

CIRCULATING TUMOR DNA IN KIDNEY CANCER

Vitaly Margulis, MD FACS

Professor

Urologic Oncology

Harold C. Simmons Comprehensive Cancer Center

What we will cover today

- How the circulating tumor DNA = ctDNA test works
- Why does this matter for patients?
- Some current data and future directions

Traditional tools have limitations measuring cancer burden and relapse



Scans



**Clinicopathologic
characteristics**



**Tissue-based
biomarkers**

Limitations

Limited ability to detect
micrometastatic disease;
radiation exposure

Features can be subjective and
not always correlated to
outcomes

Snapshot; does not reflect real-
time disease dynamics

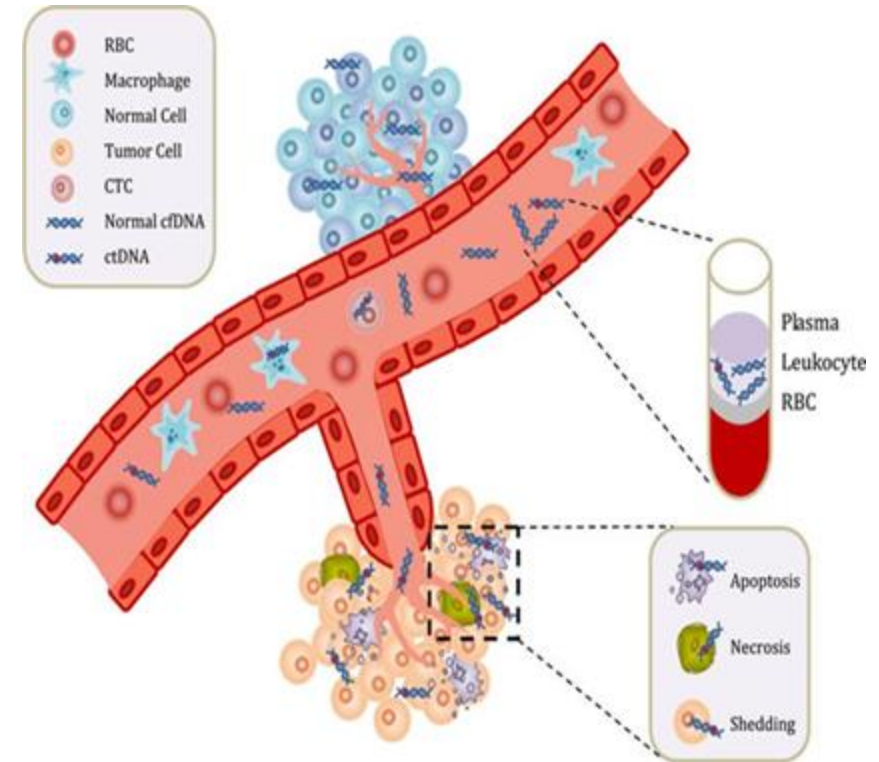
What is ctDNA? Tracking Fingerprints in the Blood

Genetic Fingerprints: Every cell in the body contains DNA. Cancer cells have altered DNA unique to the tumor.

Natural Shedding: As kidney tumor cells expand, they release their DNA into the bloodstream.

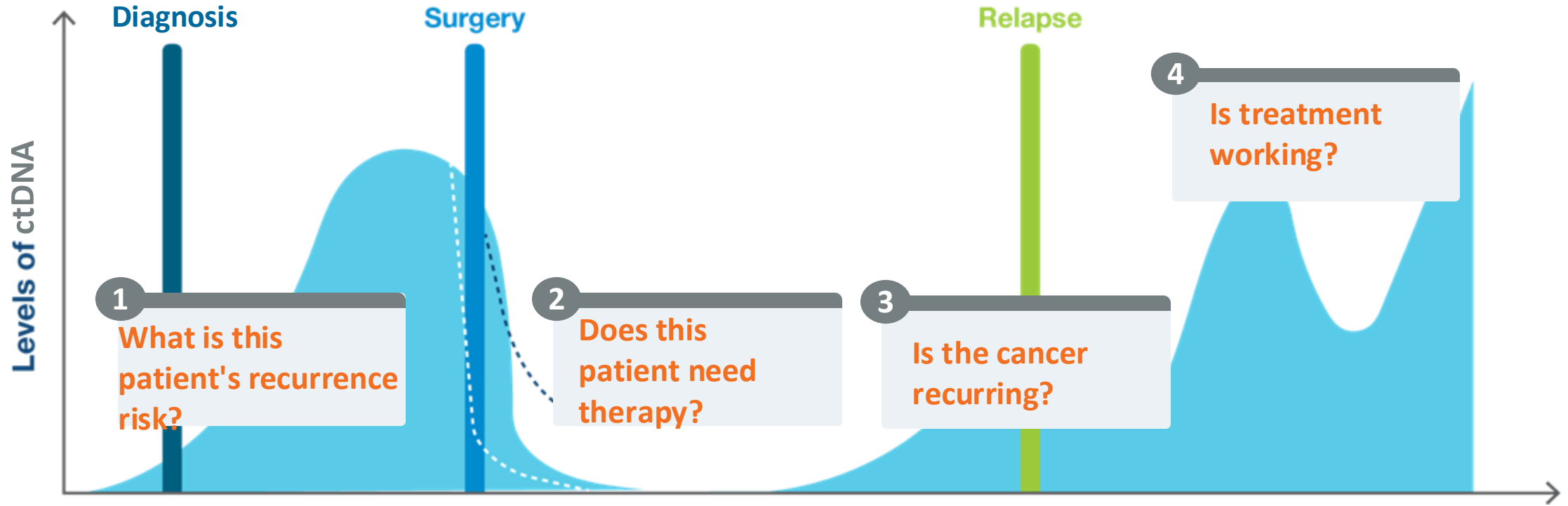
Liquid Biopsy: By taking a blood sample, specialized laboratory tests can detect these microscopic tumor DNA fragments.

