**APPENDIX: PBTC-049: A Phase I study of Savolitinib in Recurrent, Progressive or Refractory Primary CNS Tumors**

**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 | **Contrast Injection a** | 3D T1 Post |
| Sequence | TSE/FSEb – (turbo dark fluid) | EPI | MPRAGEd | TSE/FSEb | SPACE/Cube/VISTAc |
|  |  |  |  |  |  |
| Plane | Axial | Axial | Axial/Sagittal | Axial | Axial/Sagittal |
| Mode | 2D | 2D | 3D | 2D | 3D |
| TR [ms] | >6000 | >5000 | 2100e | >2500 | 2100e |
| TE [ms] | 100-140 | Min | Min | 80-120 | Min |
| TI [ms] | 2500 |  | 1100f |  | 1100f |
| 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 |
| FOVg | 240mm | 240mm | 256mm (for 1mm isotropic) | 240mm | 256mm (for 1mm isotropic) |
| Slice Thickness | ≤4mm | ≤4mm | 1mmg | ≤4mm | 1mmg |
| Gap/Spacing | 0 | 0 | 0 | 0 | 0 |
| Diffusion Options |  | *b* = 0 and 1000 s/mm2 |  |  |  |
| 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 |

a0.1 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 | **Contrast Injection a** |  | 3D T1 Post |
| Sequence | TSE/FSEb – (turbo dark fluid) | EPI | MPRAGEd | TSE/FSEb |  | SPACE/Cube/VISTAc |
|  |  |  |  |  |  |  |
| Plane | Axial | Axial | Sagittal/Axial | Axial |  | Sagittal/Axial |
| Mode | 2D | 2D | 3D | 2D |  | 3D |
| TR [ms] | >6000 | >5000 | 2100e | >3500 |  | 2100e |
| TE [ms] | 100-140 | Min | Min | 100-120 |  | Min |
| TI [ms] | 2200 |  | 1100f |  |  | 1100f |
| 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 Optionsg |  | *b* = 0 and 1000 s/mm2 |  |  |  |  |
| 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 |

a0.1 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)

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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 Older model MR scanners that are not capable of >2 *b*-values should use *b* = 0 and 1000 s/mm2.

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