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Neoadjuvant botensilimab plus balstilimab in MMR proficient and deficient early-stage cancers: first results of the pan-cancer NEOASIS study

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Disclosure Information

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Myriam Chalabi

I have the following relevant financial relationships to disclose:

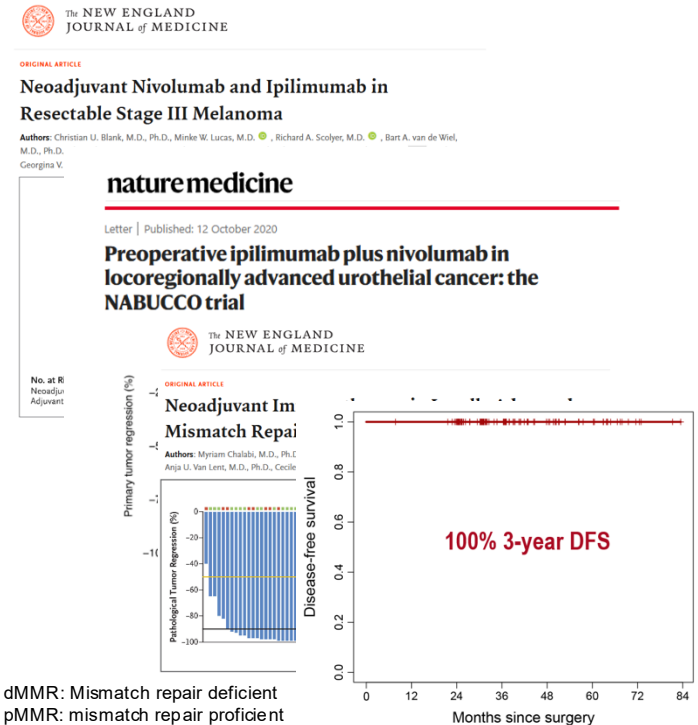
Advisory role: BMS, MSD, Roche, Agenus (paid to the institution)

Grant/Research support: BMS, Roche, MSD, Agenus

All funding and honoraria are made to the institution

Introduction

- Several studies have demonstrated the remarkable potential of neoadjuvant immunotherapy across tumor types
- Response to neoadjuvant IO associated with survival
- Highest response rates in MMR-deficient colon cancers
  - MMR-deficiency also occurs in other solid tumors
  - Majority of tumors across cancers are MMR-proficient



dMMR: Mismatch repair deficient
pMMR: mismatch repair proficient

Blank et al, NEJM 2024; Chalabi et al, ESMO 2024; Latham et al, JCO 2019

Rationale

- Next-generation CTLA-4i botensilimab (bot) & balstilimab (bal, anti PD-1) effective in a range of previously immune non-responsive tumors
  - pMMR mCRC, metastatic sarcoma, metastatic ovarian cancer

Does the efficacy seen in dMMR CRC translate to dMMR tumors of other origins?

Does neoadjuvant bot/bal induce responses in “immune cold” tumors?

NEOASIS: a pan-cancer neoadjuvant trial for patients with solid tumors

Bullock et al, Nat Med 2024; Wilky et al, JCO 2025; Bockorny et al, Gyn Onc 2023

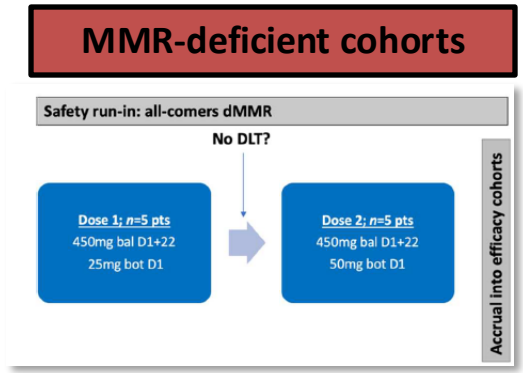
mCRC: metastatic colorectal cancer
pMMR: MMR-proficient
dMMR: MMR-deficient

