IASLC
2020 HOT TOPIC MEETING:
LIQUID BIOPSY
OCTOBER 2-3, 2020 | WORLDWIDE VIRTUAL EVENT
#LiquidBiopsy20

Utility of Liquid Biopsy in Diagnosis and Treatment Response in EGFR Mutant NSCLC Patients with Leptomeningeal Involvement

David Berz, MD

Beverly Hills Cancer Center

USA

DISCLOSURES

Commercial Interest	Relationship(s)
Biocept, Inc	Clinical Advisory Board ; Consultant
SunPharma	Speakers Bureau; Consultant
AstraZeneca	Speakers Bureau
Genentech	Speakers Bureau
PreludeDX	Consultant
Merck	Speakers Bureau
Natera	Speakers Bureau
Novartis	Speakers Bureau
Caris Life Science	Consultant/ Research
Oncocyte	Speakers Bureau

INTRODUCTION:

- Leptomeningeal Metastasis (LM) occurs in ~ 3-4% of patients with Non-Small Cell Lung Cancer (NSCLC) and increases to up to 9% in patients with EGFR mutations.
- The gold standard in diagnosing LM is identification of tumor cells in cerebrospinal fluid (CSF) by cytologic methods based on conventional stains and light microscopy (“cytology”).
- Due to the qualitative nature of cytology, diagnosing and measuring treatment response in LM remains challenging, calling for more robust and quantitative methods.
- We retrospectively compared tumor cell detection using standard Cytology and Target Selector ™ in the CSF of patients enrolled in Clinical Trial KD-019-206, a Phase II Multicenter Study of Tesevatinib in subjects with NSCLC EGFR Activating Mutations (NCT02616393).
- Target Selector ™ is novel combined approach to capture and characterize both circulating tumor cells (CTCs) and cell free DNA (cfDNA) using high sensitivity methods.
- In the same cohort, absolute counts of EGFR mutations in the CSF derived cell free DNA (cfDNA) using Target Selector ™ single gene qPCR assays based on Biocept’s proprietary Switch-Blocker enrichment technology was correlated with treatment response.

OBJECTIVES:

1. To compare CTC capture rates between standard Cytology with Target Selector ™ in the CSF of patients with metastatic Non-Small Cell Lung Cancer

2. To correlate CTC enumeration and absolute counts of EGFR mutations (Del19, L858R and T790M) of the CSF derived cfDNA with treatment response

METHODS

- Samples were obtained from subjects enrolled in Clinical Trial KD-019-206, a Phase II Multicenter Study of Tesevatinib in subjects with NSCLC EGFR Activating Mutations, Prior Treatment with a TKI and Brain- or Leptomeningeal Metastases (NCT02616393).

- CSF was collected at baseline and at different time intervals throughout treatment and analyzed by cytology as well as by Biocept's Target Selector ™ platform with n=15 unique patients, and 27 matched sample collections in total.

- Target Selector ™ is a novel combined platform technology that uses proprietary advanced microfluidics with antibody cocktail-based capture of CTCs and high sensitivity target ctDNA amplification (see figure 1) designed to provide more sensitive detection and both phenotypic and genomic characterization of tumor involvement in CSF or blood by most solid tumor types.

Figure 1. Workflow of the Target Selector ™ Platform using Biocept's CEE-Sure ™ blood collection tubes for CTCs and cfDNA detection

