VIRTUAL ESMO congress 2020

# 701O

# Assessment of circulating cell-free tumor DNA (ctDNA) in 847 patients (pts) with metastatic renal cell carcinoma (mRCC) and concordance with tissue-based testing

Z.B. Zengin[1], C. Weipert[2], J. Hsu[1], N. Salgia[1], J. Saam[2], T.K. Choueiri[3], N. Agarwal[4], S. Pal[1]

[1] Medical Oncology, City of Hope Comprehensive Cancer Center, Duarte, CA, USA, [2] Medical Affairs, Guardant Health, Inc., Redwood City, CA, USA, [3] Department of Medical Oncology, Dana-Farber Cancer Institute, The Lank Center for Genitourinary Oncology, Boston, MA, USA[4] Oncology/Internal Medicine, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA

## Background

ctDNA analysis is a non-invasive method used to assess tumor-derived genomic alterations (GAs). Previous work in mRCC has shown that ctDNA profiles evolve with treatment in mRCC. We utilized a commercially available ctDNA assay to identify common GAs in mRCC and compared ctDNA and tissue-based GAs in pts with mRCC.

## Methods

We retrospectively identified consecutive pts with mRCC who underwent ctDNA testing using a clinically-validated 73- to 74-gene panel (Guardant360) between November 2016–December 2019. The targeted next-generation sequencing (NGS) ctDNA assay included analysis of sequence alterations, small insertions/deletions, amplifications, and fusions. In a subset of pts, GAs identified with ctDNA were compared to GAs detected via tissue-based platforms with using either whole-exome sequencing (Ashion Analytics) or targeted NGS (Foundation Medicine). Tissue test results included variants of unknown significance (VUS), as some clinically relevant alterations were classified as such.

## Results

Across 847 mRCC pts (600 male, 247 female), ≥1 GAs were detected in 669/929 (72%) ctDNA samples. After excluding VUS and synonymous variants, TP53 (37%), VHL (22%), and EGFR (6%) were the most frequently altered genes in ctDNA. Tissue DNA analysis of 47 pts was also assessed; VHL (63.8%), PBRM1 (44.7%) and SETD2 (31.9%) were most frequently mutated (the latter two genes were not included on the ctDNA assay). Median time between tissue and ctDNA assays was 15.3 months (IQR, 7.5-29.8). When restricted to only the genes included on the ctDNA assay, a total of 154 GAs were found across both assays. Of these, 41 (26.6%) GAs were exclusive to blood, 92 (59.7%) were exclusive to tissue, and 21 (13.6%) were found on both platforms. The cumulative concordance rate between ctDNA and tissue DNA samples was 96.6%. Sequential ctDNA assessment was available in 65 pts; results will be presented at the meeting.

## Conclusions

With the largest mRCC cohort to date, our study shows ctDNA analysis is feasible and highly concordant with tissue genomic analysis. Exclusive GAs found on both platforms suggests tumor evolution over time and treatment, which may assist in guiding treatment selection in mRCC.

## Legal entity responsible for the study

The authors.

## Funding

Has not received any funding.

## Disclosure

C. Weipert: Shareholder/Stockholder/Stock options, Full/Part-time employment: Guardant Health. J. Hsu: Shareholder/Stockholder/Stock options, Full/Part-time employment: Guardant Health. S. Pal: Advisory/Consultancy, Research grant/Funding (institution): Pfizer; Honoraria (self), Advisory/Consultancy: Novartis; Advisory/Consultancy, Research grant/Funding (institution): Aveo; Advisory/Consultancy: Genentech; Advisory/Consultancy, Research grant/Funding (institution): Exelis; Advisory/Consultancy, Research grant/Funding (institution): Bristol Myers Squibb; Advisory/Consultancy: Astellas Pharma; Advisory/Consultancy: GlaxoSmithKline; Advisory/Consultancy, Research grant/Funding (institution): Eisai; Advisory/Consultancy: Roche; Advisory/Consultancy: Ipsen; Honoraria (self): Medivation; Honoraria (institution): Astellas Pharma; Research grant/Funding (institution): Nektar Therapeutics; Research grant/Funding (institution): QED. All other authors have declared no conflicts of interest.