



Supplementary Materials for

Neural Stem Cell Engraftment and Myelination in the Human Brain

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The PDF file includes:

Table S1. Inclusion criteria.

Table S2. Schedule of major procedures during screening, surgery, and posttransplant follow-up in the PMD phase 1 clinical study.

Table S3. Brain volumes (cm³) of PMD subjects at baseline and time points in months.

Fig. S1. Structure of mutant PLP1 protein in study subjects.

Supplementary Materials**Table S1. Inclusion Criteria**

Male subjects 6 months to 5 years of age
Molecular genetic confirmation of mutation in the <i>PLP1</i> gene
MRI appearance of reduced white matter development consistent with PMD as interpreted by a qualified neuro-radiologist
Confirmed clinical diagnosis of form of PMD by either a pediatric neurologist or metabolic/genetic specialist. <i>Connatal</i> PMD will be distinguished from the <i>Classic</i> form of PMD using the following criteria: <ul style="list-style-type: none"> a) Nystagmus must be present by 1 month of age. b) Onset of neurological signs and symptoms (hypotonia with significant head lag) consistent with PMD prior to the post-natal age of 6 months. c) No attainment of gross motor milestones by post-natal age of 6 months.
Compliance with follow-up visits and diagnostic evaluations.
Family able to provide informed consent

Table S2. Schedule of major procedures during screening, surgery, and posttransplant follow-up in the PMD phase 1 clinical study.

Assessment	Screen	HuCNS-SC Cell Transplantation			F/U Day		F/U Month				
	Day -90 to -30	Pre-Tx Day -3	Surgery Day 0	Post-Tx Days 1-3	7, 14	28	2	3, 5	6, 7, 8, 9	10	12
Visit #	1	2	2	2	3, 4	5	6	7 --	8 -- -- 9	10	11
Informed Consent	x										
HLA tissue type	x										
Medical & Surgical History	x										
Physical exam, vital signs	x	x	x	x	x	x	x	x	x	x	x
Concomitant medications	x	x	x	x	x	x	x	x	x	x	x
Adverse Events		x	x	x	x	x	x	x	x	x	x
Neurologist Exam (with	x	x			x ¹	x	x	x	x	x	x
Neurosurgeon Exam	x	x	x	x	x	x	x	x	x	x	x
Transplantation Physician	x	x	x	x	x	x	x	x	x	x	x
Anesthesiologist Exam	x	x	x								
Ophthalmology Exam	x							x			x
HuCNS-SC Cell			x								
Tacrolimus		x	x	x	x	x	x	x	x ²		
MMF immunosuppression		x	x	x	x	x ³					
SMZ-TMP Prophylactic		x	x	x	x	x		x	x ²		
Dexamethasone		x	x	x	x ⁴						
Hematology, Chemistry, LFT	x	x			x ⁵	x	x	x	x	x	x
Virology (CMV, EBV, Hepatitis)	x										
Coagulation	x	x									
Varicella titer	x										
HIV	x										
Tacrolimus level		x	x	x	x	x	x	x	x ²		
MMF levels			x								
Urinalysis	x					x	x	x	x	x	x
Chest X-ray	x							x	x		x
12-lead ECG	x							x	x		x
Bayley-III	x								x		x
Callier Azusa G-Scale	x							x	x	x	x
WeeFIM	x							x	x		x
CHQ-PF50	x							x	x		x
Head CT Scan			x				x ¹¹			x ¹¹	
Brain MRI ⁶	x ¹²	x ⁷	x	x ⁸				x	x		x
Proton MR Spectroscopy	x							x	x		x
Seizure Frequency	x	x	x	x	x	x	x	x	x	x	x
Electroencephalogram (EEG)	x								x ⁹		x
Somatosensory-Evoked	x								x ¹⁰		x

1. Neurologist Exam on Day 14 (Visit #4) only.

2. Tacrolimus immunosuppression and prophylactic antibiotic ends on Month 9 (Visit #8). In addition to the Visits in Table 1, blood samples for immunosuppression levels will be also be obtained at

Months 4, 5, 7, and 8 in the subject's local community and the results conveyed to the transplantation physician.

3. MMF immunosuppression ends on Day 28 (Visit #5).
4. Dexamethasone may be administered for 5 to 10 days posttransplant.
5. Day 14 only (Visit #4).
6. MRI to include standard sequences (with and without contrast), Diffusion imaging, MTI, and cerebral volume.
- 7 Pre-Tx MRI for intraoperative guidance and localization: standard MRI stereotactic sequences.
8. Post-Tx MRI (non-contrast) with standard sequences only.
9. Month 6 (Visit #8) only.
10. Month 9 (Visit #9) only.
11. Head CT to be performed at Month 2 (Visit # 6) and Month 10 (Visit #10) after withdrawal of MMF at Day 28 and withdrawal of tacrolimus at Month 9, respectively. The PI may elect to obtain a Bran MRI during Visit #6 and Visit #10 based on the results of the Head CT examination.

Table S3. Brain volumes (cm³) of PMD subjects at baseline and time points in months

	Months					
	0	3	6	9	10	12
Subject 1						
GMV	501	524	n/d	542	543	549
WMV	360	374	n/d	397	393	399
Brain	861	898	n/d	939	935	948
CSFv	26	27	n/d	28	28	29
Subject 2						
GMV	565	577	585	588	582	589
WMV	423	427	413	397	417	385
Brain	988	1003	998	986	999	974
CSFv	22	21	21	21	22	22
Subject 3						
GMV	507	514	544	565	567	579
WMV	351	385	396	417	418	419
Brain	858	899	940	982	985	997
CSFv	36	35	34	42	46	47
GMV	507	514	544	565	567	579
Subject 4						
GMV	696	701	703	703	703	n/d
WMV	496	504	502	502	502	n/d
Brain	1192	1205	1205	1205	1205	n/d
CSFv	37	37	38	39	40	n/d

GMV: Grey matter volume; WMV: White matter volume; CSFv: Ventricular CSF volume

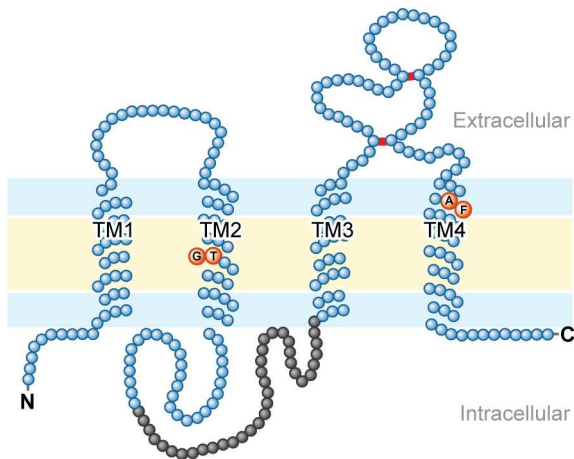


Figure S1. Structure of mutant PLP1 proteins in study subjects. An illustration of the structural domains of the PLP1 protein (light blue circles indicated amino acids) and DM20 (gray circles), including its four transmembrane spanning domains. Mutated amino acids in Subject 1 and 3 in TM2, and 2 and 4 in TM4 are indicated by red circles.