BERLIN 2025 ESMO congress

Emerging survival plateaus with botensilimab and balstilimab: Pan tumor data from a large phase 1b trial of advanced solid tumors

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#1517MO | October 17, 2025

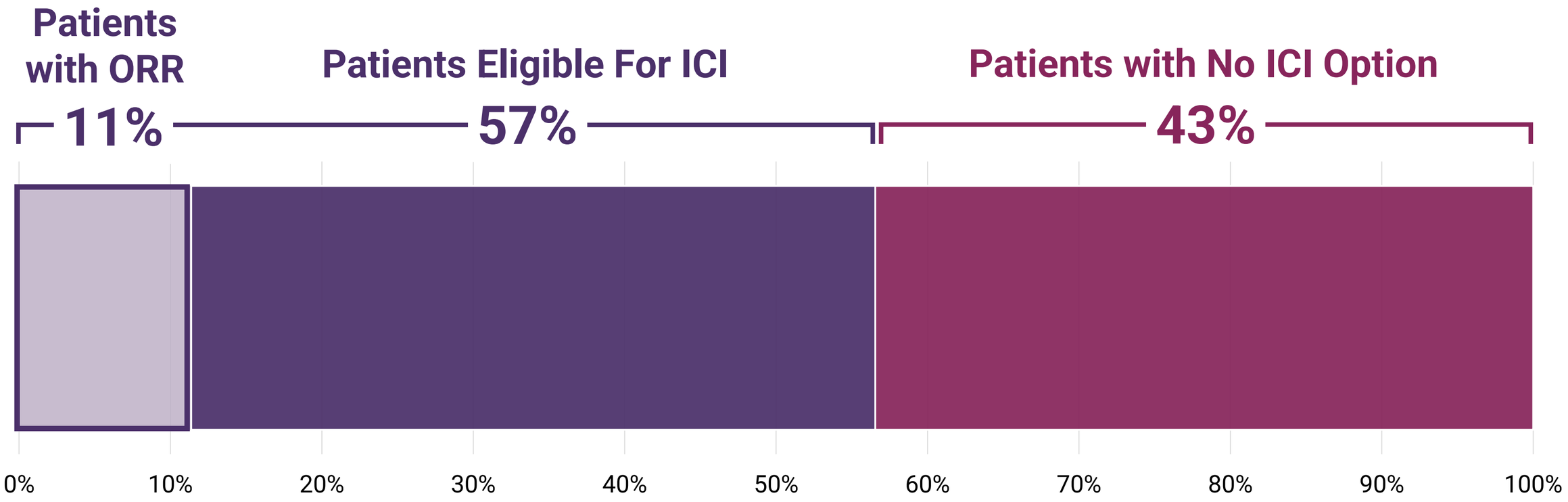
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY

DECLARATION OF INTERESTS

Michael S. Gordon declares the following:

- **Stock and other ownership interests** at Sphinx Health Solutions (previously CAREMISSION)
- **Consulting or advisory role** with Imaging Endpoints, Morphic Therapeutic, Viracta Therapeutics, Qualigen Therapeutics, OnQuality Pharmaceuticals, SpringWorks Therapeutics, and Deciphera
- **Research funding** from Genentech/Roche (Inst), GlaxoSmithKline (Inst), AbbVie (Inst), Merck Serono (Inst), Pfizer (Inst), Plexxikon (Inst), Deciphera (Inst), Corcept Therapeutics (Inst), Syndax (Inst), Tolero Pharmaceuticals (Inst), ImaginAb (Inst), Arcus Biosciences (Inst), Agenus Inc (Inst), Novartis (Inst), Revolution Medicines (Inst), IgM Biosciences (Inst), Veru (Inst), Forma Therapeutics (Inst), DynamiCure Biotechnology (Inst), Fore Biotherapeutics (Inst), NiKang Therapeutics (Inst), Nimbus Therapeutics (Inst), OncoResponse (Inst), Pionyr (Inst), Riboscience (Inst), Sirnaomics (Inst), Theseus Pharmaceuticals (Inst), SQZ Biotech (Inst), Shenzen Ionova (Inst), and Pyxis (Inst)
- **Patents, royalties, or other intellectual property**: Application Serial No.: PCT/US24/27766 Filing Date: May 3, 2024 Title: Planet atmosphere gases enwrapped into composite nanomaterials with medical treatment applications

Historical Challenges with Immune Checkpoint Inhibitors in Solid Advanced Cancers



Haslam A, Olivier T, Prasad V. *Int J Cancer*. 2025;156(12):2352-2359.

