USE OF REAL-WORLD (RW) DATA TO ASSESS THE ABILITY OF CIRCULATING CELL-FREE TUMOR DNA (CTDNA) MOLECULAR RESPONSE TO ASSESS THERAPEUTIC OUTCOMES IN PATIENTS WITH NON-SMALL CELL LUNG CANCER (NSCLC)

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Background Data suggests that changes in ctDNA quantity correlate with response to therapy in patients with advanced solid malignancies. However, there is little consistency on how to calculate and interpret such changes. Here, we apply a clinically-validated molecular response algorithm to a RW cohort of patients with NSCLC to further evaluate its ability to assess treatment outcomes.

Methods We queried the Guardant INFORM database, which comprises aggregated commercial payer health claims and de-identified records from over 173,000 individuals with comprehensive ctDNA testing via Guardant360 (G360) from September 2018-March 2022. Patients with NSCLC treated with either EGFR tyrosine kinase inhibitors (TKI) or immune checkpoint inhibitors (ICI) (monotherapy or in combination) who received a ctDNA test within 15 weeks prior to treatment initiation and a second test 3–15 weeks after treatment initiation were retrospectively evaluated using the G360 Response algorithm. Cox proportional hazards (CPH) were used for RW time to next treatment (TTNT) and time to treatment discontinuation (TTD) analyses. A >50% decrease in mean variant allele fraction ratio from pre-treatment to on-treatment was used to define the molecular response categorical variable. Gender, age, line of therapy (LOT) and comorbidities were included as covariates. Median TTNT and TTD were calculated by Kaplan Meier.

Results 282 patients with NSCLC were identified: 38% of patients received ICI, 26% received an EGFR-TKI, and 36% received other therapies. Of patients receiving either EGFR-TKI or ICI, 34% were classified as molecular responders, 47% were non-responders, and 19% were not evaluable by the algorithm due to no/low ctDNA at one or both time-points. Molecular responders had significantly longer TTNT on EGFR TKIs and ICI compared to non-responders receiving the same therapy. TTD was significantly longer for molecular responders compared to non-responders in the EGFR-TKI cohort (table 1).

Conclusions Patients with NSCLC classified as molecular responders via the G360 Response algorithm had prolonged TTD and TTNT on both EGFR-TKI and ICI compared to non-responders. This data supports the use of ctDNA molecular response, as calculated by this algorithm, in assessing patient response to therapy; exploration of the utility of this algorithm in adaptive clinical trial design to evaluate the impact of early treatment interventions on patient outcome is ongoing.

Ethics Approval This research was approved by the Quorum Institutional Review Board (IRB) for the generation of de-identified datasets for research purposes.