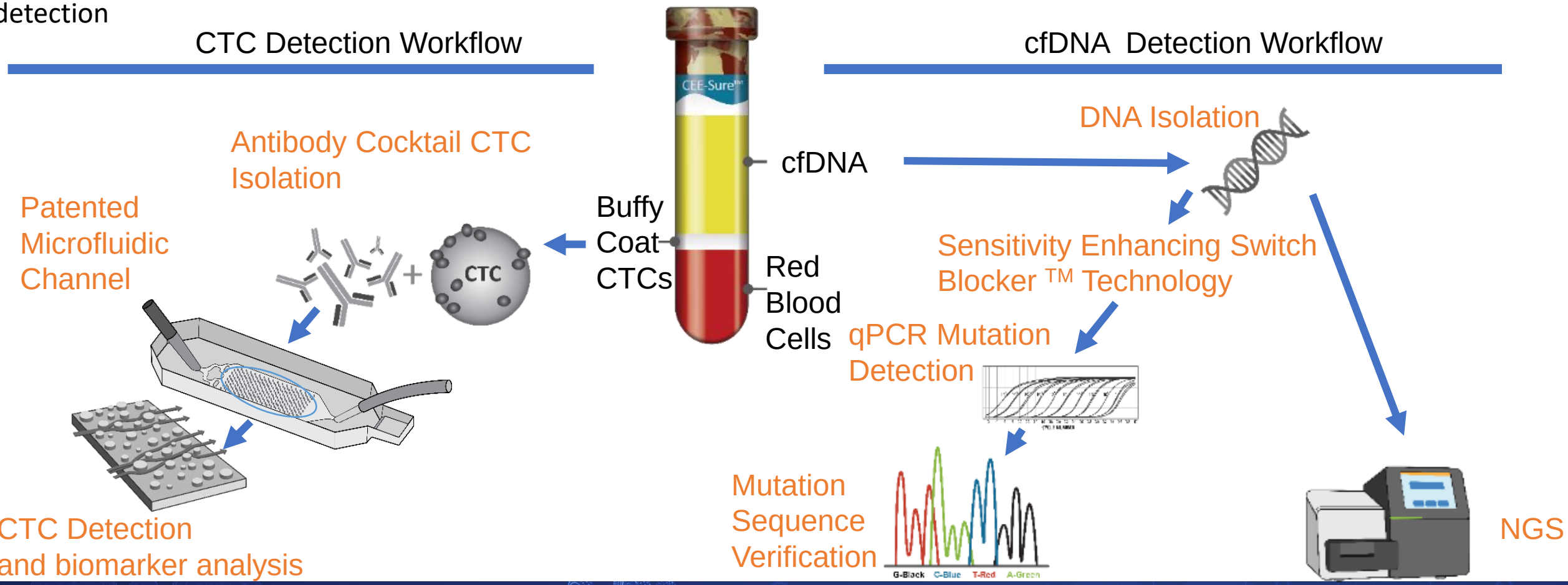


Figure 2. Improved tumor cell detection by Target Selector ™ compared to standard Cytology

