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

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## Background

Lung cancer remains the leading cause of cancer-related deaths in the United States. Afatinib was developed as a therapy for lung cancer which has been expanded to other indications in hope for more viable treatment for other indications. In addition to financial concerns surrounding afatinib a broader concern regarding the efficiency of drug development exists.

Evidence suggests a fewer number of positive clinical endpoints is required for a drug to earn additional FDA approvals. Additionally, over-testing for cancer drugs after initial approval illustrates a lack of efficacy in non-FDA approved indications. This pattern of redundant trials provides cause for concern as cancer drugs are inherently toxic and expose patients to unnecessary adverse events with little benefit.

## Methods

In this cross-sectional investigation, we screened PubMed/MEDLINE, Embase, Cochrane CENTRAL, and ClinicalTrials.gov for clinical trials of afatinib as monotherapy or in combination with other interventions for solid cancer treatment. We extracted adverse event rates, median progression free survival, median overall survival, and objective response rate for each included trial. Studies were considered positive if they met their primary endpoint and retained safety, negative if neither criteria were met, and indeterminate if no endpoint was prespecified.

## Results

- Our search yielded 2,444 articles; we excluded 2,352 articles for a final inclusion of 92 trials of 8,859 patients.
- Our sample had 49 (53%) positive trials, 27 (29%) negative trials, and 16 (17%) indeterminate trials.
- The most common off-label indications for afatinib were breast cancer and squamous cell carcinoma of head and neck.
- The median OS for all trials was 8.4 months, median PFS 3.4 months, and the total ORR was 29.6%.

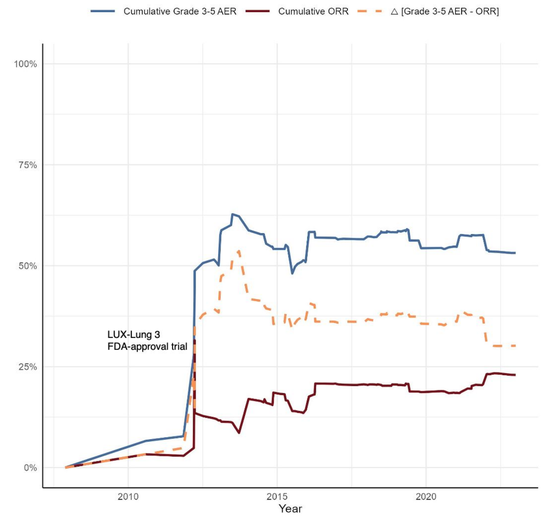


**Figure 1:** Cumulative adverse event rates vs cumulative overall response rate plotted over time. Time points encompass all published trial results within a given year.

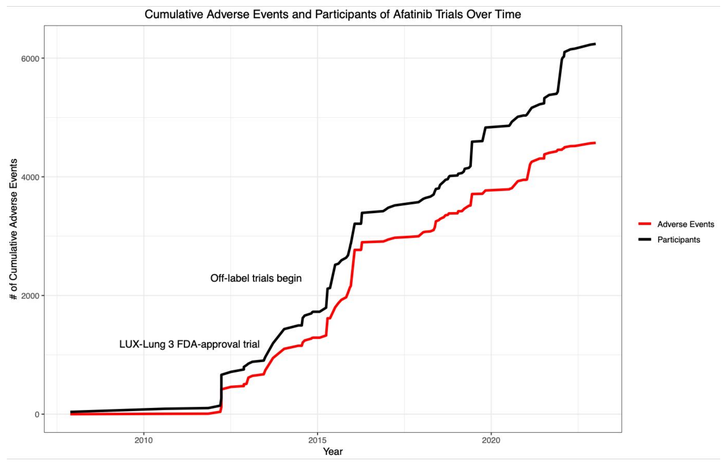


**Figure 2:** Adverse Events vs. Participants over time, 2007 to 2023.

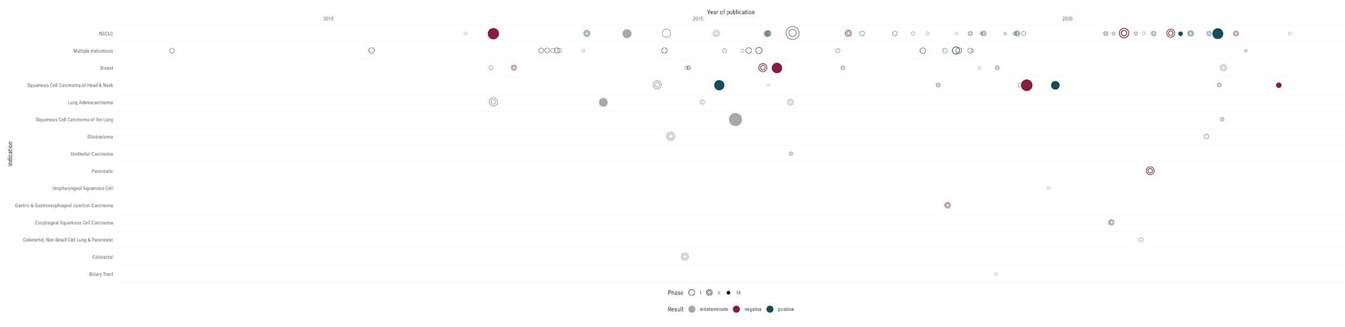


**Figure 3:** Aerogram; Afatinib trials are stratified by indication and are mapped by the date of initial publication. The shape of each point indicates the trial phase, and the relative size of the point represents the relative number of trial participants. Green points indicate positive results, red points indicate negative results, and blue points are indeterminate.

## Discussion

Our study found that beyond its primary indication for lung cancer there was little success. The recurring breast cancer trials consistently show negative results with more adverse events when compared to other indications. We recommend that in clinical practice, physicians closely consider the risk/benefit portfolio when considering afatinib as treatment.

## References

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