

Table 6: PBTC Protocols [001 – 009]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-001	A Pilot Study of Systemic and Intrathecal Chemotherapy followed by Conformal Radiation for Infants with Embryonal Intracranial Central Nervous System Tumors	None	Study completed	No correlative objective. Estimate PFS, pattern of failure. Central review of MRI scan at end of study
PBTC-002	A Phase I Study of SU5416 in Pediatric Patients With Recurrent or Progressive Poor Prognosis Brain Tumors	<u>Stratum 1</u> : Patients not on enzyme-inducing anticonvulsant drugs <u>Stratum 2</u> : Patients receiving enzyme-inducing anticonvulsant drugs	Study completed	To identify the signal characteristics and biologic correlates of tumors after SU5416 treatment.
PBTC-003	A Phase I Trial of Escalating Oral Doses of SCH 66336 in Pediatric Patients with Refractory or Recurrent Brain Tumors	None	Study completed	No correlative objective. MRI for response only. No central review.
PBTC-004	A Phase I Study of Intrathecal Spartaject™-Busulfan in Children with Neoplastic Meningitis	None	Study completed	No correlative objective. MRI for response only with central review
PBTC-005	A Phase I Trial of Temozolomide and O ⁶ -Benzylguanine in Pediatric Patients with Recurrent Brain Tumors	<u>Stratum 1</u> : patients previously not treated with RT or only focal RT <u>Stratum 2</u> : patients with prior craniospinal irradiation or myeloblastic therapy.	Study completed	No correlative objective. MRI for response only with central review
PBTC-006	A Phase I/II Trial of STI571 in Children with Newly Diagnosed Poor Prognosis Brainstem Gliomas and Recurrent Intracranial Malignant Gliomas	<u>Stratum 1</u> : newly diagnosed localized brainstem tumors <u>Stratum 2A</u> : recurrent intracranial malignant gliomas - not using EIACD <u>Stratum 2B</u> : recurrent intracranial malignant gliomas - using EIACD	Study completed	To develop exploratory data concerning surrogate endpoints of therapeutic activity, using physiological neuroimaging studies and correlative biological studies
PBTC-007	A Phase I/II Trial of ZD1839 (Iressa™) and Radiation in Pediatric Patients Newly Diagnosed with Brain Stem Tumors or Incompletely Resected Supratentorial Malignant Gliomas with Phase II Limited to Brain Stem Tumors	<u>Stratum 1</u> : Newly diagnosed intrinsic brain stem glioma or incompletely resected supratentorial malignant gliomas not receiving enzyme-inducing anti-convulsant drugs <u>Stratum 2</u> : Incompletely resected supratentorial malignant gliomas receiving enzyme-inducing anti-convulsant drugs	Study completed	To compare hemodynamic MR parameters to metabolic FDG-PET scanning and correlate both with clinical response or progression in this population
PBTC-009	A Phase I Trial of GLIADEL® and O ⁶ -Benzylguanine in Pediatric Patients with Recurrent Malignant Gliomas	None	Study completed	MRI / MRS / MR perfusion & diffusion for assessment of response and toxicity

*If neutropenia is the dose limiting toxicity, additional patients will be accrued allowing the use of G-CSF to establish whether higher doses of temozolomide can be administered with this form of hematological support (Stratum 1b &/or 2b)