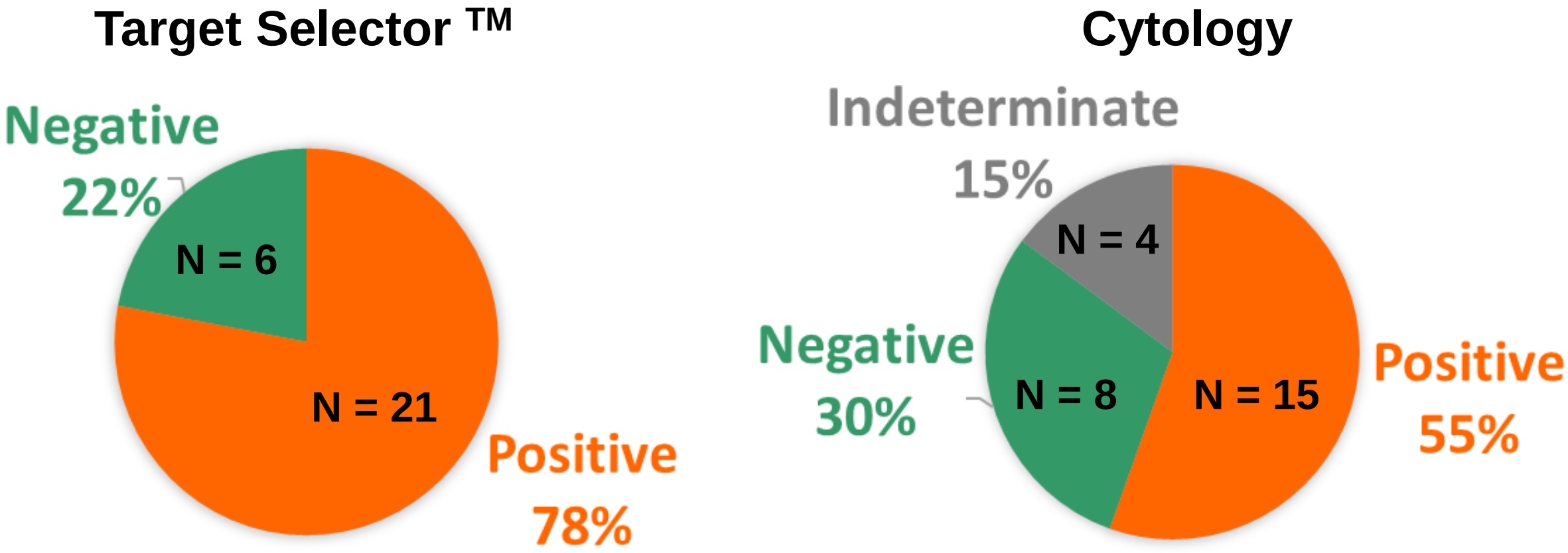


Figure 3. Improved detection of tumor derived material (CTCs and/or cfDNA) in the CSF by Target Selector ™ compared to standard Cytology

