Does the Use of a Surrogate Outcome in Solid-state Oncology HTAs Decrease the Chance of a Positive Recommendation?

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OBJECTIVE

Both the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA) accept progression-free survival (PFS) and disease-free survival (DFS) as appropriate surrogate outcomes for overall survival (OS) in clinical trials. Does using PFS or DFS decrease the likelihood of a positive recommendation from Health Technology Assessment (HTA) agencies.

METHODS

HTAs for six solid-state oncology conditions that were published between 2005 and 2013 from 10 agencies were analyzed.* Reviews were grouped by primary outcome as follows: OS, PFS, DFS, co-primary outcomes of OS and PFS, and other. Decisions (for those agencies that make decisions) were categorized as positive ("recommend" and "recommend - restricted population" decisions) and negative ("do not recommend" and "deferred" decisions). Decisions were compared to the primary outcome to determine whether the choice of primary outcome was related to the reimbursement decision. Due to the lack of variety in the primary outcome used in Melanoma, Small-cell Lung Cancer, and Ovarian Cancer, rates of positive recommendations associated with the choice of primary outcome could not be calculated.

RESULTS

The sample for outcome analysis included 245 reviews. Reviews that did not report a primary outcome were excluded (17%; n=42). The use of primary outcome was highly dependent on the type of cancer. OS was overwhelmingly used in Melanoma and Small-cell Lung Cancer (77% and 100%, respectively), while PFS was frequently used in Ovarian Cancer (64%). Colorectal Cancer used OS, PFS, and DFS at similar rates (25%, 27% and 22% respectively; n=68); Non Small-cell Lung Cancer used OS and PFS at similar rates (44% and 36% respectively; n=61). Most Prostate Cancer reviews used OS (66%; n=25), but 32% (n=12) used other outcomes (mostly related to measuring testosterone levels).

Only those HTA agencies issuing decisions were included in the decision analysis. This exclusion resulted in a sample of 198 reviews including 109 positive decisions (55%) and 89 negative decisions (45%). There was no statistical difference between the use of outcomes and the rate of positive recommendation in Colorectal Cancer, Non-small-cell Lung Cancer, and Prostate Cancer.

CONCLUSION

The choice of primary outcome was dependent on the oncology condition. The relationship between choice of primary outcome and reimbursement decision was not significant for the three oncology conditions that used a variety of outcomes. Further research and multivariate analysis is needed to determine if the choice of a surrogate outcome in oncology HTA reviews decreases the chances of a positive approval.

* Solid-state oncology conditions included in the analysis: Colorectal Cancer, Melanoma, Non Small-cell Lung Cancer, Ovarian Cancer, Prostate Cancer and Small-cell Lung Cancer. Health technology agencies included in the analysis: Agency for Healthcare Research and Quality (United States; AHRQ), Canadian Agency for Drugs and Technologies in Health (Canada; CADTH), Cancer Care Ontario (Canada; COO), Haute autorité de santé (France; HAS), Healthcare Improvement Scotland (Scotland; HIS), Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Germany; IQWiG), National Institute for Health and Care Excellence (United Kingdom; NICE), Pharmaceutical Benefits Advisory Committee (Australia; PBAC), pan-Canadian Oncology Drug Review (Canada; pCODR), and Scottish Medicines Consortium (Scotland; SMC).

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Use of Surrogate Outcomes as Primary Outcomes in Solid-state Oncology HTAs

Oncology Condition	OS	PFS	DFS	Co-primary OS & PFS	Other	Total
Colorectal Cancer	17 (25%)	18 (27%)	15 (22%)	7 (10%)	11 (16%)	68 (100%)
Non-small-cell Lung Cancer	27 (44%)	22 (36%)	7 (12%)	1 (2%)	4 (7%)	61 (100%)
Prostate Cancer	25 (66%)	1 (3%)	0 (0%)	0 (0%)	12 (32%)	38 (100%)
Melanoma	13 (77%)	0 (0%)	0 (0%)	4 (24%)	0 (0%)	17 (100%)
Ovarian Cancer	2 (18%)	7 (64%)	2 (18%)	0 (0%)	0 (0%)	11 (100%)
Small-cell Lung Cancer	8 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (100%)
Total	92 (45%)	48 (24%)	24 (12%)	12 (6%)	27 (13%)	203

Note: A primary outcome was not reported in 42 reviews (17%); these reviews were excluded from the table.

Decision Outcomes Associated with Type of Outcome Used