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Early evaluation of the effectiveness and cost-effectiveness of ctDNA-guided selection for adjuvant chemotherapy in stage II colon cancer

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Presenting author does not have conflics of interest

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Background

- After curative surgery for stage II colon cancer (CC), patients with high-risk features are offered adjuvant chemotherapy (ACT) to reduce their risk of recurrence.
- Current selection is suboptimal: undertreatment in low-risk patients (~13% recurrence rate), and overtreatment in high-risk patients (73% already cured by surgery).
- Presence of circulating tumor DNA (ctDNA) in blood plasma after surgery indicates minimal residual disease and a high risk of recurrence (1).

Post-operative ctDNA-testing could improve ACT decisions in colon cancer.

Study aim: We performed an early model-based evaluation of the (cost-)effectiveness of ctDNA-guided selection strategies for ACT in stage II CC in the Netherlands.

Methods

PATTERN-model
The validated PATTERN model simulates disease progression in CC-II patients from diagnosis to death (Figure 1) (2). The model takes the pathological-, clinical-, and biomarker features of the patient population into account.

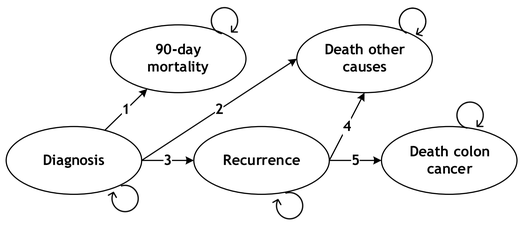

Figure 1. PATTERN-model

ctDNA parameters
The model was supplemented with observational data on the prognostic value of ctDNA from 86 patients included in the MEDOCC-study.

MEDOCC-study:
- ctDNA test: tumor-informed targeted NGS
- Median time of blood collection: 11 days post-surgery
- Median follow-up time: 47 months

ctDNA input:
- 5.8% of patients were ctDNA positive post-surgery
- HR 9.23 for recurrence for ctDNA positive vs ctDNA negative
- Costs of tumor-informed ctDNA test: €2400

The following ACT strategies were evaluated with the model:

1. **No ACT**	2. **Current guideline** *pT4 & MSS*	3. **ctDNA-only** *ctDNA positive*
4. **Combination 1** *ctDNA positive & MSS* *or* *pT4 & MSS*	5. **Combination 2** *ctDNA positive* *or* *pT4 & MSS*	6. **Combination 3** *ctDNA positive* *or* *pT4*

The impact of ctDNA related parameters was explored in sensitivity analyses by varying the input of these parameters:
- **Costs of ctDNA testing** (costs of ctDNA testing decrease)
- **Predictive of ACT response** (ctDNA positive patients respond better to ACT than ctDNA- patients)
- **Performance of ctDNA test** (ctDNA test identifies more ctDNA positive patients, with the same recurrence risk as in the base-case)

Results

Base-case analysis (Table 1)
- The ctDNA-only strategy was **less effective** than current guideline strategy, in terms of recurrences and quality-adjusted life years (QALYs).
- Combination strategies 1-3 were **more effective** than current guideline strategy, but not cost-effective (ICER > €50,000/QALY)

Table 1. Results base-case analysis

Strategy	%ACT treated	Recurrences[1]	QALYs	Costs	ICER[2]
No ACT	0.00%	163	8.027	€ 26,227	Reference
Current guideline	10.98%	155	8.079	€ 26,911	€ 13,223
ctDNA-only	5.81%	158	8.063	€ 28,735	Dominated
Combination 1	15.24%	151	8.108	€ 28,970	Dominated[3]
Combination 2	16.16%	150	8.113	€ 29,402	Dominated[3]
Combination 3	18.10%	149	8.117	€ 29,481	€ 67,413

[1] Number of recurrences in a simulated cohort of 1000 patients
[2] Incremental cost-effectiveness ratio = costs per QALY gained
[3] Dominated through extended dominance

Sensitivity analyses (Figure 2)
- In terms of cost-effectiveness, combination strategies 1-3 were more favorable than current guideline if:
  - the costs of ctDNA testing were lower than €1500 per patient
  - if ACT effectiveness was substantially better in ctDNA positive patients than in ctDNA negative patients
  - if the ctDNA test identified 12% ctDNA positive patients

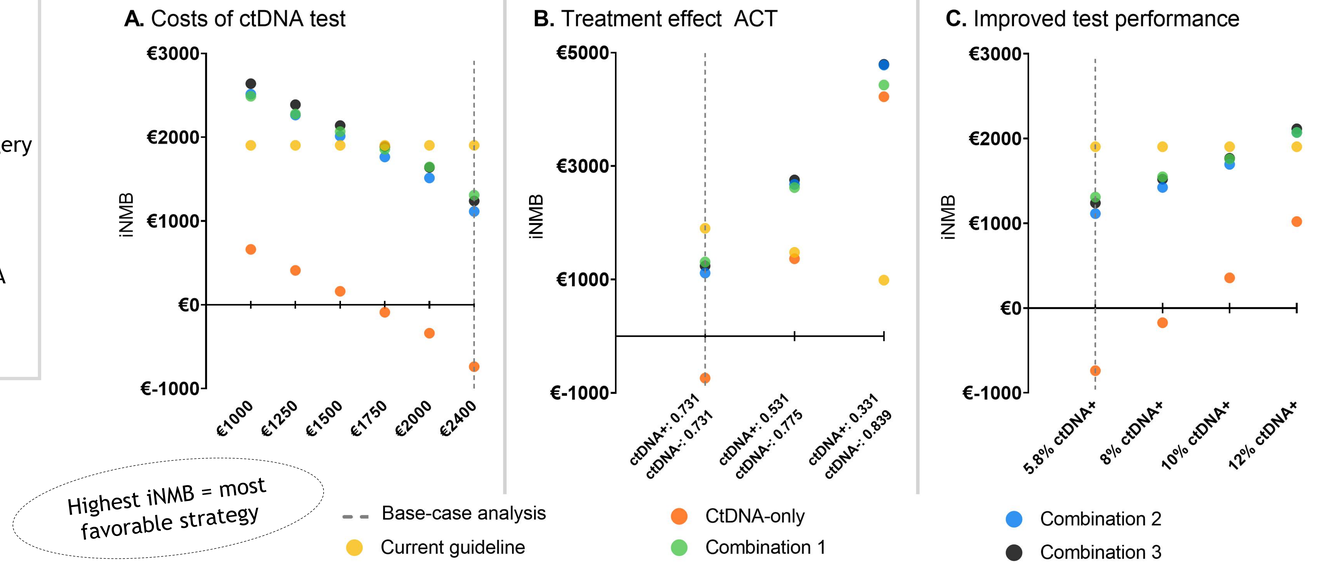

Figure 2. Results sensitivity analyses. iNMB = incremental Net Monetary Benefit compared to No ACT.

Conclusions

- **Adding ctDNA testing to current criteria for ACT can improve the selection of patients for ACT in stage II CC in the Netherlands in terms of CC recurrences and survival.**
- **The combination strategies were not cost-effective due to the high costs of ctDNA testing. However, the field is quickly developing, and these strategies have the potential to be cost-effective.**
- **Most importantly, for future research it is important to investigate if ctDNA status is predictive of ACT response.**

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