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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)

Authors: Anthony B. El-Khoueiry, MD[1], Marwan G. Fakih, MD[2], Michael S. Gordon, MD[3], Apostolia M. Tsimberidou, MD, PhD[4], Andrea J. Bullock, MD, MPH[5], Breelyn A. Wilky, MD[6], Jonathan C. Trent, MD, PhD[7], Kim A. Margolin, MD, FACP, FASCO[8], Daruka Mahadevan, MD, PhD[9], Ani S. Balmanoukian, MD[10], Rachel E. Sanborn, MD[11], Gary K. Schwartz, MD[12], Bruno Bockorny, MD[5], Justin C. Moser, MD[3], Joseph E. Grossman, MD[13], Waldo Ortuzar Feliu, MD[13], Katherine Rosenthal, RN, MSN, OCN, CCRP[13], Steven J. O'Day, MD[13], Heinz-Josef Lenz, MD, FACP[1], Benjamin L. Schlechter, MD[14]

[1]University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, USA, [2]City of Hope Comprehensive Cancer Center, Duarte, CA, USA, [3]Honor Health Research and Innovation Institute, Scottsdale, AZ, USA, [4]The University of Texas MD Anderson Cancer Center, Houston, TX, USA, [5]Beth Israel Deaconess Medical Center, Boston, MA, USA, [6]University of Colorado Cancer Center, Aurora, CO, USA, [7]Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA, [8]Providence Saint John's Cancer Institute, Santa Monica, CA, USA, [9]The University of Texas Health Sciences Center at San Antonio, San Antonio, TX, USA, [10]The Angeles Clinic and Research Institute, Los Angeles, CA, USA, [11]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, USA, [12]Herbert Irving Comprehensive Cancer Center, Columbia University Medical Center, New York, NY, USA, [13]Agenus Inc., Lexington, MA, USA, [14]Dana-Farber Cancer Institute, Boston, MA, USA

Presented by: Anthony B. El-Khoueiry, MD

University of Southern California
Norris Comprehensive Cancer Center
Los Angeles, California, United States

January 21, 2023
Abstract Number: LBA8

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Active in 'Cold' and IO Refractory Tumors

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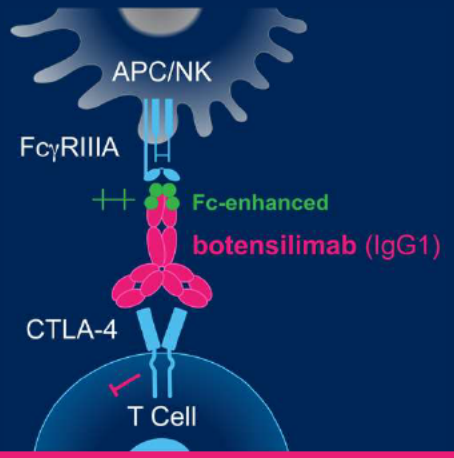
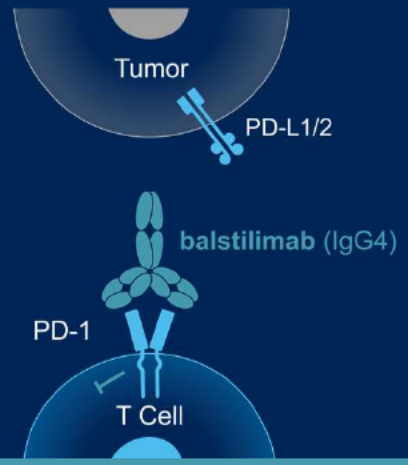
botensilimab
Fc-enhanced CTLA-4 Inhibitor



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 cancer[1]

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

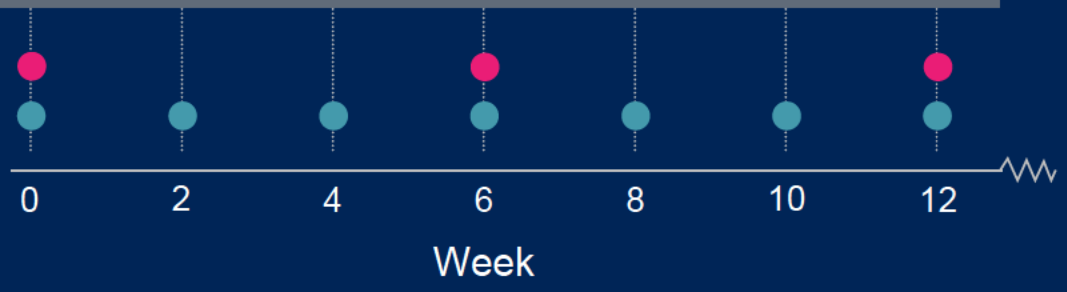
Treated with 1 or 2 mg/kg bot + bal as of 29 August 2022 with ≥1 Q6W imaging assessment

