BARCELONA 2024 ESMO congress

Value of Immune Checkpoint Blockade in Microsatellite Stable/Mismatch Repair Proficient Metastatic Colorectal Cancer

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Akershus University Hospital / University of Oslo

Lørenskog / Oslo, Norway, 15 September 2024

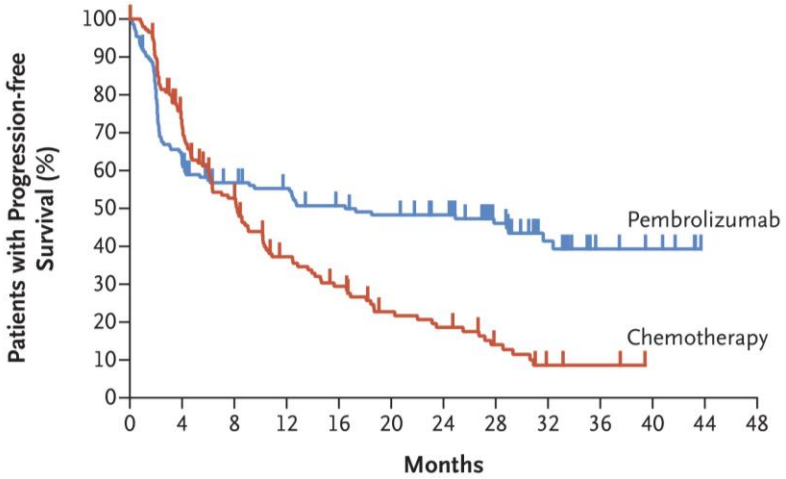
DECLARATION OF INTERESTS

Benjamin P. Geisler, MD MPH

In-kind drug donation and research funds (to institution): Bristol-Myers Squibb

Background: 1st-line ICB for metastatic CRC

MSI/dMMR



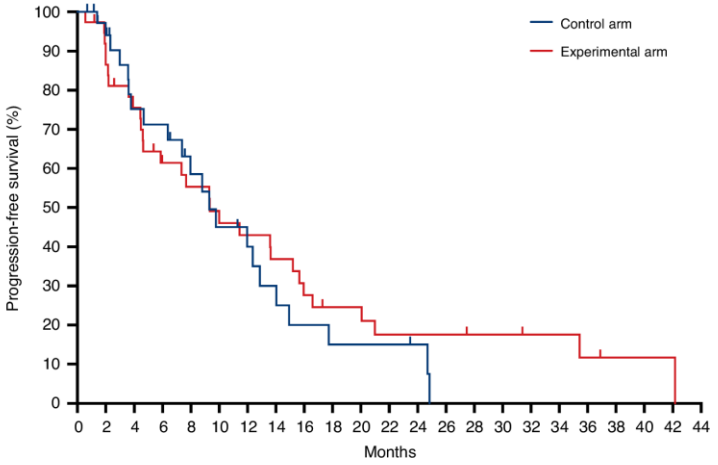
KeyNOTE-177

André *et al. N Engl J Med* 2020

Pembrolizumab vs. 5FU-based ±bevacizumab or cetuximab

HR (PFS): 0.60 (95% CI: 0.45; 0.80)

