Forgone health gains from PASKWIL-negative oncology drugs in the palliative setting: a model-based analysis

HTA184

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Introduction

- The Dutch National Health Care Institute (ZIN) uses the PASKWIL criteria for overall survival (OS) as its limit of clinical relevance for non-curative oncological drugs.[1,2]
- In the palliative setting, with a comparator median OS of 12 months or less, a treatment is PASKWIL-positive if it meets at least one of two criteria:[2]
  - **Criterion 1:** a median OS gain of more than 12 weeks **and** a hazard ratio (HR) below 0.70.
  - **Criterion 2:** an OS rate at 2 years at least 10 percentage points higher than the comparator, with more than 20% of the patients alive at 2 years.
- This limit keeps treatments that do give a survival gain, and might be cost-effective after negotiation, from reaching a cost-effectiveness assessment, price negotiation and, in the end, reimbursement.
- **Aim:** to quantify the forgone health and value of treatments that fail the PASKWIL OS criteria but could be cost-effective.

Methods

- **Population:** women with recurrent or metastatic cervical cancer who receive single-agent chemotherapy after progression on doublet chemotherapy.
- **Comparator:** single-agent chemotherapy. Survival was taken from the chemotherapy arm of a phase 3 trial in a comparable population:[3,4] we reconstructed the individual patient data[5] and fitted seven survival distributions.
- **Intervention:** a hypothetical treatment without a price that replaces the chemotherapy. Its survival follows from the comparator: $S_{int}(t) = S_{comp}(t)^{HR}$. We varied the hazard ratio (HR) for overall survival from 0.70 to 1.00 and set the HR for progression-free survival equal. Administration, toxicity and quality of life were assumed equal to chemotherapy.
- **Model:** partitioned survival model (weekly cycles, 30 years, societal perspective, discounting 3% for costs and 1.5% for effects) per the Dutch guideline;[6] utilities from a NICE appraisal for recurrent or metastatic cervical cancer.[7]
- **Outcomes:** QALY gain and net monetary value (NMV): QALY gain × €80,000 minus all incremental costs except the price of the treatment. The NMV is the maximum average drug cost per patient at which the treatment is still cost-effective. €80,000 is the highest Dutch reference value (proportional shortfall 0.97).[8,9] We focused on the effective PASKWIL boundary: the lowest HR at which neither criterion is met. Criterion 2 can still be met just above HR 0.70 (at HR 0.72 the 2-year OS rate is 10.2 percentage points higher), so the boundary lies at HR 0.725.
- **Uncertainty:** one-way analysis (±20%) and eight scenarios (extrapolation, utilities, administration, adverse events, comparator, time horizon, unrelated medical costs).

Results

0.23
QALY gain per patient at the boundary (HR 0.725), 40% on top of 0.59 QALY with chemotherapy

€11,940
NMV per patient at the boundary (base case: generalised gamma extrapolation)

€3,834
NMV at HR 1.00: the saving on the chemotherapy that is replaced

- At the boundary (HR 0.725, median OS gain 12.6 weeks) the QALY gain is worth €18,610; after incremental costs of €6,670 (excluding the price of the treatment) €11,940 remains. Criterion 2 determines the boundary for all seven distributions (0.725 to 0.735).

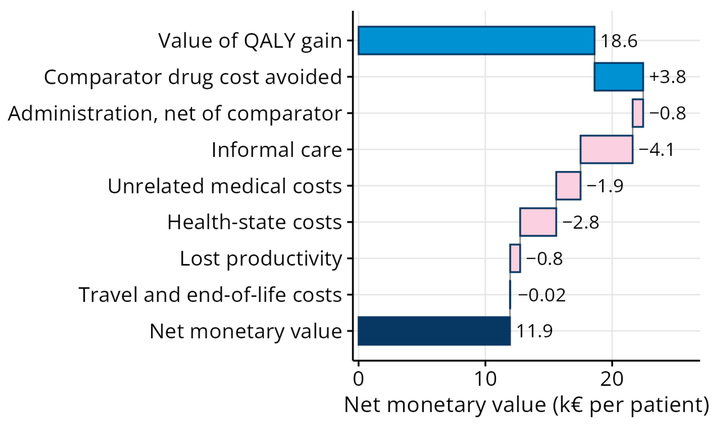

Figure 1. Composition of the NMV at the effective PASKWIL boundary (k€ per patient).

- The NMV falls towards HR 1.00 but stays positive across the whole PASKWIL-negative region, for all seven distributions (€10,150 to €17,660 at their own boundary).