Non-Invasive Tracking: This allows doctors to track the tumor over time. In some cases, it enables assessing if the tumor has changed (new DNA mutations).



Critical clinical decisions in Kidney Cancer require reliable risk assessment tools

From diagnosis to advanced disease - the clinical question changes



1

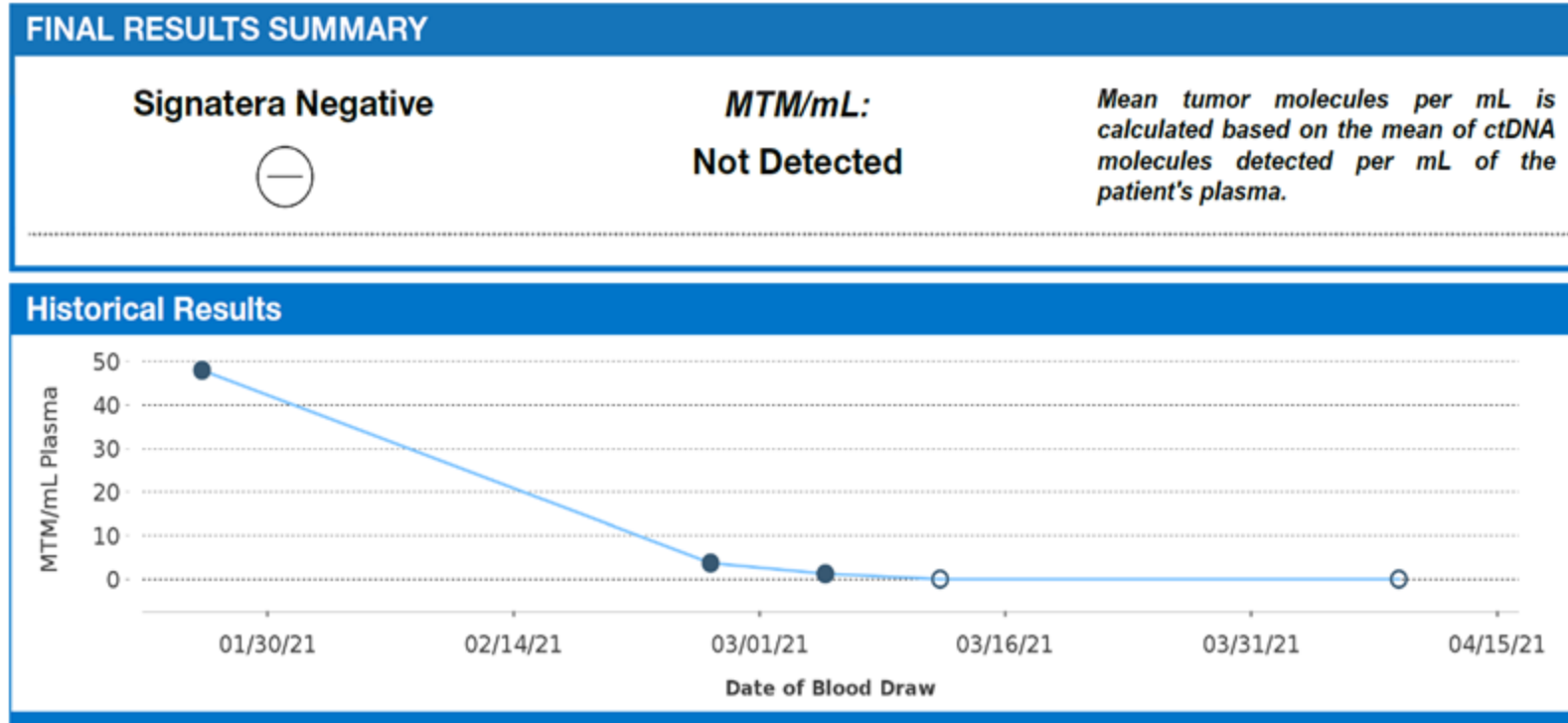
2. THE PROBLEM OF THE SUBSTITUTION

2

3

Figure 1 is a line graph showing the change in viral load (log copies/mL) over time for HIV-1 infected patients. The x-axis represents time from 01/12/2016 to 01/03/2017. The y-axis represents viral load in log copies/mL, ranging