

Using Cerebrospinal Fluid Tumor Cell (CSF-TC) Assays to Track Disease Burden and Treatment Response in Patients with Leptomeningeal Metastasis

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Background

- Leptomeningeal metastasis (LM) is diagnosed in approximately 5% of patients with metastatic cancer and has a dismal prognosis (4-6 weeks, untreated)
- Imaging, clinical exam, and cytology all have limited capability for diagnosis and disease monitoring of LM

Methods

- Five (5) cases of LM were diagnosed and followed using the Biocept™ CNSide™ platform
- For each specimen, approximately 6-8 mL of CSF was obtained and transported using the CNSide assay's proprietary tubes
- Each specimen underwent CSF-TC capture, immunocytochemistry (ICC), and (when applicable) fluorescence in situ hybridization (FISH)

Patient Demographics

Patient	Sex	Age	Primary	Treatment	OS
1	F	40	Breast (HER2+)	Tucatinib, IT Methotrexate, IT Cytarabine, IT Trastuzumab (Added), IT Pemetrexed (Added)	17 mos
2	M	70	Melanoma (PD-L1+)	IT Cytarabine, IT Thiotepa	10 mos
3	M	63	Esophageal (HER2+)	IT Topotecan, IT Trastuzumab (Added)	2 mos
4	F	59	Breast (ER+, PR+)	IT Cytarabine, IT Methotrexate	7 mos
5	M	76	Neuroendocrine Carcinoma	Capecitabine, Temozolomide	5 mos

OS - Overall Survival, IT - Intrathecal

Learn more about the CNSide assay



Conclusions

The CNSide assay shows significant advantages in monitoring treatment response and disease course in LM

- The CNSide assay identifies biomarkers in LM patients for which targeted therapeutic interventions can significantly improve neurological symptoms and survival
- Additional longitudinal trials to assess the utility of this platform for LM patients are warranted

CSF-TC Capture Demonstrates Improved Tumor Cell Capture Rate Compared To Cytology

CSF tumor cell capture and HER2 amplification on CSF Tumor cells

Patient 1					
Collection	Cytology Result	CNSide Result	CSF-TC/mL	HER2 Amplification	HER2%
7/22/2020	Positive	Positive	3133.00	Detected	2.17
8/11/2020	Positive	Positive	1625.67	Detected	0.64
8/25/2020	Positive - rare	Positive	23.81	Detected	17.91
9/1/2020	Positive - rare	Positive	1.45	Not Detected	0
9/8/2020	Negative	Positive	1.40	Not Detected	0
9/15/2020	Positive	Positive	0.20	Not Detected	0
9/29/2020	Negative	Positive	1.18	Not Detected	0
10/6/2020	Negative	Positive	3.00	Not Detected	0
10/20/2020	Negative	Positive	1.17	Not Detected	0
10/27/2020	Negative	Positive	1.25	Not Detected	0
11/3/2020	Negative	Positive	0.69	Not Detected	0
11/17/2020	Negative	Negative*	0.17	NA	0
12/1/2020	Negative	Positive	1.83	Not Detected	0
1/12/2021	Positive	Positive	204.56	Detected	2.00
1/19/2021	Positive	Positive	207.83	Detected	6.00
1/27/2021	Positive	Positive	17.00	Detected	2.74
2/3/2021	Negative	Positive	0.50	Not Detected	0
2/6/2021	N/A	Negative	0.00	NA	0
2/16/2021	Negative	Positive	0.20	Not Detected	0
2/23/2021	Negative	Negative	0.00	NA	0
3/2/2021	Negative	Negative	0.00	NA	0
3/23/2021	Negative	Positive	0.33	Not Detected	0
6/1/2021	Positive	Positive	14411.00	Not Detected	0
6/15/2021	Positive	Positive	5010.00	Detected	25.00
6/22/2021	Positive	Positive	2494.71	Not Detected	0
6/29/2021	Positive	Positive	559.57	Not Detected	0
7/6/2021	Positive	Positive	439.33	Not Detected	0
7/13/2021	Positive	Positive	516.63	Detected	1.00
7/20/2021	Positive	Positive	144.67	Not Detected	0
7/27/2021	Positive	Positive	527.00	Detected	4.00
8/3/2021	Positive	Positive	245.17	Not Detected	0
8/10/2021	Positive	Positive	258.33	Not Detected	0
8/17/2021	Positive	Positive	535.67	Not Detected	0
9/30/2021	N/A	Positive	1728.00	Detected	1.00
10/14/2021	N/A	Positive	8006.00	Not Detected	0
10/28/2021	N/A	Positive	748.00	Detected	3.00
11/4/2021	N/A	Positive	257.25	Not Detected	0
11/19/2021	N/A	Positive	2211.56	Not Detected	0

