

Results from a phase 1a/1b study of botensilimab (BOT), a novel innate/adaptive immune activator, plus balstilimab (BAL; anti-PD-1 antibody) in metastatic heavily pretreated microsatellite stable colorectal cancer (MSS CRC)

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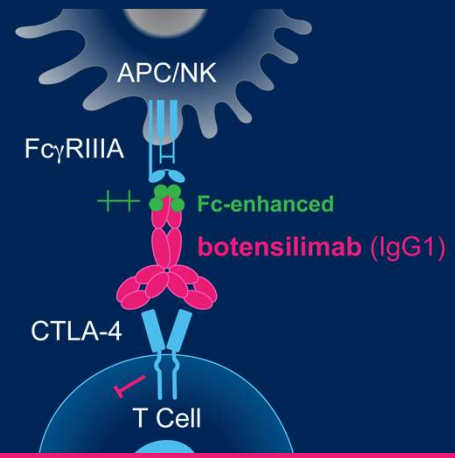
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Active in 'Cold' and IO Refractory Tumors

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botensilimab

Fc-enhanced CTLA-4 Inhibitor

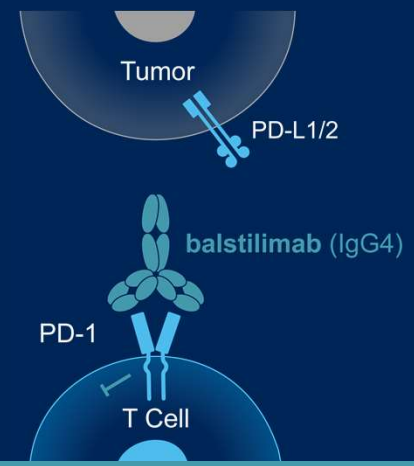


Active in 'cold' and IO refractory tumors^{1,2}

- >300 patients treated across 4 trials
- ↑ T cell priming, expansion, memory^{3,4}
- ↑ Frequency of activated APCs
- ↑ Treg depletion
- ↓ Complement mediated toxicity

balstilimab

PD-1 Inhibitor



Safety and efficacy analogous to approved anti-PD-1 mAbs^{5,6}

- >750 patients treated; 10 ongoing trials / 2 completed
- Complete blocker of PD-1-PD-L1/2 interactions
- Enhanced T cell activation and effector function

1. El-Khoueiry AB. SITC 2021 Annual Meeting. Poster #479. 2. Wilky B. SITC 2022 Annual Meeting. Oral #778. 3. Waight et al. Cancer Cell. 2018;33(6): 1033-1047. 4. Levey D. SITC 2022. Annual Meeting. Oral #470. 5. O'Malley, et al. Gynecol Oncol. 2021; 163: 274-280. 6. O'Malley et al, J Clin Oncol. 2022; 40(7): 762-771.

