomography; CTLA-4, cytotoxic T-lymphocyte associated protein 4; DCR, disease control rate (CR, PR, or SD ≥6 weeks); DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; Fc, fragment crystallizable; FcγR, fragment crystallizable gamma receptor; H&E, hematoxylin and eosin; I-O, immunotherapy; mCRC, metastatic colorectal cancer; MSS, microsatellite stable; MRI, magnetic resonance imaging; NK, natural killer; NLM, no active liver metastases; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression free survival; PD, progressive disease; PD-1, programmed cell death protein 1 ; PR, partial response; PS, performance status; Q[X]W, every X weeks ; SD, stable disease; TMB, tumor mutational burden; Treg, regulatory T cell.

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RESULTS

Baseline Characteristics

	N=77
Median Age, years (range)	56 (36–82)
Sex, n (%)	
Male	37 (48%)
Female	40 (52%)
Race, n (%)	
White	59 (77%)
Black	1 (1%)
Asian	10 (13%)
Other or not specified	7 (9%)
Ethnicity, n (%)	
Hispanic or Latino	13 (17%)
Not Hispanic or Latino	61 (79%)
Not specified	3 (4%)
ECOG PS, n (%)	
0	32 (42%)
1	45 (58%)
Prior Lines of Therapy, n (%)	
Median (range)	4 (2–6)
≥3	56 (73%)
Prior PD-(L)1/CTLA-4, n (%)	16 (21%)
Prior regorafenib, n (%)	17 (22%)
Prior trifluridine/tipiracil, n (%)	12 (16%)
Prior bevacizumab, n (%)	65 (84%)

	N=77
TMB >10, Mut/Mb, n/N (%)[a]	2/39 (5%)
RAS mutation, n/N (%)	47/72 (65%)
BRAF mutation, n/N (%)	2/39 (5%)
Time from metastatic disease to first dose of study drug, months	
Median (range)	36.7 (0.2–179.4)
≥18 months, n (%)	59 (77%)
<18 months, n (%)	18 (23%)
Location of metastases, n (%)	
Lungs	62 (81%)
Peritoneal disease	33 (43%)
Lymph nodes	32 (42%)
Soft tissue	15 (19%)
Other[b]	18 (23%)
Bone	3 (4%)
Brain	2 (3%)
Metastatic sites, n (%)	
1 organ	28 (36%)
Lung only	22 (29%)
Lymph nodes only	2 (3%)
Peritoneal disease only	4 (5%)
≥2 organs	49 (64%)

Data cutoff: 01-MAR-2024
[a]Only two patients had a TMB >10 Mut/Mb and <13.
[b]Other organ involvement includes adrenal glands, bone, brain, kidney, pleura, retroperitoneum, and spleen.

Table 1. Baseline demographics and patient characteristics.

Efficacy

	Number of patients	ORR, % (n/nn)	DCR, % (n/nn)	Median OS, months (95% CI)
NLM MSS mCRC (efficacy evaluable population)	70	26% (18/70)	80% (56/70)	**NR** (20.7–NR)
NLM MSS mCRC (safety analysis population)	77	23% (18/77)	73% (56/77)	**21.2** (16.5–NR)
Any lung involvement	62	26% (16/62)	74% (46/62)	**21.2** (20.7–NR)
Lung only	22	18% (4/22)	82% (18/22)	**NR** (13.3–NR)
Any peritoneal involvement	33	18% (6/33)	67% (22/33)	**20.7** (6.3–NR)
Any soft tissue involvement	15	27% (4/15)	73% (11/15)	**20.7** (3.6–NR)
Any other organ involvement	18	33% (6/18)	72% (13/18)	**20.9** (6.3–NR)

Data cutoff: 01-MAR-2024
Median follow-up for NLM MSS mCRC (safety analysis population) patients (N=77) was 13.6 months (range, 0.6–41.8 months), with 11/18 responses ongoing/censored.

Table 2. Efficacy outcomes by sites of metastatic disease in patients with NLM MSS mCRC.

- Across different NLM sites:
  - Response rates ranged from **18–33%**
  - Disease control rate ranged from **67–82%**
  - Median OS remained consistent and ranged from **20.7 months to not reached (NR)**

Case Study: Radiologic Growth of an Occult Brain Metastasis With a Pathologic Response and No Recurrence

