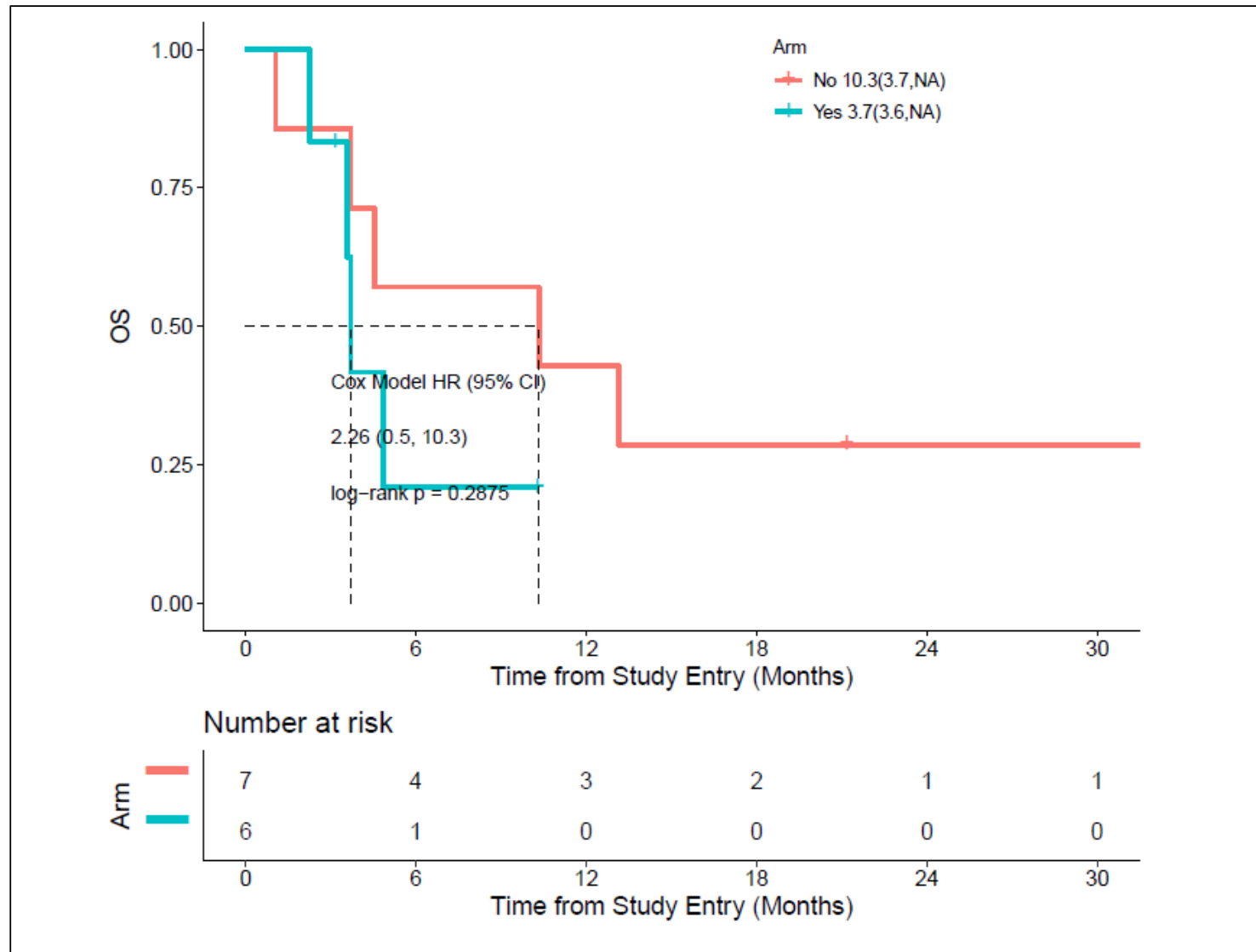