Botensilimab (BOT)* and Balstilimab (BAL):

*Multifunctional, Fc-Enhanced CTLA-4 Inhibitor

BOT[1-3]

CTLA-4 Inhibitor

- Enhances T cell priming, activation and memory
- Activates APCs/myeloid cells
- Reduces intratumoral regulatory T cells
- Improves safety by reducing complement-mediated toxicities (e.g., hypophysitis)

BAL[4,5]

PD-1 Inhibitor

- Functionally comparable to other PD-1 inhibitors

We present updated, pan-tumor data from the phase 1b C-800-01 trial of BOT+BAL in advanced cancers

1. Bullock AJ, et al. *Nat Med.* 2024;30(9):2558-2567. **2.** Waight JD, et al. *Cancer Cell.* 2018;33(6):1033-1047.e5. **3.** Chand D, et al. *Cancer Discov.* 2024;14(12):2407-2429. **4.** O'Malley DM, et al. *Gynecol Oncol.* 2021;163(2):274-280. **5.** O'Malley DM, et al. *J Clin Oncol.* 2022;40(7):762-771.

C-800-01: Phase 1b Trial Design

First-in-Human, Phase 1b Trial of BOT ± BAL in Patients with Advanced Cancer (NCT03860272)[a,1-3]

KEY ELIGIBILITY

- Advanced solid tumors refractory to standard treatment
- Prior I-O therapy allowed

COMBINATION THERAPY ARM[b]

BOT Q6W
1 mg/kg or 2 mg/kg

Fc-enhanced, multifunctional, anti–CTLA-4 mAb

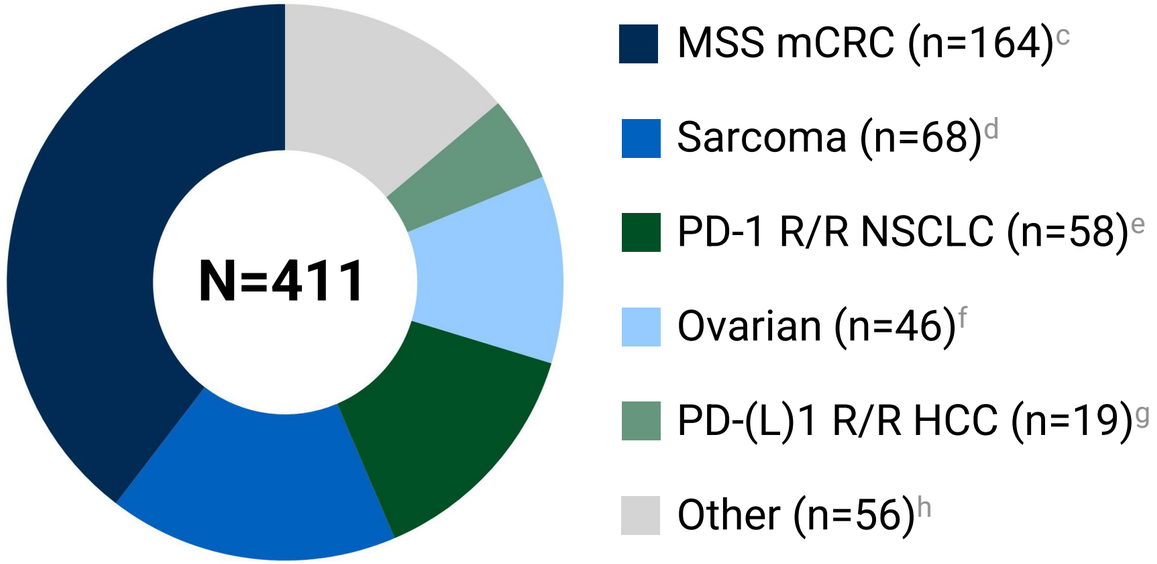
+

BAL Q2W
3 mg/kg

Inhibitory anti–PD-1 mAb

PAN TUMOR POPULATION

Immunologically "Cold" Tumors; I-O Relapsed/Refractory



Data cutoff: 13-MAR-2025. Safety analysis set (N=411; participants who received ≥1 dose of study drug).