BOT + **BAL**

Fc-enhanced CTLA-4
1 or 2 mg/kg Q6W

PD-1
3 mg/kg Q2W

Combination therapy



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

Patient Characteristics

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Characteristic	Overall (N=70)*
Age, median (range)	57 (25-83)
Sex, n (%)	
Female	40 (57)
Male	30 (43)
ECOG PS at baseline, n (%)	
0	28 (40)
1	42 (60)
Prior lines of therapy, n (%)	
Median (range)	4 (1-10)

Characteristic	Overall (N=70)
Prior immunotherapy, n (%)	22 (31)
Botensilimab dose, n (%)	
1 mg/kg Q6W + bal (PD-1) Q2W	17 (24)
2 mg/kg Q6W + bal (PD-1) Q2W	53 (76)
TMB>10, n/N (%)	1/57 (2)
RAS mutation, n/N (%)	41/70 (59)
BRAF mutation, n/N (%)	2/65 (3)

* 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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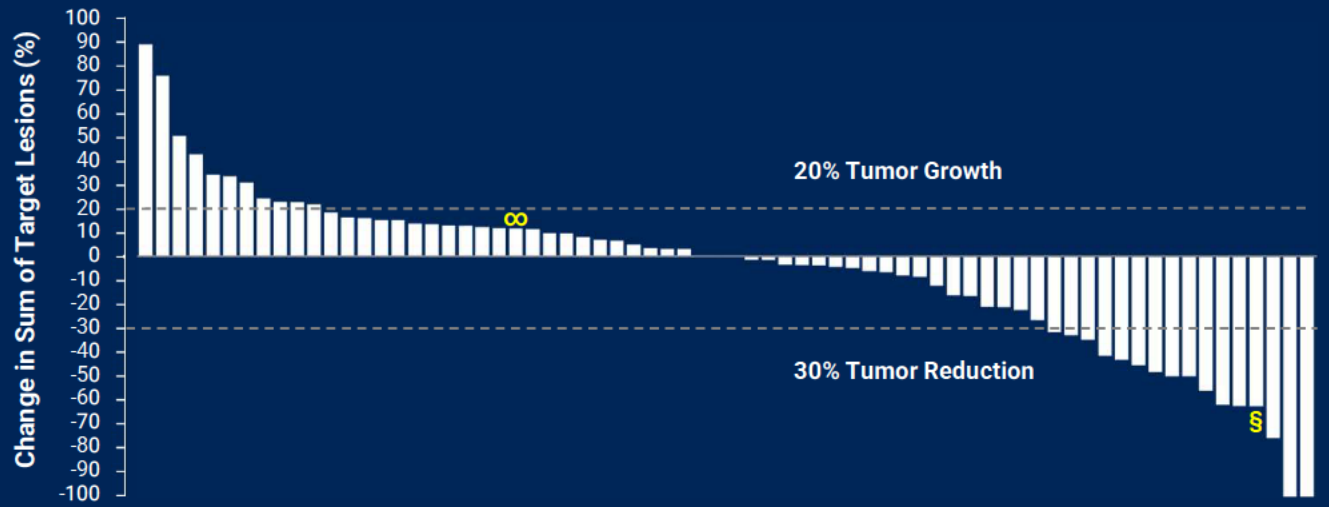

Efficacy	N=70
ORR*, % (95% CI)	23 (14-34)
BOR, n (%)	
CR	1 (1)
PR	15 (21)
SD	37 (53)
DCR (CR + PR + SD), % (95% CI)	76 (64-85)
Median, OS (95% CI)	NR (10.3-NR)
Median PFS, months (95% CI)	4.1 (2.8-5.5)
Median F/U, months (Min, Max)	7 (2, 31)