*Test Result did not Exceed Normal Cutoff Value (1 CK+ Cell and/or 2 CK- Cells)

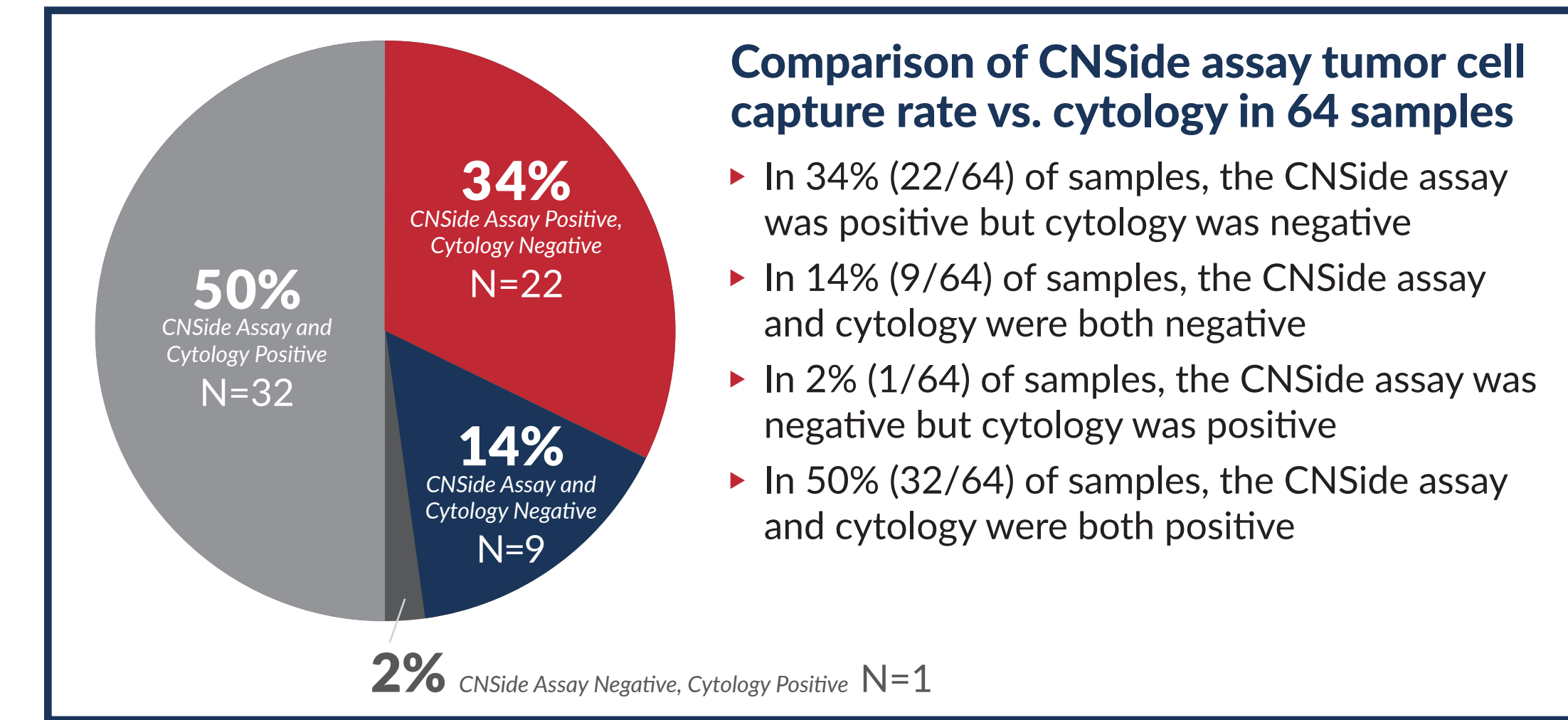
Patient 2			
Collection	Cytology Result	CNSide Result	CSF-TC/mL
1/26/2021	Positive	Positive	46.62
3/9/2021	Positive	Positive	0.10
3/23/2021	Positive	Positive	4.10
3/30/2021	Positive	Positive	12.40
4/13/2021	Positive	Positive	9.57
4/27/2021	Negative	Positive	0.33
5/11/2021	Positive	Positive	5.67
5/25/2021	Positive	Positive	5.25
6/8/2021	Negative	Positive	7.60
6/22/2021	Positive	Positive	29.88
7/6/2021	Negative	Positive	8.50
7/20/2021	Positive	Positive	5.17
8/3/2021	Positive	Positive	9.75
8/17/2021	Positive	Positive	1.00
9/28/2021	Negative	Positive	0.86
10/12/2021	Negative	Positive	0.38