MSS/pMMR



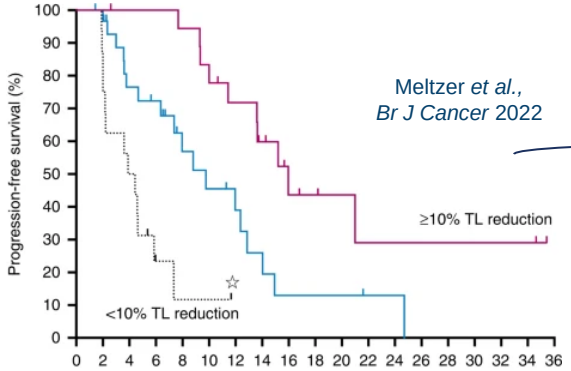
METIMMOX

Ree *et al. Br J Cancer* 2024

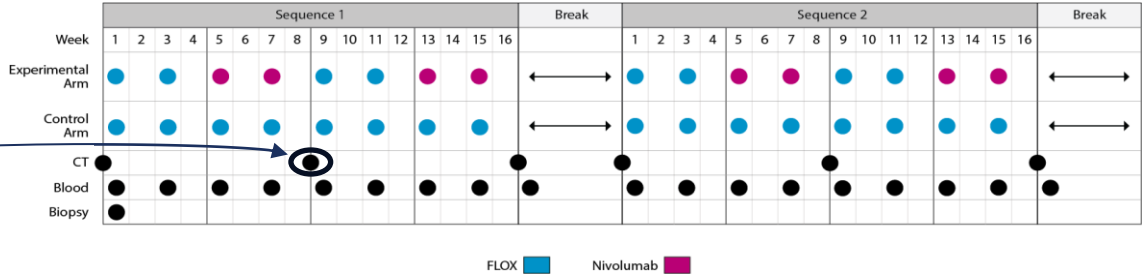
Alternating two cycles each of FLOX and nivolumab

HR (PFS): 0.88 (95% CI: 0.50; 1.57)

Background: MSS/pMMR Biomarker Subgroups



Meltzer *et al.*,
Br J Cancer 2022



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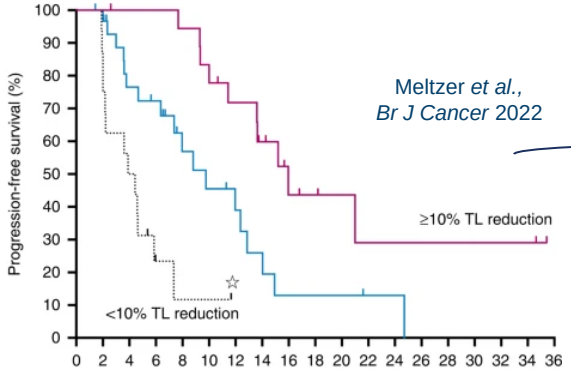
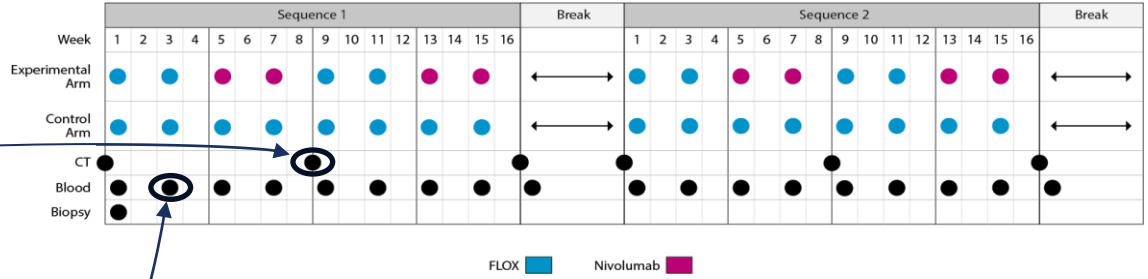
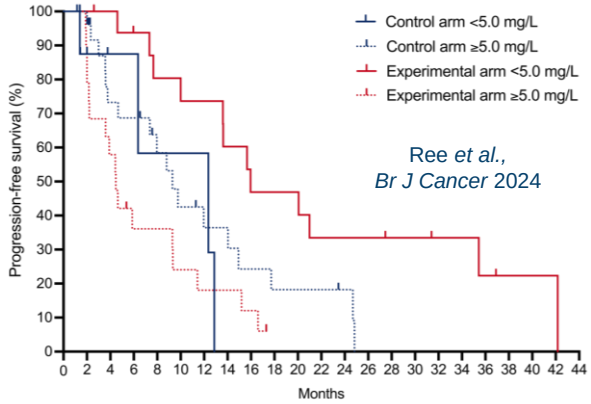


