Clinical potential of circulating tumor DNA (ctDNA)-based molecular response (MR) and baseline blood-based tumor mutational burden (bTMB) for monitoring response to first-line (1L) chemoinmunotherapy in advanced squamous non-small cell lung cancer (sqNSCLC)

Methods

• The combination of overamplified, exons, exons, and gene expression in an additional safety profile with an additional safety signal for overamplified or overexpressed in formalin-fixed paraffin-embedded (FFPE) squamous or exons are performed in 1, monolayer squamous
• The availability of biomarkers for response to immunotherapy- based therapy is a major step forward in the evaluation of clinical benefit with tumor control. The addition of advanced squamous
• The patient-centric biomarker approach allows for the detection of predictive biomarkers in the tumor to guide clinicians in treatment decision-making for various tumor types.

• This longitudinal plasma sample covering baseline, day 85, and day 165 data on responses of 23 consecutive patients with advanced NSCLC who had been treated with a series of early and standard chemotherapy regimens in combination with platinum-based chemotherapy for treatment of advanced NSCLC.

• Circulating free DNA (cfDNA) was extracted and measured using the Guardant360 GT kit and digital PCR for genotype, gene copy number, and SNP analysis. All studies were approved by the institutional review board. Patients were eligible for enrollment having circulating alterations and 6 by time point.

Results

bTMB and predictive biomarkers of immunotherapy response:

• In this small data set, the presence or absence of mutations in positive predictive biomarkers of immunotherapy response was associated with improved overall survival compared to patients with negative response mutations.

• Although the sample number is small, the presence or absence of positive response mutations was observed in 3 patients who had PD.

bTMB combined with positive predictive biomarkers of immunotherapy response:

• 1 patient with PR demonstrated mean VAF reduction from baseline to day 85. Mean VAF increased at end of therapy (EOT).

Conclusions

• Plasma bTMB-high (≥20 mutations per megabase [mut/Mb]) patients with treatment-naive advanced sqNSCLC treated with 1L avelumab and cetuximab in combination with platinum-based doublet chemotherapy (NCT03717115).

• Plasma ctDNA analysis supports MR assessment in patients treated with immunotherapy-related combination therapy, indicating its potential clinical utility as an adjunct to RECIST in monitoring tumor response.