CAR-NK cell therapy for ovarian cancer treatment in the first relapse: Assessing conditions needed for cost-effectiveness in the Netherlands using early health-economic modelling

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INTRODUCTION

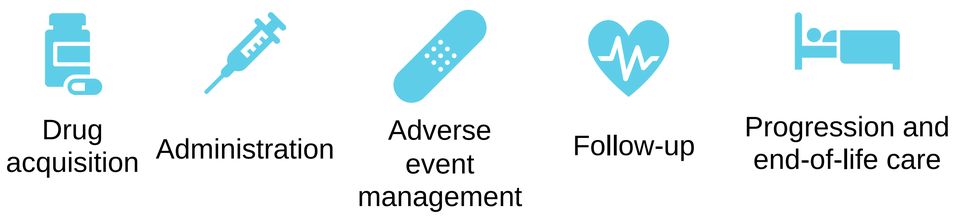
- Ovarian cancer (OC) is often diagnosed at an advanced stage due to the absence of early symptoms, making it highly fatal.[1]
- In the Netherlands, 5-year survival for patients diagnosed with advanced OC ranges between 14 and 29%.[2]
- The majority of cases (85–90%) are of epithelial origin (epithelial ovarian cancer, EOC). [3]
- Preclinical evidence has shown that EOC is susceptible to Natural Killer (NK) cell attack.[4]
- A Phase 1 clinical study, showed that intraperitoneal administration of NK cells to EOC patients is safe and well tolerated.
- NK cells can be genetically modified to express chimeric antigen receptors (CARs), which optimizes their therapeutic efficacy.
- Despite showing great clinical promise, cell therapies are associated with high manufacturing costs.
- Health economic modeling conducted early in product development can help identify the conditions necessary for a product to be cost-effective and guide the development process to fully realize the technology's value.[5]

OBJECTIVE

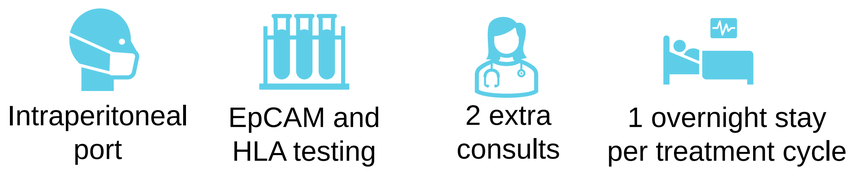
The aim of this study was to develop an early health economic model to explore the conditions under which the addition of CAR-NK cells to the Standard of Care (SoC) would be cost-effective for patients with high-grade EpCAM+ epithelial ovarian cancer at the first recurrence.

METHODS

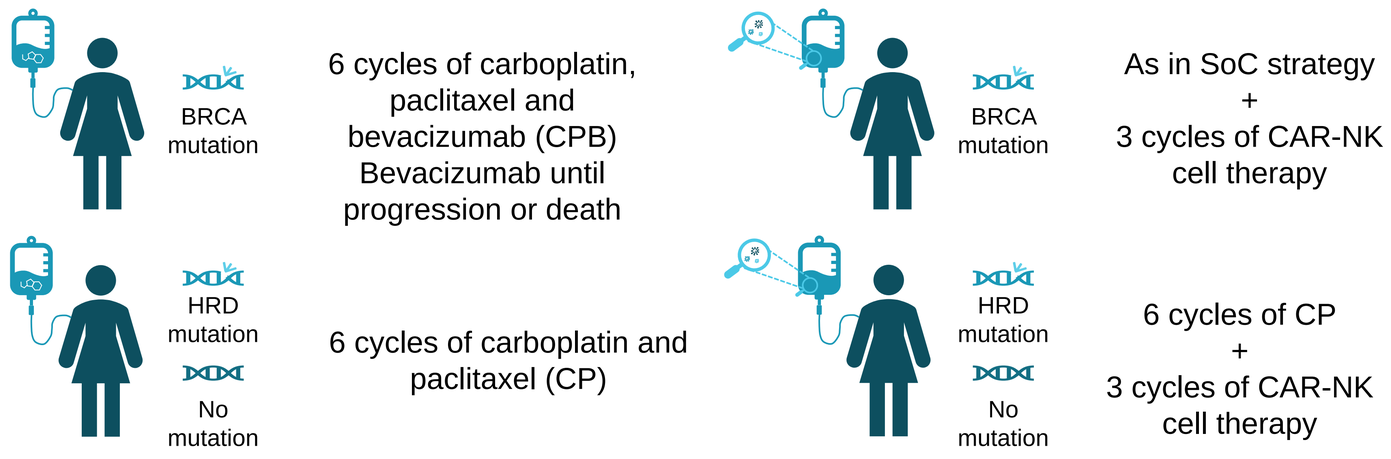
- Partitioned survival model estimating costs and (quality-adjusted) life years from a healthcare perspective, over a lifetime horizon
- Progression-free survival (PFS) and overall survival (OS) curves reconstructed from pivotal trials and fitted with parametric models.[6,7,8,9,10]
- CAR-NK strategy: treatment effect modelled by applying a scaling factor (α) to PFS and OS SoC-curves: SCAR-NK Cell therapy = $[SSoC(t)]^{\alpha}$
- Manufacturing costs were estimated using a modified version of the framework by Ten Ham et al.[11]
- Included costs:



- CAR-NK strategy associated with (extra resources):



Population: Women with platinum sensitive high grade EpCAM+ EOC at first recurrence.
Average age: 66 years.[12]



- Costs (€, 2023) discounted at 3% annually. Effects discounted at 1.5%.[13]
- Model was validated using AdViSHE checklist.[14]

RESULTS

- SoC strategy yielded on average 2.47 QALYs and 3.2 LYs, with a mean cost of €34,340 per patient.
- For CAR-NK cell therapy costs of €15,000 per cycle (€ 45,000 total treatment costs per patient), it would need to provide an average gain of 0.76 QALYs to be considered cost-effective. In our model this would be associated with a gain in LYs of 1.00, associated with an average gain of 3.08 months in median PFS and 10.82 months in median OS.
- At €20,000 per cycle (€60,000 total treatment costs per patient), the required benefit would be 0.95 QALYs, equivalent to 1.25 LYs, associated with an average gain of 3.08 months in median PFS, and 13.60 months in median OS.

Utilities	Base case	Scenario	Incremental costs	Incremental QALYs	Incremental LYs
Using alternative utility values for PFS and RD	PFS: 0.82; RD: 0.753	PFS: 0.718; RD: 0.649	€75,979	0.95	1.44
Adverse Events					
Inclusion of ICANS and CRS	ICANS incidence: 0% CRS incidence: 0%	ICANS incidence: 10% CRS incidence: 10%	€78,186	0.98	1.28
Exclusion of CAR-NK cell therapy related disutilities	Disutility associated with NK cell therapy AEs included	Assume no extra disutility associated with NK cell therapy AEs	€76,021	0.95	1.21
Alternative treatment schemes					
HRD patients get niraparib	HRD patients get CP	50% of HRD patients with complete response after CP get niraparib	€82,233	1.03	1.34
All patients get CPB	Only BRCA patients get CPB	All patients get CPB	€96,485	1.21	1.55
All patients get CP	Only BRCA patients get CPB	All patients get only CP	€70,259	0.88	1.16

Table 1. Scenario analyses. Analyses were conducted with CAR-NK cell therapy cost fixed at €20,000 per cycle. The table presents the resulting incremental costs and incremental QALYs of the CAR-NK strategy versus the SoC strategy. For each scenario, parameters were adjusted so that any scenario-induced changes in incremental costs or QALYs were offset by corresponding adjustments in LYs gained to maintain the target ICER of €80,000/QALY.

CAR-NK Cost (cycle) QALYs Gained	€5,000	€10,000	€15,000	€20,000	€25,000	€30,000	€35,000	€40,000	€45,000	€50,000
0.13	-€14,943	-€29,928	-€44,913	-€59,898	-€74,883	-€89,868	-€104,854	-€119,839	-€134,824	-€149,809
0.33	-€756	-€15,742	-€30,729	-€45,716	-€60,703	-€75,690	-€90,677	-€105,663	-€120,650	-€135,637
0.56	€16,433	€1,445	-€13,544	-€28,532	-€43,521	-€58,509	-€73,498	-€88,486	-€103,475	-€118,463
0.86	€37,723	€22,733	€7,743	-€7,247	-€22,238	-€37,228	-€52,218	-€67,208	-€82,198	-€97,188
1.24	€64,842	€49,851	€34,859	€19,867	€4,875	-€10,117	-€25,108	-€40,100	-€55,092	-€70,084
1.75	€100,699	€85,706	€70,713	€55,719	€40,726	€25,732	€10,739	-€4,254	-€19,248	-€34,241
2.48	€150,588	€135,593	€120,598	€105,603	€90,608	€75,613	€60,618	€45,623	€30,628	€15,632
3.57	€225,034	€210,037	€195,041	€180,044	€165,048	€150,052	€135,055	€120,059	€105,062	€90,066
5.35	€346,462	€331,465	€316,468	€301,471	€286,475	€271,478	€256,481	€241,484	€226,487	€211,491

Table 2. Multivariate sensitivity analysis. Light-blue cells indicate scenarios with a positive iNMB. Orange cells show scenarios with a negative iNMB.

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CONCLUSION

- CAR-NK cell therapy has the potential to become a cost-effective treatment option.
- CAR-NK therapy would need to deliver a substantial improvement in OS.
- CAR-NK costs are a major driver of the model; cost and upscaling optimization essential.
- Early HTA can help guide product development and optimize resource use.

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