[a]Dose-escalation and expansion cohort design with BOT monotherapy and BOT+BAL (N=496 participants treated). Assessments of ORR, DOR, DCR and PFS were per Response Evaluation Criteria in Solid Tumors version 1.1 based on investigator assessment. [b]Crossover to combination from BOT monotherapy permitted, as well as fixed-dosing (BOT 150 mg Q6W + BAL 450 mg Q3W, which was pooled with the 2 mg/kg BOT Q6W + 3 mg/kg BAL Q2W population for analysis). [c]BOT dose 1mg/kg n=79; 2 mg/kg n=85. [d]BOT dose 1mg/kg n=48; 2 mg/kg n=20. [e]BOT dose 1mg/kg n=43; 2 mg/kg n=15. [f]BOT dose 1mg/kg n=22; 2 mg/kg n=24. [g]BOT dose 1mg/kg n=9; 2 mg/kg n=10. [h]BOT dose 1mg/kg n=27; 2 mg/kg n=29. Other tumor types included endometrial carcinoma (n=14), pancreatic cancer (n=14), prostate cancer (n=4), melanoma (n=3) and other (n=21, ≤2 participants per indication; adrenocortical carcinoma, ampullary, anal cancer, breast cancer, carcinoma of unknown primary, cervical cancer, digital papillary, esophageal cancer, fibrolamellar hepatocellular cancer, gallbladder cancer, gastric cancer, head and neck cancer, neuroendocrine carcinoma, renal cell carcinoma, testicular cancer, urothelial carcinoma).

1. ClinicalTrials.gov identifier: NCT03860272. Updated February 6, 2026. Accessed August 7, 2025. https://clinicaltrials.gov/ct2/show/NCT03860272
2. El-Khoueiry AB, et al. Poster presented at SITC Annual Meeting. Washington, DC, USA. 2021. Poster 479. **3.** Wilky BA, et al. Oral presentation at SITC Annual Meeting. Boston, MA, USA. 2022. Oral 778.

Patient Characteristics

Characteristic	Overall Population (N=411)
Median age (range)	61 (19–82)
Female, n (%)	242 (59)
ECOG PS, n (%)	
0	177 (43)
1	234 **(57)**
Prior lines of therapy	
Median no. of prior lines (range)	**3** (0–17)
≥3 prior lines, n (%)	251 **(61)**
Prior PD-(L)1 and/or CTLA-4, n (%)	136 **(33)**
Multiple metastatic sites n (%)	284 **(69)**
Active liver metastases, n (%)	126 **(31)**

Data cutoff: 13-MAR-2025. Safety analysis set (N=411; participants who received ≥1 dose of study drug).

Durable Responses Across Tumor Types

Efficacy Outcome	Efficacy Evaluable (N=339)
Confirmed ORR, % n, 95% CI	**17%** 58, 13–22
BOR, n (%)	
CR	7 (2)
PR	51 (15)
SD	164 (48)
PD	117 (35)
Median DOR, months 95% CI	**14.6** 9.7–NR
DCR at 6 weeks, % n, 95% CI	**66%** 222, 60–71
CBR at 24 weeks, % n, 95% CI	**26%** 89, 22–31

Median follow-up was 13.0 months (range, 1.3–53.3)