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

Durable Objective Responses

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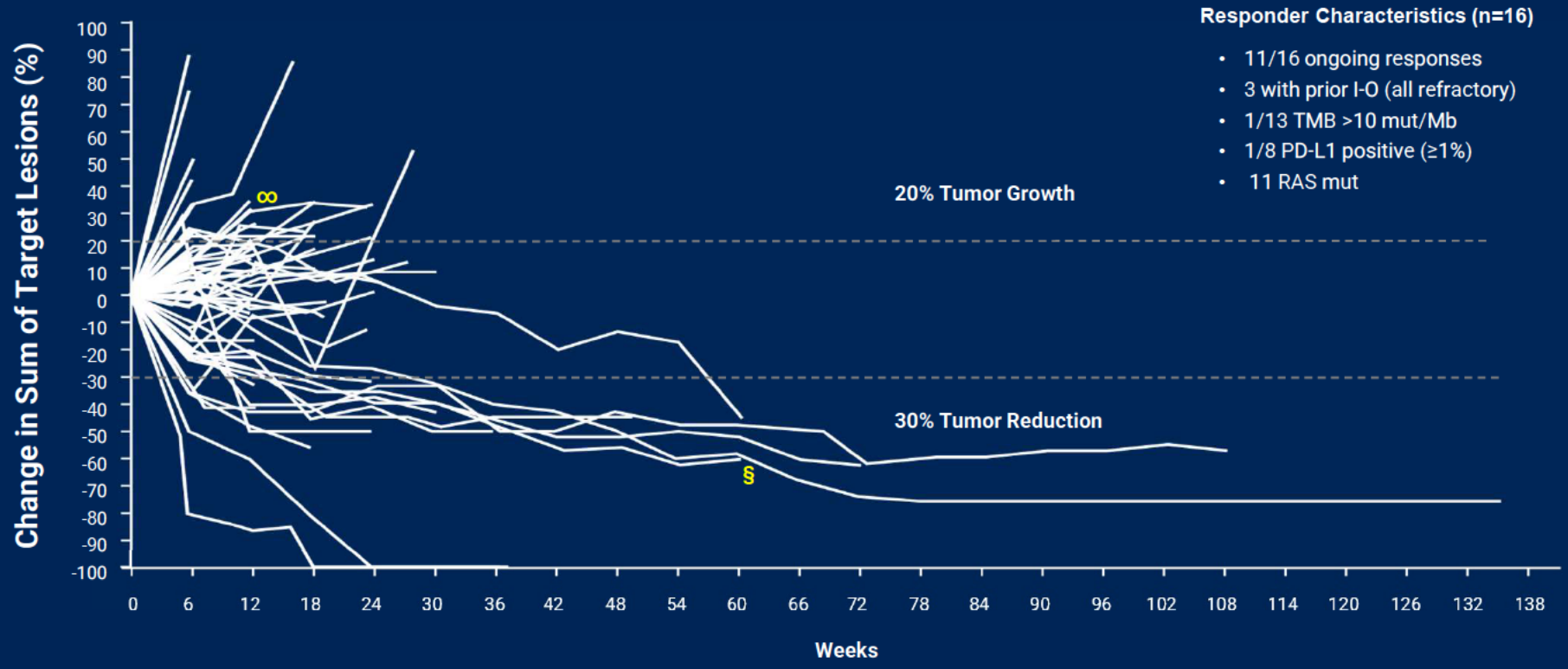

Responder Characteristics (n=16)

- 11/16 ongoing responses
- 3 with prior I-O (all refractory)
- 1/13 TMB >10 mut/Mb
- 1/8 PD-L1 positive (≥1%)
- 11 RAS mut

