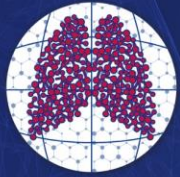


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2020 HOT TOPIC MEETING:  
LIQUID BIOPSY

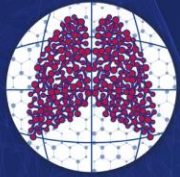
OCTOBER 2-3, 2020 | WORLDWIDE VIRTUAL EVENT

#LiquidBiopsy20

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

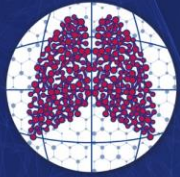
**David Berz, MD**

**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                      |



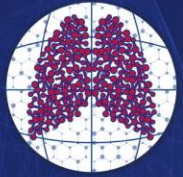
## 2020 HOT TOPIC MEETING: LIQUID BIOPSY

OCTOBER 2-3, 2020 | WORLDWIDE VIRTUAL EVENT

# #LiquidBiopsy20

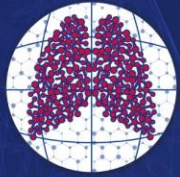
### INTRODUCTION:

- 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.

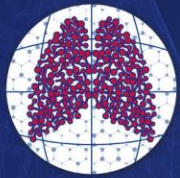


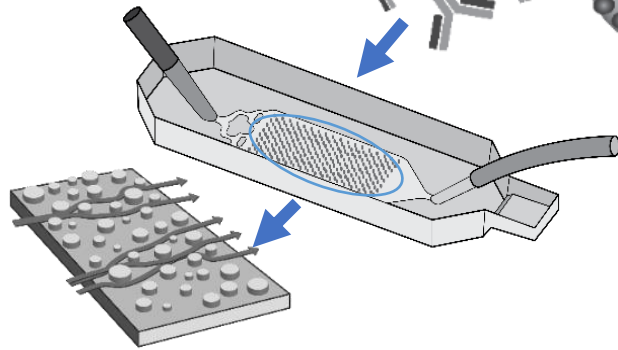
Figure 1. Workflow of the Target Selector™ Platform using Biocept's CEE-Sure™ blood collection tubes for CTCs and cfDNA detection

CTC Detection Workflow

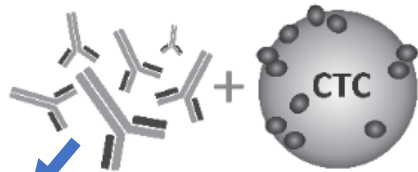
cfDNA Detection Workflow

Antibody Cocktail CTC Isolation

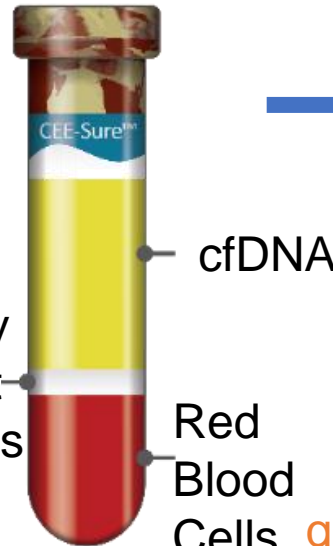
Patented Microfluidic Channel



CTC Detection and biomarker analysis



Buffy Coat CTCs

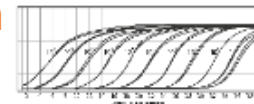


DNA Isolation

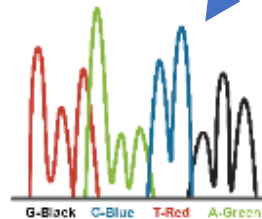


Sensitivity Enhancing Switch Blocker™ Technology

qPCR Mutation Detection



Mutation Sequence Verification



NGS



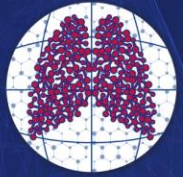


Figure 2. Improved tumor cell detection by Target Selector™ compared to standard Cytology