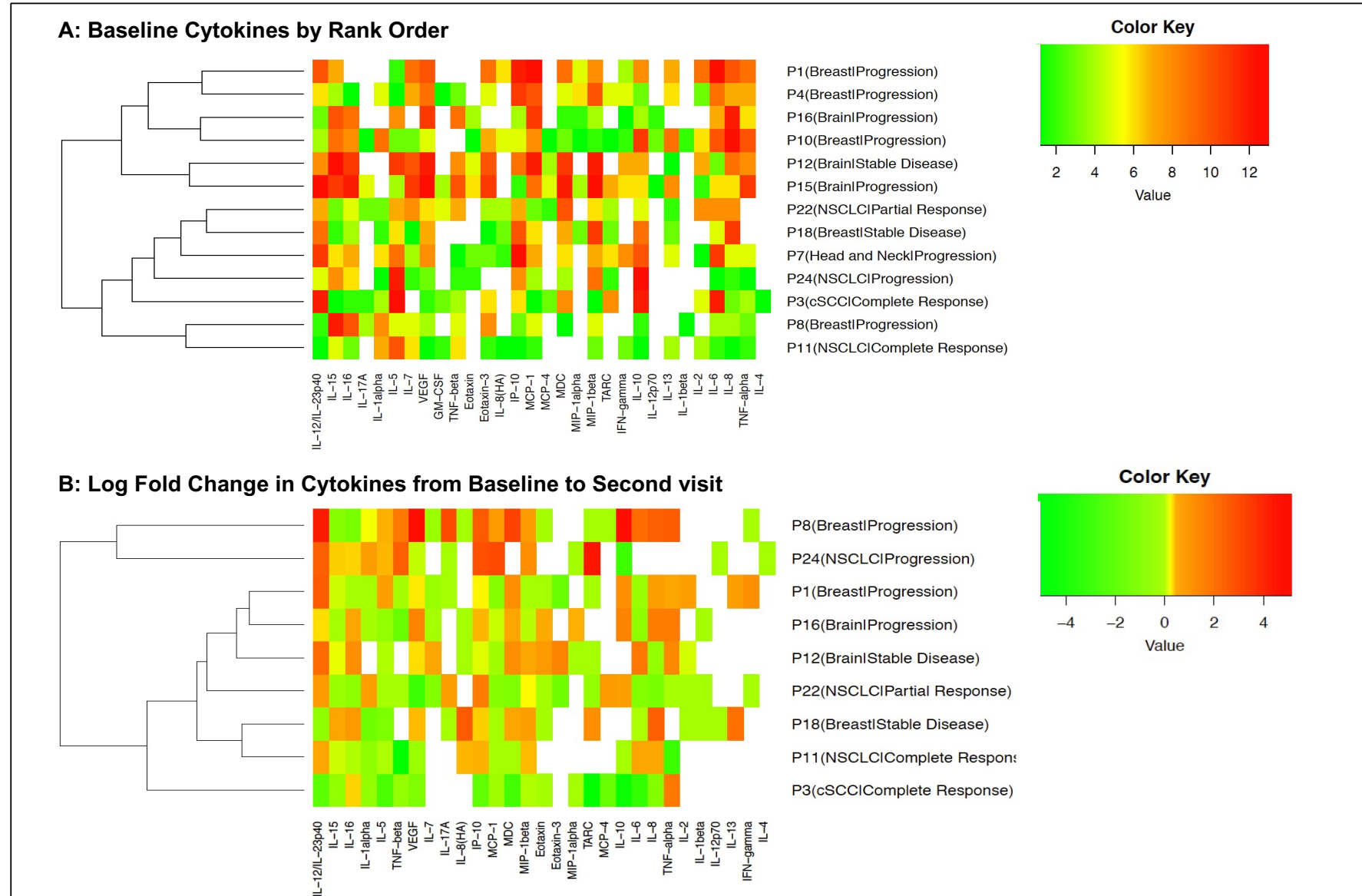