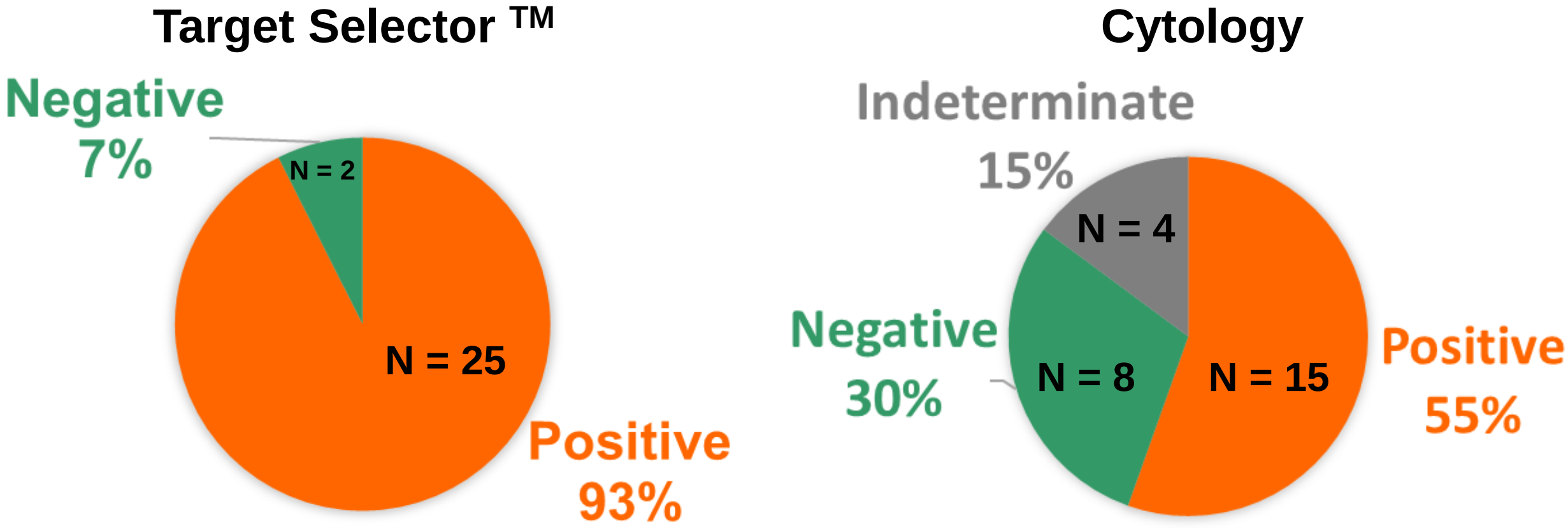


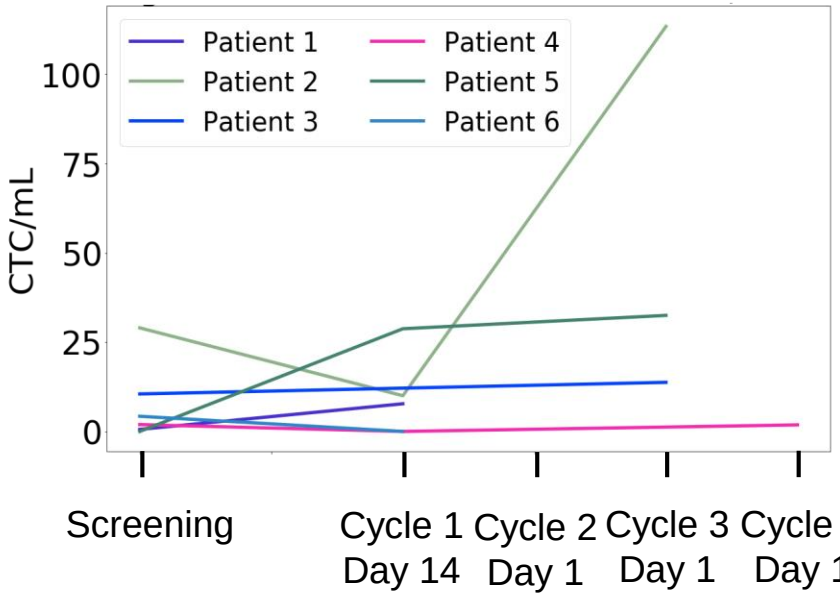
Figure 4. Treatment responses observed in Leptomeningeal Disease (N = 9)

Clinical Response	N
Stable Disease (SD)	6
Partial Response (PR)	1
Progressive Disease (PD)	2

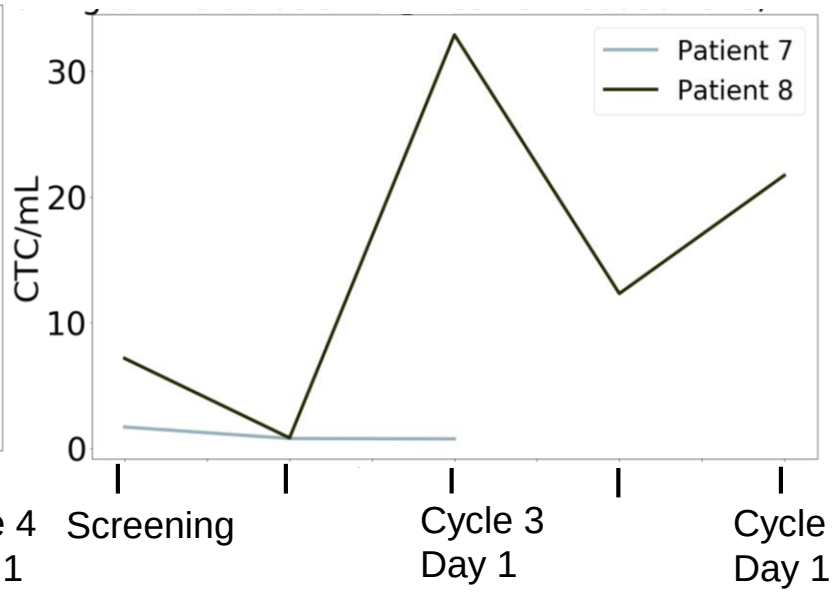
Figure 5. Decrease in CTC density associates with Stable Disease and Partial Response in the LM Tumor