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

Overall Survival

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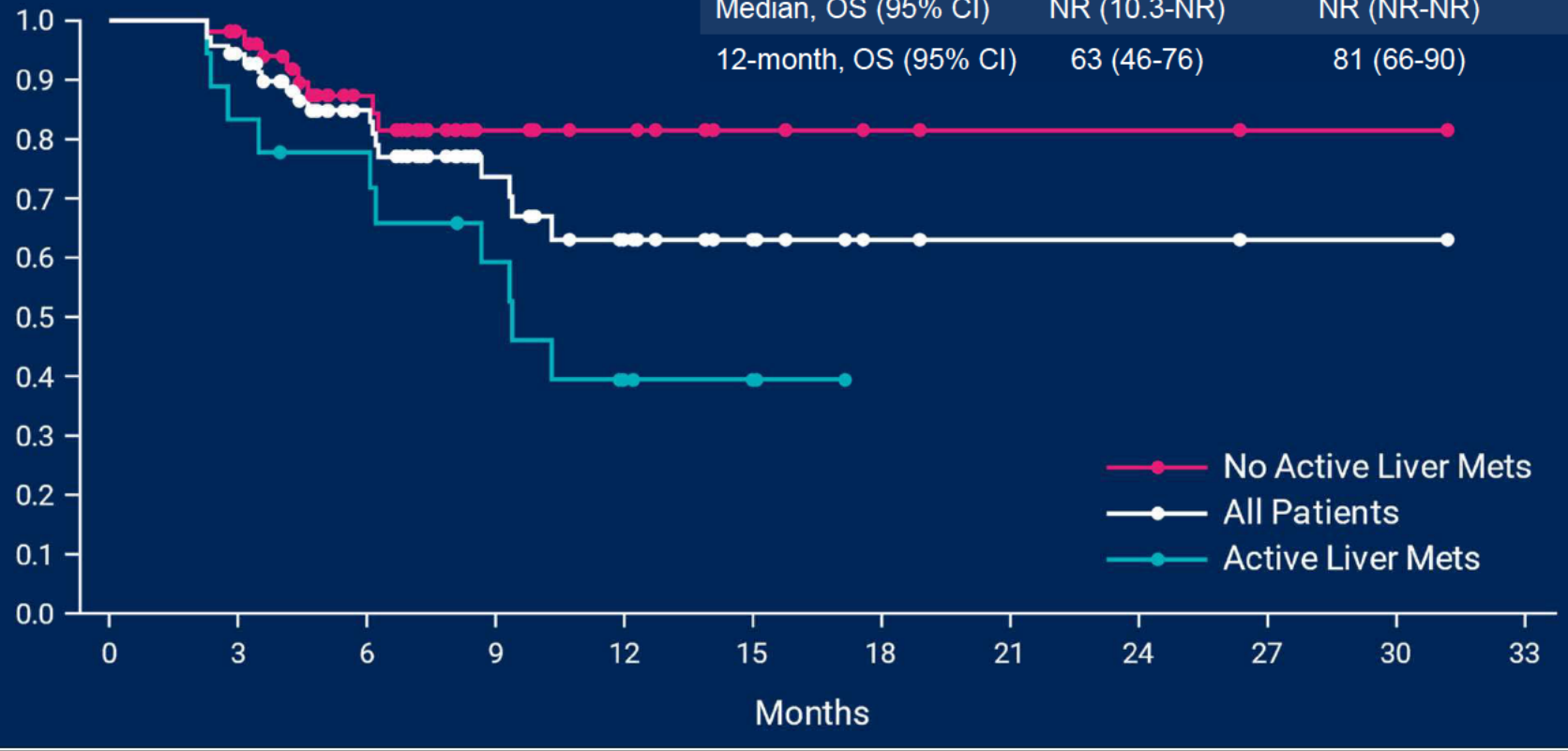
Efficacy evaluable population, N=70

	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 ≥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

- 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

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Abbreviations

AE, adverse event
ALT, alanine aminotransferase
APC, antigen presenting cell
AST, aspartate aminotransferase
bal, balstilimab
BOR, best overall response
bot, botensilimab
BRAF, v-raf murine sarcoma viral oncogene homolog B1
CR, complete response
CPK, creatine phosphokinase
CRC, colorectal cancer
CTLA-4, cytotoxic T-lymphocyte antigen-4
DC, dendritic cell
DCR, disease control rate
DOR, duration of response
ECOG, Eastern Cooperative Oncology Group
Fc, fragment crystallizable
FcγRIIIA, Fc gamma receptor IIIA
F/U, follow-up
HCC, hepatocellular carcinoma
ICI, immune checkpoint inhibitor
IgG, immunoglobulin G
I-O, immunotherapy
L, line
LOT, lines of therapy
mAb, monoclonal antibody
Mets, metastases
MSI, microsatellite instability
MSS, microsatellite stable
NK, natural killer
NSCLC, non-small cell lung cancer
ORR, objective response rate
OS, overall survival
PD, progressive disease
PD-1, programmed death receptor-1
PD-L1/2, programmed death-ligand ½
PFS, progression-free survival
PR, partial response
PS, performance status
QXW, every X weeks
RAS, rat sarcoma virus
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

Acknowledgements

Agenus Inc. funded and is the sponsor of this study.

- The authors would like to thank the patients and their families for participating in the C-800-01 study, as well as the trial coordinators and investigators for their contributions.