## Supplemental Figure 1: Association between Cytologic Leptomeningeal Metastasis and Overall Survival in Patients Treated with Pembrolizumab



## Supplemental Figure 2: CSF multiplex cytokine analysis



**Supplemental Table 1: Determination of CNS Response to Leptomeningeal Metastasis**

Clinical Response*	Radiologic Response by RECIST 1.1**	Cytologic Response***	Overall CNS Response Determination
No neurologic symptoms	None detectable	None detectable	Complete Response
Improved	Stable	Stable	Partial Response
Stable	Improved	Improved	Partial Response
Stable	Stable	Stable	Stable
Improved	Progression	Progression	Progression
Stable	Progression	Progression	Progression
Progression	Improved or Stable	Improved or Stable	Progression

\* Clinical response was defined as an improvement in objective neurologic signs or symptoms attributable to LMM by the treating investigator.

\*\* Radiologic response was defined as a reduction in size of a measurable lesion on a contrast-enhanced MRI scan of the brain. Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 was the primary radiologic response criteria used, however Immune-related Response Criteria was also used.

\*\*\* Cytologic response was defined as a negative CSF cytology result in 2 consecutive samples, in patients who have initial positive cytology prior to treatment

**Supplemental Table 2: Distribution of Patients by Highest Grade Adverse Event by Event For All Reported Adverse Events without Regard to Attribution**

