

Beyond Cytology – A Single Institution Experience Using CNSide™ for Diagnosing and Monitoring Treatment Response in Non-Small Cell Lung Cancer with Leptomeningeal Carcinomatosis (LMC)



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Background

- Leptomeningeal Carcinomatosis (LMC) is a complication that occurs in 3-9% of patients with Non-Small Cell Lung Cancer (NSCLC).
- Diagnosis of LMC occurs via Clinical Evaluation, Imaging and Cytology, which has limited sensitivity.
- When untreated, average survival for patients with LMC is 4-6 weeks.
- CNSide is a platform that detects tumor cells and actionable mutations in the CSF in patients with LMC
- We report a single institution experience using CNSide to diagnose and manage LMC in patients with NSCLC and show that patients with LMC treated with a targetable treatment can demonstrate survival exceeding 3 years.

Methods

CSF of 15 unique patients was collected via a Lumbar Puncture or Ommaya Reservoir. Frozen (6 unique patients) and Fresh samples (7 unique patients) were included. For 2 patients, both fresh and frozen samples were analyzed. Fresh CSF was analyzed for tumor cell number and actionable mutations by CNSide. Frozen samples were analyzed by NGS. CNSide allows for the analysis of both tumor cells and ctDNA from a single CSF sample collected in the same CEE-Sure™ tubes. CNSide captures cells with a 10-antibody capture cocktail combined with a microfluidic chamber and analyzes the ctDNA by NGS and/or single gene analysis (Switch Blocker™). For 3 patients, fresh serial CSF draws taken throughout treatment were analyzed for cell number and quantification of EGFR mutations. LMC negative was based on overall evaluation with 3 month follow up.

Patient Demographics

Patient Nr.	F/M	Age (yr)	Fresh/Frozen	LMC (+/-)	Clinical Findings	Survival (Days)	Status
1	F	55	Frozen	+	Asymmetric facial numbness	515	Expired
2	M	39	Frozen	+	Imbalance, Seizures, hydrocephalus	155	Expired
3	M	56	Frozen	+	Cranial Neuropathy, vision, gait, incontinence	449	Expired
4	M	63	Frozen	+	Imbalance, confusion	206	Expired
5	F	43	Frozen	+	Speech, anal numbness	37	Expired
6	F	63	Frozen & Fresh	+	Speech, light sensitivity, non-ambulatory	1568	Expired
7	M	57	Frozen	+	Non-ambulatory	1557	Alive
8	F	72	Frozen & Fresh	+	Deaf, imbalance	1011	Alive
9	F	61	Fresh	+	Vision changes, headaches	275	Alive
10	F	62	Fresh	+	Headaches	113	Expired
11	M	65	Fresh	+	Confusion, imbalance	102	Alive
12	M	67	Fresh	+	Diplopia, headaches, swallow dysfunction, facial numbness	18	Alive
13	F	67	Fresh	-	Facial numbness	NA	Alive
14	F	78	Fresh	-	Floater	NA	Alive
15	F	65	Fresh	-	Swallow dysfunction, numbness right side of face	NA	Alive

- The age and gender of patients was similarly distributed amongst LMC positive and LMC negative patients

CNSide is More Often Positive Compared to Cytology in LMC Positive Patients

Table 2. LMC Positive patients (Fresh samples)

Patient Nr.	# Draw	Cytology (Positive/Negative)	CNSide (Positive/Negative)
9	1 *	Negative	Positive
	2	Negative	Positive
	3	Negative	Positive
	4	Negative	Positive
12	1 *	Negative	Positive
8	1	Negative	Negative
	2	Negative	Positive
10	1 *	Negative	Positive
	2	Positive	Positive
	3	Positive	Positive
	4	Positive	Positive
11	1*	Positive	Positive
	2	Positive	Positive
	3	Positive	Positive
	4	Positive	Positive
6	1	Positive	Positive
	2	Positive	Positive