CTC Density

Stable Disease



Progressive Disease



Partial Response

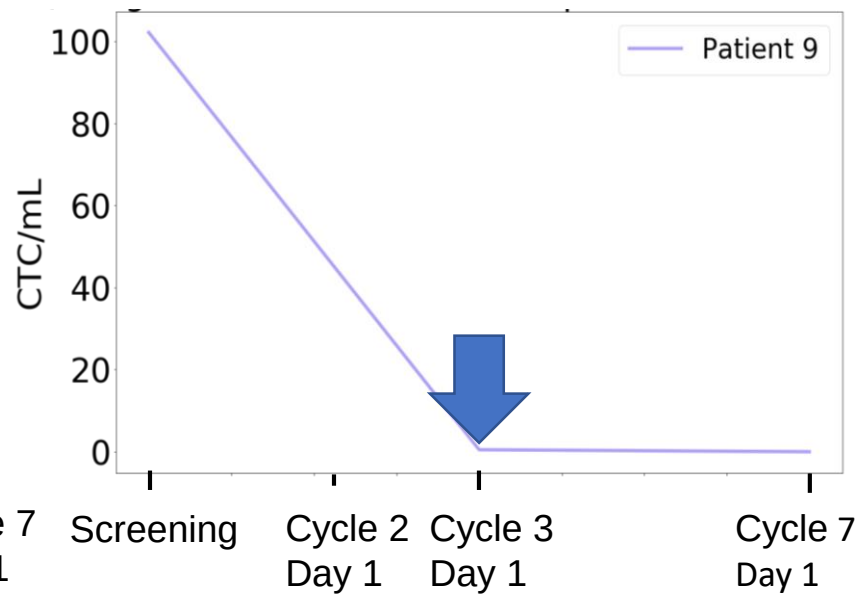
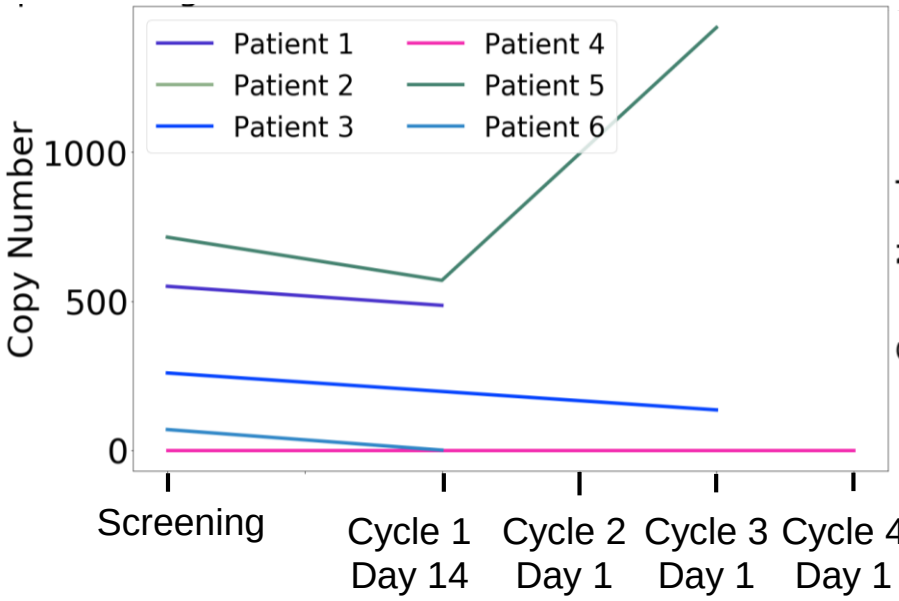