	All Grades (n, %)	Grade 1 (n, %)	Grade 2 (n, %)	Grade 3+ (n, %)
Overall Highest Grade	13 (100)	1 (7.7)	2 (15.4)	10 (76.9)
Dyspnea	6(46.2)	2(15.4)	4(30.8)	0 (0)
Fatigue	6(46.2)	1(7.7)	2(15.4)	3(23.1)
Generalized Muscle Weakness	6(46.2)	1(7.7)	2(15.4)	3(23.1)
Back Pain	5(38.5)	2(15.4)	1(7.7)	2(15.4)
Headache	5(38.5)	2(15.4)	2(15.4)	1(7.7)
Nausea	5(38.5)	1(7.7)	4(30.8)	0 (0)
Pain In Extremity	5(38.5)	2(15.4)	2(15.4)	1(7.7)
Pruritus	5(38.5)	5(38.5)	0 (0)	0 (0)
Anorexia	3(23.1)	0 (0)	2(15.4)	1(7.7)
Arthralgia	3(23.1)	3(23.1)	0 (0)	0 (0)
Confusion	3(23.1)	0 (0)	0 (0)	3(23.1)
Constipation	3(23.1)	2(15.4)	1(7.7)	0 (0)
Dry Skin	3(23.1)	3(23.1)	0 (0)	0 (0)
Edema Limbs	3(23.1)	2(15.4)	1(7.7)	0 (0)
Ataxia	2(15.4)	1(7.7)	1(7.7)	0 (0)
Diarrhea	2(15.4)	2(15.4)	0 (0)	0 (0)
Dry Mouth	2(15.4)	2(15.4)	0 (0)	0 (0)
Eye Disorders-Other	2(15.4)	2(15.4)	0 (0)	0 (0)
Joint Range Of Motion Decreased	2(15.4)	1(7.7)	1(7.7)	0 (0)
Memory Impairment	2(15.4)	1(7.7)	0 (0)	1(7.7)
Musculoskeletal Disorder	2(15.4)	2(15.4)	0 (0)	0 (0)
Neck Pain	2(15.4)	0 (0)	2(15.4)	0 (0)
Paresthesia	2(15.4)	0 (0)	2(15.4)	0 (0)
Rash Maculo-Papular	2(15.4)	2(15.4)	0 (0)	0 (0)
Urinary Incontinence	2(15.4)	2(15.4)	0 (0)	0 (0)
Urinary Tract Infection	2(15.4)	0 (0)	1(7.7)	1(7.7)
Weight Loss	2(15.4)	2(15.4)	0 (0)	0 (0)
Abdominal Pain	1(7.7)	1(7.7)	0 (0)	0 (0)
Blurred Vision	1(7.7)	0 (0)	1(7.7)	0 (0)
Bone Pain	1(7.7)	0 (0)	0 (0)	1(7.7)
Cerebrospinal Fluid Leakage	1(7.7)	0 (0)	1(7.7)	0 (0)
Cognitive Disturbance	1(7.7)	0 (0)	0 (0)	1(7.7)
Concentration Impairment	1(7.7)	0 (0)	0 (0)	1(7.7)
Creatinine Increased	1(7.7)	0 (0)	1(7.7)	0 (0)
Dehydration	1(7.7)	0 (0)	1(7.7)	0 (0)
Delusions	1(7.7)	0 (0)	1(7.7)	0 (0)
Vomiting	1(7.7)	1(7.7)	0 (0)	0 (0)
Depressed Level Of Consciousness	1(7.7)	0 (0)	1(7.7)	0 (0)
Dizziness	1(7.7)	1(7.7)	0 (0)	0 (0)
Dry Eye	1(7.7)	1(7.7)	0 (0)	0 (0)
Dysarthria	1(7.7)	1(7.7)	0 (0)	0 (0)
Dyspepsia	1(7.7)	1(7.7)	0 (0)	0 (0)
Dysphagia	1(7.7)	0 (0)	1(7.7)	0 (0)
Dysphasia	1(7.7)	0 (0)	1(7.7)	0 (0)
Edema Cerebral	1(7.7)	0 (0)	0 (0)	1(7.7)
Edema Face	1(7.7)	1(7.7)	0 (0)	0 (0)
Epistaxis	1(7.7)	1(7.7)	0 (0)	0 (0)
Fever	1(7.7)	0 (0)	1(7.7)	0 (0)
General Disorders	1(7.7)	1(7.7)	0 (0)	0 (0)
Hoarseness	1(7.7)	1(7.7)	0 (0)	0 (0)
Hypotension	1(7.7)	0 (0)	1(7.7)	0 (0)
Hypothyroidism	1(7.7)	1(7.7)	0 (0)	0 (0)
Infusion Related Reaction	1(7.7)	1(7.7)	0 (0)	0 (0)
Insomnia	1(7.7)	1(7.7)	0 (0)	0 (0)
Lethargy	1(7.7)	0 (0)	1(7.7)	0 (0)
Muscle Weakness Lower Limb	1(7.7)	0 (0)	0 (0)	1(7.7)
Myalgia	1(7.7)	1(7.7)	0 (0)	0 (0)
Nasal Congestion	1(7.7)	1(7.7)	0 (0)	0 (0)
Neoplasia Benign-Malignant-Unspecified-Other	1(7.7)	1(7.7)	0 (0)	0 (0)
Non-Cardiac Chest Pain	1(7.7)	1(7.7)	0 (0)	0 (0)
Pelvic Pain	1(7.7)	0 (0)	0 (0)	1(7.7)
Peripheral Motor Neuropathy	1(7.7)	0 (0)	0 (0)	1(7.7)
Peripheral Sensory Neuropathy	1(7.7)	1(7.7)	0 (0)	0 (0)
Pneumonitis	1(7.7)	0 (0)	1(7.7)	0 (0)
Productive Cough	1(7.7)	0 (0)	1(7.7)	0 (0)
Seizure	1(7.7)	1(7.7)	0 (0)	0 (0)
Skin And Subcutaneous Tissue Disorders-Other	1(7.7)	1(7.7)	0 (0)	0 (0)
Surgical And Medical Procedures-Other	1(7.7)	0 (0)	1(7.7)	0 (0)
Thromboembolic Event	1(7.7)	0 (0)	0 (0)	1(7.7)
Tremor	1(7.7)	1(7.7)	0 (0)	0 (0)
Urinary Retention	1(7.7)	0 (0)	1(7.7)	0 (0)
Urinary Tract Obstruction	1(7.7)	0 (0)	0 (0)	1(7.7)

**Supplemental Table 3: Assay sensitivity for detecting LMM in cerebrospinal fluid.**

Timepoint of Assessment	Patients with Detectable Leptomeningeal Disease by CSF Assay (n)	
	CSF Aneuploidy	CSF Cytopathology
Baseline, Pre-Pembrolizumab (n = 13)	11	6
Post cycle 2 Pembrolizumab (n = 10)	7	5
Post cycle 2 Pembrolizumab (n = 4)	3	2
Assay Sensitivity* (95% CI)	84.6% (54.6-8.1%)	53.9% (25.1-80.8%)