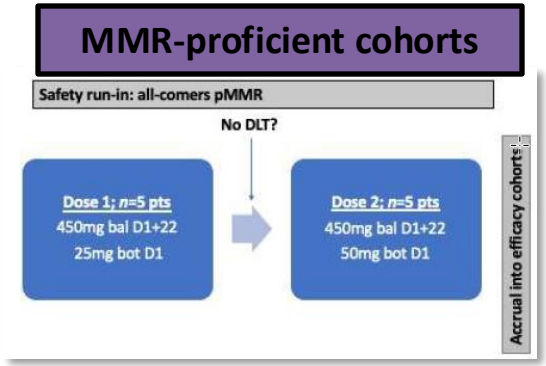
Study design

- Investigator-initiated, non-randomized basket study

- **Safety run-ins:**
  - First 5 pts in each cohort (dMMR or pMMR) receive 25mg bot
  - Dose-escalation from 25 to 50mg allowed if ≤1 DLT in first 5 patients (IDMC)
  - If no more than 2 DLTs with 50mg bot → continue accrual in efficacy cohorts with 50mg

Dose limiting toxicity (DLTs) definition:
- Any grade 5 event
- Grade 4 event persisting ≥3 weeks
- Any grade 3 event persisting ≥ 6 weeks
- Any treatment related toxicity resulting in a delay of surgery >2 weeks





Treatment and main selection criteria

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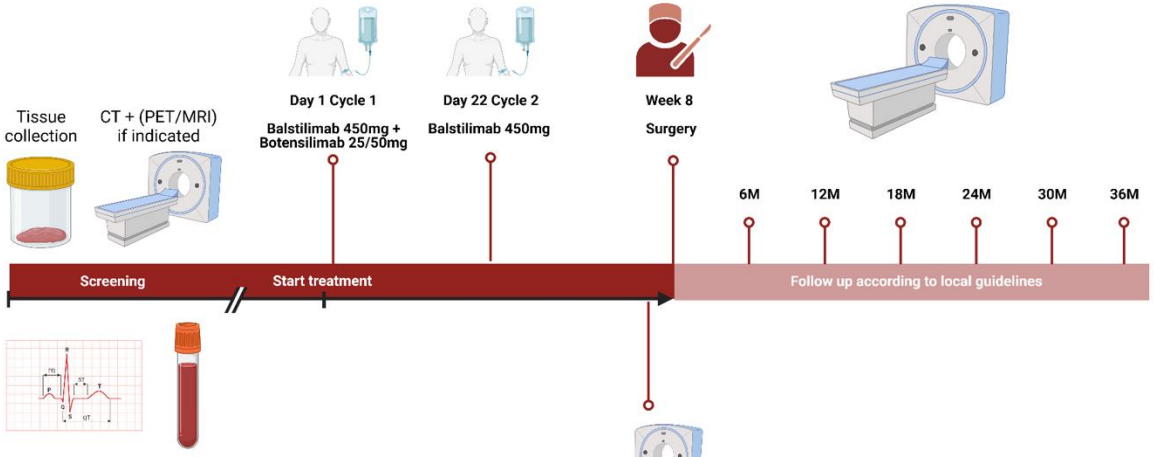
- Patients with non-metastatic solid tumors who will undergo surgery
- In case of pMMR tumors; no standard of care neoadjuvant therapy unless adjuvant equivalent available
- No previous chemo- or immunotherapy



Baseline characteristics

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Characteristic	pMMR population (*n*=10)	dMMR population (*n*=10)
Age, median (range)	54 (34 - 78)	67 (50-71)
Gender		
Female	**9 (90%)**	5 (50%)
Male	1 (10%)	5 (50%)
ECOG performance status		
0	8 (80%)	6 (60%)
1	2 (20%)	4 (40%)
Tumor type		
Duodenal cancer	-	1 (10%)
Colorectal cancer	-	**9 (90%)**
Estrogen receptor+ breast cancer	2 (20%)	-
Merkel cell carcinoma	1 (10%)	-
Triple negative breast cancer	**6 (60%)**	-
Undifferentiated pleiomorphic sarcoma	1 (10%)	-

Results – Safety of 25mg bot

- All 10 patients received both cycles of therapy
- No grade ≥ 3 immune related adverse events (irAEs)
- No DLTs / No delays of surgery
- Grade 1-2 irAEs mild & manageable

Immune related adverse events	25mg botensilimab (*n*=10)
Patients with any grade irAE *n* (%)	7 (70%)
Grade ≥3 irAEs	0
irAEs type	
Cutaneous toxicity	3 (30%)
Fatigue	2 (20%)
Hypothyroidism	2 (20%)