Table 6: PBTC Protocols [010 – 016]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-010	A Phase II Study of Oxaliplatin in Children with Medulloblastoma, Supratentorial Primitive Neuroectodermal Tumors and Atypical Teratoid Rhabdoid Tumors after Failure of Initial Therapy	<u>Stratum IA</u> : medulloblastoma patients with measurable disease <u>Stratum IB</u> : medulloblastoma patients with only positive CSF cytology or with linear leptomeningeal disease; <u>Stratum II</u> : will include patients with supratentorial primitive neuroectodermal tumor (S-PNET) including pineoblastomas, and ependymoblastomas; <u>Stratum III</u> : patients with atypical teratoid rhabdoid tumors (ATRT).	Study completed	No correlative objective. MRI for response only with central review.
PBTC-011	A Phase I/II Trial of Intracerebral IL13-PE38QQR Infusions in Pediatric Patients with Recurrent Malignant Glioma	No strata in Phase I	Study completed	No correlative objective. MRI for response only with central review.
PBTC-012	A Phase I Study of Cilengitide (EMD 121974) in Children with Refractory Brain Tumors	No strata	Study completed	MRI, MRS, MR perfusion, PET for tumor blood flow, metabolic activity and volume.
PBTC-013	A Phase I/II Study of a Recombinant Chimeric Protein Composed of Transforming Growth Factor (TGF)- α and a Mutated Pseudomonas Exotoxin Termed PE38 (TP-38) in Pediatric Patients with Recurrent or Progressive Supratentorial High Grade Gliomas	No strata	Study completed	No correlative objective. MRI for response only with central review.
PBTC-014	A Phase I/II Trial of R115777 and Radiation in Pediatric Patients Newly Diagnosed Non-disseminated Intrinsic Diffuse Brainstem Gliomas	No strata	Study completed	To characterize radiographic changes using MRI, MRS, perfusion and diffusion imaging and PET scans.
PBTC-015	A Phase II Trial of 06-Benzylguanine and Temozolomide in Pediatric Patients with Recurrent or Progressive High-Grade Gliomas and Recurrent or Progressive Brainstem Tumors	<u>Stratification</u> Patients will be stratified according to tumor type: <u>Stratum A</u> Recurrent or progressive high grade gliomas <u>Stratum B</u> Recurrent or progressive brain stem tumors	Study completed	To evaluate changes in MR spectroscopic patterns, MR diffusion and MR perfusion in children with refractory or recurrent high-grade gliomas or brainstem gliomas who are treated with the combination of O6-BG and TMZ.
PBTC-016	A Phase I, Molecular Biology and Phase II Study of Lapatinib (GW572016) in Pediatric Patients with Recurrent or Refractory Medulloblastoma, Malignant Glioma or Ependymoma	Phase I: <u>Stratum 1</u> : those who are not receiving steroids; <u>Stratum 2</u> : those who are receiving steroids;	Study completed	To characterize radiographic changes using MRI, MRS, perfusion and diffusion imaging and PET scans.

Table 6: PBTC Protocols [017 – 021]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-017	A Phase I Study of CLORETAZINE™ (VNP40101M) in Children with Recurrent, Progressive or Refractory Primary Brain Tumors	<u>Stratum 1</u> : no prior XRT or focal XRT only and/or < 2 prior myelosuppressive chemotherapy regimens; <u>Stratum 2</u> : prior craniospinal XRT, high-dose chemotherapy, and/or > 2 prior myelosuppressive chemotherapy regimens	Study completed	No correlative component. Central review for response based on the first MRI scan obtained after 2 courses of chemotherapy.
PBTC-018	A Phase I Trial of CC-5013 in Pediatric Patients with Recurrent or Refractory Primary CNS Tumors	No strata	Study completed	1. To evaluate changes in circulating endothelial cells, circulating endothelial cell precursors, and angiogenic modulators and correlate these changes with changes in MR perfusion and clinical outcome. 2. To evaluate changes in MR spectroscopy, MR perfusion and diffusion during treatment.
PBTC-019	A Phase I Pharmacokinetic Optimal Dosing Study of Intrathecal Topotecan for Children with Neoplastic Meningitis	No strata	Study completed	MRI central review for treatment effects and response at study completion.
PBTC-020	A Phase I Clinical Trial of AZD2171 in Children with Recurrent or Progressive Central Nervous System (CNS) Tumors	<u>Stratum 1</u> : Those who are not receiving enzyme inducing anticonvulsant drugs (EIACD) <u>Stratum 2</u> : Stratum 1: Those who are receiving enzyme inducing anticonvulsant drugs (EIACD)	Study completed	1. To explore correlations in changes in CECs, CEPs and angiogenic modulators with changes in MR perfusion. 2. To obtain preliminary evidence of biologic activity of AZD2171 by evaluating alterations in tissue perfusion, tumor blood flow and metabolic activity using MR perfusion and diffusion imaging, MRS as well as PET analysis and correlating these findings with changes in tumor size by standard MRI. 3. To continue the PBTC investigation of imaging assessments of antiangiogenesis effects by combining data from this trial with other PBTC trials of similar agents.
PBTC-021	A Phase I Trial of Capecitabine Rapidly Disintegrating Tablets and Concomitant Radiation Therapy in Children with Newly Diagnosed Brainstem Gliomas and High Grade Gliomas	No strata	Study completed	To characterize radiographic changes in non-disseminated, newly diagnosed intrinsic brainstem gliomas and high-grade gliomas treated with radiation and capecitabine using MRI, MRS, perfusion and diffusion imaging and PET scans