### Target Selector™

Negative

22%

N = 6

N = 21

Positive

78%

### Cytology

Indeterminate

15%

N = 4

Negative

30%

N = 8

N = 15

Positive

55%

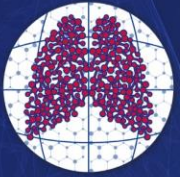
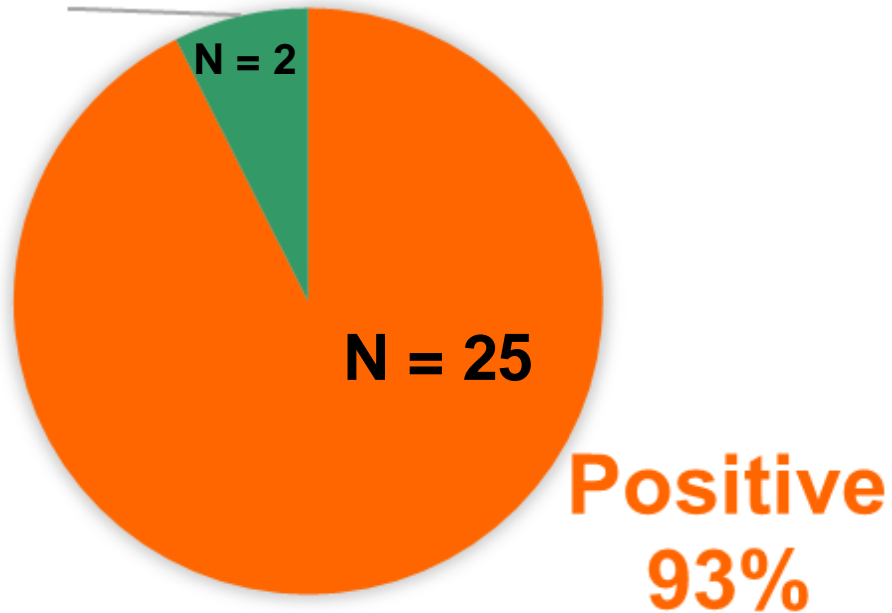


Figure 3. Improved detection of tumor derived material (CTCs and/or cfDNA) in the CSF by Target Selector™ compared to standard Cytology

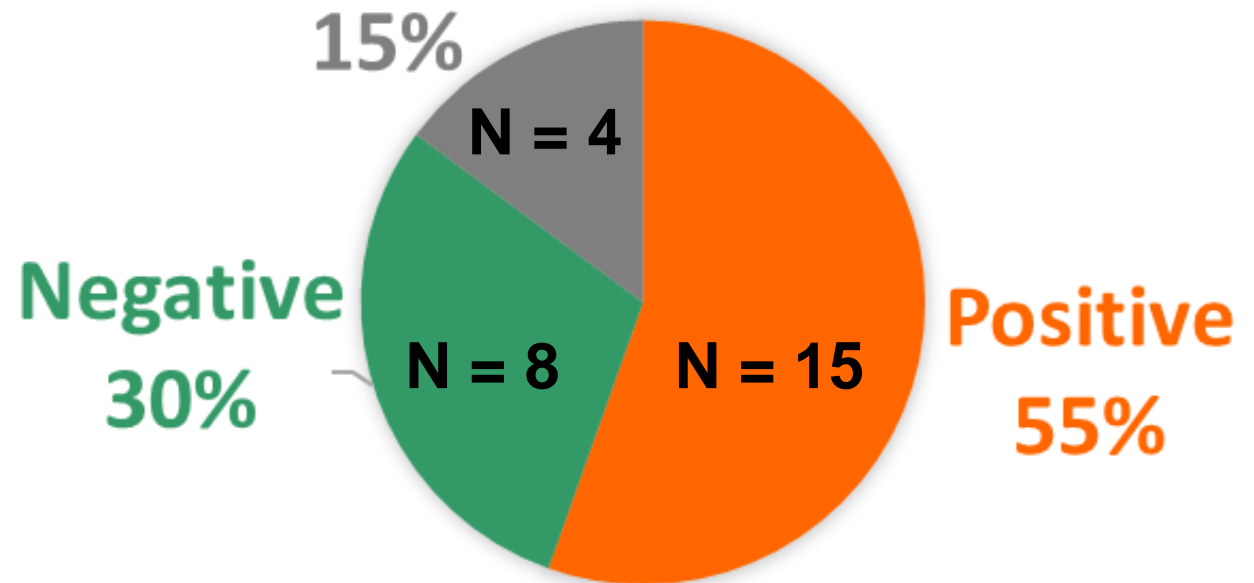
### Target Selector™

Negative  
7%



### Cytology

Indeterminate  
15%





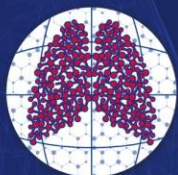


Figure 4. Treatment responses observed in Leptomeningeal Disease (N = 9)