Patient 3			
Collection	Cytology Result	CNSide Result	CSF-TC/mL
8/31/2021	Positive	Positive	1790.00
9/7/2021	Positive	Positive	17593.13

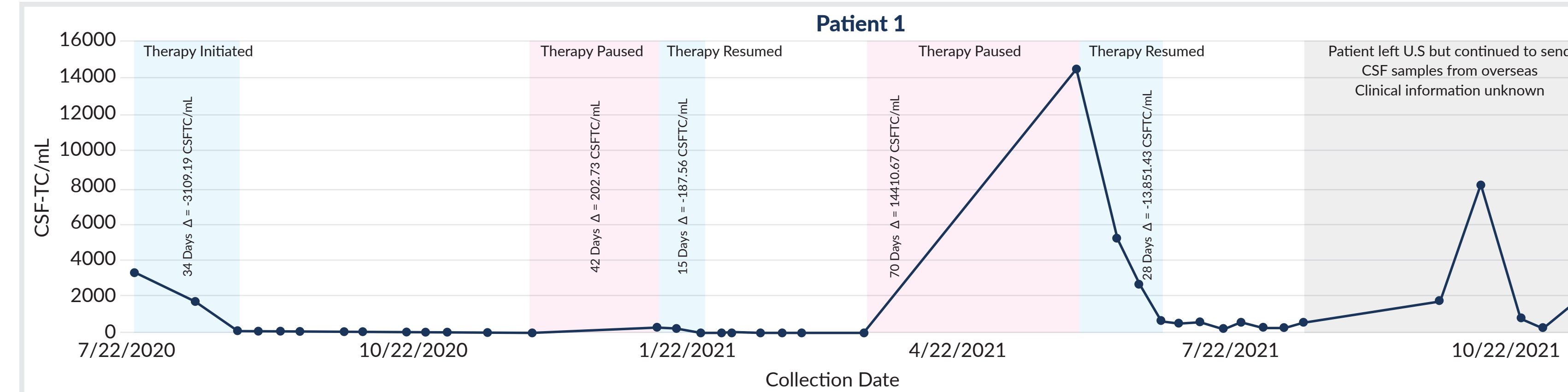
Patient 4			
Collection	Cytology Result	CNSide Result	CSF-TC/mL
2/24/2021	Positive	Positive	142.67
3/10/2021	Negative	Positive	1.29
3/17/2021	Positive	Negative	0
3/24/2021	Negative	Negative	0
4/21/2021	Negative	Positive	0.25
4/28/2021	Negative	Positive	0.13
5/5/2021	Negative	Negative	0
5/12/2021	Negative	Negative	0
6/2/2021	Negative	Negative	0
6/16/2021	Negative	Negative	0
6/30/2021	Negative	Negative	0
7/14/2021	Negative	Positive	0.13
7/28/2021	Negative	Negative	0