Table 6: PBTC Protocols [022 – 025]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-022	Phase II study of Bevacizumab plus Irinotecan (Camptosar™) in Children with Recurrent, Progressive, or Refractory Malignant Gliomas, Diffuse/Intrinsic Brain Stem Gliomas, Medulloblastomas, Ependymomas and Low Grade Gliomas	<p><u>Stratum A:</u> Recurrent, progressive or refractory high-grade gliomas</p> <p><u>Stratum B:</u> Recurrent, progressive or refractory Intrinsic brain stem tumors</p> <p><u>Stratum C:</u> Recurrent or progressive Medulloblastomas</p> <p><u>Stratum D:</u> Recurrent or progressive Ependymomas</p> <p><u>Stratum E:</u> Recurrent low grade gliomas</p>	Study completed	<p>1. To document changes in MR perfusion and diffusion scans obtained within 24-48 hours following the 2nd dose of Bevacizumab as compared to baseline and correlate with response.</p> <p>2. To correlate functional changes in tumor with responses to treatment with Bevacizumab + irinotecan using MR perfusion/diffusion imaging, and Fluoro-deoxyglucose (FDG) positron emission tomography (PET).</p> <p>3. To estimate vascular endothelial growth factor receptor-2 (VEGF-R2) expression in peripheral blood mononuclear cells (PBMC) prior to treatment and its down-regulation following two doses of single-agent Bevacizumab and correlate this finding with permeability changes in the tumor on MR perfusion imaging obtained 24-48 hours following the 2nd dose Bevacizumab</p>
PBTC-023	Phase I and Pharmacokinetic Study of Enzastaurin (LY317615) in Children and Adolescents with Refractory Primary CNS Tumors	No strata	Study completed	<p>To explore changes in correlative magnetic resonance imaging in children receiving enzastaurin. Specifically to evaluate changes in MR perfusion and diffusion scans obtained within 15 ± 2 days after initiation of enzastaurin therapy as compared to baseline and to correlate these changes with clinical outcome, as applicable.</p> <p>1. Results of imaging studies will be combined across similar PBTC protocols to increase the power for detecting correlations among scans and with outcome.</p>
PBTC-024	A Phase I Study of MK-0752 in Pediatric Patients with Recurrent or Refractory CNS Malignancies	No strata	Study completed	<p>To explore changes in correlative magnetic resonance imaging in children receiving MK-0752. Volumetric MR imaging findings may be combined across similar PBTC protocols to increase the power for detecting correlations among scans and associations with outcome.</p>
PBTC-025	A Phase I Pharmacokinetic and Safety Study in Children with Recurrent or Refractory Medulloblastoma to Identify a Pharmacokinetic Based Dose for GDC-0449	No strata	Study completed	Central review of MR knee, standard MR brain and spine.