Meltzer *et al.*,
Br J Cancer 2022





Ree *et al.*,
Br J Cancer 2024

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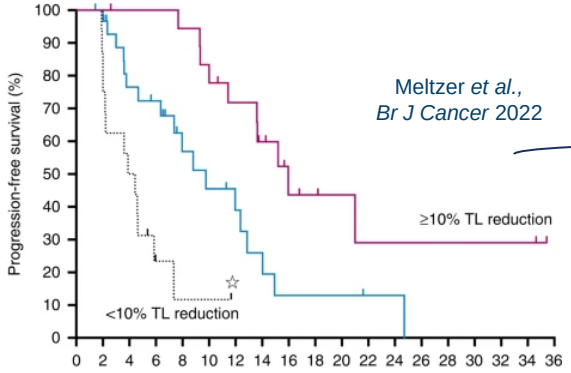
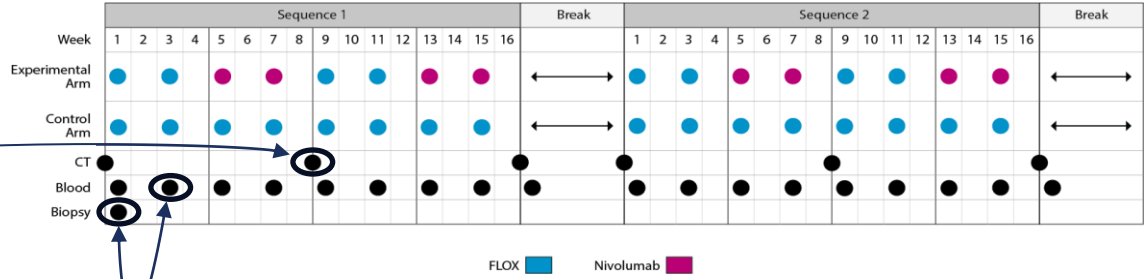
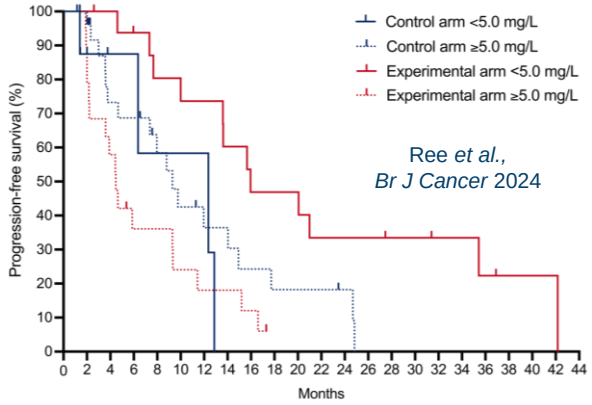
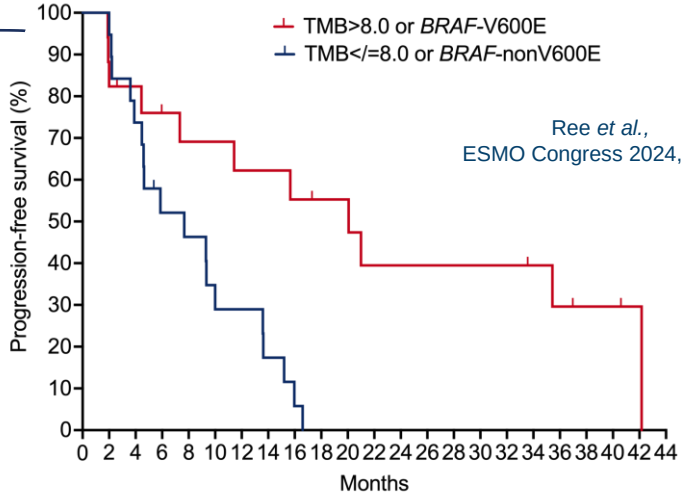


Meltzer *et al.*,
Br J Cancer 2022





Ree *et al.*,
Br J Cancer 2024



Ree *et al.*,
ESMO Congress 2024, **543P**

Objective

- To quantify the **value for money** of alternating two cycles each of oxaliplatin-based chemotherapy (**FLOX**) and ICB (**nivolumab**) for unresectable metastatic **MSS/pMMR** colorectal cancer, compared with standard-of-care FLOX alone, with and without **biomarker-selected subgroups**

Methods

- **Model-based cost-effectiveness analysis** (**partitioned survival model** via parametric fitting of progression-free and overall survival) using **individual participant data from METIMMOX-1**
- Health-related **quality of life** via **EQ-5D-5L** surveys collected **in-trial**
- Costs in **2023 Euros** were estimated from a **healthcare perspective** and included the study drugs, diagnostic testing, second-line and end-of-life care
- Outcomes were extrapolated to **lifetime** and **discounted** at 4% per year
- We estimated incremental cost-effectiveness ratios (ICERs) and compared to a Norwegian **cost-effectiveness threshold** of NOK 605,000/QALY (~**€51,000/QALY**)

