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Results from an expanded phase 1 trial of **botensilimab**, a multifunctional anti-CTLA-4, plus balstilimab (anti-PD-1) for metastatic heavily pretreated microsatellite stable colorectal cancer

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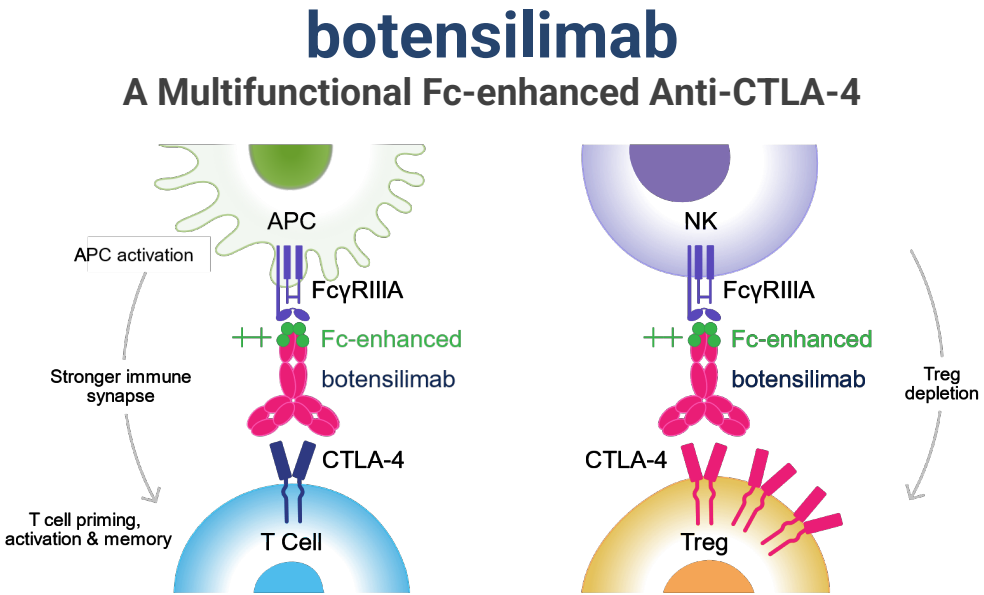
DISCLOSURES

Andrea J. Bullock

Consulting fees: Exelixis, Panovance, Oncolytics

BOTENSILIMAB IS A NOVEL INNATE & ADAPTIVE IMMUNE ACTIVATOR

Expanding the Reach of Immunotherapy

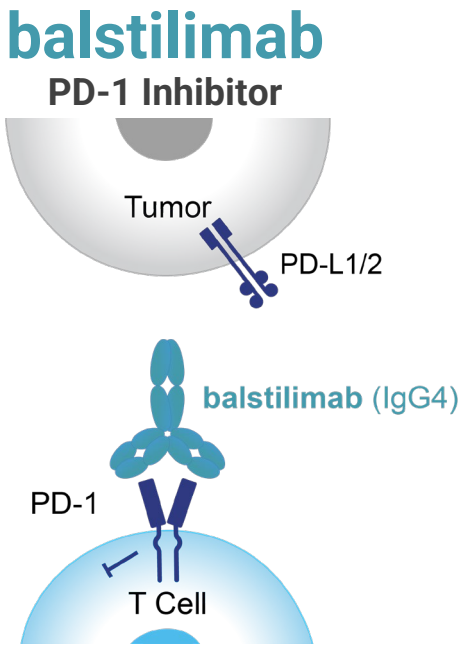


Driving Activity in Cold or I-O Refractory Tumors[1-4]

- **Enhanced** T cell priming, expansion, memory[5,6]
- **Enhanced** frequency of APCs
- **Enhanced** Treg depletion
- **Reduced** complement mediated toxicity

1. Wilky B. SITC 2022 Annual Meeting. Oral #778. 2. Wilky B, et al. Oral Presentation at CTOS 2022. Vancouver, CA. #1294633. 3. El-Khoueiry A, et al. Oral Presentation at ASCO GI 2023. San Francisco, CA, USA. Rapid Oral #LBA8. 4. Bockorny B, et al. Scientific Plenary Presentation at SGO 2023. Tampa, Florida. #2.
5. Waight et al. *Cancer Cell*. 2018;33(6): 1033-1047. 6. Delepine C, et al. Poster Presentation at SITC 2022. Boston, MA, USA. #470.