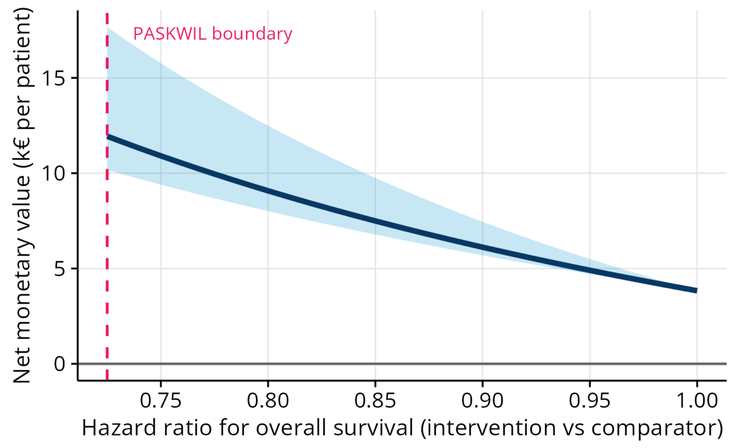

Figure 2. NMV across the PASKWIL-negative region; the shaded area shows the seven fitted OS distributions.

- In the one-way analysis the utility in progressed disease had the largest influence (€9,591 to €14,271). With all parameters unfavourable simultaneously the NMV at the boundary is €4,500 (€20,500 when all are favourable).
- Scenarios gave €9,115 (comparator of the cheapest agent only) to €18,769 (alternative utilities). 84% of the NMV arises within the observed follow-up.

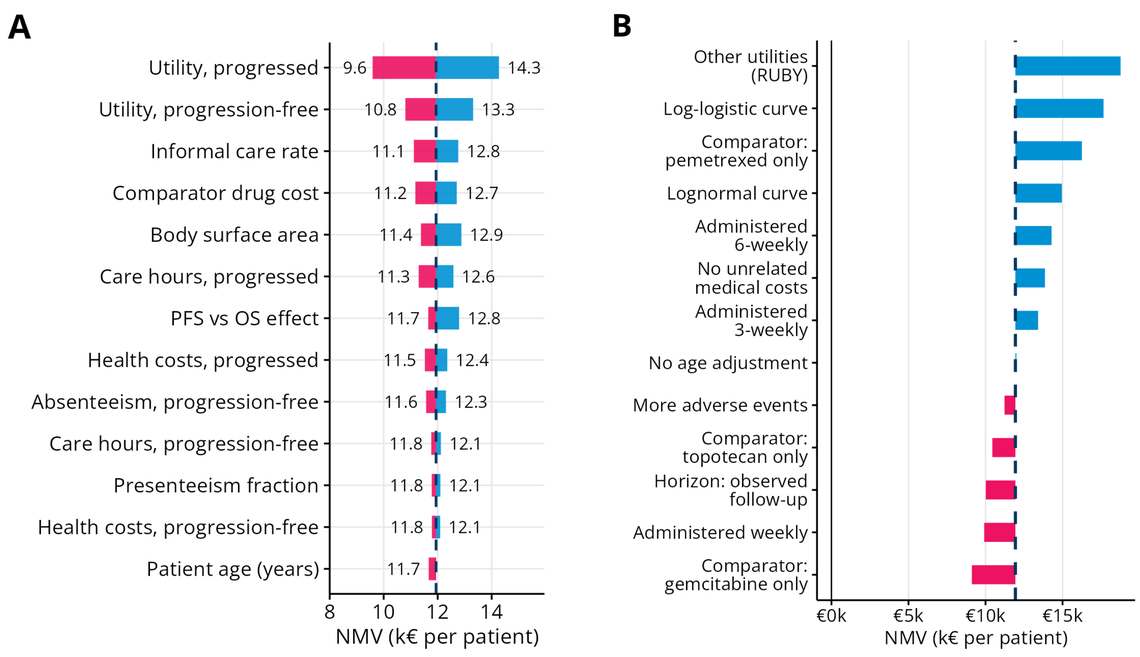

Figure 3. (A) One-way sensitivity analysis at the boundary (±20%). (B) NMV by scenario; the dashed line is the base case.

Conclusion

- Not meeting the PASKWIL OS criteria does not mean that a treatment has no value: treatments that just fall short can still give a substantial QALY gain.
- The willingness to pay states what we want to pay per QALY gained; a smaller gain allows a lower payment, which the NMV expresses.
- The NMV was positive in every analysis, even when all parameters were set unfavourably.
- Limitations:
  - Hypothetical, unpriced treatment: the NMV is a cost ceiling, not a price.
  - Toxicity, quality of life and administration equal to chemotherapy (to be shown for a real drug).
  - Proportional hazards, often not true for immunotherapy.
  - Extrapolation: 16% of the NMV arises beyond the trial follow-up (6% to 42% across distributions); the choice of distribution moves the NMV between €10,150 and €17,660.
  - Comparator mix from the trial control arm, not Dutch practice.
  - One indication.

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