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$$ICER = \frac{\text{Costs Strategy A} - \text{Costs Strategy B}}{\text{QALYs Strategy A} - \text{QALYs Strategy B}}$$

i.e., incremental € per incremental QALY gained

Methods: Baseline Characteristics and Key Input Parameters (i)

	Overall	Control Arm	Experimental Arm
n	76	38	38
Median age [years, IQR]:	64.5 [57.8; 72.0]	65.0 [58.5; 72.8]	60.5 [57.0; 72.0]
Female (%):	35 (46.1)	15 (39.5)	20 (52.6)
ECOG status of 0 (%):	44 (57.9)	21 (55.3)	23 (60.5)
RAS/BRAF-mutant (%):	55 (72.4)	29 (76.3)	20 (68.4)
Left-sided (%):	54 (71.1)	(71.1)	(71.1)
Median TL reduction [%; IQR]:	–24 [–1; –35]	–27 [–16; –38]	–11 [+13; –31]
Median CRP [mg/L; IQR]	6.0 [2.0; 15.0]	9.0 [5.0; 17.0]	5.0 [1.0; 9.32]
Median TMB [mut/MB, IQR]:	n.a.	n.a.	8.0 [4.1; 10.2]

Methods: Baseline Characteristics and Key Input Parameters (ii)

Cost per FLOX cycle:	€ 427	
Cost per nivolumab cycle:	€ 13,923	
Cost for CT scan incl. reading:	€ 386	(standard of care)
Cost for laboratory analysis:	€ 6	(standard of care)
Cost for NGS (Illumina TSO-500):	€ 1,439	(**additional costs**)
Cost for last month of life:	€ 13,803	
Health-related QoL *before* PFS is reached (SD):	0.952 ±0.111	
Health-related QoL *after* PFS is reached (SD):	0.895 ±0.093	

Results: Basecase Cost-effectiveness Analysis

	Arm	Costs	Incremental Costs	QALYs	Incremental QALYs	ICER (€/QALY)
METIMMOX ITT population	Control arm	€ 34,520	€ 75,057	1.5712	0.1175	638,798
	Exp. arm	€ 109,577		1.6887		
TL reduction ≥10%	Control arm	€ 66,081	€ 30,386	1.9557	0.2112	143,850
	Exp. arm	€ 96,467		2.1669		
CRP <5.0 mg/L	Control arm	€ 45,197	€ 32,945	1.9639	0.2920	112,840
	Exp. arm	€ 78,142		2.2558		
TMB >8.0 mut/MB	Control arm	€ 34,530	€ 16,616	1.5712	0.3656	45,451
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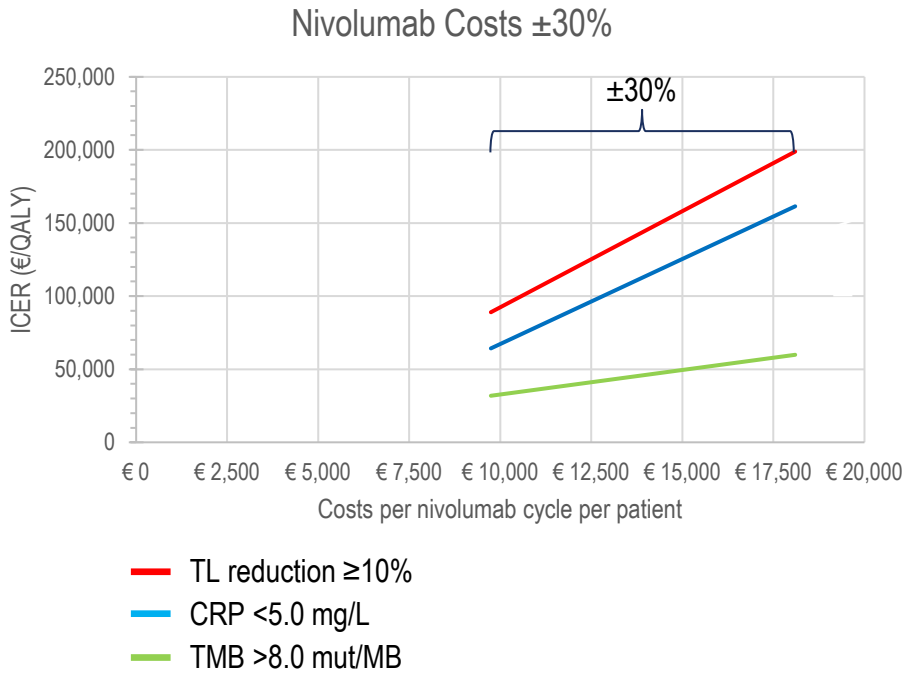
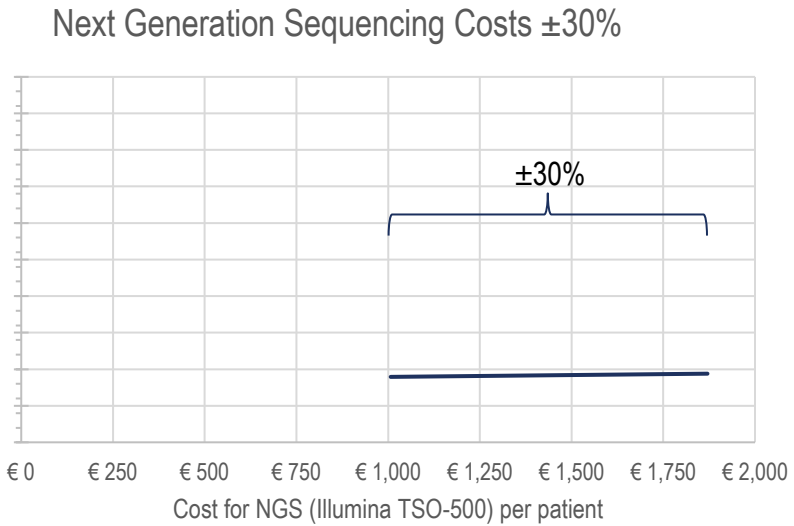
Results: Key Deterministic Sensitivity Analysis





