

E. van den Berg\*, L.D.W. van den Dungen, P.G.M. de Gooyer, M.H. Geukes Foppen, S. Dokter, P. Snaebjornsson, K.F.D. Kuhlmann, A.G. den Hartog, W.A. van Hattem, S. Balduzzi, T.N. Schumacher, J.B.A.G. Haanen, D.M.J. Lambregts, B.A. Grotenhuis, J.G. van den Berg, M. Chalabi  
Netherlands Cancer Institute, Amsterdam, Netherlands  
\* Nothing to declare

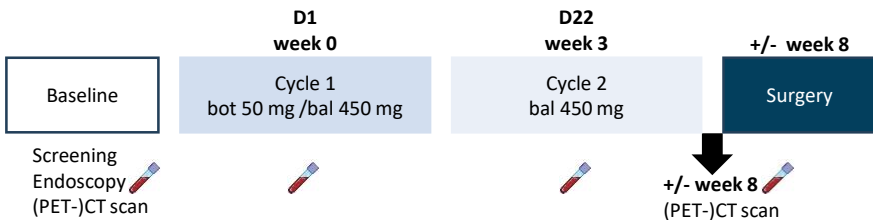
Study sponsored by the Netherlands Cancer Institute

## BACKGROUND

- Immune checkpoint inhibition has shown remarkable efficacy in mismatch repair-deficient (dMMR) colorectal cancer (CRC)
- Botensilimab is a new-generation, Fc-enhanced anti-CTLA-4 that harnesses novel mechanisms by binding to Fcγ receptors on APCs and NK cells, thereby augmenting T-cell priming, reducing regulatory T-cells, and activating APCs
- Botensilimab combined with balstilimab (anti-PD-1) has shown efficacy across tumor types, including immune-cold tumor types such as MMR-proficient colorectal cancer and sarcoma
- NEOASIS is a platform study in which patients are treated with botensilimab (bot) plus balstilimab (bal) and, depending on the tumor type, combined with other treatments such as chemotherapy
- Based on previously reported safety run-in data, patients are treated with a low dose of bot at 50 mg. Here we report results from the dMMR CRC basket

## METHODS

- Investigator-initiated, single center, phase II platform study
- Patients with colorectal, non-metastatic, resectable, dMMR adenocarcinoma. MMR deficiency confirmed by IHC
- Botensilimab 50 mg I.V. on D1 + balstilimab 450 mg I.V. on D1 and D22, followed by surgery within 8 weeks after start of treatment
- PRIMARY ENDPOINT:** Major pathologic response (MPR, ≤ 10% residual viable tumor, RVT, in primary tumor and lymph nodes);
  - Simon's two-stage design: 8 patients in stage 1, expanding to 18 if > 2 MPRs. Primary endpoint met if ≥ 7/18 MPRs.
- SECONDARY ENDPOINTS:**
  - Pathologic complete response (pCR, no RVT in both primary tumor and lymph nodes), partial pathologic response (10 – 50 % RVT), no pathologic response (> 50% RVT);
  - EFS, DFS, OS;
  - Translational analyses including WES, scRNAseq, and ctDNA.



## CONCLUSION

**Bot + bal leads to high rates of pathologic response** in patients with locally advanced dMMR CRC, including an MPR in 83% and pCR in 72% of patients

These data support further evaluation of bot + bal in dMMR CRC, including a currently ongoing **dMMR rectal organ preservation** cohort within NEOASIS

## BASELINE CHARACTERISTICS

| Characteristic                                               | n = 18                                     |
|--------------------------------------------------------------|--------------------------------------------|
| Median age (range) – yr                                      | 58 (21-78)                                 |
| Male sex - no. (%)                                           | 11 (61%)                                   |
| ECOG PS - no. (%)                                            | 0 18 (100%)<br>1 0 (0%)                    |
| Tumor stage - no. (%)                                        | cT3 or cT3-4a 6 (33%)<br>cT4a + b 12 (67%) |
| Lymph node stage - no. (%)                                   | N0 5 (28%)<br>N+ 13 (72%)                  |
| Tumor location - no. (%)                                     | rectum 0* (0%)<br>colon 18 (100%)          |
| Lynch syndrome – no. (%)                                     | 6 (33%)                                    |
| Non-lynch syndrome dMMR - no. (%)                            | 12 (67%)                                   |
| *One patient had a synchronous colon and rectal tumor (T3N0) |                                            |

