

2024

ESMO GASTROINTESTINAL CANCERS

Annual Congress

#743; NEOADJUVANT BOTENSILIMAB (BOT) PLUS BALSTILIMAB (BAL) IN RESECTABLE MISMATCH REPAIR PROFICIENT AND DEFICIENT COLORECTAL CANCER

NEST-1 Clinical Trial

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DECLARATION OF INTERESTS

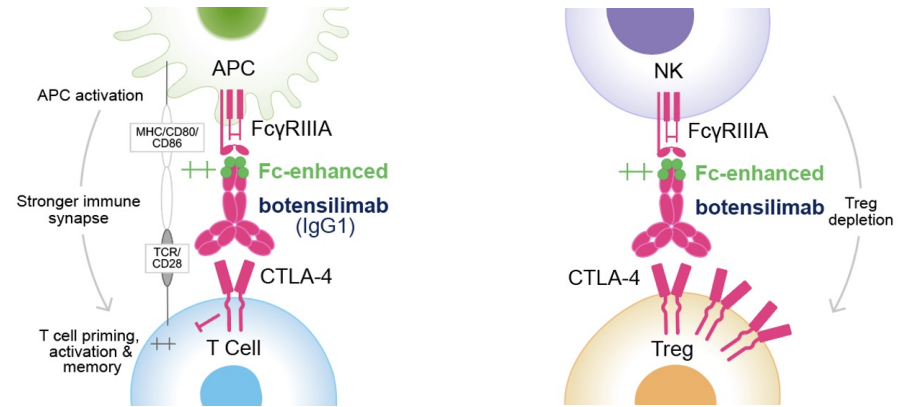
No Relevant Disclosures

Investigator-initiated trial supported by Agenus Inc.

BACKGROUND

- There is a lack of effective therapies for proficient mismatch repair/ microsatellite stable (pMMR/MSS) colorectal cancer (CRC)¹
- Response Rates of > 20% in metastatic MSS CRC² with combination therapy of
 - Botensilimab (BOT):** multifunctional next-generation anti-CTLA-4 antibody
 - Balstilimab (BAL):** an anti-PD-1 antibody
- NEST-1**⁴ (NCT05571293) is the first study to evaluate neoadjuvant BOT/BAL in resectable colon cancer

Botensilimab (BOT)³ Fc-enhanced CTLA-4 Inhibitor



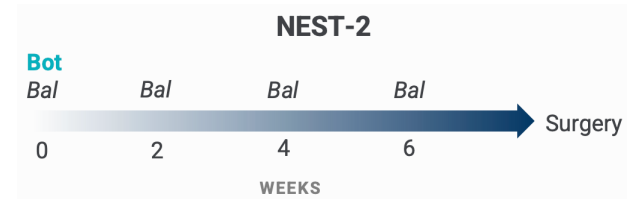
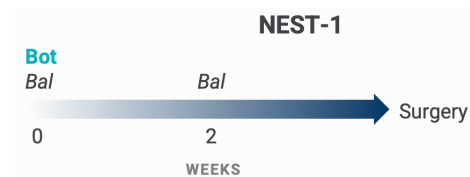
- ↑ T cell priming, expansion, memory
- ↑ Frequency of activated APCs
- ↑ Treg depletion
- ↓ Complement mediated toxicity

