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902.HEALTH SERVICES AND QUALITY IMPROVEMENT - LYMPHOID MALIGNANCIES

Use of Single-Arm Trials in FDA Approvals of Treatments in Relapsed or Refractory B-Cell Lymphoma

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Background: Single-arm trials are commonly used to evaluate therapies targeting life-threatening or rare diseases (e.g., late-stage cancers that are relapsed or refractory to prior interventions). A number of oncology products supported by single-arm trials have been approved by the United States Food and Drug Administration (FDA). The draft guidance issued by the FDA on 24 March 2023 recommended key considerations for trial design and analysis when a single-arm trial is considered appropriate to support accelerated approval. The objective of this study was to assess how often anticancer drugs approved by the FDA were based on single-arm trials in a typical relapsed or refractory indication and to evaluate the quality of trial design and data leading to approvals.
Methods: We reviewed past approvals between 2006 and 2023 listed on the FDA website, focusing on the indication of relapsed or refractory B-cell lymphoma. Of 11 approvals identified, eight were supported by single-arm trials and three were based on randomized controlled trials. Approvals based on single-arm trials were further investigated, and each trial was analyzed for the following criteria as recommended by the draft FDA guidance: 1) if the endpoint was based on response rate assessed using appropriate criteria; 2) if the sample size was sufficient to provide robust estimates of efficacy and safety profile; and 3) if the magnitude and duration of response were adequate.
Results: Among the eight approvals based on single-arm trials, one was approved in 2017, one in 2018, and two each in 2020, 2021, and 2023. Three were chimeric antigen receptor T-cell (CAR-T) therapies and were granted regular approval; the other five were non-CAR-T therapies which were granted accelerated approval. The primary endpoints adopted by all the trials were overall response rates (defined as complete and partial responders) and duration of response determined by an independent review committee. The magnitude of overall response rates reported by most trials ranged from 48% to 72% (with more than 50% of them with a complete response); one trial reported an overall response rate of 29% with complete response rate of 13%. A minimal median follow-up of six months after response was achieved in all trials. The estimated median duration of response varied from 10.3 to 21.7 months, with three trials reporting medians not reached. Based on the trial description, the analysis population was pre-specified for the evaluation of efficacy, ranging from 68 to 192 participants.
Conclusion: Submissions based on single-arm trials for oncology therapies in the relapsed and refractory setting tended to be well accepted by FDA for accelerated and regular approval when the key criteria of trial design and data quality were adequately met.

Disclosures Rose: *PPD, Part of ThermoFisher Scientific:* Current Employment, Current equity holder in publicly-traded company.

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