Poster #HTA85

Will the new Dutch criteria for therapeutic value for oncology drugs create inequalities in access between countries? A review of health technology assessment oncology submissions

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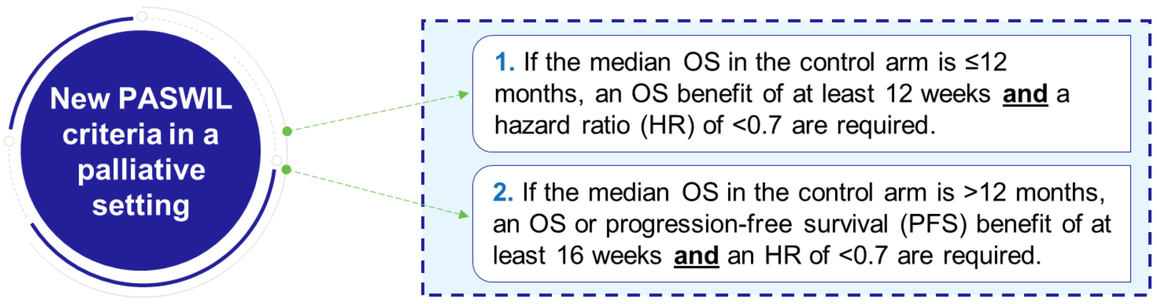
The revised PASKWIL criteria are likely to lower the acceptance rate of oncology drugs and/or delay patient access to care in the Netherlands. This may create inequalities across countries, especially considering the new European Union Joint Clinical Assessment aiming to unify patient access to promising drugs.

Background

- In the Netherlands, the clinical benefit of new oncology drugs licensed by the European Medicines Agency (EMA) is assessed against the current standard of care according to the PASKWIL (palliative, adjuvant, specific side effects, quality of life, impact of treatment and level of evidence) framework.
- Since its inception in 2000, the PASKWIL framework has been repeatedly revised, most recently in May 2023.
- The most recent revision with a stronger focus on demonstrating a survival benefit based on a patient-relevant endpoint (i.e., overall survival [OS]) was considered necessary by the Dutch Oncology Society (NVMO) given the increasing speed at which new drugs have become available and the increasingly flexible marketing authorisation approaches by the EMA.



- There have been concerns that high drug costs may not be proportional to the health benefit offered.
- Previously, a 12-week survival benefit of an HR of <0.7 was required, regardless of life expectancy in the control arm. The new criteria may therefore present a higher barrier to reimbursement and thus a more restricted availability of new oncology drugs in the Netherlands.

Objective

- The objective of this study was to assess the potential impact of the revised PASKWIL criteria on reimbursement decisions for oncology drugs in a palliative setting in the Netherlands and compare them with reimbursement decisions for duplicate submissions in Germany and the United Kingdom (UK).