Table 6: PBTC Protocols [025B – 029]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-025B	A Phase I Pharmacokinetic and Safety Study in Children with Recurrent or Refractory Medulloblastoma to Identify a Pharmacokinetic Based Dose for GDC-0449	<u>Stratum 1: Without SHH activation</u> <u>Stratum 2: With SHH activation</u>	Study completed	Central review of neuro-imaging studies by neuro-radiologists will be conducted to confirm response only in patients reported by the treating site to have experienced an objective response. MRI of the Brain and spine with and without contrast (brain) and post contrast (spine) will be performed.
PBTC-026	A Feasibility Study of SAHA combined with Isotretinoin and Chemotherapy in Infants with Embryonal Tumors of the Central Nervous System	No strata	Study completed	To estimate the preliminary response rate of thi approach in patients with measurable residual disease (primary site and/or metastatic sites. Central review of standard MR brain and spine.
PBTC-027	A Phase I Study of ABT-888, an Oral Inhibitor of Poly(ADP-ribose) Polymerase and Temozolomide in Children with Recurrent/Refractory CNS Tumors	No strata	Study completed	No correlative objective. MR for response only.
PBTC-029	Phase I and Pharmacokinetic Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	No strata	Study completed	Central review of MR imaging studies. To assess diffusion imaging contributions to tumor behavior (type, grade) and response to therapy.
PBTC-029B	A Phase 1 and Phase II Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	<u>Stratum 1:</u> Patients with non NF-1 associated progressive, recurrent or refractory pilocytic astrocytoma with pre-trial tumor material available and with a BRAF aberration excluding patients with optic pathway glioma. <u>Stratum 2:</u> Patients with non NF-1 associated progressive, recurrent or refractory pilocytic astrocytoma with pre-trial tumor material available and without BRAF aberration excluding patients with optic pathway glioma. <u>Stratum 3:</u> Patients with NF-1 associated progressive, recurrent or refractory low grade glioma (WHO I or II), with or without tissue <u>Stratum 4:</u> Patients with non-NF1 associated progressive, recurrent or refractory optic pathway glioma (OPG) with or without tissue available for BRAF evaluation. <u>Stratum 5:</u> Patients with non NF-1 associated progressive, recurrent or refractory low grade glioma (other than pilocytic astrocytoma or optic pathway glioma) with a BRAF aberration.	Study completed	To describe MRI characteristics of the tumors before and after treatment to determine if there is an early diffusion indicator of response.

		Stratum 6: Patients with non NF-1 associated progressive, recurrent or refractory low grade glioma (other than OPG) with tissue available for BRAF analysis who cannot be classified into Stratum 1, 2 or 5 due to inadequate tissue quality		
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Table 6: PBTC Protocols [029C – 033]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-029C - Retreatment	A Phase 1 and Phase II Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	No strata	Study completed	To describe MRI characteristics of the tumors before and after treatment to determine if there is an early diffusion indicator of response.
PBTC-030	A Phase II Trial of Capecitabine Rapidly Disintegrating Tablets and Concomitant Radiation Therapy in Children with Newly Diagnosed Brainstem Gliomas	No strata	Study completed	To describe and explore changes in diffusion tensor imaging variables in brainstem gliomas in response to therapy and prior to progression.
PBTC-031	Phase I and Pharmacokinetic Trial of PTC299 in Pediatric Patients with Refractory or Recurrent CNS Tumors	No strata	Study completed	To obtain preliminary evidence of biologic activity of PTC299 by using MR diffusion to assess tumor cellularity.
PBTC-032	A Phase II Clinical Trial Evaluating the Efficacy and Safety of GDC-0449 in Children with Recurrent or Refractory Medulloblastoma	<u>Strata A:</u> Patients without evidence of activation of Hedgehog signaling pathway <u>Strata B:</u> Patients with evidence of activation of Hedgehog signaling pathway	Study completed	MR of the knee: To assess for side effects of this drug on growth cartilage MR of brain/spine: Central review of MR scans of brain and spine will be performed to confirm sustained responses and other clinical events as may be needed.
PBTC-033	A Phase I/II Study of ABT-888, an Oral Poly (ADP-ribose) Polymerase Inhibitor, and Concurrent Radiation Therapy, Followed by ABT-888 and Temozolomide, in Children with Newly Diagnosed Diffuse Pontine Gliomas (DIPG)	No strata	Study completed	To explore the quantitative MR measures of relative cerebral blood volume (rCBV), vascular permeability (K _{trans} , v _p , and v _e values), and apparent diffusion coefficient (ADC) within the first six months of initiating protocol treatment to correlate with disease outcome and determine whether such metrics differentiate patients with pseudoprogression from those with true early progressive disease.

