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Assessing the Correlation Between Surrogate Endpoints and Clinical Benefit in Oncology Accelerated Approvals: A Comparative Analysis

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Background/Purpose

There has been a rise in the number of oncology therapeutics seeking approval through the accelerated approval pathway, which allows manufacturers to use surrogate endpoints as substitutes for clinical endpoints as a quicker way to evaluate the efficacy. In oncology, surrogate endpoints are meant to predict clinically meaningful outcomes such as overall survival. However, these surrogate endpoints may not always accurately predict the desired clinical outcomes; thus validation of these endpoints is necessary.

Methods

A search within the Food and Drug Administration (FDA) website was conducted to collect information regarding Oncology (Cancer) / Hematologic Malignancies Approvals. The target population was accelerated oncology clinical trials that received traditional approval, were withdrawn, or are still ongoing from January 1, 1995 to October 31, 2023. The trials were stratified based on endpoints, including objective response rate (ORR), progression free survival (PFS), and duration of response (DOR).

Results

ORR with DOR has the highest endpoint used for withdrawn (38.89%) and ongoing approvals (51.61%), while evolving endpoints, which includes all other endpoints used apart from the traditional clinical endpoints, are most prevalent in verified approvals (38.64%).

88.89% of withdrawn approvals, 52.27% of verified approvals, and 100% of ongoing approvals utilized ORR either alone or with supporting endpoints for the basis of accelerated approval.

The utilization of PFS as a surrogate endpoint is varied across approval status, with approvals that have been subsequently withdrawn demonstrating a higher reliance on PFS (27.78%) compared to verified approvals (12.5%) and ongoing approvals (0%).

Conclusion

ORR with DOR is the most utilized endpoint among withdrawn and ongoing approvals. However, ORR, either alone or with supporting endpoints, yields inconsistent results and may not predict meaningful clinical benefit. Therefore, there is a growing recognition of the need to shift towards evolving endpoints that hold promise to predict clinically meaningful outcomes.