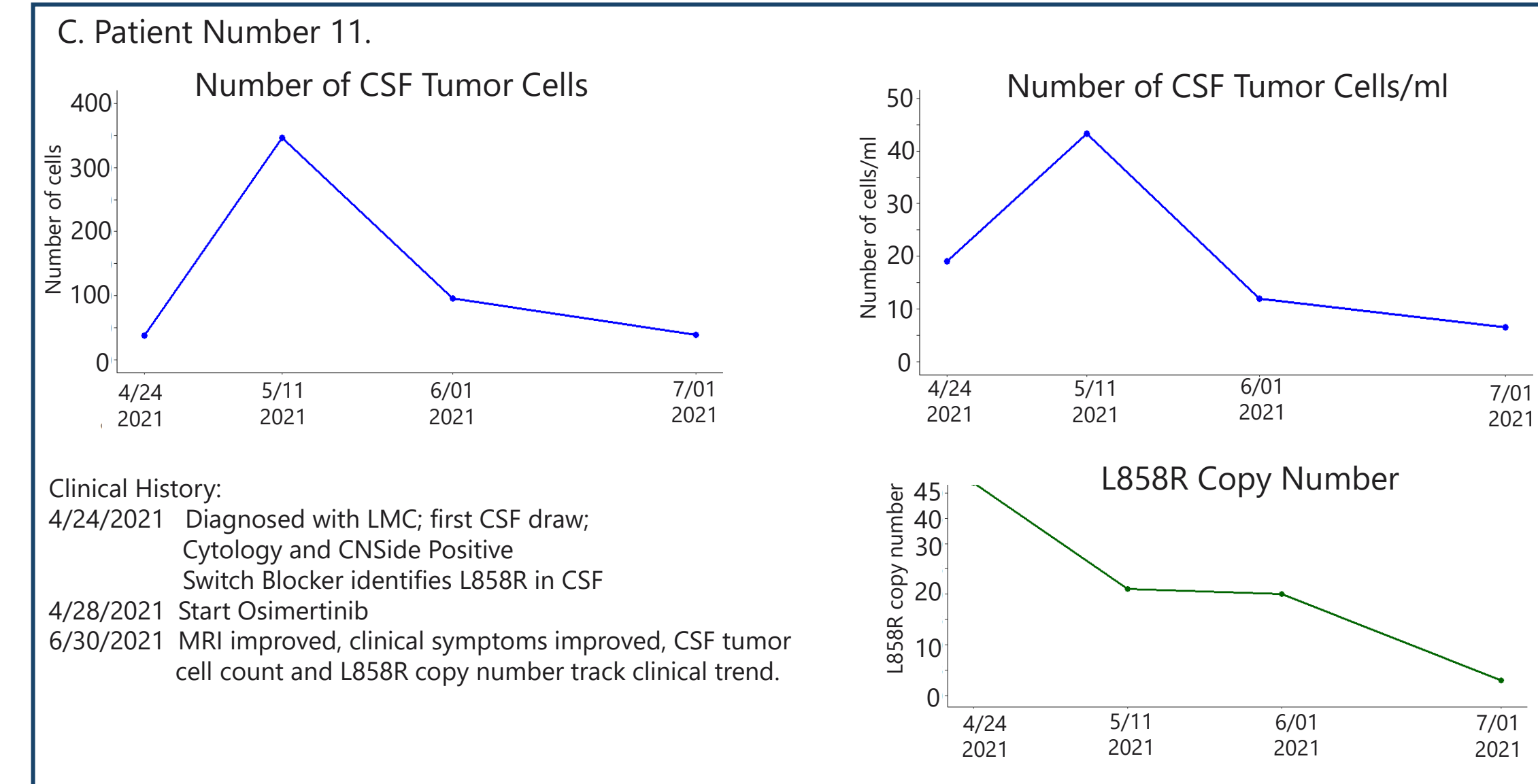
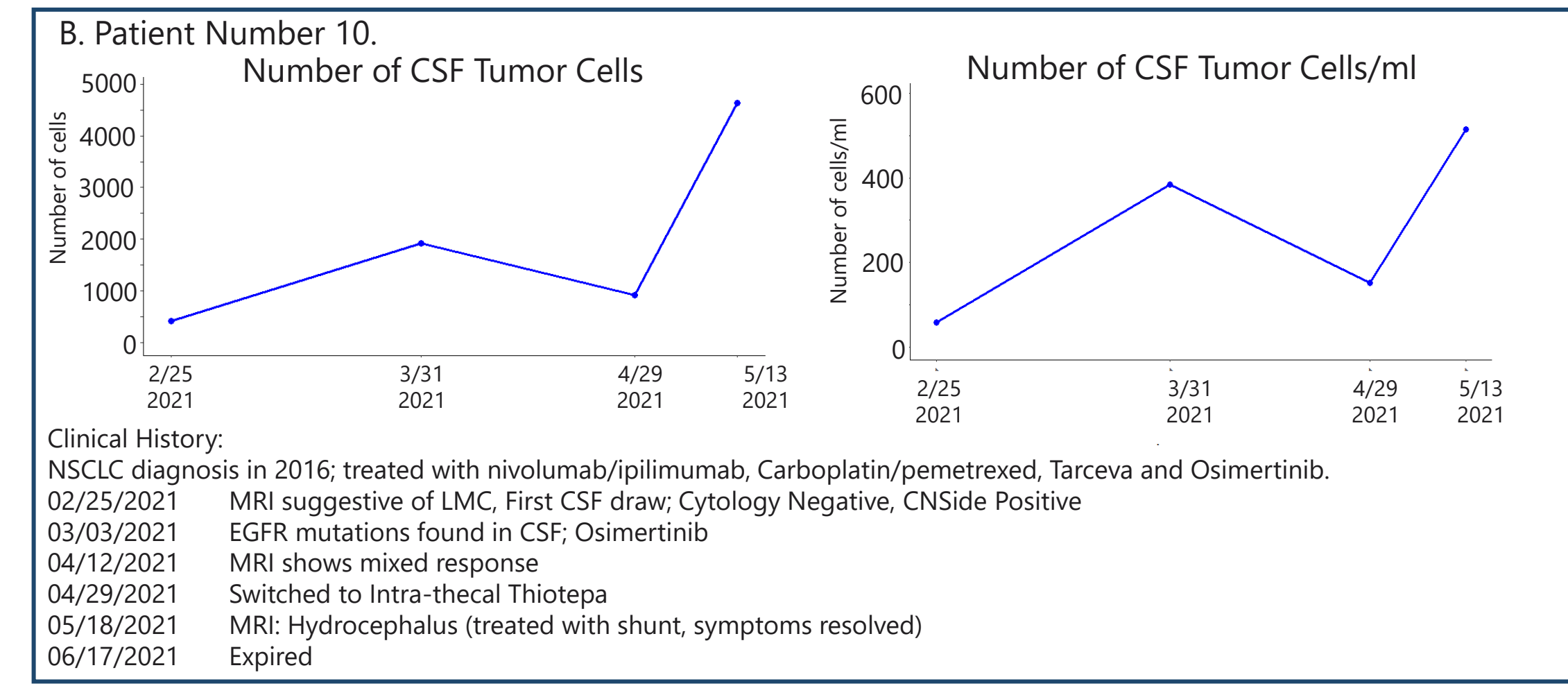
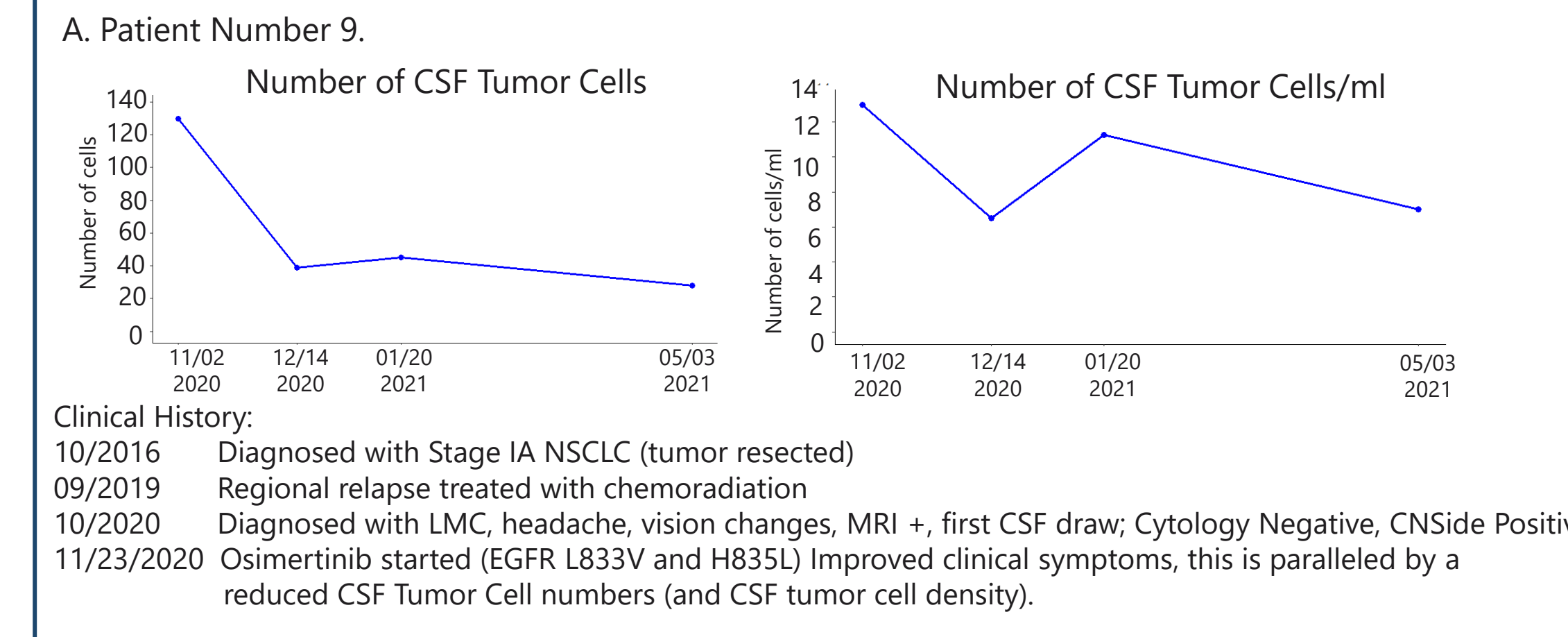
- Concordance between Cytology and CNSide is 59%. This likely due to differences in sensitivity in CSF tumor cell detection between the two platform.
- * = CSF collected at time of diagnosis.
- Conventional Cytology missed 3 out of 4 diagnosis.