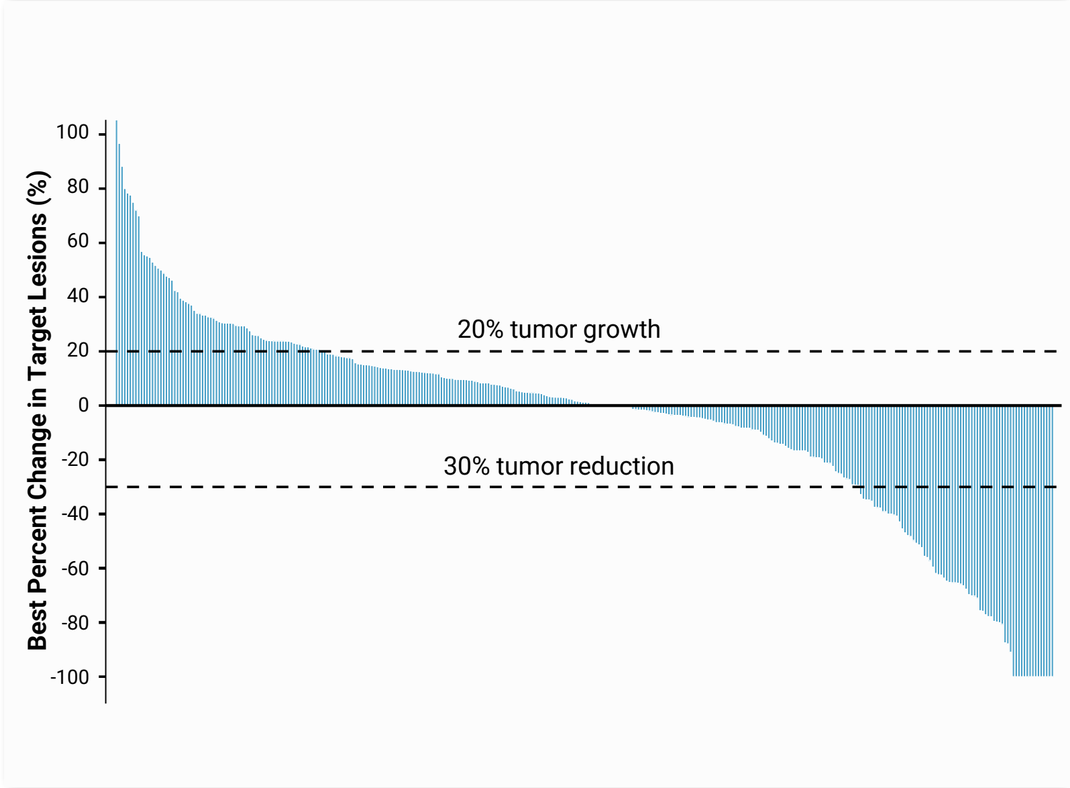
ORR consistent by dose:

- **1 mg/kg:** 17% ORR (95% CI, 12–23; n=33/192)
- **2 mg/kg:** 17% ORR (95% CI, 11–24; n=25/147)

