Use of circulating tumor DNA (ctDNA) for early assessment of treatment response in patients with non-small cell lung cancer (NSCLC): A real-world (RW) analysis incorporating baseline ctDNA level and molecular response

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Background

Background: Data suggests that changes in ctDNA quantity correlate with response to therapy in patients with advanced solid malignancies. Furthermore, absolute baseline (pre-treatment) ctDNA level has been shown to be associated with patient prognosis. However, there is little information on how these variables can be combined to better interpret ctDNA results and enhance predictive power of treatment response. Here, we develop approaches to incorporate the effects of both baseline ctDNA level as well as relative ctDNA change in order to identify very high/low risk patient populations as measured by real-world data.

Methods

- We queried the Guardant INFORM database, which comprises aggregated commercial payer health claims and de-identified records from >225,000 individuals with ctDNA testing via Guardant360.
- Patients with aNSCLC who received a ctDNA test within 15 weeks prior to treatment initiation (any line of therapy) and a second test 3-15 weeks after treatment initiation were retrospectively evaluated using the G360 Response algorithm.
  - Patients were grouped by treatment into immune checkpoint inhibitor-based combination therapy (ICI) and EGFR kinase inhibitor-based (osimertinib, erlotinib, afatinib, gefitinib) therapy (TKI).
  - Cox proportional hazards (CoxPH) were used for RW time to next treatment (TTNT) and overall survival (OS) analyses.
  - A ≥60% and 10% decrease in mean variant allele fraction ratio from pre-treatment to on-treatment was used to define TTNT molecular responder (R)/non-responder (N) molecular status in ICI and TKI cohorts, respectively.
  - Patients classified as ctDNA-low (i.e. having low tumor shed at both timepoints) were grouped with molecular responders when assessing response.
  - 1.6% and 0.6% maximum variant allele fraction (MVAF) was used as thresholds to assign TTNT high/low baseline ctDNA tumor fraction categories in ICI and TKI cohorts, respectively.

Conclusions

Patients with aNSCLC classified as molecular responders via the G360 Response algorithm had significantly prolonged time on treatment and overall survival compared to non-responders. Further stratification of molecular response by baseline ctDNA level identifies patients at particularly high/low risk. Preliminary data shows that methylation-based estimate of ctDNA tumor fraction (see poster 3123) is significantly associated with rwTTNT and may be an improvement over MVAF-based estimates (data not shown).

Compared to tumor biomarkers, ctDNA has a short half-life, which can allow for early response assessment, as shown in this study. These findings are relevant for clinical care, with future potential to allow for adaptive clinical trial design.

References