Table 6: PBTC Protocols [036-042]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-036	A Molecular Biology and Phase II Study of Imetelstat (GRN163L) in Children with Recurrent High-Grade Glioma, Ependymoma, Medulloblastoma/Primitive Neuroectodermal Tumor and Diffuse Intrinsic Pontine Glioma	No strata	Study completed	To assess changes in tumor size, enhancement, and diffusion characteristics.
PBTC-037	A phase I study of intratumoral/peritumoral herpes simplex virus-1 mutant HSV1716 in patients with refractory or recurrent high grade gliomas (HGG)	No strata	Study completed	<ol style="list-style-type: none"> 1. To evaluate changes in tumor enhancement, quantitative MR measures of tumor 1.1.4perfusion (relative cerebral blood volume (rCBV), ktrans, Vp and Ve values and apparent diffusion coefficient (ADC) in response to HSV1716 injection 2. To evaluate changes in FDG-PET uptake in response to HSV1716 injection. 3. To evaluate changes in tumor choline values using MR spectroscopy in response to HSV1716 injection and further delineate from progressive disease versus pseudo-progression post therapy.
PBTC-039	A Phase II study of Peginterferon alfa-2b (PEGIntron) for pediatric patients with unresectable or recurrent craniopharyngioma	<p><u>Stratum 1:</u> Patients with progressive unresectable or recurrent craniopharyngiomas treated with surgery alone who have not received radiation therapy. Patients with unresectable craniopharyngiomas (i.e., residual measurable disease following surgical resection) will be enrolled at the time of progression</p> <p><u>Stratum 2:</u> Patients with progressive or recurrent craniopharyngiomas following radiation therapy.</p>	Study completed	To compare the protocol specific disease assessment criteria to MacDonald criteria during the first year of treatment in stratum I and at the time of objective response and progressive disease in both strata.
PBTC-041	A Phase I Trial of p28 (NSC745104), a Non-HDM2 mediated peptide inhibitor of p53 ubiquitination in pediatric patients with recurrent or progressive CNS tumors	No strata	Study completed	No correlative objective. MR for response only.
PBTC-042	PBTC-042 Phase I study of CDK 4-6 inhibitor PD-0332991 in children with recurrent, progressive or refractory central nervous system tumors	<p><u>Stratum A:</u> DIPGs</p> <p><u>Stratum B:</u> non-brainstem HGGs</p>	Study completed	No correlative objective MR for response only