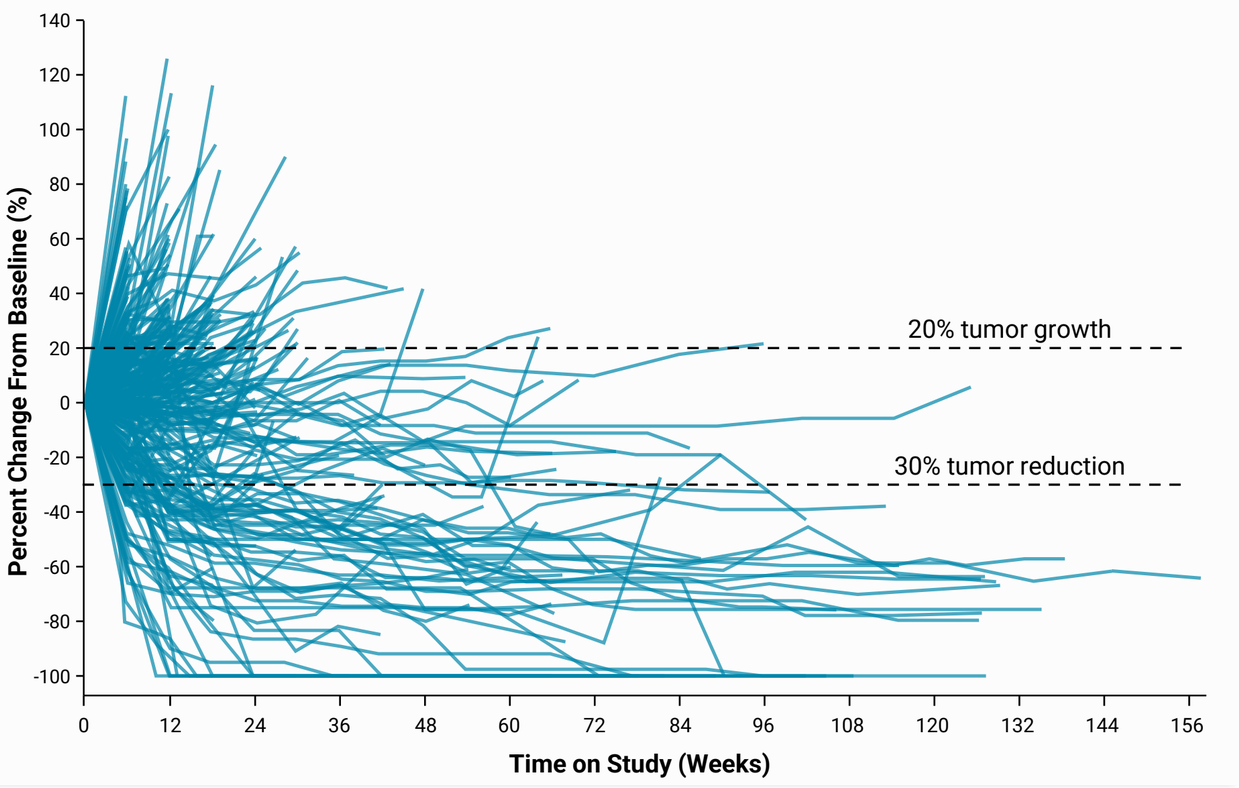
Data cutoff: 13-MAR-2025. Per investigator assessment in efficacy evaluable set (N=339; participants who received ≥1 post-baseline 6-week imaging scan).
CBR, clinical benefit rate (CR, PR, or SD ≥24 weeks); DCR, disease control rate (CR, PR, or SD ≥6 weeks).

