Case Series of Multi-Institutional Utility of CNSide™ to Manage Leptomeningeal Disease in Patients with Metastatic Breast Cancer

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Background

- Atypical Leptomeningeal Disease is a devastating complication of Breast Cancer.
- Median survival after diagnosis is two to three months.
- Standard Of Care (SOC) methods to diagnose LMD are cytology, MRI and Clinical Evaluation, which suffer from limited sensitivity and specificity and are unable to adequately monitor the response to treatment of the LMD tumor.
- The CNSide assay is a platform that captures tumor cells in the CSF, yields a quantitative CSF tumor cell result and can detect actionable mutations of CSF tumor cells.
- Here we present how CNSide was used to manage LMD in patients with breast cancer who were treated at four different institutions and demonstrate its impact on clinical management.

Methods

- CNSide was analyzed by CNSide for tumor cell number and presence of HER2 amplification by FISH on the tumor cells.
- Patients were treated at the Smilow Cancer Hospital at New Haven (n=1 patient), Northwestern Medicine Lou and Jean Malnati Brain Tumor Institute and UT Southwestern (n=1 patient), and Barrow Neurological Institute (n=2 patients).
- All patients received intrathecal (IT) treatment via an Ommaya reservoir.
- In eleven (11) matched CNSide and cytology in parallel, CNSide detected tumor cells in 100% (11/11) of the samples, whereas cytology detected tumor cells in 54% (6/11- including one sample with atypical cells) of the samples.
- For patient 1 at the second CNSide draw, CNSide was positive for the detection of tumor cells, whereas cytology detected atypical cells.
- For patients 2 and 3 CNSide was not performed on matched CNSide CSF draws.

CNSF Tumor Cell Number Detection by CNSide during Treatment Tracks Clinical Response (Patient 1)

Patient 1

- 2015 Stage IV breast cancer diagnosis
- 2018 Bone Metastasis diagnosed
- 2020: Oct. Diagnosed with LMD
- Nov. Methotrexate IT BW, this resolved the LMD symptoms and was paralleled by a decline in the number of CSF tumor cells
- Late Dec. IT treatment suspended, capetitabine systemic treatment started.
- 2021: April – May: progression of systemic cancer to bone marrow (low platelet counts) and bone scan positive for cancer
- May: minor LMD symptoms (dizziness)
- June: patient expired due to systemic progression

Patient 2

- 2017 Stage IV breast cancer diagnosis.
- 2020: July: suspicion for LMD, cytology negative for CSF tumor cells; on a subsequent draw, CNSide assay was positive for CSF tumor cells and CSF HER2 amplification by FISH was detected.
- Aug: start IT treatment with topotecan and trastuzumab-biosimilar; LMD symptoms resolved, corresponding with a decreased number of CSF tumor cells.
- 2021: April: patient sustained an injury; IT treatment was suspended for 3-4 months, patient progressed during this time (no CSF was drawn) and expired in Aug.

Patient 3

- 2014 Stage II Breast Cancer Diagnosis
- 2019 Suspicion for LMD (cytology neg.); start IT trastuzumab
- 2020: April: CNSide positive for CSF tumor cells and HER2 amplification (FISH) on CSF detected; IT trastuzumab continued; decreased CSF tumor cell numbers tracked clinical response.
- 2021: June: tumor cell numbers increased prior to worsening of LMD symptoms and MRI progression; treatment switched to IR.
- Sept: IR discontinued, and treatment switched to IT topotecan.
- Oct: LMD symptoms resolved, concomitant by a decrease in CSF tumor cell numbers, patient doing well.

Patient 4

- 2020 Dec. suspicion for LMD, cytology and CNSide positive.
- 2021: Jan: start IT treatment with methotrexate; LMD symptoms resolved, which was held by a decrease in number of CSF tumor cells.
- March: patient moved back home, her care was transferred to UT Southwestern.
- Apr: LMD acquired de novo HER2 amplification detected by CNSide (primary tumor was HER2 negative) and IT trastuzumab was added to IT topotecan; CSF tumor cell numbers remained low. Patient exhibits minor cognitive impairment and Leptomeningeal tumor is under control.

Conclusions

- Using CNSide for quantitative CSF tumor cell detection may aid in monitoring the response to treatment of the LMD tumor.
- CNSide can detect actionable mutations of the CSF tumor cells, allowing targetable therapy to treat LMD.
- CNSide may predict clinical progression prior to MRI evidence of progression.
- Larger prospective controlled clinical trials are needed to further establish the role of CNSide in managing LMD.

Comparison CNSF Tumor Cell Detection by CNSide vs Cytology

Patient Characteristics

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<tr>
<th>Patient</th>
<th>Gender</th>
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