Table 3. LMC Negative patients (Fresh Samples)

Patient Number	# Draw	Cytology (Positive/Negative)	CNSide (Positive/Negative)
13	1	Negative	Negative
	1	Negative	Negative
14	2	Negative	Negative
	3	Negative	Negative
15	1	Negative	Negative

- Cytology and CNSide did not detect cells in the CSF of LMC negative patients

CSF Tumor Cell Number Changes Measured by CNSide Tracks Clinical Response in Patients with LMC



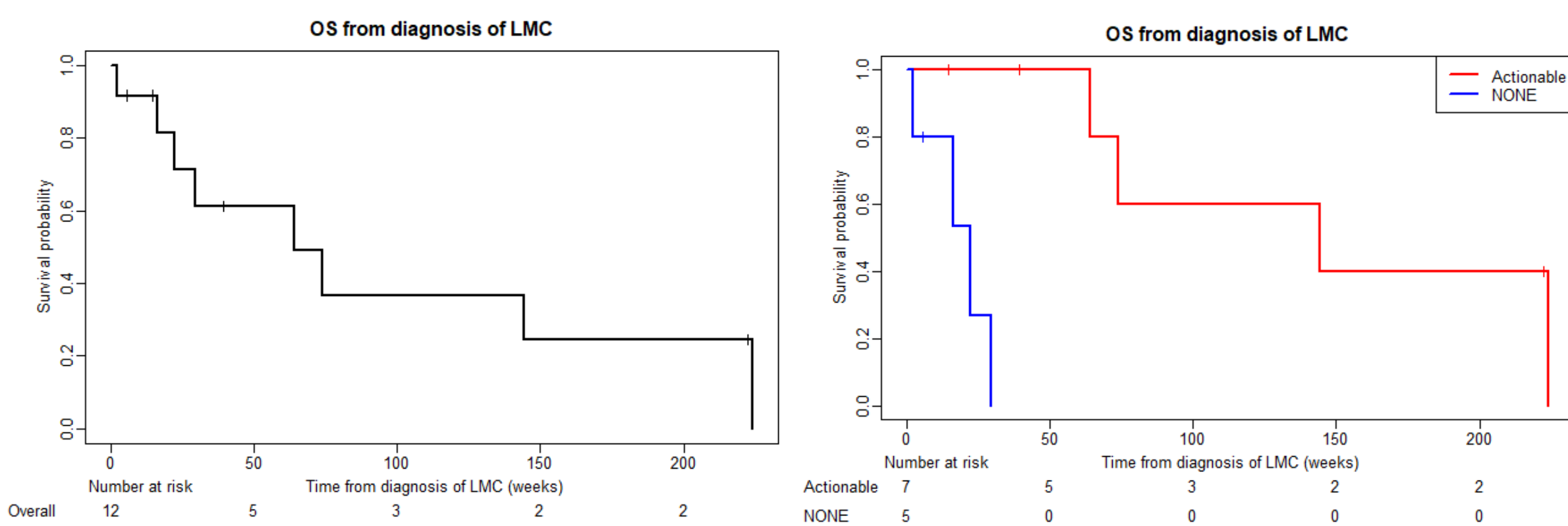
Mutations in CSF from Tissue or Blood in Matched Patients

Patient Number	Tissue/Blood	Mutations CSF
1	EGFR (Del19) *	None (Responded to Therapy)
2	EGFR (Exon 20)	EGFR (M766Q)
3	BRAF (600E) *	BRAF, PIK3CA and p53
4	No actionable mutations	NRAS
5	ALK	ALK (p.G1269A), (p.E1210K), (p.E1210K) and PIK3CA
6	EGFR*	EGFR (Del19, T790M, M766Q)
7	ALK*	None (Responded to Therapy)
8	ALK*	None (Responded to Therapy)
9	EGFR L833V and H835L *	None
10	EGFR	EGFR (L858R, T790M)
11	EGFR (L858R) *	EGFR (L858R)
12	No actionable mutations	None
13	EGFR	None (LMC Negative)
14	EGFR	EGFR (LMC Negative)
15	EGFR (L858R, T790M)	None (LMC Negative)

- Analysis of Tissue, Blood and CSF were not done at the same time
- * Patients with actionable targeted therapy

Survival in LMC Positive Patients From Time of Diagnosis

- A. Median survival for the whole group is 64 weeks
- B. Median survival for patients treated with actionable targeted therapy is 144 weeks and 22 weeks for those without.



Conclusions

- Quantitative measurement of CSF tumor cells LMC clinical disease course
- CNSide appears to be more sensitive than cytology
- Survival of patients with LMC can be prolonged if an actionable target is identified
- Larger controlled clinical trials are needed to better establish the clinical utility of CNSide in diagnosing and managing LMC