from 0 to 10. A vertical yellow bar indicates the period of treatment with efavirenz (EFV). The legend shows two groups: efDNA (+) (filled circles) and efDNA (-) (open circles). The efDNA (+) group shows a significant decrease in viral load during the EFV treatment period, while the efDNA (-) group remains relatively stable.

ctDNA tells the story of your cancer over time

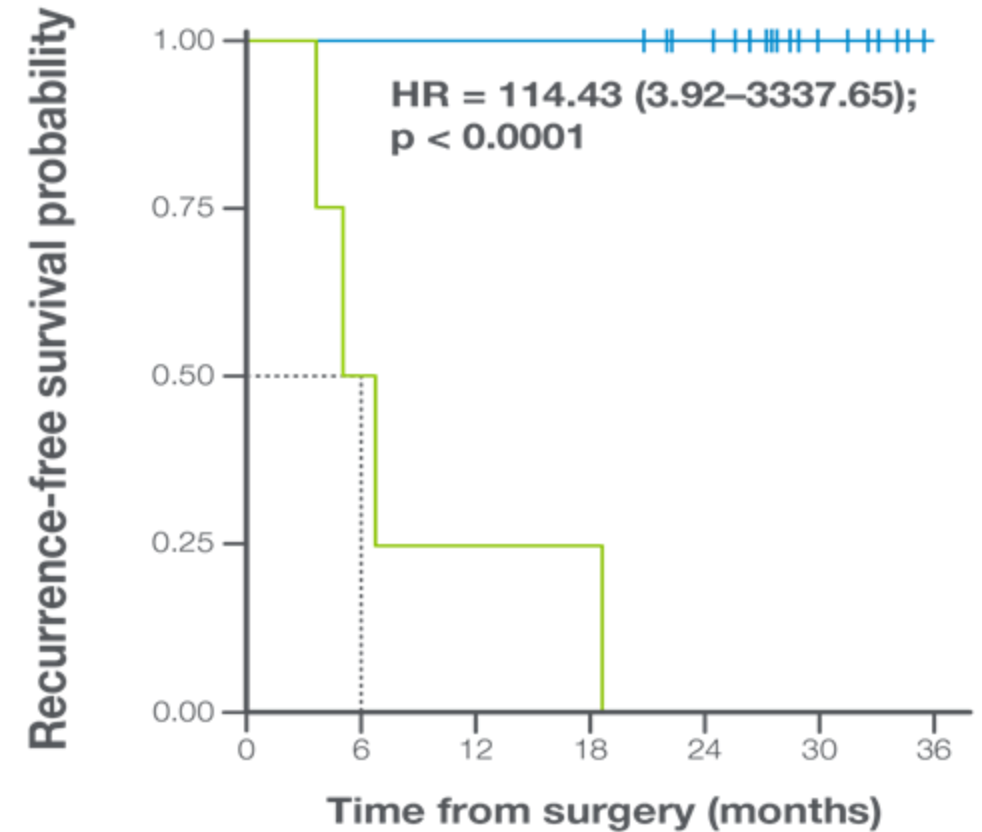


- Tracking ctDNA levels over time can indicate how your cancer is responding to treatment.
- ctDNA is meant for serial use in combination with other test including scans as part of your overall cancer care.