C-800 Study Design: MSS CRC Cohort

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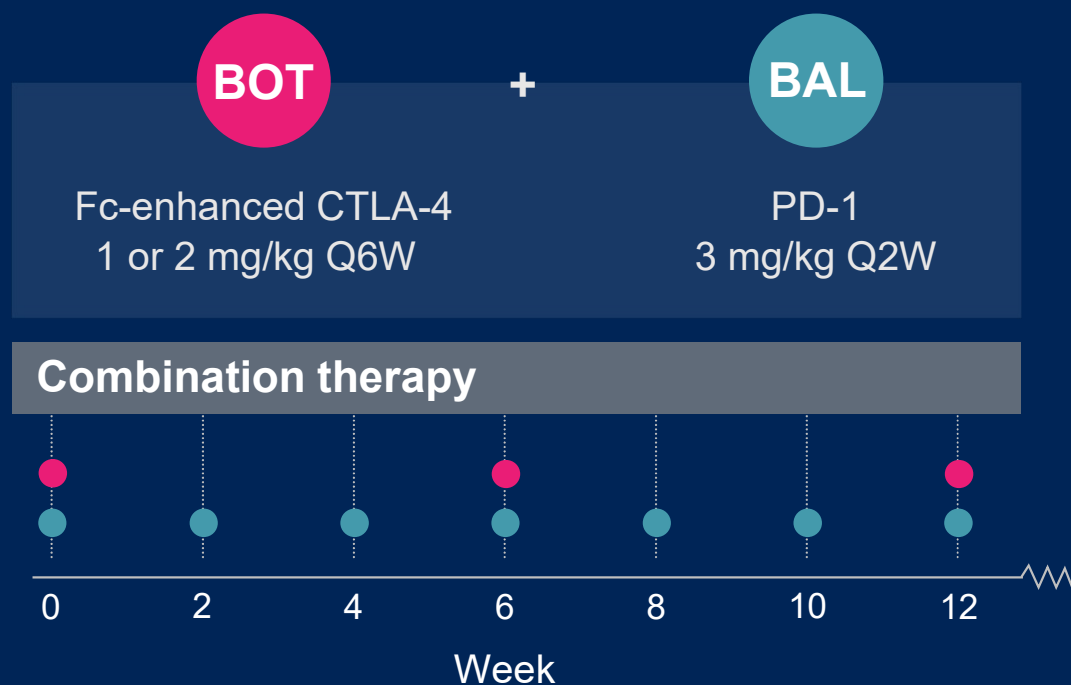
NCT03860272: First-in-human trial of botensilimab ± balstilimab in patients with advanced cancer¹

Key Eligibility for CRC

- Refractory Metastatic CRC
- MSS by local assessment
- Prior IO allowed
- Tbili ≤ 1.5 x IULN
- AST/ALT ≤ 2.5 x IULN

Evaluable Population

Treated with 1 or 2 mg/kg bot + bal as of 29 August 2022 with ≥1 Q6W imaging assessment



1. <https://clinicaltrials.gov/ct2/show/NCT03860272>.