BALSTILIMAB IS A CLINICALLY VALIDATED PD-1 INHIBITOR



A Highly Active Anti-PD-1 mAb[1,2]

- **Complete blocker** of PD-1- PD-L1/2 interactions
- **Enhanced** T cell activation and effector function

1. O'Malley, et al. *Gynecol Oncol*. 2021; 163: 274-280. 2. O'Malley et al, *J Clin Oncol*. 2022; 40(7): 762-771.

STUDY DESIGN (C-800-01): NON-MSI-H CRC COHORT

NCT03860272: First-in-human trial of **botensilimab (bot)** ± **balstilimab (bal)** in patients with advanced cancer[1]

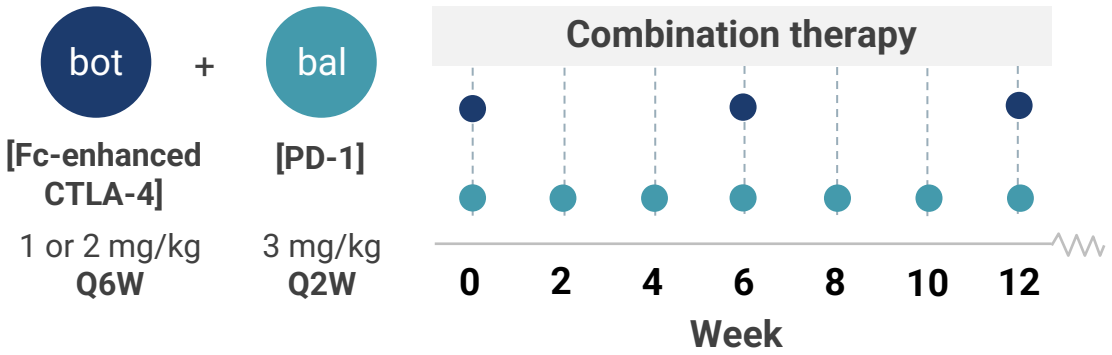
Key Eligibility

- Refractory Metastatic CRC
- MSS by local assessment
- Prior I-O allowed

Study Endpoints

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

Treatment *(up to 2 years)*



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

PATIENT DISPOSITION

Intent-to-treat Population (ITT; All Treated Patients)
Safety Evaluable
101 Non-MSI-H patients received ≥1 dose
(1 or 2 mg/kg botensilimab Q6W + 3 mg/kg balstilimab Q2W)
- **77** with no active liver metastases
- **24** with active liver metastases

14 patients (including **6** with active liver metastases) did not receive ≥1 post-baseline 6-week imaging scan:
- **9** early progression
- **4** withdrew consent
- **1** related AE

Efficacy Evaluable (EE)
87 had ≥1 post-baseline 6-week imaging scan
- **69** with no active liver metastases
- **18** with active liver metastases

Data cutoff: 26-MAY-2023

PATIENT CHARACTERISTICS

	ITT Population N=101
Age, median (range)	54 (25–82)
Sex, n (%)	
Male	45 (45)
Female	56 (55)
ECOG PS at baseline, n (%)	
0	44 (44)
1	57 (56)
Primary Site*	
Colon	64 (64)
Rectal	37 (36)

	ITT Population N=101
Prior lines of therapy, n (%)	
Median (range)†	4 (1–10)
≥3	73 (72)
Prior I-O, n (%)*‡	25 (25)
TMB >10, mut/Mb, n/N (%)*	3/76 (4)
RAS mutation, n/N (%)*	58/100 (58)
BRAF mutation, n/N (%)*	3/71 (4)

*Per internal medical review.
†Excludes two patients with unknown prior treatments.
‡Includes prior PD-1 or CTLA-4 inhibitors, anti-CD137 monoclonal antibodies, and other immune checkpoint inhibitors.