Clinical Benefit Beyond ORR

Best Overall Responses

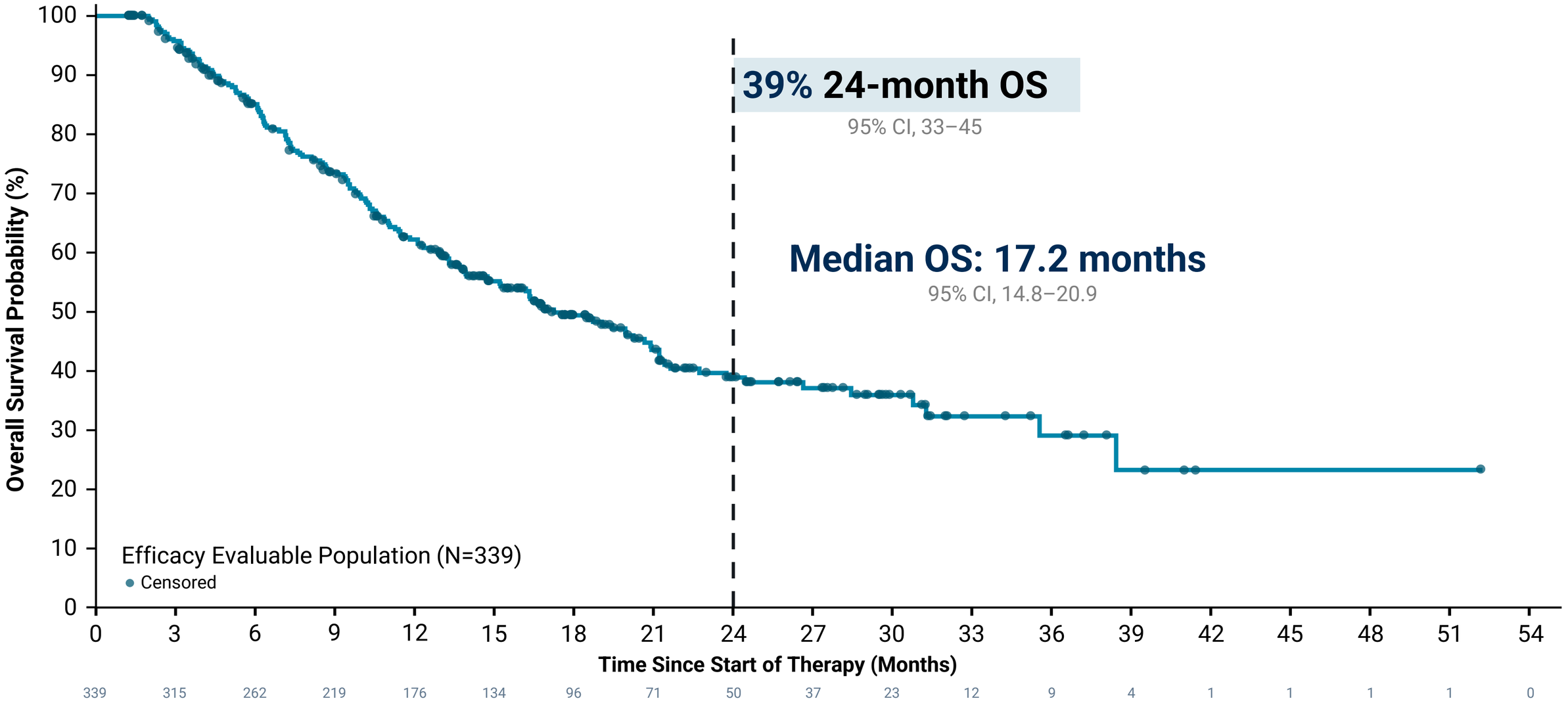


Responses Over Time



Data cutoff: 13-MAR-2025. Per investigator assessment in efficacy evaluable set (N=339; participants who received ≥1 post-baseline 6-week imaging scan).

Overall Survival



Data cutoff: 13-MAR-2025. Efficacy evaluable set (N=339; participants who received ≥1 post-baseline 6-week imaging scan).

Safety Overview

Safety event, n (%)	1 mg/kg (n=228)		2 mg/kg (n=183)		Overall (N=411)	
Any grade TRAE	**194 (85)**		**157 (86)**		**351 (85)**	
Grade ≥3 TRAEs	63 (28)		69 (38)		132 (32)	
	Any grade	**Grade ≥3**	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**
Any treatment-related imAE[a,b]	96 (42)	42 (18)	99 (54)	49 (27)	195 (47)	91 (22)
Most common (≥3%) treatment-related imAEs[a]						
Diarrhea/colitis[c]	61 (27)	22 **(10)**	73 (40)	34 (19)	134 (33)	56 (14)
Thyroid[d]	17 (8)	**0**	15 (8)	0	32 (8)	0
Hepatitis[e]	6 (3)	2 **(1)**	13 (7)	8 (4)	19 (5)	10 (2)
Skin[f]	4 (2)	2 **(1)**	9 (5)	3 (2)	13 (3)	5 (1)
Pneumonitis[g]	5 (2)	3 **(1)**	6 (3)	2 (1)	11 (3)	5 (1)

- No new safety signals were observed
- The most common imAEs were GI-related, which were reversible
- There was a low incidence of visceral toxicities outside the GI tract
- No treatment-related deaths were observed (grade 5)

Data cutoff: 13-MAR-2025. Safety analysis set (N=411; participants who received ≥1 dose of study drug).