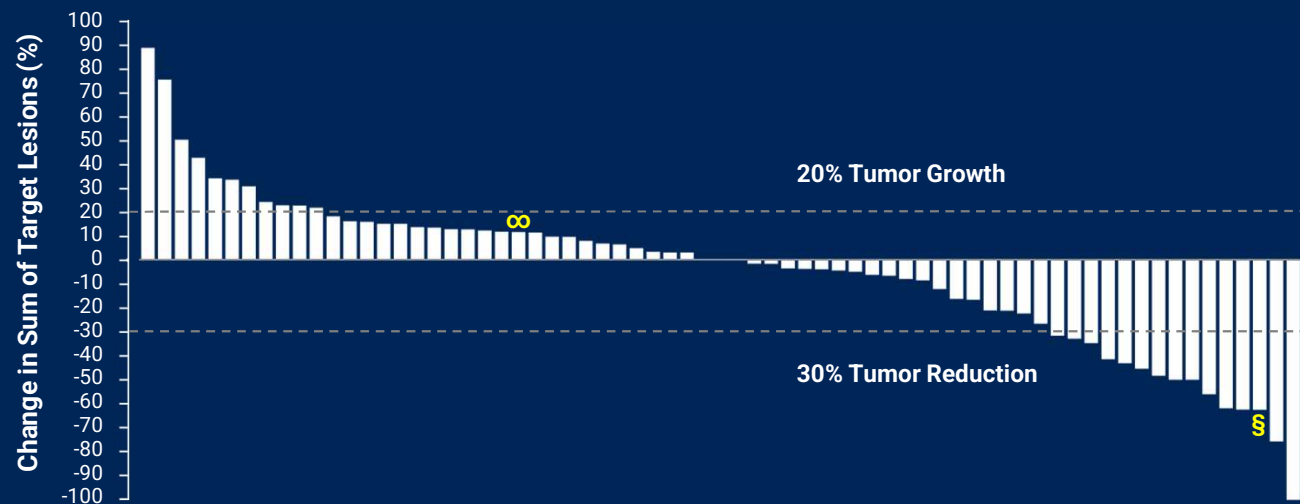
Patient Characteristics

Characteristic	Overall (N=70)*	Characteristic	Overall (N=70)
Age, median (range)	57 (25-83)	Prior immunotherapy, n (%)	22 (31)
Sex, n (%)		Botensilimab dose, n (%)	
Female	40 (57)	1 mg/kg Q6W + bal (PD-1) Q2W	17 (24)
Male	30 (43)	2 mg/kg Q6W + bal (PD-1) Q2W	53 (76)
ECOG PS at baseline, n (%)		TMB>10, n/N (%)	1/57 (2)
0	28 (40)	RAS mutation, n/N (%)	41/70 (59)
1	42 (60)	BRAF mutation, n/N (%)	2/65 (3)
Prior lines of therapy, n (%)			
Median (range)	4 (1-10)		

* 12 patients treated as of 29 AUG 2022 who did not have a post-baseline scan at least 39 days after the first dose were excluded, 3 of these withdrew consent. Data cutoff date 15 Dec 2022.

Deep Objective Responses

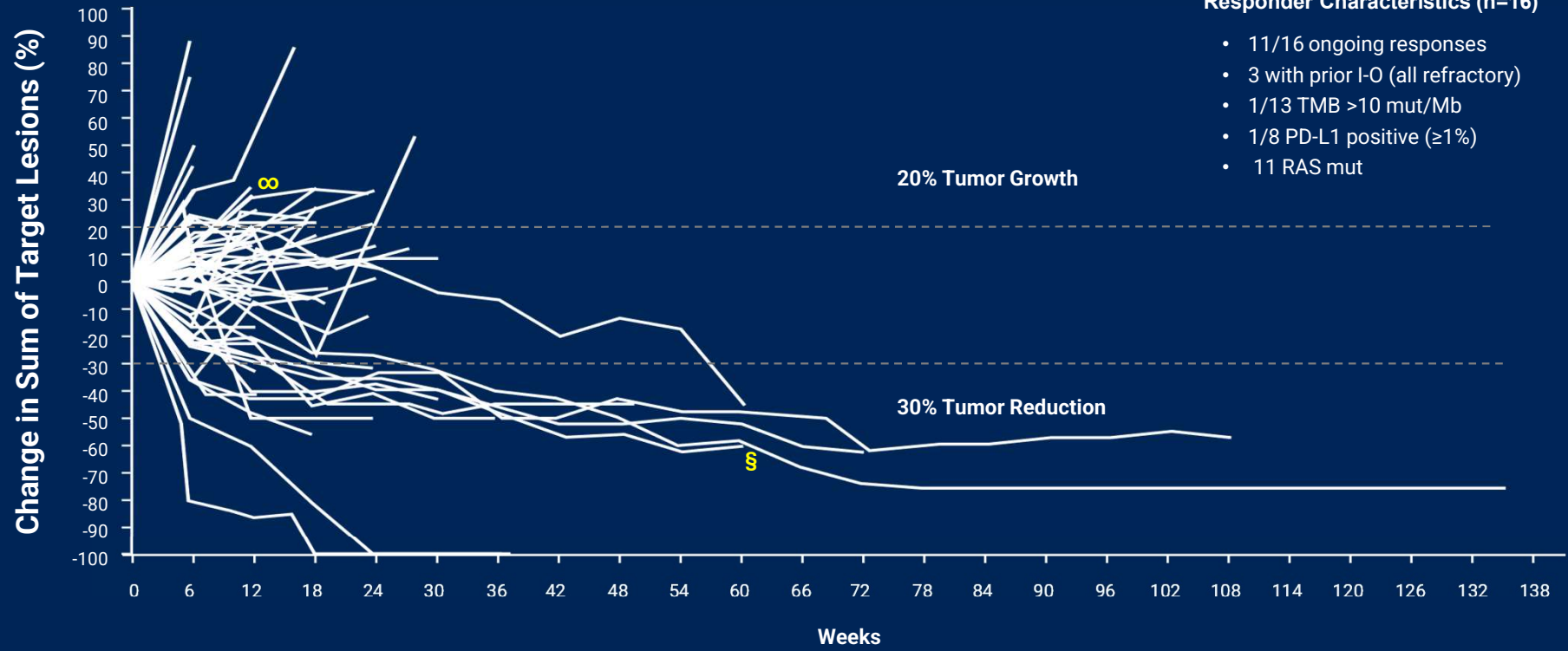
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Efficacy	N=70
ORR*, % (95% CI)	23 (14-34)
BOR, n (%)	
CR	1 (1)
PR	15 (21)
SD	37 (53)
DCR (CR + PR + SD), % (95% CI)	76 (64-85)
Median OS (95% CI)	NR (10.3-NR)
Median PFS, months (95% CI)	4.1 (2.8-5.5)
Median F/U, months (Min, Max)	7 (2, 31)

