APPENDIX: PBTC-056: A Phase I study of the ADAM-10 inhibitor, INCB7839 in children with recurrent/progressive high-grade gliomas to target microenvironmental neuroligin-3

Standard Brain MR Imaging:

The specific acquisition parameters, the sequence of imaging acquisition, and the plane of imaging are all required as stated in these protocols. Additionally, individual patients must be consistently imaged at the same field strength as their baseline registration scan. Additional sequences that the site wants can be added prior to injection or after the 3DT1 post but the time between injection and the 3DT1 post must be the same for each scan.

All MRI scans for every patient for the duration of the study are to be transferred to the PBTC Operations, Biostatistics and Data and Management Core at St. Jude Children's Research Hospital and then to the PBTC Neuroimaging Center.

Any questions, please contact Tina Young Poussaint, MD, FACR, Department of Radiology, Boston Children's Hospital, tina.poussaint@childrens.harvard.edu, 617-355-6450.

3T Protocol:

	Ax FLAIR	Ax DWI	3D T1 Pre	Ax T2		3D T1 Post
Sequence	TSE/FSE[b] – (turbo dark fluid)	EPI	MPRAGE[d]	TSE/FSE[b]		SPACE/Cube/VISTA[c]
Plane	Axial	Axial	Axial/Sagittal	Axial		Axial/Sagittal
Mode	2D	2D	3D	2D		3D
TR [ms]	>6000	>5000	2100[e]	>2500		2100[e]
TE [ms]	100-140	Min	Min	80-120		Min
TI [ms]	2500		1100[f]			1100[f]
Flip Angle	90/≥160	90/180	10-15	90/≥160		10-15
Frequency	≥256	128	256	≥256		256
Phase	≥256	128	256	≥256		256
NEX	≥1	≥1	≥1	≥1		≥1
Frequency Direction	A/P	R/L	A/P	A/P		A/P
FOV[g]	240mm	240mm	256mm (for 1mm isotropic)	240mm		256mm (for 1mm isotropic)
Slice Thickness	≤4mm	≤4mm	1mm[g]	≤4mm		1mm[g]
Gap/Spacing	0	0	0	0		0
Diffusion Options		*b* = 0 and 1000 s/mm^2 ≥3 directions				
Parallel Imaging	Up to 2x	Up to 2x	Up to 2x	Up to 2x		Up to 2x
Scan Time (Approx)	4-5 min	3-5 min	5-8 min	3-5 min		5-8 min

Contrast Injection [a]

[a] 0.1 mmol/kg or up to 20cc (single, full dose) of MR contrast.

[b] TSE = turbo spin echo (Siemens & Philips) is equivalent to FSE (fast spin echo; GE, Hitachi, Toshiba)

[c] SPACE= Sampling Perfection with Application optimized Contrasts using different flip angle Evolution (Siemens) is equivalent to Cube (GE) and VISTA=Volume Isotropic Turbo spine echo Acquisition (Phillips)

[d] MPRAGE = magnetization prepared rapid gradient-echo (Siemens & Hitachi) is equivalent to the inversion recovery SPGR (IR-SPGR or Fast SPGR with inversion activated; GE), 3D turbo field echo (TFE; Philips), or 3D fast field echo (3D Fast FE; Toshiba).

[e] For Siemens and Hitachi scanners. GE, Philips, and Toshiba scanners should use a TR = 5-15ms for similar contrast.

[f] For Siemens and Hitachi scanners. GE, Philips, and Toshiba scanners should use a TI = 400-450ms for similar contrast.

[g] FOV and matrix size should be chosen to keep resolution at 1mm isotropic voxel size. Note that all voxel measurements should be equal in x, y, and z dimensions. *Smaller FOV (200mm) may be required for smaller head sizes (young child vs adolescent)*

Acronyms:

Ax = Axial; ADC = apparent diffusion coefficient. FLAIR = fluid attenuated inversion recovery; DWI = diffusion-weighted imaging; 3D = three dimensional; TSE = turbo spin echo; EPI = echo planar imaging; MPRAGE = magnetization prepared rapid gradient-echo; A/P = anterior to posterior; R/L = right to left; NEX = number of excitations or averages; FOV = field of view; SPACE= Sampling Perfection with Application optimized Contrasts using different flip angle Evolution; VISTA=Volume Isotropic Turbo spine echo Acquisition.

1.5T Protocol:

	Ax FLAIR	Ax DWI	3D T1 Pre	Ax T2		3D T1 Post
Sequence	TSE/FSE[b] – (turbo dark fluid)	EPI	MPRAGE[d]	TSE/FSE[b]		SPACE/Cube/VISTA[c]
Plane	Axial	Axial	Sagittal/Axial	Axial		Sagittal/Axial
Mode	2D	2D	3D	2D		3D
TR [ms]	>6000	>5000	2100[e]	>3500		2100[e]
TE [ms]	100-140	Min	Min	100-120		Min
TI [ms]	2200		1100[f]			1100[f]
Flip Angle	90/≥160	90/180	10-15	90/180		10-15
Frequency	≥256	128	≥172	≥256		≥172
Phase	≥256	128	≥172	≥256		≥172
NEX	≥1	≥1	≥1	≥1		≥1
Frequency Direction	A/P	R/L	A/P	A/P		A/P
FOV	240mm	240mm	256mm (for ≤1.5mm isotropic)	240mm		256mm (for ≤1.5mm isotropic)[h]
Slice Thickness	≤4mm	≤4mm	≤1.5mm	≤4mm		≤1.5mm
Gap/Spacing	0	0	0	0		0
Diffusion Options[g]		*b* = 0 and 1000 s/mm^2 ≥ 3 directions				
Parallel Imaging	Up to 2x	Up to 2x	Up to 2x	Up to 2x		Up to 2x
Scan Time (Approx)	4-5 min	3-5 min	5-8 min	3-5 min		5-8 min

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[f] For Siemens and Hitachi scanners. GE, Philips, and Toshiba scanners should use a TI = 400-450ms for similar contrast.

[g] Older model MR scanners that are not capable of >2 *b*-values should use *b* = 0 and 1000 s/mm^2.

[h] FOV and matrix size should be chosen to keep resolution *less than* 1.5mm isotropic voxel size. Note that all voxel measurements should be equal in x, y, and z dimensions. *Smaller FOV(200m) may be required for smaller head sizes (young child vs adolescent).*

Acronyms:
Ax = Axial; ADC = apparent diffusion coefficient. FLAIR = fluid attenuated inversion recovery; DWI = diffusion-weighted imaging; 3D = three dimensional; TSE = turbo spin echo; EPI = echo planar imaging; MPRAGE = magnetization prepared rapid gradient-echo; A/P = anterior to posterior; R/L = right to left; NEX = number of excitations or averages; FOV = field of view; SPACE= Sampling Perfection with Application optimized Contrasts using different flip angle Evolution; VISTA=Volume Isotropic Turbo spine echo Acquisition