DEEP AND DURABLE OBJECTIVE RESPONSES

	All EE n=87*	No Active Liver Mets EE n=69†	Active Liver Mets EE n=18‡
Confirmed ORR, n % (95% CI)	18% (11–28)	23% (14–35)	0% (0–19)
BOR, n (%)			
CR	1 (1)	1 (1)	0
PR	15 (17)	15 (22)	0
SD	45 (52)	39 (57)	6 (33)
PD	26 (30)	14 (20)	12 (67)
DCR (CR + PR + SD), % (95% CI)	70% (59–80)	80% (68–88)	33% (13–59)
12-month OS, % (95% CI)	62% (49–73)	74% (59–84)	30% (11–52)
Ongoing responses§	11/16 (69%)		0

*Excludes patients with unconfirmed responses, among them one with a response in lung lesions who then became non-evaluable after a hemicolectomy which showed a pathologic CR, and another patient with a -60% reduction through week 60 who had a perisplenic nodule retrospectively identified as a new lesion at week 18.

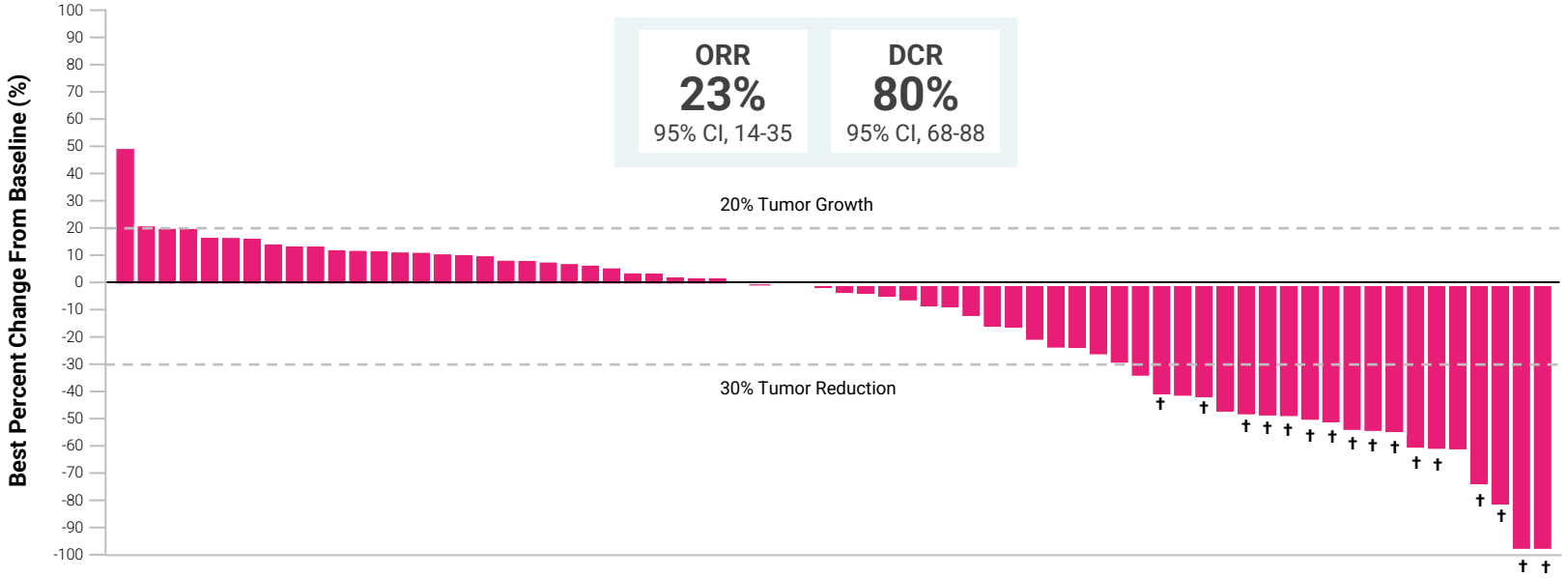
†In the ITT population with no active liver metastases (n=77), ORR was 21% (95% CI, 12–32) and DCR was 71% (95% CI, 60–81).

‡In the ITT population with active liver metastases (n=24), ORR was 0% (95% CI, 0–14) and DCR was 25% (95% CI, 10–47).

§Median DOR is immature as 11/16 (69%) patients are ongoing.