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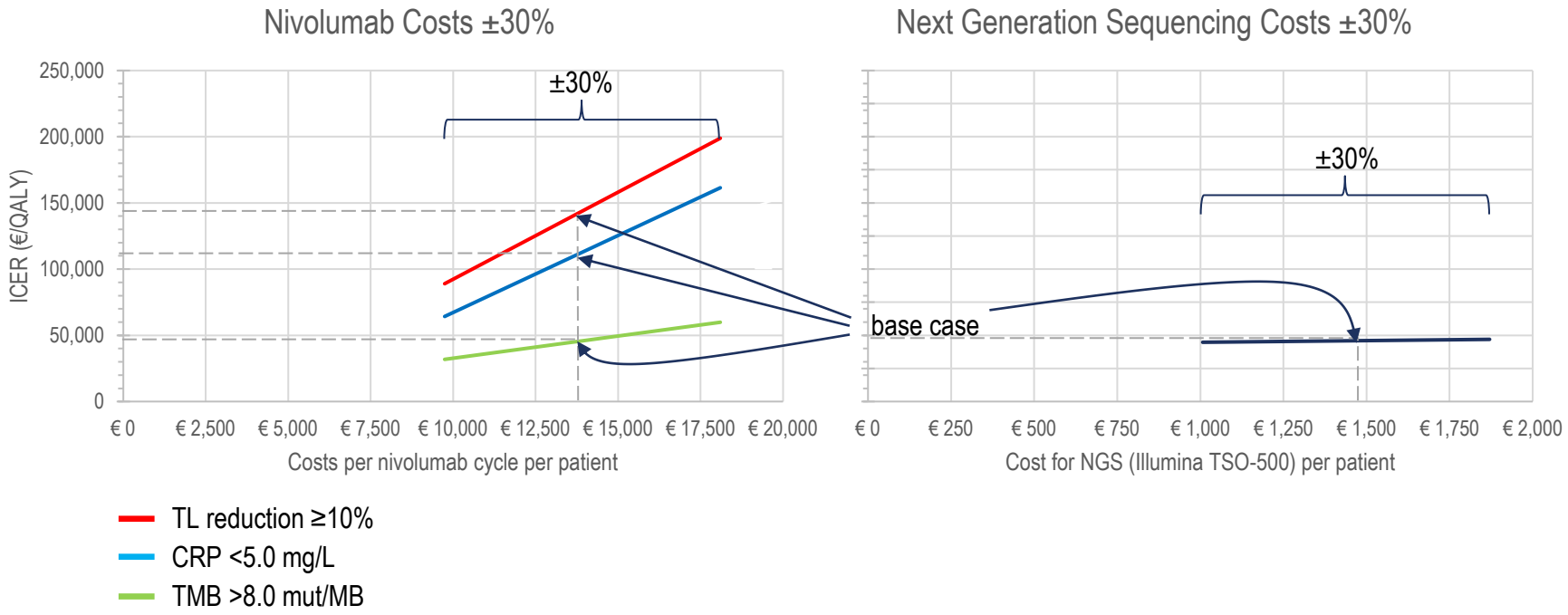

