TPS3676: The CO.33/BATTMAN trial: A phase 3 randomized study of botensilimab + balstilimab versus best supportive care in chemorefractory unresectable colorectal adenocarcinoma that is not dMMR/MSI-H.

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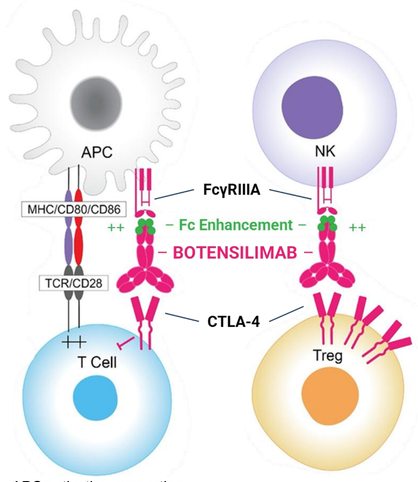
BATTMAN
CO.33 STUDY
YOUR IMMUNE SYSTEM IS THE REAL SUPERHERO

Unmet Need

- Despite recent advances, patients with metastatic colorectal cancer (mCRC) have a poor prognosis after progression on standard cytotoxic chemotherapies.
- Approximately 95% of patients with mCRC have non–mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) disease, which is associated with less effective treatment options compared with dMMR/MSI-H mCRC, resulting in substantial unmet need.[1,2]
- Standard later-line salvage therapies include regorafenib, trifluridine/tipiracil ± bevacizumab, and fruquintinib, with objective response rates (ORRs) of 1%–6% and median overall survival (OS) of approximately 6–11 months for each agent.[3-8]
- Once refractory, patients receiving best supportive care (BSC) have a median OS of 4–6 months.[9-10]
- Although conventional immune checkpoint inhibitors (ICIs) show limited activity in mCRC that is not dMMR/MSI-H, the CCTG CO.26 randomized phase 2 trial (NCT02870920) demonstrated that doublet ICI with durvalumab + tremelimumab improved OS compared with BSC,[10] suggesting that next-generation ICI with improved immune engagement may drive meaningful benefit in this setting.

Botensilimab and Balstilimab

- **Botensilimab (BOT)** is an investigational Fc-enhanced multifunctional anti–CTLA-4 antibody that augments T-cell priming, depletes intratumoral Tregs, and activates antigen-presenting cells to overcome resistance and extend activity to "cold" or ICI-refractory tumors.[11-12]
- **Balstilimab (BAL)** is an investigational anti–PD-1 antibody pharmacologically comparable to approved PD-1 inhibitors.[13-14]
- The combination of BOT+BAL has shown meaningful clinical activity in heavily-pretreated non–MSI-H/dMMR mCRC, with ORRs of ~20%, median OS 20.9 months, and a 2-year OS rate of 42%.[15-16]



APC activation supporting enhanced T-cell priming, activation, and memory

Treg depletion

The phase 3 randomized CO.33/BATTMAN trial (registrational intent) will evaluate next-generation ICI with BOT + BAL + BSC versus BSC alone in patients with refractory non–MSI-H/dMMR mCRC, a historically immunotherapy-resistant population with limited treatment options.

Study Design

CO.33/BATTMAN Trial (NCT07152821): A Phase 3 Trial of **B**otensilimab + B**a**lstilimab *versus* Bes**t** Suppor**t**ive Care in Che**m**o-Refractory **A**dvanced Colorectal Ade**n**ocarcinoma[17]

Patients with non-dMMR, non-MSI-H unresectable colorectal cancer refractory to available agents

Randomize 1:1

- Botensilimab 75 mg IV Q6W x 4 doses + Balstilimab 450 mg IV Q3W
- Best Supportive Care (BSC)

No systemic anticancer treatment; care focuses on symptom management and quality of life.

Primary Endpoint:
- Overall Survival[a]

Select Secondary Endpoints:
- Progression-Free Survival
- Overall Response Rate
- Clinical Benefit Rate
- Quality of Life
- Safety and Toxicity

[a]Overall survival with pre-planned subgroup analysis based on presence or absence of liver metastases

Stratification:
- ECOG Performance Status (0 *vs* 1)
- Active liver metastases (yes *vs* no)
- Region of enrollment (CA *vs* AU/NZ *vs* FR)

No cross-over permitted

Select Eligibility Criteria

- Colorectal adenocarcinoma that is not MSI-H or dMMR by local testing.
- ECOG 0/1 with RECIST 1.1 evaluable lesions.
- Life expectancy of ≥12 weeks at the time of study enrollment.
- Refractory or intolerant to all available systemic therapies.
- Adequate bone marrow and end organ function.

Select Ineligibility Criteria

- Prior organ transplantation, active autoimmune disorder, or autoimmune condition requiring treatment within 2 years of starting protocol therapy.
- Requirement for >10 mg prednisone equivalent per day corticosteroids within 7 days of starting protocol therapy.
- Unresolved CTCAE grade ≥2 adverse events from prior therapy (excluding toxicities not expected to be exacerbated by protocol treatment).
- Refractory ascites.
- Prior anti–PD-(L)1 or CTLA-4 therapy.
- Active, untreated brain metastases.
- Recent bowel obstruction.

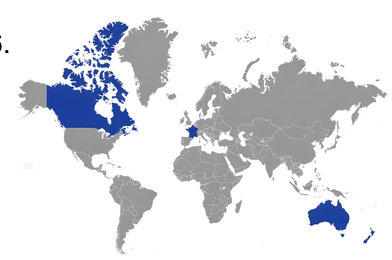
Immune-Mediated Diarrhea/Colitis (imDC) Management

Across ICI therapies, imDC management has shifted from prolonged high-dose steroids toward early TNF-α blockade (i.e., infliximab) to minimize treatment interruption and support rapid steroid tapering.[18-20] This strategy is being employed in BOT/BAL trials to support a manageable and reversible imDC profile (details below).

Key Management Steps	Details
Early Intervention and Bridging Steroids	• Early intervention (all grades) with "bridging" prednisone 0.5-1 mg/kg daily within 24 hours, followed by dose 1 of infliximab 5 mg/kg in clinic <72 hours after onset of symptoms
Initial Infliximab Administration	• Give infliximab dose 1 in the clinic, even if good response to oral "bridging" steroids is observed
Assess Response and Taper Steroid	• Expect rapid and marked improvement in imDC following infliximab within 24–48 hours • If a good response to infliximab occurs, taper prednisone from 40 mg to 0 mg over 1 week (or at most 2 weeks)
Consolidation and BOT Continuation	• Give dose 2 and 3 of infliximab at weeks 2 and 6 for consolidation and prophylaxis. BOT dosing may be continued if diarrhea is not considered immune related OR symptoms resolve rapidly *and* imDC did not exceed grade 2
Evaluate Non-Response and Alternative Causes	• If no substantial response to dose 1 of infliximab occurs after 2–3 days, consider infliximab 10 mg/kg (particularly if patient has low albumin <2.5 g/dL) and workup for other causes of diarrhea (e.g., infectious, or *C. diff,* or CMV or celiac [both rare])

Trial Status

- Centrally activated: February 12, 2026.
- First patient enrolled: March 31, 2026.
- Canadian sites actively enrolling.
- Australia, New Zealand and France activation planned imminently.
- Expected sample size: 834 patients.



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