DEEP OBJECTIVE RESPONSES

No Active Liver Metastases (Efficacy Evaluable, n=69*)



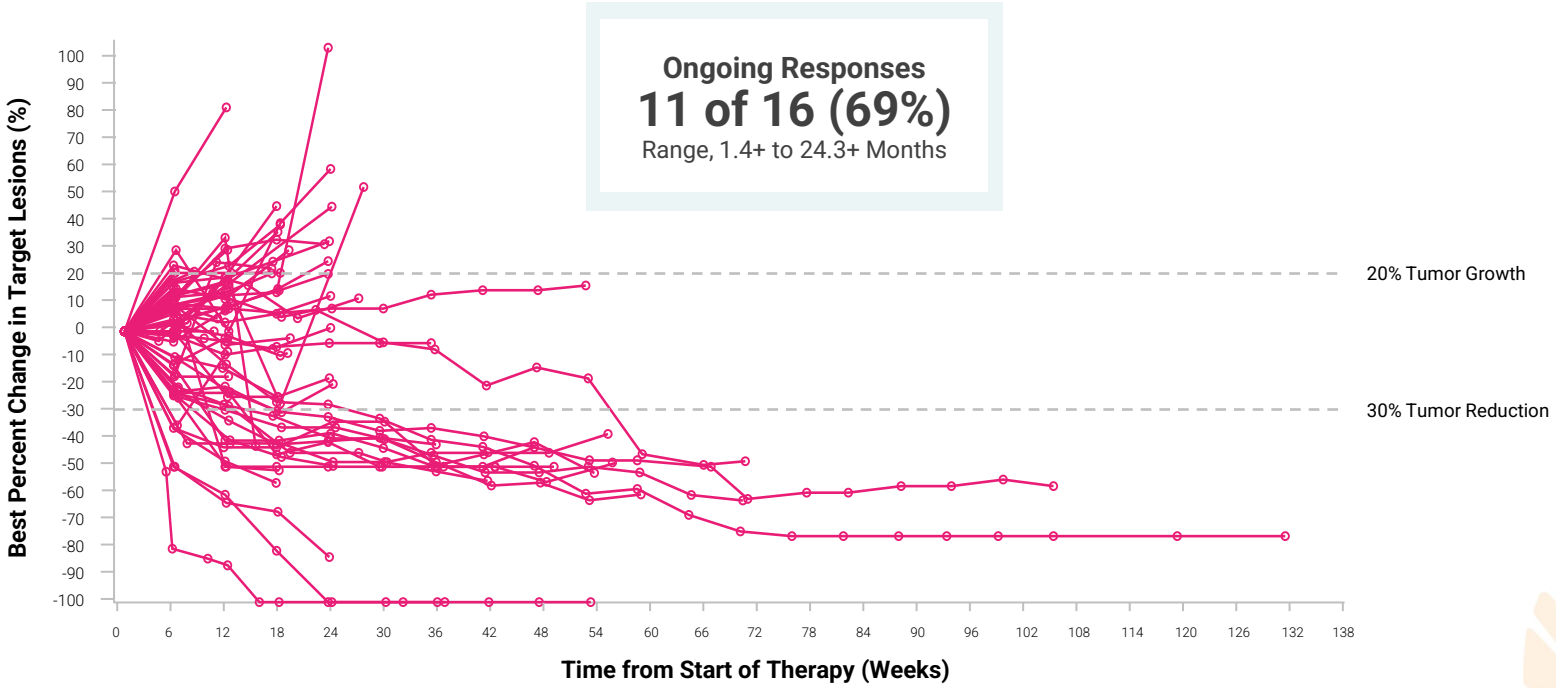
Data cutoff: 26-MAY-2023

*69 patients were evaluable with ≥1 post-baseline scan. One patient out of the 69 is not included in the waterfall plot because RECIST was recorded as SD but no percent change was recorded as of the data cutoff.

†Confirmed response (CR or PR).