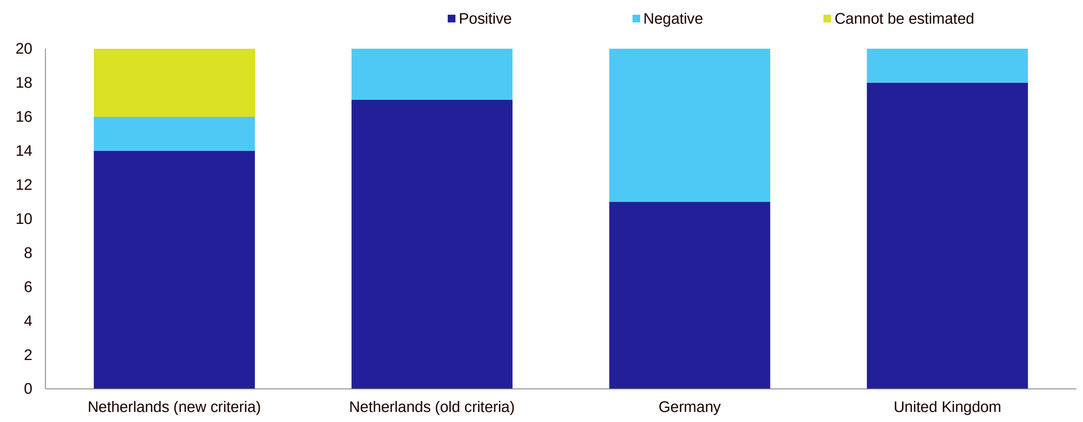
Methods

- We comprehensively reviewed health technology assessment (HTA) submissions (January 2017 to May 2023) on solid tumours in a palliative setting (locally advanced or metastatic disease) in the Netherlands (Zorginstituut Nederland [ZiN]), UK (National Institute for Health and Care Excellence [NICE]) and Germany (Institute for Quality and Efficiency in Health Care [IQWiG]).
- Only relevant submissions for the same treatment and indication available from all three agencies identified through each agency's website were included.
- Using a pre-designed extraction sheet, information on the submission scope, source of clinical efficacy data, OS and PFS results (median and HR), median follow-up duration and data cut was extracted.
- For Dutch submissions, the new PASKWIL criteria were retrospectively applied to determine their hypothetical impact on the reimbursement decision.

Results

- In total, 78 relevant dossiers (both primary submissions and resubmissions) were identified across the three agencies, accounting for 19 primary ZiN submissions and their corresponding submissions to NICE and IQWiG.
- These 19 submissions covered lung (N=7), breast (N=6), renal (N=3), ovarian (N=2) and bladder cancer (N=1); programmed death-1/ligand-1 inhibitors were the most evaluated treatment (N=8).
- Sixteen submissions received a positive decision in the Netherlands based on the old PASKWIL criteria compared with 17 in the UK and 11 in Germany (Table 1, Figure 1).
- Given an indication for a sufficiently long survival, OS or PFS data (accepted for decision-making in these cases) would likely result in a positive recommendation being maintained in 13 ZiN submissions, while for the remaining six submissions, a negative decision would be likely, or the decision could not be predicted based on the available data (Table 2).
- Of those six submissions, two submissions would result in a negative recommendation due to an insufficiently large OS (atezolizumab for non-small cell lung cancer) or OS/PFS benefit (nivolumab + ipilimumab for pleural mesothelioma) over the control group.

Figure 1. Distribution of reimbursement decisions by HTA agency



Results (cont.)

- In two submissions (avelumab + axitinib, nivolumab)—both of which had previously received a negative recommendation—the provided OS data were too immature for an evaluation under the new criteria.
- As the same data cut was used across all three agencies, the potential impact of more mature data on the decision could not be assessed.
- The remaining two submissions (entrectinib and pralsetinib) were based on single-arm trials without a control arm and did not include any OS data due to data immaturity; thus, the added benefit over a control group could not be estimated against the new PASKWIL criteria.
- Decision changes to three ZiN submissions would result in differences to reimbursement decisions made in Germany (N=2) and the UK (N=3).
- Only oncology drugs submitted and assessed within the lock for expensive drugs (i.e., drugs with a substantial budget impact) were considered in this review. As oncology drugs not placed in the lock were assessed using the same criteria, the potential impact of the change in PASKWIL criteria on their reimbursement status could not be assessed.

Table 1. Overview of included submissions and their decisions across HTA agencies