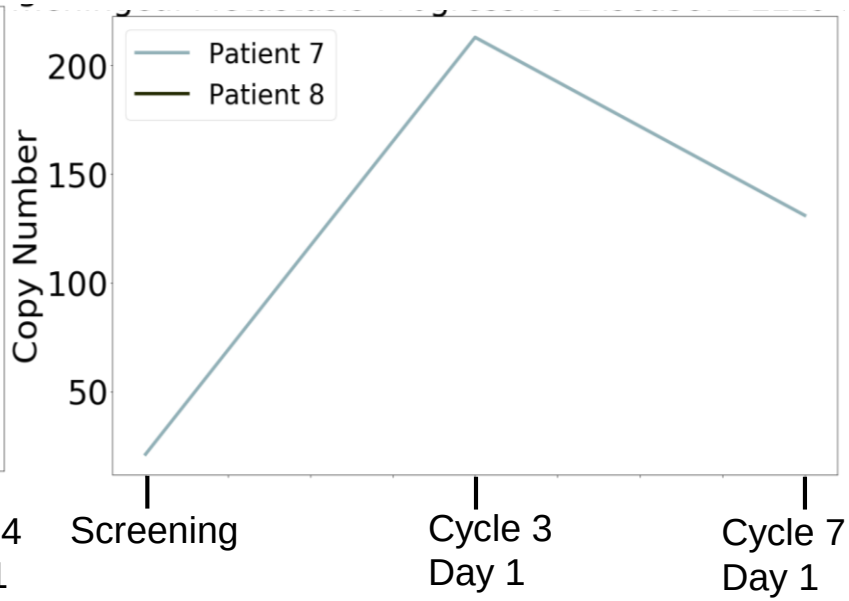
Figure 6. Decrease in EGFR mutation Exon Deletion 19 copy number associates with Stable Disease and Partial Response

EGFR Exon 19 Deletion

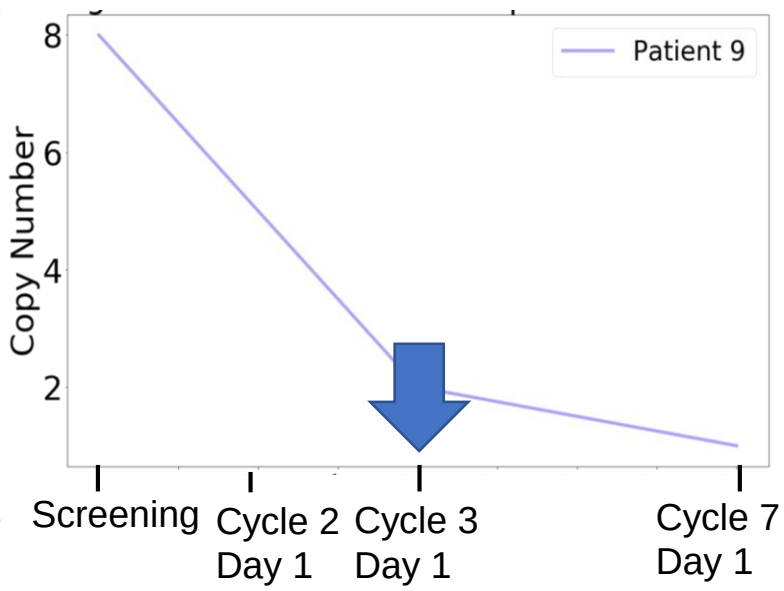
Stable Disease



Progressive Disease



Partial Response



- Liquid biopsy analyses of the CSF in patients with Leptomeningeal tumors:
  - May provide a more sensitive method than standard cytology for the diagnosis and assessment of treatment response.
  - Allows for detection of actionable biomarkers such as EGFR mutations with the potential to treat with targeted therapies.

- Alterations in CSF CTC density and mutational EGFR copy number have the potential to indicate a treatment response prior to traditional clinical measures.

- Larger clinical trials are needed to fully define the clinical impact of these observations.

IASLC
2020 HOT TOPIC MEETING:
LIQUID BIOPSY
OCTOBER 2-3, 2020 | WORLDWIDE VIRTUAL EVENT
#LiquidBiopsy20

Authors:

David Berz[1], MD, PhD
Veena Singh[2], MD, FCAP, FACMG
Ross Camidge[3], MD, PhD
Deepa Subramaniam[4], MD
Barbara O'Brien[5], MD,
Laurie Green[6],
Masha Poyurovsky[6], PhD
Sanjay Aggarwal[7], MB
Linghui Li[6], MD, PhD
Jorge Nieva[8], MD,
Thierry Jahan[9], MD
Sarah Suh[6],
Beth MacGillivary[10],
Dave Eiznhamer[6], PhD
Mark Berger[11], MD
Lan Huynh[2],
Edgar Sales[2],
Heeje Cho[2],
Barbara Blouw[2], PhD
Melissa Johnson[12], MD
Santosh Kesari[13], MD, PhD