TRIAL DESIGN AND ELIGIBILITY

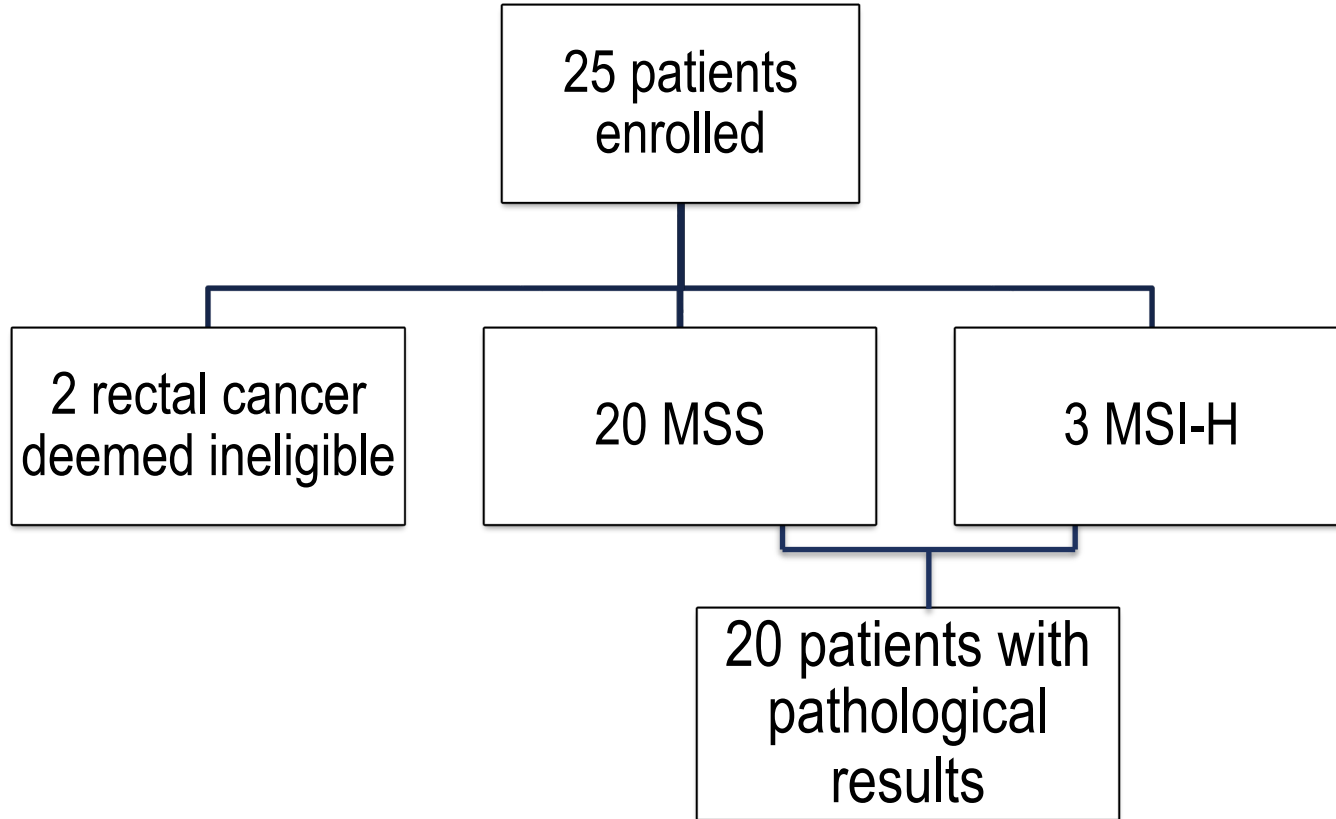
- Resectable non-metastatic colon cancer
- No contraindication for IO administration
- Surgical resection occurs within 1-6 weeks after completion of therapy

NEST Protocol (NCT05571293):

- **NEST-1** 1 dose of 75mg Botensilimab (BOT)
 - 2 doses of 240mg Balstilimab (BAL) 2 weeks apart
- **NEST-2**
 - 1 dose of 75mg Botensilimab (BOT)
 - Up to 4 doses of 240mg Balstilimab (BAL) 2 weeks apart