Patient 5			
Collection	Cytology Result	CNSide Result	CSF-TC/mL
8/4/2021	Negative	Positive	40.42
9/21/2021	Negative	Positive	17.08
10/13/2021	Negative	Positive	103.28

- Patient 1 - Breast cancer HER2+**
- CNSide assay HER2 FISH results informed the addition of IT Trastuzumab
 - Patient moved overseas in August 2021, expired in late 2021
- Patient 2 - Melanoma with multiple intracranial recurrences**
- LM was well controlled throughout treatment course
 - Patient went on hospice after parenchymal mass invaded optic chiasm, causing blindness
- Patient 3 - Esophageal cancer**
- CNSide assay HER2 FISH results informed the addition of IT Trastuzumab
 - Patient transferred providers, no treatment information following 9/7/21
- Patient 4 - Breast cancer ER/PR+**
- Diagnostic LP (2/24/21) - CNSide assay detected 1284 tumor cells; cytology was positive, but a differential count by pathologist found only 72 tumor cells
 - Patient responded well to IT chemo and her LM remained under control but she progressed with systemic disease and expired
- Patient 5 - Large cell neuroendocrine carcinoma**
- Diagnostic LP (8/4/21) - Cytology negative; the CNSide assay detected 194 tumor cells
 - Cytology consistently negative in this patient
 - Functional status declined and patient transitioned to hospice

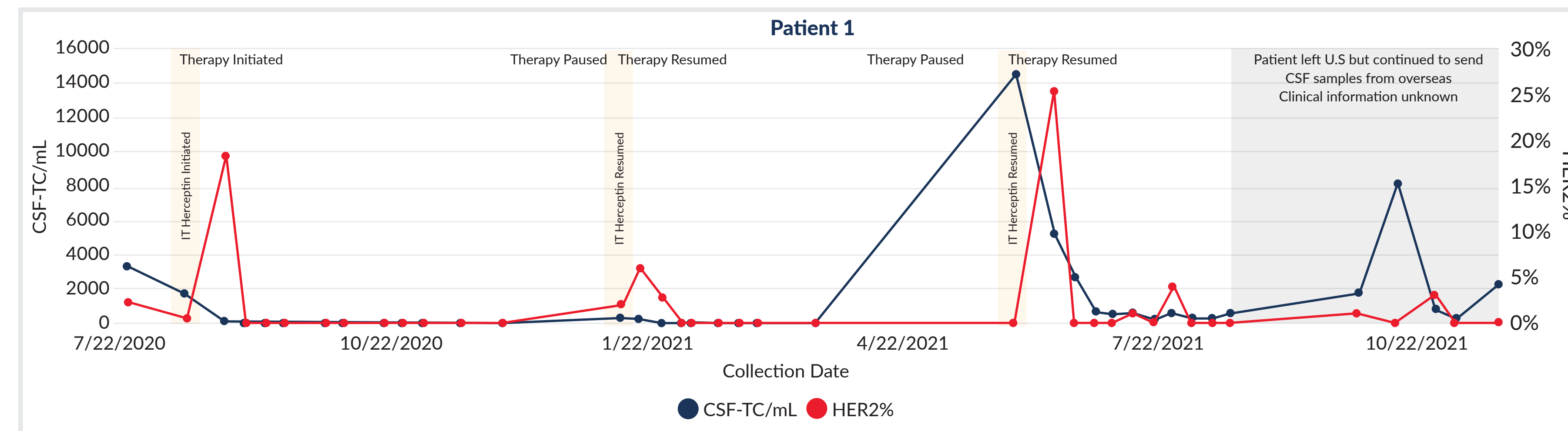


CSF-TCs Track Disease Status and Therapy Response



CSF tumor cell numbers detected by the CNSide assay correlated with treatment status

- 38 unique CSF specimens (Median=7, SD=3.36 mL)
- CSF-TC counts are normalized by volume
- LM directed treatment and cessation correlated with CSF tumor cell number



Percentage of HER2 amplified CSF-TC increases after start of therapy while total cell count declines

- HER2 amplification determined by FISH according to ASCO/CAP scoring criteria
- Equivocal results (so-called "HER2-low") were not counted as amplified