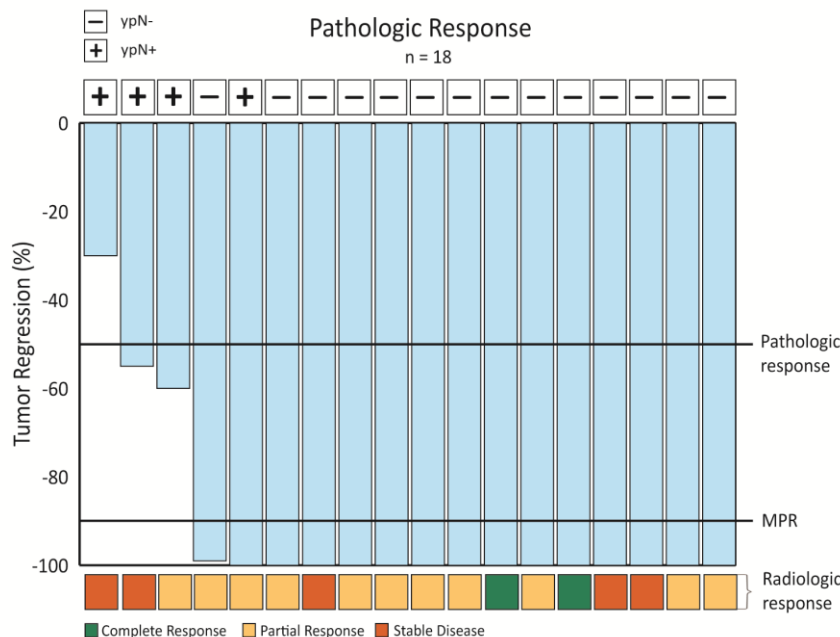
## SAFETY

| Immune related adverse events | n = 18   |
|-------------------------------|----------|
| Grade 1 - 2 irAE – no. (%)    | 13 (72%) |
| Flu-like symptoms             | 6 (24%)  |
| Rash                          | 5 (30%)  |
| Hypothyroidism                | 5 (20%)  |
| Grade 3 irAE – no. (%)        | 1 (6%)   |
| Colitis                       |          |

- Grade 1-2 irAEs were mild and manageable
- One case of grade 3 colitis resolved with infliximab and steroids, and 2<sup>nd</sup> bal dose was withheld
- Two patients developed an ileus: one underwent surgery as planned, while the other was operated prematurely on day 41. Both had a pCR. All other patients underwent surgery as planned.

## EFFICACY

- 17/18 (94%) patients had a pathologic response:
  - 15/18 (83%) an MPR, meeting the primary endpoint;
  - 13/18 (72%) had a pCR;
  - Two patients had a partial response and one patient with 70% RVT was a non-responder.
- In the patient with a synchronous colon and rectal tumor, the rectal tumor showed a complete endoscopic response and patient opted for rectal organ preservation, while surgery was performed for the colon tumor (partial response)
- Radiographic assessment did not accurately predict pathologic response



## SURVIVAL

After a median FU of 15 months (range 13,7 – 21,6):

- All patients were alive;
- One patient (partial responder; ypT4abN2), who received adjuvant chemotherapy, developed peritoneal metastases a year later;
- One patient with an MPR experienced a solitary lymph node metastasis 6 months after surgery;
- The patient with complete clinical response of the rectal tumor has no signs of regrowth at 7 months FU.

Corresponding email address: m.chalabi@nki.nl