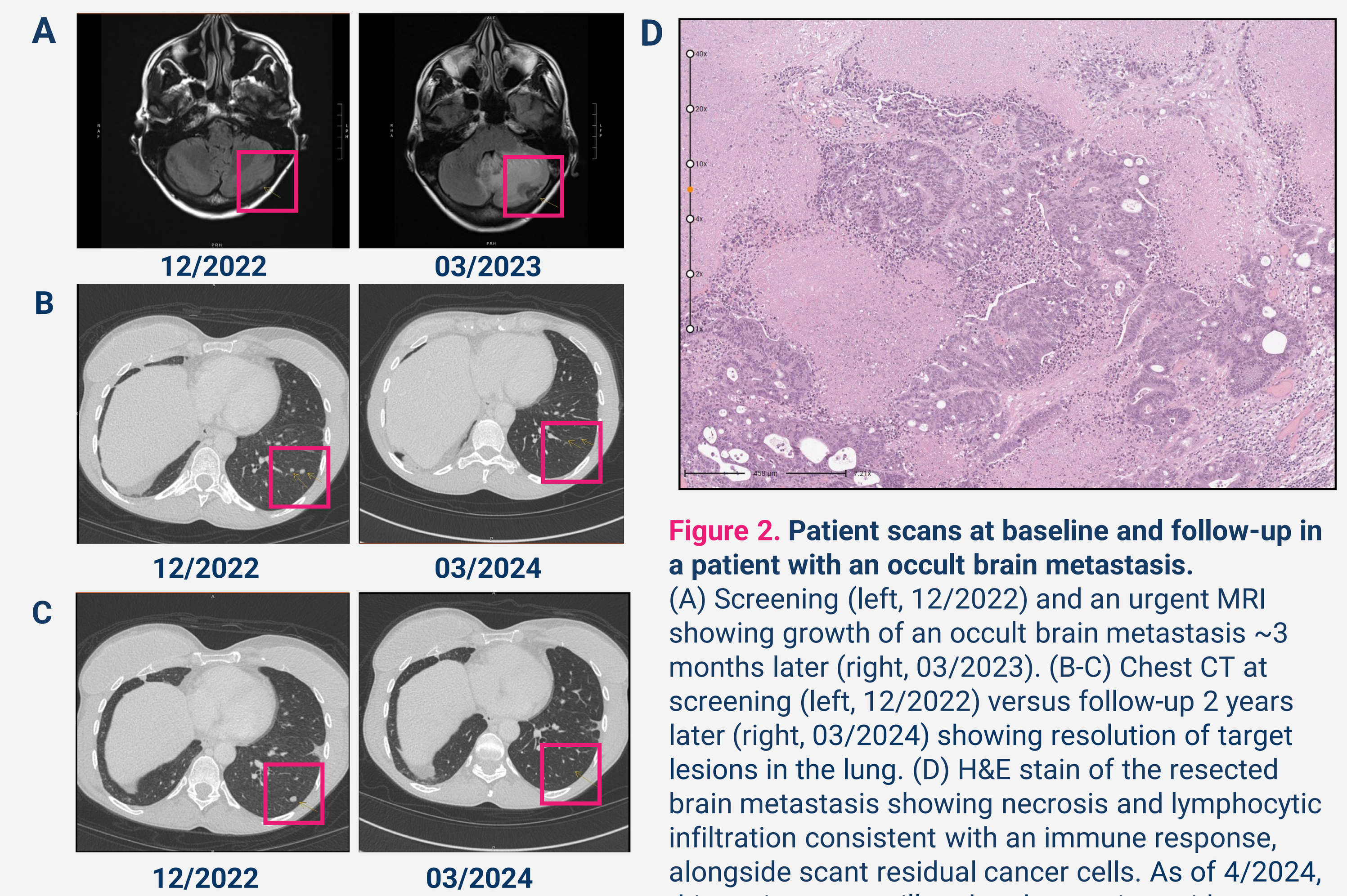

Figure 2. Patient scans at baseline and follow-up in a patient with an occult brain metastasis. (A) Screening (left, 12/2022) and an urgent MRI showing growth of an occult brain metastasis ~3 months later (right, 03/2023). (B-C) Chest CT at screening (left, 12/2022) versus follow-up 2 years later (right, 03/2024) showing resolution of target lesions in the lung. (D) H&E stain of the resected brain metastasis showing necrosis and lymphocytic infiltration consistent with an immune response, alongside scant residual cancer cells. As of 4/2024, this patient was still under observation, with an ongoing PR in lung lesions.

Safety Overview

- No new safety signals
- Safety in CRC consistent across tumor types in study
- No treatment-related deaths

CONCLUSIONS

- In patients with NLM MSS mCRC, response rates were comparable across different sites of metastatic disease, including historically poor prognostic sites such as the peritoneum, soft tissue, pleura and brain
- This broader clinical activity outside the lungs and lymph nodes has not previously been reported with other IO and IO/non-IO combinations
- A global randomized phase 2 trial of BOT ± BAL (versus standard of care) in MSS mCRC is fully enrolled (NCT05608044) and a global phase 3 trial is planned

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Disclosures

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