Post-nephrectomy ctDNA status stratifies recurrence risk in localized RCC

- ctDNA positivity strongly associated with risk of recurrence
- 100% longitudinal sensitivity and specificity for all relapses

Suri, Margulis et al. ESMO 2025



Number at-Risk

ctDNA-negative

24

24

24

24

20

9

0

ctDNA-positive

4

2

1

1

0

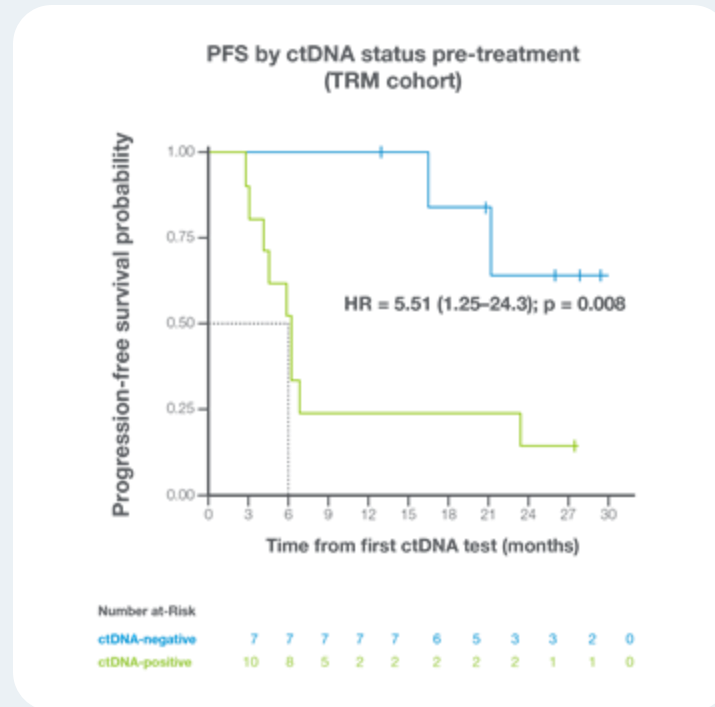
0

0

ctDNA stratified risk of progression in metastatic RCC patients during treatment and surveillance

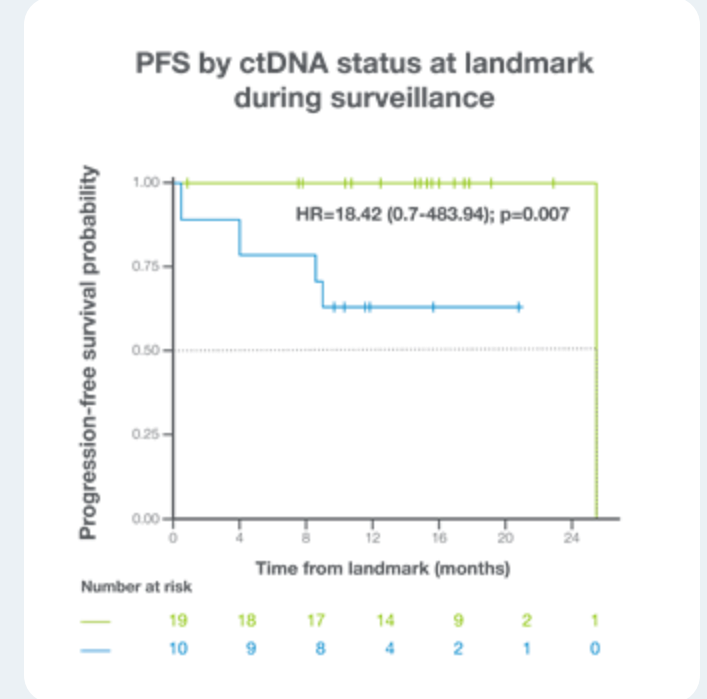
Pre-Treatment

- ctDNA positivity was associated with higher chances of progression (HR 5.51; $p=0.008$)
- On-treatment dynamics reflected treatment outcomes



Surveillance

- ctDNA positivity predicted recurrence (HR 18.42; $p=0.007$)
- Favorable dynamics associated with delayed progression (10.3 vs 1.7 months)



Suri, Margulis et al. ESMO 2025 — Cohort B: 48 patients with metastatic RCC

Key takeaways

ctDNA IS STANDARD OF CARE IN MANY TUMORS

WE ARE NOT THERE YET IN KIDNEY CANCER BUT TECHNOLOGY IS IMPROVING

ctDNA is a personalized test that helps determine:

- If there are signs of cancer remaining in the patient after surgery (or initial treatment)
- Whether a patient may benefit from additional treatment to reduce risk of recurrence
- If the treatment is working (tracking disease burden over time through serial testing)
- If the cancer is returning by detecting relapse earlier than with scans

When used serially, along with other tools, it may provide additional insights and help guide shared decisions between patients and providers

THANK YOU

PATIENTS that have contributed to clinical studies
and their FAMILIES
moving the field forward towards better outcomes

PLEASE SUPPORT CLINICAL TRIALS

vitaly.margulis@utsouthwestern.edu