DURABLE OBJECTIVE RESPONSES

No Active Liver Metastases (Efficacy Evaluable, n=69*)

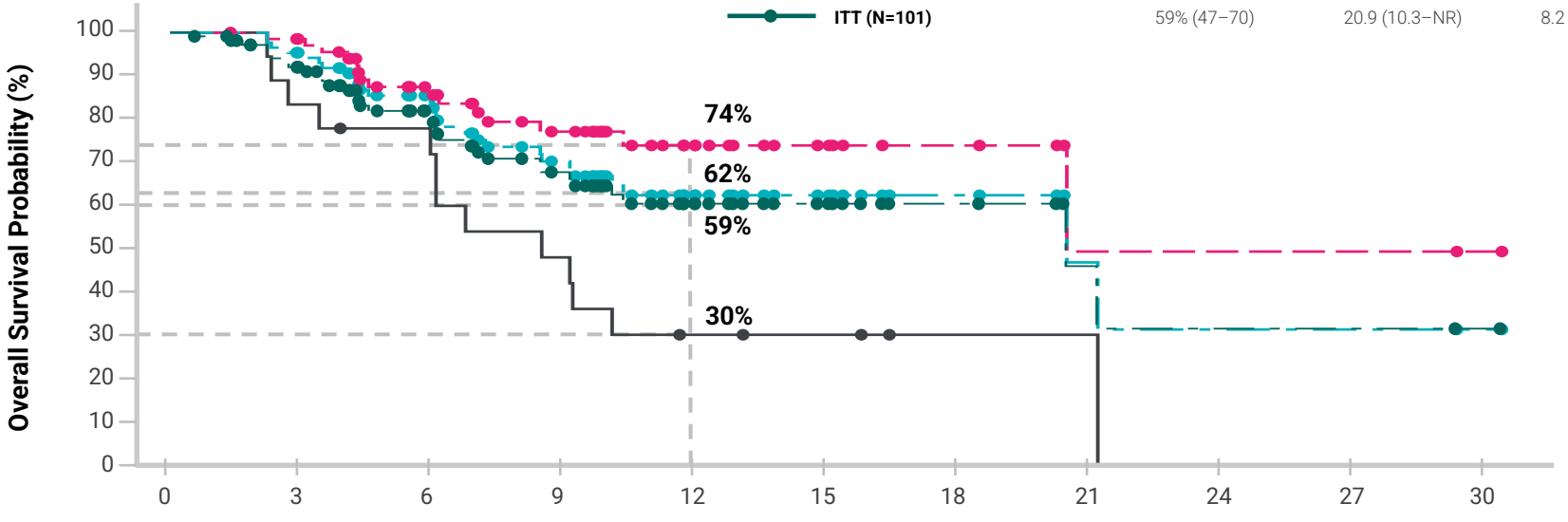


Data cutoff: 26-MAY-2023

*69 patients were evaluable with ≥1 post-baseline scan. One patient out of the 69 is not included in the spider plot because RECIST was recorded as SD but no percent change was recorded as of the data cutoff.

OVERALL SURVIVAL

	12-month OS, % (95% CI)	Median OS, Months (95% CI)	Median F/U, Months (Range)
No Active Liver Mets EE (n=69)	74% (59–84)	20.9 (20.9–NR)	9.8 (1.4–36.5)
Active Liver Mets EE (n=18)	30% (11–52)	8.7 (6.1–NR)	7.8 (2.3–21.7)
All EE (n=87)	62% (49–73)	20.9 (10.6–NR)	9.3 (1.4–36.5)
ITT (N=101)	59% (47–70)	20.9 (10.3–NR)	8.2 (0.5–36.5)



Number at Risk											
No Active Liver Mets EE	69	65	47	33	18	11	6	2	2	2	2
Active Liver Mets EE	18	15	13	8	4	3	1	1	0	0	0
All EE	87	80	60	41	22	14	7	3	2	2	2
ITT	101	85	60	41	22	14	7	3	2	2	2

Data cutoff: 26-MAY-2023

SAFETY

All TEAEs in ≥15% of the ITT Population (N=101)

TEAE, n (%)	All Grades	Grade 3	Grade 4
Any*	101 (100)	58 (57)	4 (4)
Gastrointestinal			
Diarrhea	50 (50)	8 (8)	0
Nausea	41 (41)	5 (5)	0
Vomiting	30 (30)	4 (4)	0
Colitis	28 (28)	13 (13)	1 (1)
Abdominal pain	27 (27)	3 (3)	0
Constipation	15 (15)	0	0
Constitutional			
Fatigue	46 (46)	3 (3)	0
Decreased appetite	44 (44)	3 (3)	0
Pyrexia	30 (30)	4 (4)	0
Chills	28 (28)	0	0
Headache	22 (22)	2 (2)	0
Weight decreased	16 (16)	0	0
Peripheral edema	15 (15)	0	0
Hepatic			
Alanine aminotransferase increased	20 (20)	2 (2)	0
Aspartate aminotransferase increased	19 (19)	2 (2)	1 (1)
Blood alkaline phosphatase increased	16 (16)	3 (3)	0

