Target Selector™ cerebrospinal fluid (CSF) circulating tumor cells and biomarker analysis: improving sensitivity and targeted treatment options in breast and NSCLC cancer patients with CNS involvement

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Background

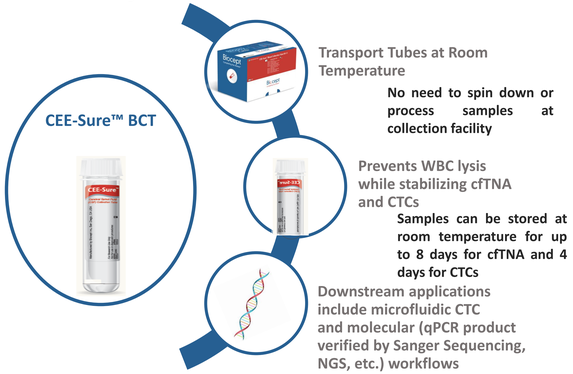
- Leptomeningeal Disease (LMD) is a deleterious complication of various types of cancer, leading to death in 4-6 months following diagnosis (1).
- LMD occurs in 2-5% of patients with metastatic breast cancer (1) and 3-4% of patients with Non-Small Cell Lung Cancer (NSCLC), which increases to 9% when these patients acquire mutations in EGFR (2).
- Cytology is the gold standard in diagnosing LMD but suffers from lack of sensitivity and does not allow for assessment of biomarker status of Cerebrospinal Fluid (CSF) derived Circulating Tumor Cells (CTCs) and cell-free TNA (cfTNA).
- Biocept's Target Selector™ allows for quantitative and biomarker analysis of CTCs and ctDNA derived from the CSF.
- Here we report the analytical and clinical validation of Target Selector™ in enumeration and biomarker status of CTCs and cfTNA in the CSF from patients with confirmed LMD.

Methods

For 98 (n=98) unique patients who had confirmed LMD by either image analysis or Cytology, CSF was prospectively collected in CEE-Sure™ sample collection tubes (Figure 1) and analyzed. CTCs were captured using a 10-antibody cocktail and subsequently analyzed in a microfluidic channel for different FISH probes. Using distinct staining antibodies, captured cells were classified for a variety of markers such as CD45 and Cytokeratin. From the same patient's CSF sample, cell-free total nucleic acids (cfTNA) were extracted from the supernatant and used for both Target Selector™ single gene and next-generation sequencing (NGS) NSCLC and breast multi-gene testing (see Figure 2 for the workflow). For NGS, data analysis was performed using Torrent Suite and Ion Reporter with annotation and curation by Oncomine Knowledgebase Reporter software (Figure 2).

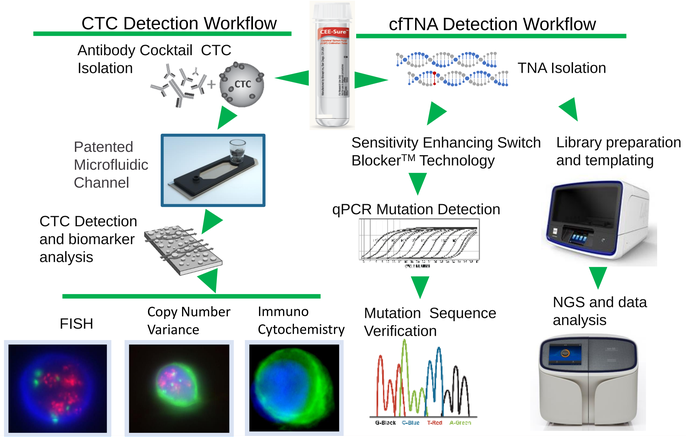
CEE-Sure™ CSF Collection Tubes

Figure 1: Schematic Illustrating the benefits of the CEE-Sure™ CSF Collection Tubes



Target Selector™ Platform for CTC and cfTNA Mutation Analysis

Figure 2. Workflow of the Target Selector™ CTC Platform and cfTNA Molecular Assays



Target Selector™ CSF CTC Assay Performance

TABLE 1: Target Selector™ CSF CTC Detection Assay Summary of Performance

STUDY		RESULTS
Clinical Accuracy		85.4%
Clinical Precision	Intra-Assay	100.0%
	Inter-Assay	100.0%
	Inter-Operator	100.0%
	Inter-Instrument	100.0%
Clinical Sensitivity		80.0%
Clinical Specificity		96.6%
Positive Predictive Value		98.0%
Negative Predictive Value		70.0%
Analytical Specificity		96.0%
Analytical Sensitivity/Limit of Detection		2 CTCs
Reportable Range		CTCs Detected ≥ 2 CTCs
		CTCs Not Detected < 2 CTCs

Target Selector™ CSF Molecular Validation

TABLE 2: Target Selector™ CSF Molecular Validation Summary

STUDY	RESULTS
Clinical Accuracy	87.4%
Clinical Sensitivity	85.2%
Clinical Specificity	88.3%
Positive Predictive Value	76.7%
Negative Predictive Value	93.0%

Representative Images of Captured CTCs

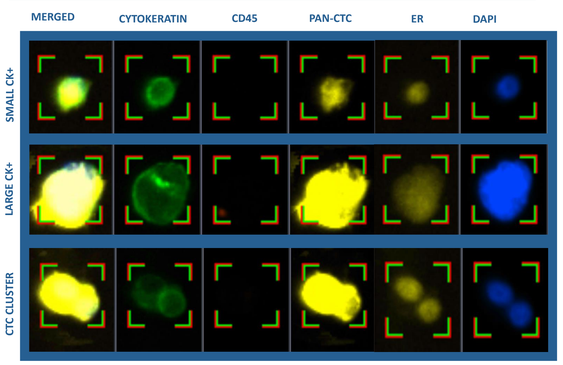


Figure 3. Examples of cells stained with Cytokeratin and CD45

Conclusions

- Target Selector™ is a viable and sensitive platform for CTC detection and molecular analysis of CSF samples from patients with NSCLC or breast cancer with CNS metastases compared to the current standard of care (CSF cytology)
- Identifying CTCs and actionable biomarkers can help to confirm CNS involvement when clinically suspected, characterize tumor mutational evolution, guide targeted therapy selection and potentially monitor for treatment response and tumor burden.

References

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