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

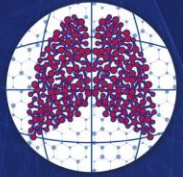


Figure 5. Decrease in CTC density associates with Stable Disease and Partial Response in the LM Tumor

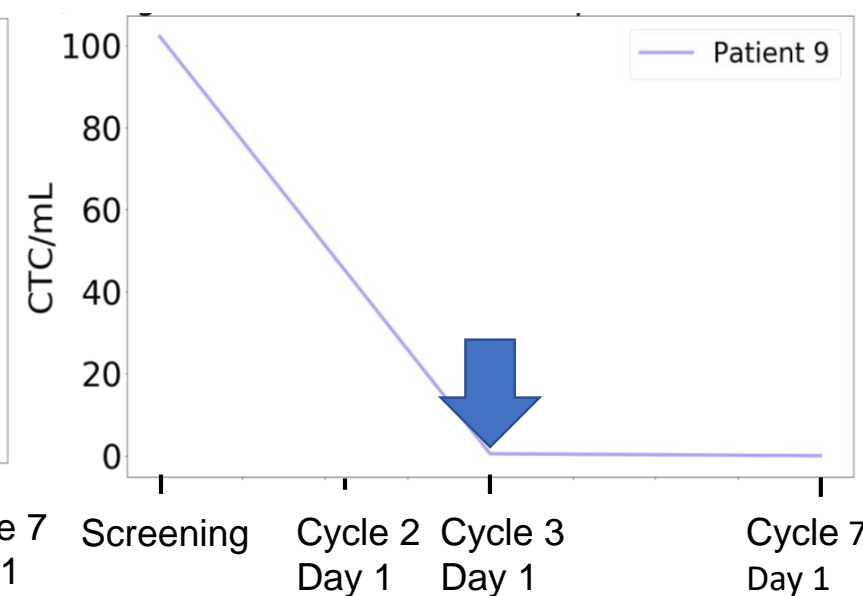
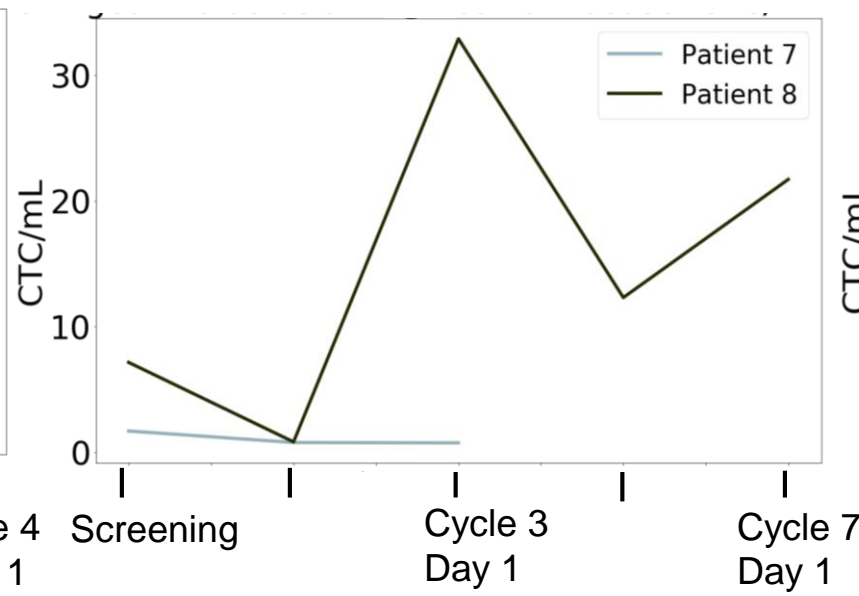
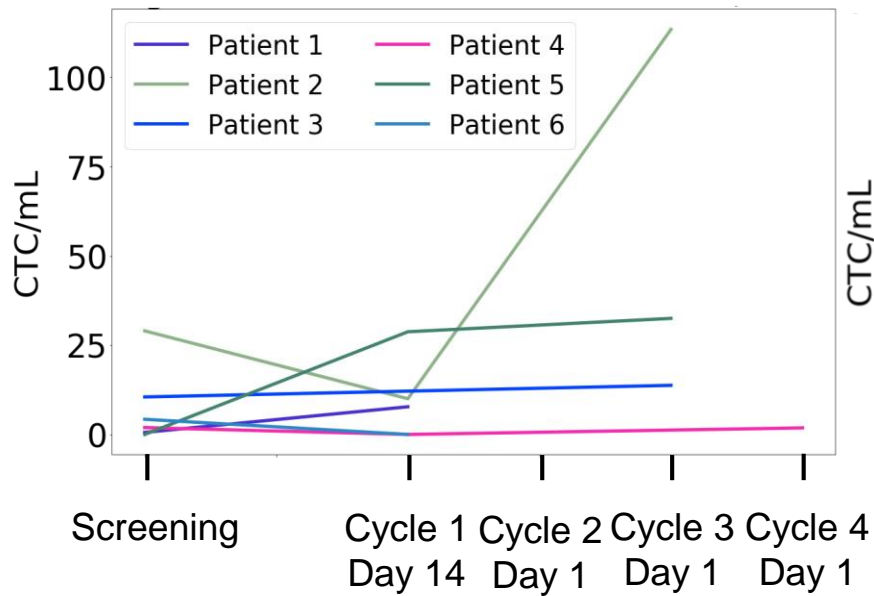
**CTC**