*Includes unconfirmed responses. ∞ Resected target lesions showed complete pathologic response. § Response by iRECIST.

Durable Objective Responses

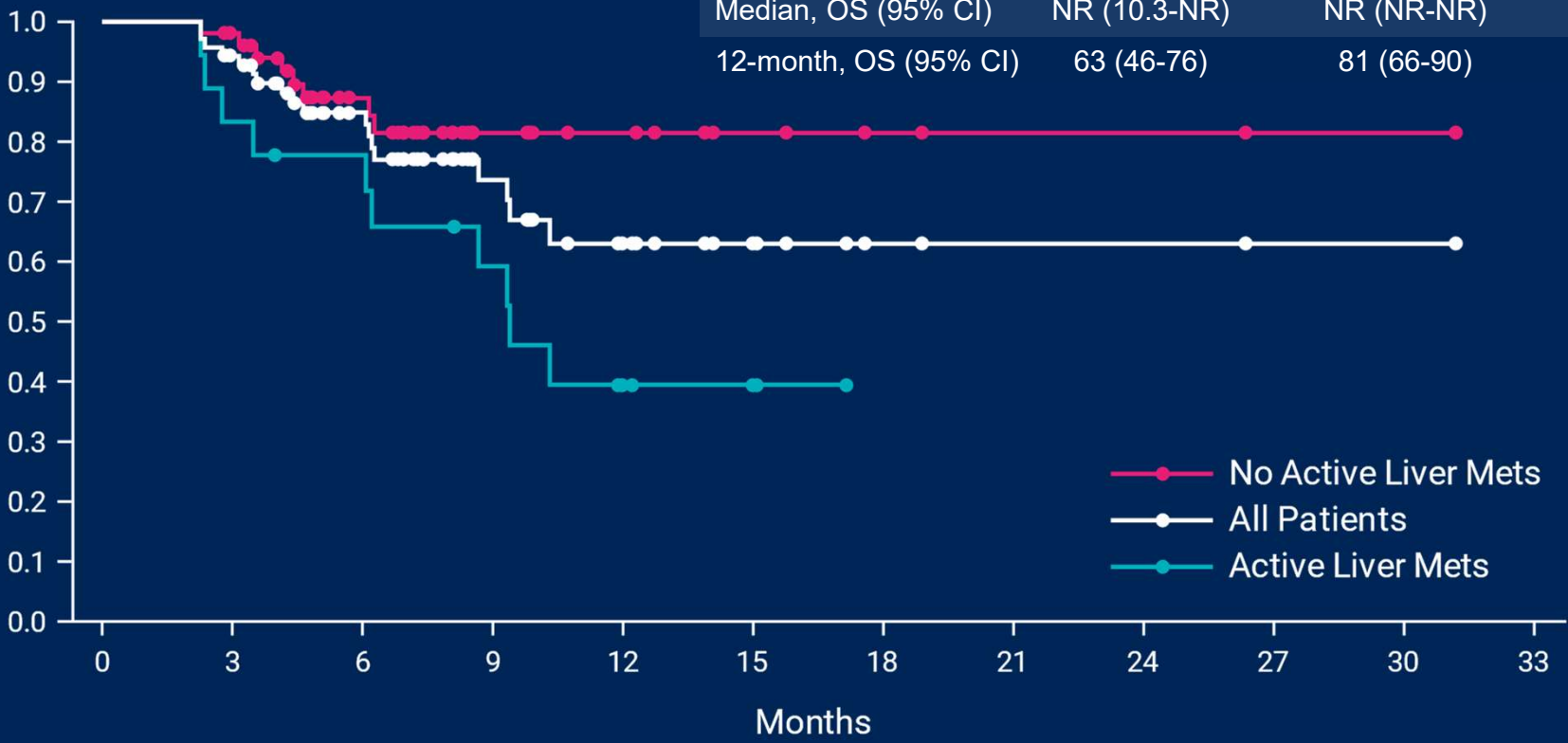


*Includes unconfirmed responses. ∞ Resected target lesions showed complete pathologic response. § Response by iRECIST.

Overall Survival

Efficacy evaluable population, N=70

	Overall	No Active Liver Mets	Active Liver Mets
Median, OS (95% CI)	NR (10.3-NR)	NR (NR-NR)	9.4 (6.1-NR)
12-month, OS (95% CI)	63 (46-76)	81 (66-90)	40 (17-62)



Safety Profile

All TRAEs of Any Grade in $\geq 15\%$ of All Patients

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n (%)	ALL GRADE	GRADE 3	GRADE 4
ANY TRAE	64 (91)	28 (40)	2 (3)
GASTROINTESTINAL			
IM diarrhea/colitis*	30 (43)	14 (20)	1 (1)
Nausea	16 (23)	1 (1)	0
CONSTITUTIONAL			
Fatigue	24 (34)	3 (4)	0
Decreased appetite	19 (27)	0	0
Chills	15 (21)	0	0
Pyrexia	16 (23)	3 (4)	0

n (%)	ALL GRADE	GRADE 3	GRADE 4
SKIN			
Rash	19 (27)	0	0
Pruritus	12 (17)	0	0
ENDOCRINE			
Hypo/hyperthyroidism	11 (16)	0	0

* Immune-mediated (IM) diarrhea/colitis is defined as patients who received steroids or infliximab.

Summary & Future Directions

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- Botensilimab is a CTLA-4 antibody with enhanced binding to activating Fc receptors enabling innate and adaptive immune activation
- Durable objective responses in heavily pre-treated patients with MSS CRC
- Manageable safety profile
- Favorable overall survival: 12-month estimate 63%