Table 6: PBTC Protocols [043-049]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-043	A Phase I Trial of Pomalidomide for children with recurrent, progressive or refractory CNS tumors	<p><u>Stratum 1:</u> Patients on or off steroids</p> <p><u>Stratum 2:</u> Patients on steroid, <12 Years Old</p> <p><u>Stratum 3:</u> Patients off steroid, <12 Years Old</p> <p><u>Stratum 4:</u> Patients on steroid, >=12 Years Old</p> <p><u>Stratum 5:</u> Patients off steroid, >=12 Years Old</p>	Study completed	No correlative response MR for response only
PBTC-045	A Safety and Preliminary Efficacy trial of MK-3475 (pembrolizumab; anti-PD-1) in Children with recurrent, progressive or refractory high-grade gliomas (HGG) and DIPGs.	<p><u>Stratum 1:</u> patients with progressive, recurrent or refractory DIPGs</p> <p><u>Stratum 2:</u> patients with progressive, recurrent or refractory non-brainstem HGGs.</p> <p><u>Stratum 3:</u> patients with hypermutated brain tumors with CMMRD syndrome</p> <p><u>Stratum 4:</u> patients with progressive, recurrent or refractory ependymoma</p> <p><u>Stratum 5:</u> patients with progressive recurrent or refractory medulloblastoma</p>	Stratum 1 completed; Stratum 2-5 Open	<p>1. To examine the ability of quantitative MR spectroscopy and diffusion/weighted imaging/ADC mapping to provide early assessment of tumor behavior and specifically distinguish pseudoprogression from true progression</p> <p>2. To explore the use of serial MR permeability (DCE) and MR perfusion (DSC) to determine if elevated rCBV and ktrans can distinguish pseudoprogression from true progression in tumors treated on this protocol</p>
PBTC-047	A Phase I Trial of Panobinostat in Children with Diffuse Intrinsic Pontine Glioma	<p><u>Stratum 1: Recurrent/progressive DIPG</u></p> <p><u>Stratum 2: Nonprogressed DIPG or H3K27M+ Thalamic Diffuse Midline Glioma (DMG)</u></p>	Study completed	No correlative response. MR for response only Will analyze diffusion and standard MR sequences
PBTC-048	Feasibility Trial of Optune for Children with Recurrent or Progressive Supratentorial High-Grade Glioma and Ependymoma	<p><u>Stratum 1: Patients with supratentorial HGG or ependymoma</u></p> <p><u>Stratum 2: Patients with newly diagnosed DIPG</u></p>	Open	To explore the association of apparent diffusion coefficient (ADC) values within the tumor and correlate with response to Optune treatment and EFS.
PBTC-049	A Phase I study of Savolitinib in Recurrent, Progressive, or Refractory Medulloblastoma, High-Grade Glioma, Diffuse Intrinsic Pontine Glioma, and CNS tumors harboring MET aberrations	<p><u>Stratum 1-3: Recurrent, progressive, medulloblastoma, HGG, DIPG and</u></p> <p><u>Stratum 4: CNS tumors harboring MET aberrations</u></p>	Stratum 1-3 completed; Stratum 4 open	MR for response only.