Results – Safety of 50mg bot

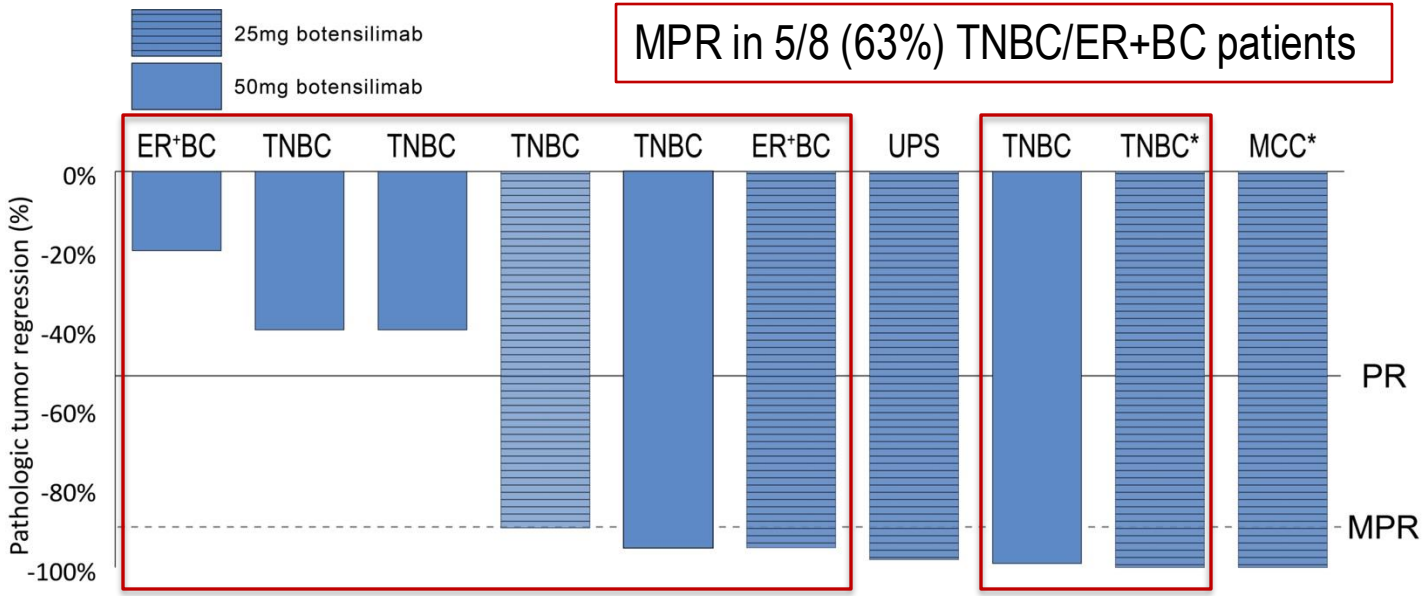
- Two patients did not receive the 2nd cycle of therapy, both due to liver toxicity
- One patient with grade 3 IR-hepatitis, full resolution upon steroid treatment
- No DLTs, no delay of surgery
- No IR-colitis at either dose levels

Immune related adverse events	50mg botensilimab (*n*=10)
Patients with any grade irAE *n* (%)	8 (80%)
Grade ≥3 irAEs	**1 (10%)**
irAEs type	
Fatigue	3 (30%)
IR-hepatitis	2 (20%)
Infusion related reaction	2 (20%)