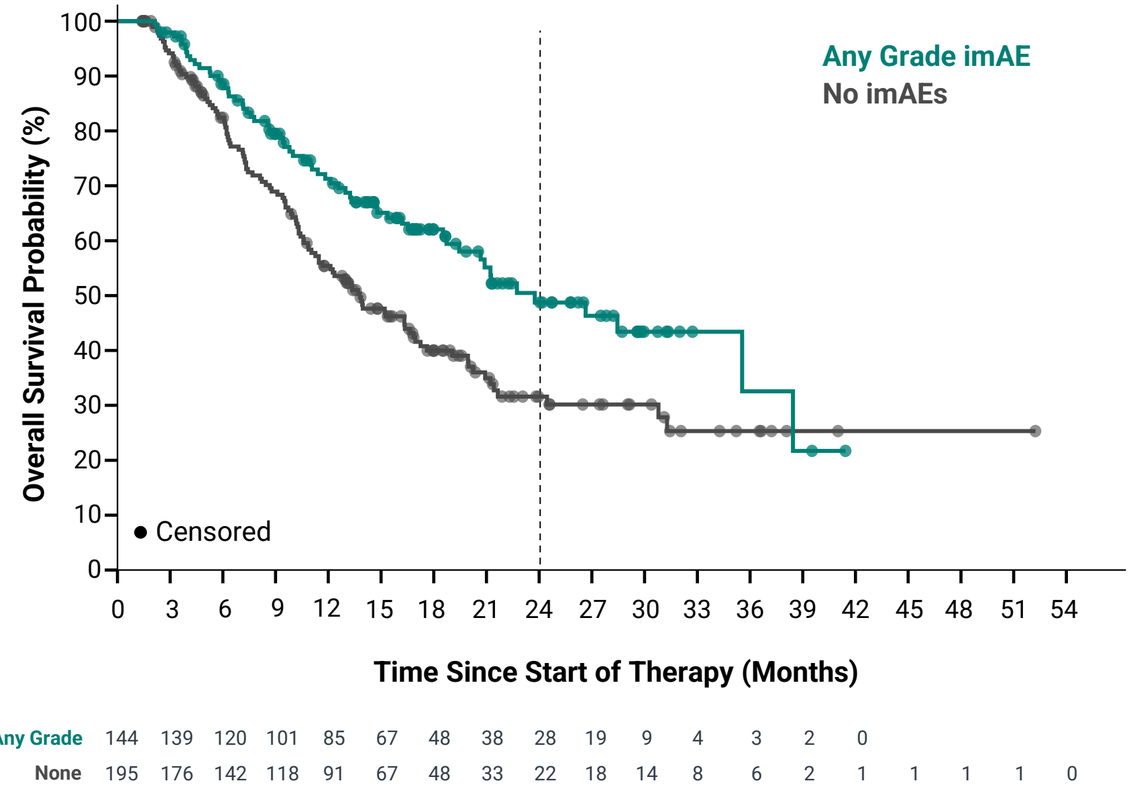
[a]imAEs were medically adjudicated. [b]Grade 4 imAEs (n=1 each) of colitis (2 mg/kg group), autonomic neuropathy (1 mg/kg group), diabetic ketoacidosis (2 mg/kg group), and thrombocytopenia (1 mg/kg group) were reported; no other grade ≥4 imAEs occurred. [c]Grouped term that included preferred term events of autoimmune colitis, colitis, diarrhea, duodenitis, enteritis, enterocolitis, and immune-mediated enterocolitis. [d]Grouped term that included preferred term events of blood thyroid stimulating hormone increased, hyperthyroidism, hypothyroidism, immune-mediated hypothyroidism, immune-mediated thyroiditis, and thyroiditis. [e]Grouped term that included preferred term events of AST increased, ALT increased, autoimmune hepatitis, blood alkaline phosphatase increased, and immune-mediated hepatitis. [f]Grouped term that included preferred term events of immune-mediated dermatitis, lichen sclerosus, linear IgA disease, rash, rash erythematous, and rash maculo-papular that were treated systemically. [g]Grouped term that included preferred term events of immune-mediated lung disease, and pneumonitis.

Survival Benefit Was Observed with imAEs

Within the first 12 weeks of treatment

Efficacy outcome	No imAEs n=195	Any Grade imAE n=144
Confirmed ORR, % n, 95% CI	**16%** 31, 11–22	**19%** 27, 13–26
Median DOR, months 95% CI	**12.3** 4.2–NR	**14.6** 9.8–NR
CBR at 24 weeks, % n, 95% CI	**25%** 48, 19–31	**29%** 41, 21–37
Median OS, months 95% CI	**13.8** 11.3–16.9	**23.8** 18.7–38.4
24-month OS, % 95% CI	**32%** 24–40	**49%** 38–59

Participants with or without imAEs during first 12 weeks of treatment



Data cutoff: 13-MAR-2025. Among the efficacy evaluable set (N=339; participants who received ≥1 post-baseline 6-week imaging scan).