- A global phase 2 (NCT05608044) randomized trial in MSS CRC is enrolling and a global phase 3 trial is planned for 2023

activate 
AGAINST COLORECTAL CANCER

Abbreviations

AE , adverse event	IgG , immunoglobulin G
ALT , alanine aminotransferase	I-O , immunotherapy
APC , antigen presenting cell	L , line
AST , aspartate aminotransferase	LOT , lines of therapy
bal , balstilimab	mAb , monoclonal antibody
BOR , best overall response	Mets , metastases
bot , botensilimab	MSI , microsatellite instability
BRAF , v-raf murine sarcoma viral oncogene homolog B1	MSS , microsatellite stable
CR , complete response	NK , natural killer
CPK , creatine phosphokinase	NSCLC , non-small cell lung cancer
CRC , colorectal cancer	ORR , objective response rate
CTLA-4 , cytotoxic T-lymphocyte antigen-4	OS , overall survival
DC , dendritic cell	PD , progressive disease
DCR , disease control rate	PD-1 , programmed death receptor-1
DOR , duration of response	PD-L1/2 , programmed death-ligand 1/2
ECOG , Eastern Cooperative Oncology Group	PFS , progression-free survival
Fc , fragment crystallizable	PR , partial response
FcγRIIIA , Fc gamma receptor IIIA	PS , performance status
F/U , follow-up	QXW , every X weeks
HCC , hepatocellular carcinoma	RAS , rat sarcoma virus
ICI , immune checkpoint inhibitor	R/R , relapsed/refractory
	SD , stable disease
	SOC , standard of care
	TMB , tumor mutation burden
	TNBC , triple negative breast cancer
	TRAE , treatment-related adverse event
	Treg , regulatory T cell

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