Results – Response pMMR cohort

Major pathologic response rate of 70% in bot 25 and 50mg dose levels combined

- MPR in 5/5 tumors at 25mg bot dose
- MPR in 2/5 tumors at 50mg bot dose



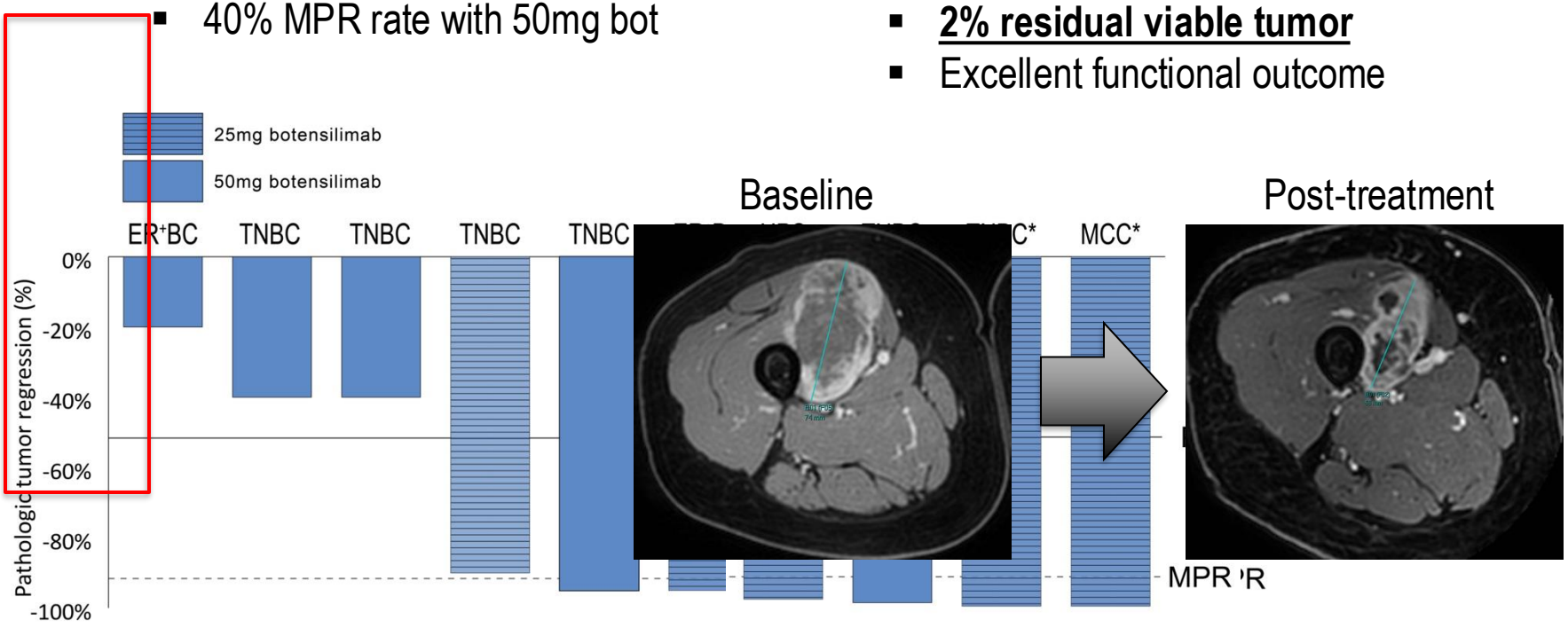
ER+BC: Estrogen receptor positive breast
TNBC: Triple negative breast cancer
UPS: Undiff. pleiomorphic sarcoma
MCC: Merkel cell carcinoma
SoC: Standard of care

Results – Response pMMR

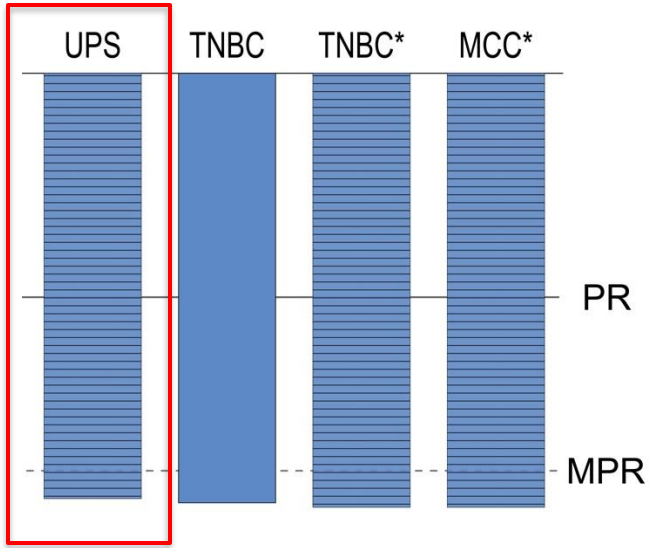
Overall 60% MPR-rate with both dose levels of bot