Clinical Benefit Was Observed Irrespective of Liver Metastases or Prior I-O Exposure

Efficacy outcome	Liver metastases status		Prior I-O status	
	Active LM n=101	No Active LM n=238	I-O R/R n=109	I-O Naïve n=230
Confirmed ORR, % n, 95% CI	**13%** 13, 7–21	**19%** 45, 14–25		
Median DOR, months 95% CI	**9.8** 2.8–NR	**16.6** 7.3–NR		
CBR at 24 weeks, % n, 95% CI	**21%** 21, 13–30	**29%** 68, 23–35		
Median OS, months 95% CI	**11.5** 9.8–17.0	**20.7** 16.4–24.4		
24-month OS, % 95% CI	**29%** 18–40	**43%** 35–51		

Data cutoff: 13-MAR-2025. Among the efficacy evaluable set (N=339; participants who received ≥1 post-baseline 6-week imaging scan).

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Efficacy outcome	Liver metastases status		Prior I-O status	
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Confirmed ORR, % n, 95% CI	**13%** 13, 7–21	**19%** 45, 14–25	**12%** 13, 7–20	**20%** 45, 15–25
Median DOR, months 95% CI	**9.8** 2.8–NR	**16.6** 7.3–NR	**12.3** 2.9–NR	**16.6** 7.3–NR
CBR at 24 weeks, % n, 95% CI	**21%** 21, 13–30	**29%** 68, 23–35	**21%** 23, 14–30	**29%** 66, 23–35
Median OS, months 95% CI	**11.5** 9.8–17.0	**20.7** 16.4–24.4	**12.4** 10.4–16.7	**20.9** 16.5–24.4
24-month OS, % 95% CI	**29%** 18–40	**43%** 35–51	**31%** 21–42	**42%** 34–50

Data cutoff: 13-MAR-2025. Among the efficacy evaluable set (N=339; participants who received ≥1 post-baseline 6-week imaging scan).

Conclusions

BOT+BAL demonstrated notable overall survival with 2-year survival plateaus, supported by deep, durable responses and prolonged stable disease in a variety of refractory solid tumors

- Tumor types included MSS mCRC, sarcoma, ovarian, PD-1 R/R NSCLC, and PD-(L)1 R/R HCC
- Efficacy was similar across doses, with improved safety at BOT 1 mg/kg
- Occurrence of imAEs was associated with survival benefit
- Clinical benefit was evident irrespective of the presence or absence of liver metastases and prior I-O status
- No new safety signals were observed outside of the I-O class and there were no treatment-related deaths

These findings in late-stage patients across tumor types complement emerging pan-tumor data in the neoadjuvant setting[1]

1. Chalabi M, et al. Oral presentation at AACR 2025. Chicago, IL, USA. 2025. Abstract #CT130.

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Acknowledgements

C-800-01 is sponsored (and funded) by Agenus Inc.

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

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Abbreviations

ALT, alanine aminotransferase
AST, aspartate aminotransferase
APC, antigen presenting cell
BAL, balstilimab
BOR, best overall response
BOT, botensilimab
CBR, clinical benefit rate (CR, PR, or SD ≥24 weeks)
CI, confidence interval
CR, complete response
CTLA-4, cytotoxic T-lymphocyte associated protein-4
DCR, disease control rate (CR, PR, or SD ≥6 weeks)
DLT, dose-limiting toxicity
DOR, duration of response
ECOG, Eastern Cooperative Oncology Group
Fc, fragment crystallizable
GI, gastrointestinal
HCC, hepatocellular carcinoma
IgA, immunoglobulin a
imAE, immune-mediated adverse event
ICI, immune checkpoint inhibitor
I-O, immuno-oncology
LM, liver metastases
mAb, monoclonal antibody
mCRC, metastatic colorectal cancer
MSS, microsatellite stable
NR, not reached
NSCLC, non-small cell lung cancer
ORR, objective response rate
OS, overall survival
PFS, progression-free survival
PD, progressive disease
PD-1, programmed cell death protein 1
PD-L1, programmed death ligand 1
PR, partial response
PS, performance status
Q[X]W, every X weeks
R/R, relapsed/refractory
SD, stable disease
TRAE, treatment-related adverse event