CURRENT ENROLLMENT



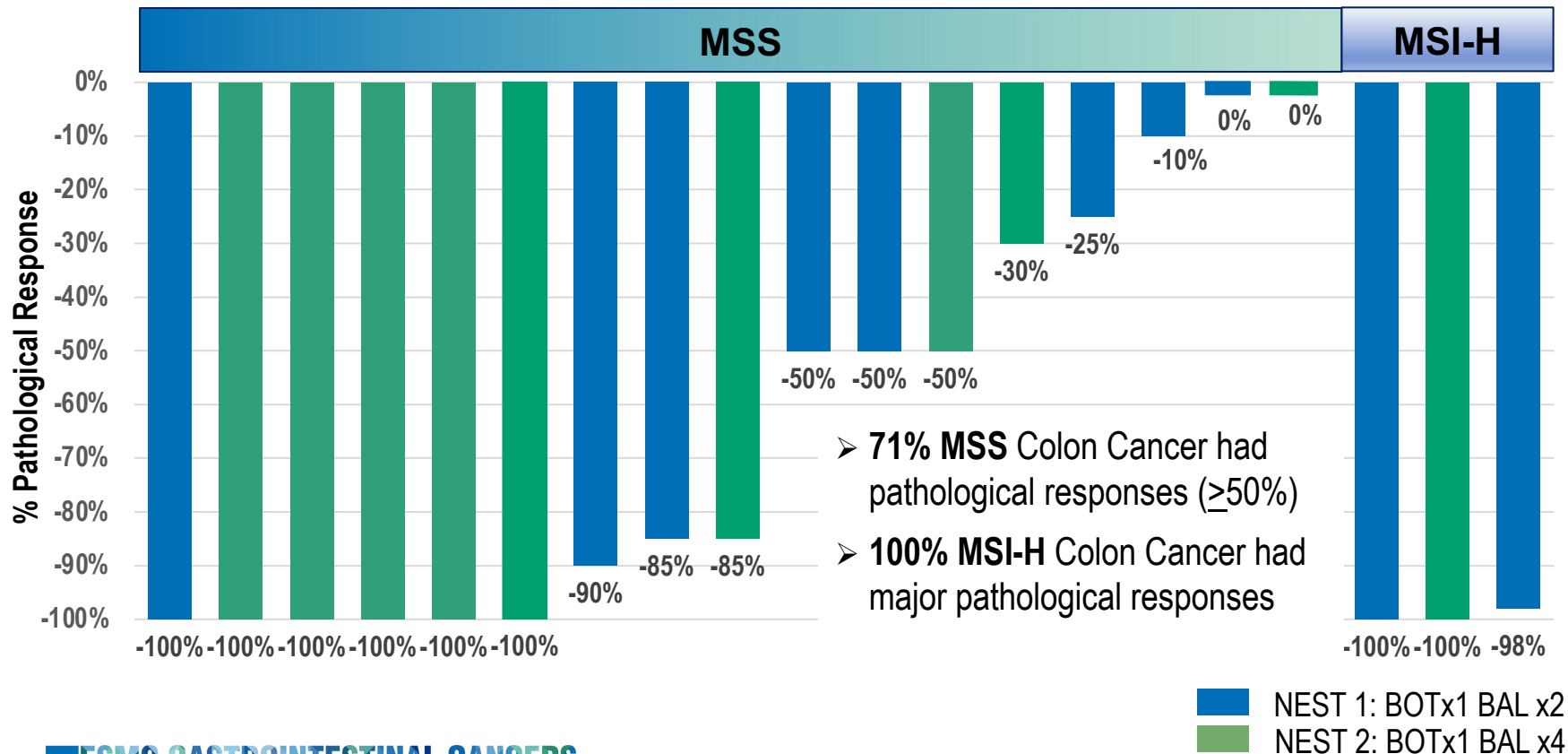
PATIENT DEMOGRAPHICS & SAFETY

	NEST 1 (N=10)	NEST 2 (N=10)
Median Age (range)-yr	67(35-79)	67 (23-76)
Sex (F)	70%	40%
Median Time to OR from C1D1 (range), days	29.5 (21-38)	57 (45-81)
Adjuvant Chemotherapy	70%	Too early to report
Unresolved irAE*	0%	0%

*2 patients with Grade 3 diarrhea/colitis managed with infliximab and short course steroids

Neoadjuvant BOT/BAL was **safe** and did **not delay** planned surgery

PATHOLOGICAL TUMOR REDUCTIONS (%) BY PATIENT



- **71% MSS** Colon Cancer had pathological responses ($\geq 50\%$)
- **100% MSI-H** Colon Cancer had major pathological responses

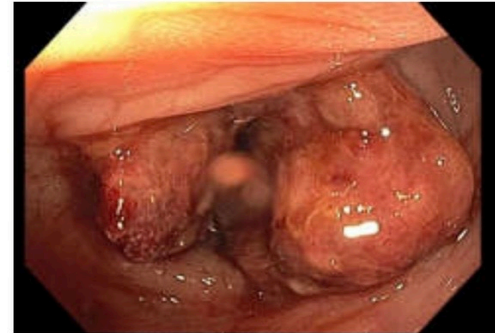
PATHOLOGICAL RESPONSE RATES

	Pathological Response (<u>></u> 50% Regression)	Complete Pathological Response (100% Regression)
NEST 1 (N=10)		
MSS (N=8)	5 (63%)	1 (13%)
MSI-H (N=2)	2 (100%)	1 (50%)
NEST 2 (N=10)		
MSS (N=9)	7 (78%)	5 (56%)
MSI-H (N=1)	1 (100%)	1 (100%)
Overall MSS (N=17)	12 (71%)	6 (35%)
Overall MSI-H (N=3)	3 (100%)	2 (67%)

CONCLUSIONS*

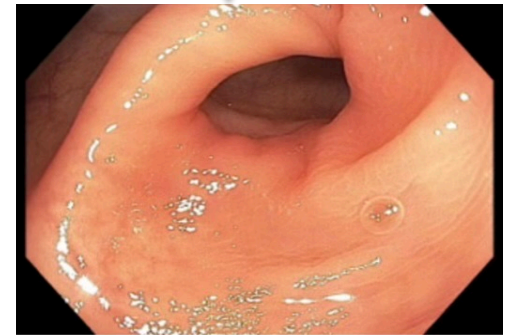
- **Neoadjuvant BOT/BAL** is a **safe** and **active** regimen in both pMMR/MSS and dMMR/MSI-H colon cancer.
- **Response rates increased with more doses of BAL in conjunction with increased interval to surgery** with up to 50% complete path response rate in pMMR colon cancer.
- **Downstaging and pathological response** may reduce reliance on surgery and/or adjuvant chemotherapy in future studies.

*This data is not final and under review by WCM.
Final results are pending completion of the study analysis.



Pretreatment MSS Sigmoid Cancer

↓
NEST 2



Week 7 after C1D1 : Complete Response

ACKNOWLEDGEMENTS

NEST CLINICAL TRIAL

Patients, Caregivers, GI, Medical Oncology, Colorectal Surgery and the Research Team at **Weill Cornell Medicine, New York.**



Weill Cornell Medicine
NewYork-Presbyterian

