Oklahoma State University / College of Osteopathic Medicine

Assessing Patient Risk, Benefit, and Outcomes in Drug Development: A Decade of Lenvatinib Clinical Trials

Patrick Crotty, B.S., Karim Kari, B.S., Griffin K. Hughes, B.A., B.S., Chase Ladd, B.S., Ryan McIntire B.S., Brooke Gardner, B.S., Andriana M. Peña, B.S., Sydney Ferrell, D.O., Jordan Tuia, B.S., Jacob Cohn, D.O., Alyson Haslam, Ph.D., Vinay Prasad, M.D., M.P.H., Matt Vassar, Ph.D.

Background

Cancer diagnoses worldwide are driving drug development and marketing strategies, which incur huge costs. The evaluation of cancer drug therapy focuses on benefits but not on adverse effects on quality of life. Novel drugs often do not progress past trials to FDA approval, costing pharmaceutical companies millions. Sunitinib and imatinib are examples of initially successful cancer drugs whose risk/benefit ratio worsened with off-label use. Reducing costs and improving therapeutic benefits can minimize risk and optimize outcomes by avoiding redundant studies.

Methods

- Searched Pubmed/MEDLINE, Embase, Cochrane CENTRAL, and ClinicalTrials.gov on May 25th, 2023 for lenvatinib clinical trials in solid cancers.
- Included clinical trials with adult participants, published in English, and focused on solid tumors.
- Collected adverse event data, trial characteristics, progression-free survival, overall survival, and objective response rate.
- Categorized trials as positive, negative, or indeterminate based on meeting primary endpoint and safety criteria.

Results

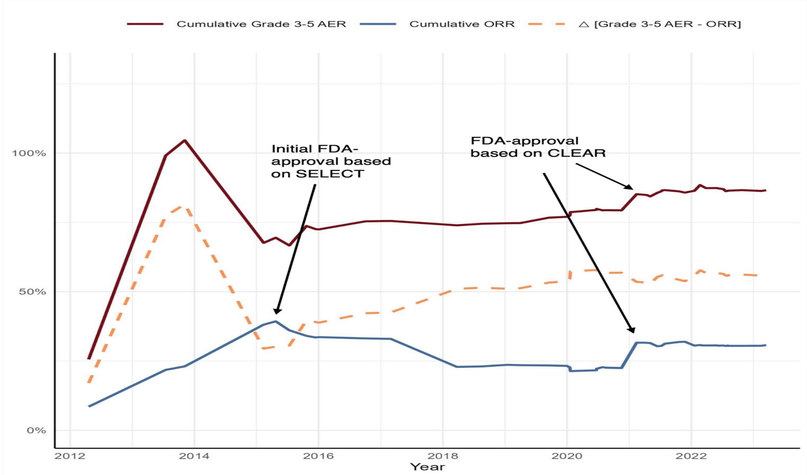

Figure 1: Cumulative adverse event rates per trial-year vs. cumulative ORR per trial-year are plotted over time. Δ[AER-ORR] represents the absolute difference between cumulative AER and cumulative ORR. Time points included all trials with results published in a given year.

- Lenvatinib was tested in 16 cancer indications, with FDA approval obtained in 4.
- Expanding clinical trials beyond the initial FDA indication showed an increase in cumulative adverse events and a decrease in drug efficacy.
- A total of 5390 Grade 3-5 adverse events occurred among 6225 clinical trial participants.
- Off-label testing revealed wide variations in objective response rate (11-69%), overall survival (6.2-32 months), and progression-free survival (3.6-15.7 months) across all indications.
- Following FDA approval, clinical trial results became more negative and indeterminate, especially in non-randomized trials.

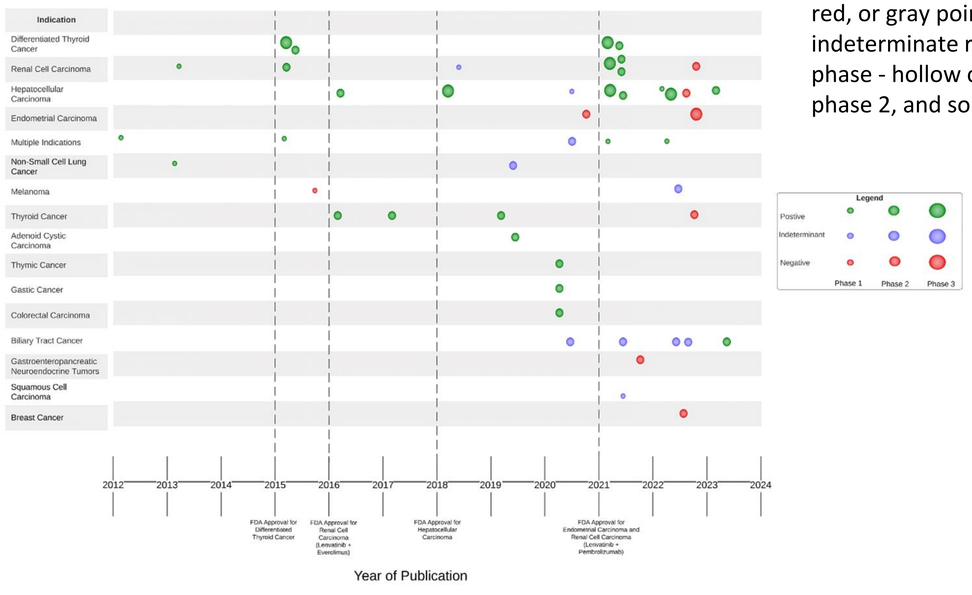

Figure 2: Lenvatinib trials visualized by indication and date of publication, with each point representing a trial's phase and relative participant number. Blue, red, or gray points represent positive, negative, or indeterminate results, and varying shapes denote the phase - hollow circles for phase 1, double circles for phase 2, and solid circles for phase 3.

Discussion

While demonstrating effectiveness for its FDA-approved indications, lenvatinib exhibited periods marked by elevated risk and reduced benefit. These periods were distinguished by a notable rise in the number of trials exploring off-label or novel indications. Future trials using lenvatinib as an intervention should carefully evaluate the effects on patients and weigh the risks and benefits involved.

References

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Acknowledgments

- We would like to thank the OSU-CHS medical library for their extraordinary contributions in facilitating the development of this project.
- Additionally we would like to thank everyone on the Vassar Team for their contributions.