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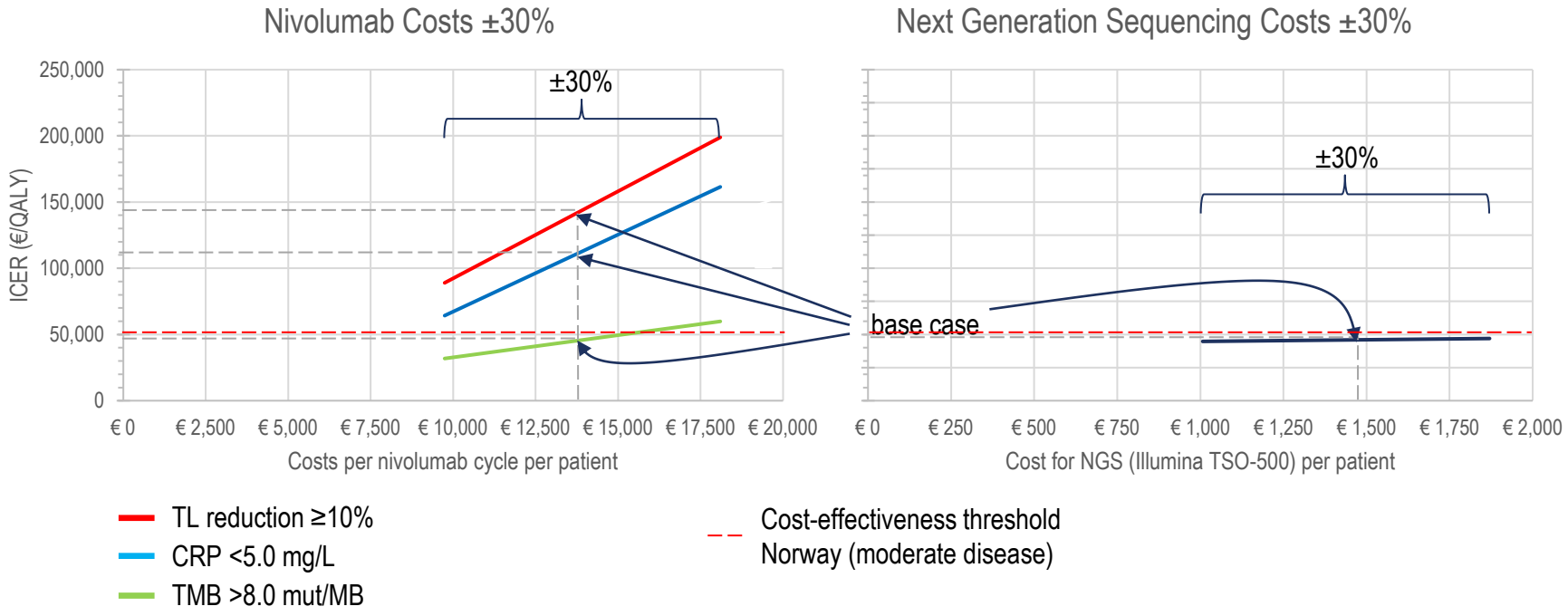

Limitations

1. Post-hoc analyses
2. Awaiting TMB data for the control group
3. Probabilistic sensitivity analysis
4. Results are set in the context of Norway

Conclusions

- **Biomarker-guided patient selection** for first-line ICB – compared to treating all unresectable metastatic **MSS/pMMR** CRC patients – may improve incremental effectiveness while lowering incremental costs, rendering it potentially **cost-effective** in Norway

- The value of a **TMB-based treatment approach** is promising, and prospective validation is warranted

Acknowledgements:
- Our patients
- Co-authors: Dr. Sebastian Meltzer, Prof. Emily A. Burger, Prof. Eline Aas, and Prof. Anne Hansen Ree
- Norwegian Cancer Society for research grants and Bristol-Myers Squibb

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