- 80% MPR rate with 25mg bot
- 40% MPR rate with 50mg bot

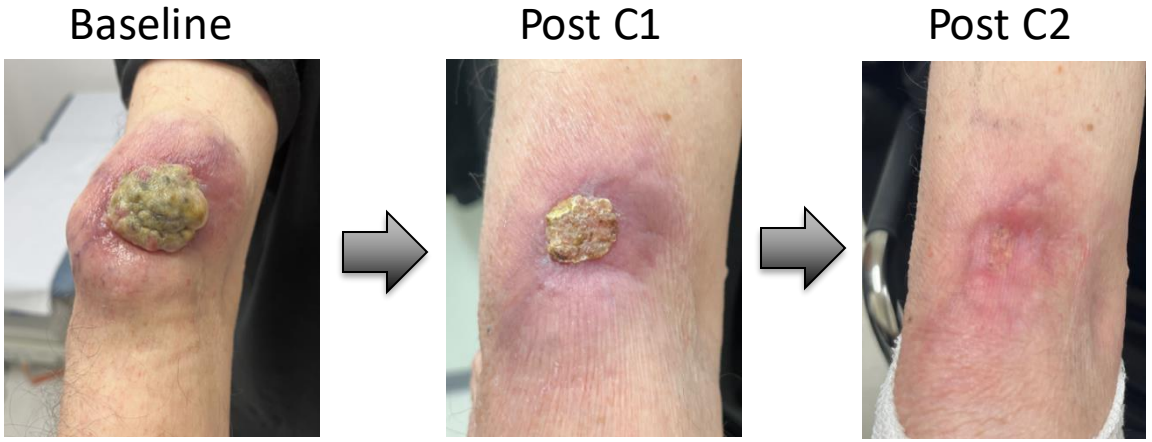
- Undifferentiated pleiomorphic sarcoma of the right upper leg
- **2% residual viable tumor**
- Excellent functional outcome



Results – Response pMMR



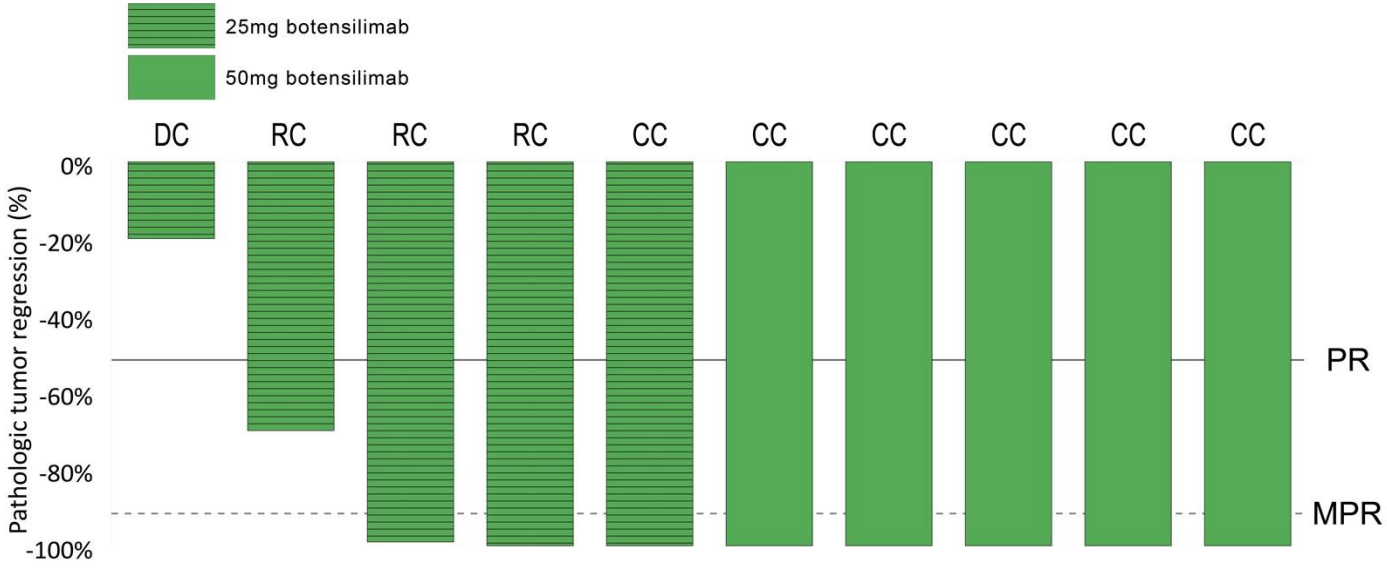
- Merkel cell carcinoma, left elbow
- Clear macroscopic regression after 3 weeks
- **Pathologic complete response** including multiple lymph nodes (tumor-positive at baseline)



Results – Response dMMR cohort

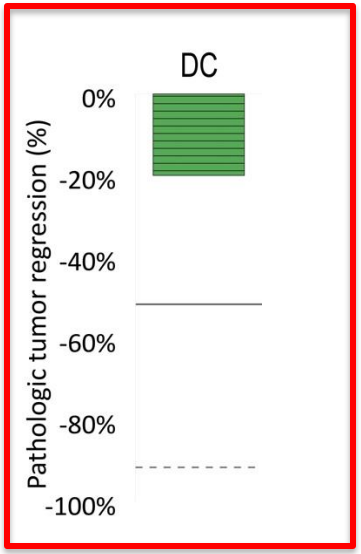
Overall 80% MPR rate with 70% pCR

- MPR in 3/5 at 25mg bot dose; of which 2 pCR
- pCR in 5/5 (100%) at 50mg bot dose