Drug	Indication	Netherlands (new criteria)	Netherlands (old criteria)	Germany	United Kingdom
Abemaciclib + fulvestrant	Breast cancer	✓	✓	✗	✓
Atezolizumab	Non-small cell lung cancer	✗	✓	✓	✓
Avelumab	Bladder cancer	✓	✓	✓	✓
Avelumab + axitinib	Renal cell carcinoma	?	✗	✓	✓
Durvalumab	Non-small cell lung cancer	✓	✓	✓	✓
Entrectinib	Non-small cell lung cancer	?	✗	✗	✓
Lenvatinib + pembrolizumab	Renal cell carcinoma	✓	✓	✗	✓
Niraparib	Ovarian cancer	?	✓	✗	✓
Nivolumab + ipilimumab	Pleural mesothelioma	✗	✓	✓	✓
Nivolumab + ipilimumab	Renal cell carcinoma	✓	✓	✓	✓
Nivolumab + ipilimumab + platinum chemotherapy	Non-small cell lung cancer	✓	✓	✓	✗
Olaparib	Ovarian cancer	✓	✓	✗	✓
Osimertinib	Non-small cell lung cancer	✓	✓	✓	✓
Palbociclib + letrozole	Breast cancer	✓	✓	✗	✓
Pralsetinib	Non-small cell lung cancer	?	✗	✗	✗
Ribociclib + letrozole	Breast cancer	✓	✓	✗	✓
Sacituzumab govitecan	Breast cancer	✓	✓	✓	✓
Trastuzumab-deruxtecan	Breast cancer	✓	✓	✓	✓
Tucatinib + trastuzumab + capecitabine	Breast cancer	✓	✓	✓	✓

Table 2. OS and PFS results for ZiN submissions that may not receive a positive recommendation under the new PASKWIL criteria

ZiN		NICE		IQWiG		Data cut
OS	PFS	OS	PFS	OS	PFS	
Atezolizumab in non-small cell lung cancer						
13.8 vs. 9.6 (0.73 [0.6-0.87])	NA (0.95 [0.82-1.10])	13.8 vs. 9.6 (0.73 [0.62-0.87])	NA	12.6 vs 9.7 (0.76 [0.58-0.99])	2.7 vs. 3.8 (0.96 [0.85-1.08])	**Different** (ZiN/NICE: July 2016; IQWiG: January 2017)
Avelumab + axitinib in renal cell carcinoma						
NE vs. NE (0.80 [0.62-1.03])	13.8 vs. 8.4 (0.69 [0.57-0.83])	NE vs. NE (0.80 [0.62-1.03])	13.8 vs. 8.4 (0.69 [0.57-0.83])	Low/intermediate risk: NE vs. NE (0.87 [0.63-1.19]) High risk: 21.2 vs. 11.0 (0.50 [0.31-0.81])	Low/intermediate risk: 15.2 vs. 11.0 (0.72 [0.59-0.88]) High risk: 17.7 vs. 18.9 (0.90 [0.39-2.10])	**Same** (28 January 2019)
Entrectinib in non-small cell lung cancer						
NA	NA	NA	16.8 vs. NA	NA	NA	NA
Niraparib in ovarian cancer						
NE vs. NE (0.70 [0.44-1.11])	13.8 vs. 8.2 (0.62 [0.50-0.76])	NE vs. NE (0.70 [0.44-1.11])	13.8 vs. 8.2 (0.62 [0.50-0.76])	NA	NA	**Same** (17 May 2019)
Nivolumab + ipilimumab in pleural mesothelioma						
18.1 vs. 14.1 (0.74 [0.60-0.91])	6.8 vs. 7.2 (1.00 [0.82-1.21])	18.1 vs. 14.1 (0.74 [0.60-0.91])	6.8 vs. 7.2 (1.00 [0.82-1.21])	18.1 vs. 14.1 (0.74 [0.60-0.91])	NA	**Same** (3 April 2020)
Pralsetinib in non-small cell lung cancer						
NA	NA	NA	NA	NA	NA	NA

Note: OS/PFS results are median (hazard ratio [95% confidence interval])
Abbreviations: IQWiG, Institute for Quality and Efficiency in Health Care; NA, not applicable, NE, not evaluable; NICE, National Institute for Health and Care Excellence; OS, overall survival; PFS, progression-free survival; ZIN, Zorginstituut Nederland

Conclusions

- Based on the assessed submissions, it is likely that the revised PASKWIL criteria will lower the acceptance rate of oncology drugs and/or delay patient access to care in the Netherlands.
- This may create inequalities across countries, especially considering the new European Union Joint Clinical Assessment aiming to unify patient access to promising drugs.

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