**Density**

**Stable Disease**

**Progressive Disease**

**Partial Response**



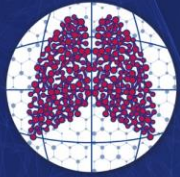
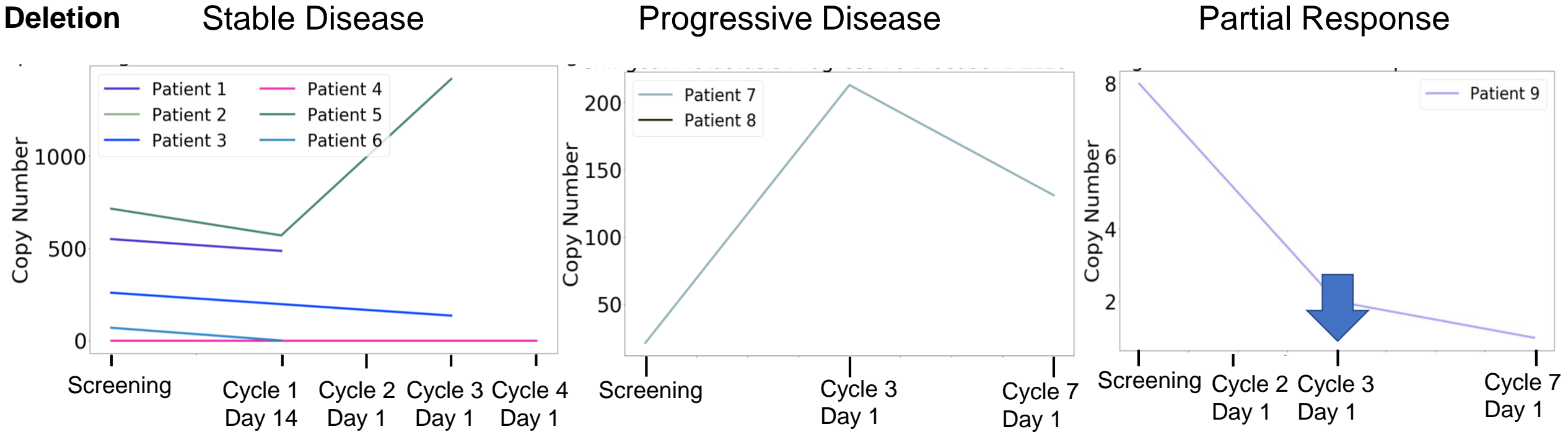
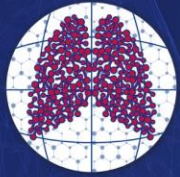


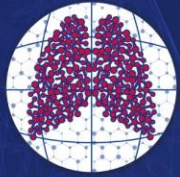
Figure 6. Decrease in EGFR mutation Exon Deletion 19 copy number associates with Stable Disease and Partial Response

**EGFR Exon 19**





- 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.



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