DC: Duodenal cancer
RC: Rectal cancer
CC: Colon cancer

Results – Response dMMR



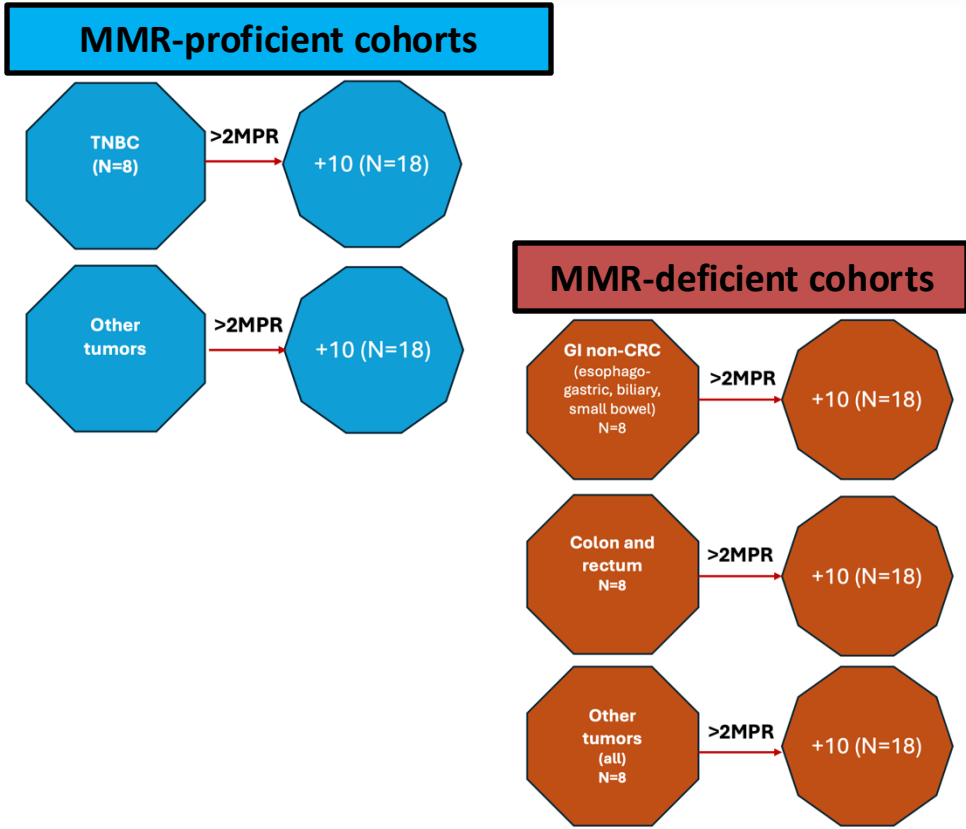
- One patient with duodenal cancer showed limited response of the primary tumor
- In contrast: during surgery multiple lesions of the peritoneum, diaphragm and liver biopsied and showed a pCR

Conclusion

- Combination treatment with bot/bal is safe with primarily low grade & manageable irAEs and no surgical delays
- Bot/bal led to remarkable responses in pMMR tumors of several origins
  - Efficacy of neoadjuvant ICB may be extended to less immunogenic tumors
- High efficacy in dMMR CRC tumors with 50mg bot → leverage to achieve immune-ablation and organ preservation by a very brief combination treatment

Future directions

- Recruitment in MMR-specific baskets ongoing (50+ pts included)
- Expand to organ preservation cohorts
- Translational analyses including WES, scRNAseq and ctDNA analyses ongoing



Acknowledgements

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Dirk Smeele
Marieke van de Belt

Talks below will also include insights from NEOASIS

SESSION **PL05 - Opportunities in Predictive Oncology**

Apr. 30, 2025, 8:59 AM - 9:26 AM
Breast cancer dynamics in predicting response to immunotherapy
Marleen Kok. Netherlands Cancer Institute, Amsterdam, Netherlands

Session ADT03 - Neoadjuvant Treatment for Solid Tumors: Why, How, and When?
- Neoadjuvant treatment across tumor types: One size does not fit all

Apr. 30, 2025, 10:20 AM - 10:40 AM
Neoadjuvant treatment across tumor types: One size does not fit all
Myriam Chalabi. Netherlands Cancer Institute, Amsterdam, Netherlands

Clinicaltrials.gov: NCT06279130