TEAE, n (%)	All Grades	Grade 3	Grade 4
Musculoskeletal			
Arthralgia	24 (24)	1 (1)	0
Skin			
Pruritus	24 (24)	0	0
Rash maculo-papular	20 (20)	0	0
Blood			
Anemia	29 (29)	12 (12)	0
Respiratory			
Cough	26 (26)	0	0
Dyspnea	24 (24)	4 (4)	0
Metabolism			
Hypokalemia	23 (23)	2 (2)	1 (1)
Hyponatremia	20 (20)	3 (3)	0
Dehydration	17 (17)	2 (2)	0
Hypoalbuminemia	17 (17)	0	0
Hypophosphatemia	16 (16)	0	0

*There were 9 grade 5 TEAEs (none related to study drug): 1 respiratory failure and 8 malignant neoplasm progression.

SAFETY

All TRAEs in ≥15% of the ITT Population (N=101)

TRAE, n (%)	All Grades	Grade 3	Grade 4
Any*	89 (88)	37 (37)	2 (2)
Gastrointestinal			
Immune-mediated diarrhea/colitis*	40 (40)	16 (16)	1 (1)
Nausea	20 (20)	2 (2)	0
Constitutional			
Fatigue	32 (32)	3 (3)	0
Decreased appetite	27 (27)	0	0
Pyrexia	25 (25)	4 (4)	0
Chills	24 (24)	0	0
Hepatic			
Alanine aminotransferase increased	16 (16)	2 (2)	0
Musculoskeletal			
Arthralgia	18 (18)	1 (1)	0
Skin			
Pruritus	18 (18)	0	0
Rash maculo-papular	15 (15)	0	0

*Investigator reported as immune-mediated or the patient received steroids and/or a TNF-α inhibitor.

- No new safety signals
- Safety in CRC consistent across tumor types
- 33% discontinued due to a TRAE
  - 33% bot
  - 17% bal
- No treatment-related deaths

CONCLUSIONS & FUTURE DIRECTIONS

- Botensilimab is a multifunctional CTLA-4 antibody with broad activity in “cold” or I-O refractory tumors
- Botensilimab plus balstilimab continues to show deep and durable objective responses and notable overall survival compared to historical data in non-MSI-H CRC
- Enhanced overall survival noted across all subgroups, including those with or without active liver metastases
- Manageable safety profile with no new safety signals reported
- Global randomized phase 2 trial (NCT05608044) of botensilimab ± balstilimab (versus standard of care) in non-MSI-H CRC is ongoing

ACKNOWLEDGEMENTS

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ABBREVIATIONS

AE, adverse event
APC, antigen presenting cell
bal, balstilimab
BOR, best overall response
bot, botensilimab
BRAF, v-raf murine sarcoma viral oncogene homolog B1
CI, confidence interval
CR, complete response
CRC, colorectal cancer
CTLA-4, cytotoxic T-lymphocyte antigen-4
DCR, disease control rate
DOR, duration of response
ECOG, Eastern Cooperative Oncology Group
EE, efficacy evaluable
Fc, fragment crystallizable
FcγRIIIA, fragment crystallizable gamma receptor IIIA
F/U, follow-up
H, high
IgG, immunoglobulin G
I-O, immunotherapy
ITT, intent-to-treat
mAb, monoclonal antibody
Mets, metastases
MSI, microsatellite instability
MSS, microsatellite stable
NK, natural killer
NR, not reached
ORR, objective response rate
OS, overall survival
PD, progressive disease
PD-1, programmed death receptor-1
PD-L1/2, programmed death-ligand 1/2
PFS, progression-free survival
PR, partial response
PS, performance status
QXW, every X weeks
RAS, rat sarcoma virus
SD, stable disease
SOC, standard of care
TEAE, treatment-emergent adverse event
TMB, tumor mutational burden
TRAE, treatment-related adverse event
Treg, regulatory T cell

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Q&A Session