Table 6: PBTC Protocols [050-056]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-050	A Phase I and Surgical Study of Ribociclib and Everolimus (RAD001) in Children with Recurrent or Refractory Malignant Brain Tumors	Phase 1 Study: Patients with recurrent or refractory CNS tumors(HGG, medulloblastoma, CNS embryonal tumors, ependymoma, ATRT and DIPG) Surgical Study: <u>recurrent or refractory disease including HGG, medulloblastoma, CNS embryonal tumor, ependymoma or ATRT)</u>	Study completed	No correlative response. MR for response only
PBTC-051	Phase I Study to Evaluate the Safety and Tolerability of the CD40 Agonistic Monoclonal Antibody APX005M in Pediatric Subjects with Recurrent/Refractory Brain Tumors and Newly Diagnosed Brain Stem Glioma	<u>Stratum 1: Recurrent or refractory CNS malignant tumor</u> <u>Stratum 2: Newly diagnosed DIPG</u>	Stratum 1 completed; Stratum 2 open	No correlative response. MR for response only.
PBTC-053	A Pediatric Brain Tumor Consortium Phase I/ II and Surgical Study of CX-4945 in Patients with Recurrent SHH Medulloblastoma	<u>Phase 1-Skeletally-immature children with recurrent SHH medulloblastoma:</u> <u>Phase 2-Skeletally-mature patients with recurrent SHH medulloblastoma:</u> <u>Surgical: To explore ability of CX-4945 to inhibit Ck-2 mediated signaling in tumor</u>	Open	No correlative response. MR for response only
PBTC-055	Phase I/II trial of Dabrafenib, Trametinib, and Hydroxychloroquine (HCQ) for BRAF V600E-mutant or Trametinib and HCQ for BRAF fusion/duplication positive or NF1-associated recurrent or progressive gliomas in children and young adults	<u>Stratum 1: LGG or HGG with BRAF V600E/D/K mutation</u> <u>Stratum 2: BRAF fusion/duplication or NF1- associated LGG</u> <u>Stratum 3: LGG with BRAF V600E/D/K mutation</u> <u>Stratum 4: HGG with BRAF V600E/D/K mutation</u> <u>Stratum 5: LGG with BRAF duplication or fusion with any partner</u> <u>Stratum 6: LGG with Neurofibromatosis Type 1</u>	Stratum 1-2 completed; Stratum 3-6 open	Standard MR imaging in phase I and II and ADC histogram analysis in phase II study
PBTC-056	A Phase 1 Study of the ADAM-10 inhibitor, INCB007839 in Children with Recurrent/Progressive High-Grade Gliomas to Target Microenvironmental Neurologlin-3	<u>Stratum 1: recurrent/progressive high-grade gliomas, including diffuse intrinsic pontine glioma (DIPG), diffuse midline glioma (DMG), glioblastoma (GBM), and anaplastic astrocytoma.</u>	Open	Standard MR imaging.

Table 6: PBTC Protocols [058-060]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-058	Phase 2 Study of Intraventricular Omburtamab-based Radioimmunotherapy for Pediatric Patients with Recurrent Medulloblastoma and Ependymoma	<u>Stratum 1: Recurrent medulloblastoma</u> <u>Stratum 2: Recurrent ependymoma</u>	Study completed	Standard MR imaging and PET imaging
PBTC-059	Phase 1 Trial of Autologous HER2-specific CAR T cells in Pediatric Patients with Refractory or Recurrent Ependymoma	<u>Stratum 1: Recurrent or refractory ependymoma</u>	Open	1. To examine the ability of quantitative MR diffusion DWI/ADC mapping to provide early assessment of tumor behavior and specifically distinguish pseudoprogression from tumor progression. 2. To explore the use of MR permeability and MR perfusion to distinguish pseudoprogression from tumor progression.
PBTC-060	A Pilot Study of Safety, Tolerability, and Immunological Effects of SurVaxM in Pediatric Patients with Progressive or Relapsed Medulloblastoma, High Grade Glioma, Ependymoma and Newly Diagnosed Diffuse Intrinsic Pontine Glioma	<u>Progressive or relapsed medulloblastoma, high grade glioma, ependymoma and newly diagnosed DIPG.</u> <u>Stratum 1 (progressive or recurrent) patients must be ≥ 10 years of age and ≤ 21 years of age at the time of study screening.</u> <u>Stratum 2 (progressive or recurrent) patients must be ≥ 1 year of age and < 10 years of age at the time of study screening.</u> <u>Stratum 3 (newly diagnosed DIPG) patients must be ≥ 1 year of age and ≤ 21 years of age at the time of study enrollment</u>	Open	1. To examine the ability of quantitative MR diffusion DWI/ADC mapping to provide early assessment of tumor behavior and specifically distinguish pseudoprogression from tumor progression. 2. To explore the use of MR permeability and MR perfusion to distinguish pseudoprogression from tumor progression.

Table 7: PBTC Protocols [001 – 013]

Protocol	Trial	MR Brain	MR Diffusion	MR Perfusion	MR Spectroscopy	Cister-nogram	MR Spine	Bone Scan	PET	CT
PBTC-001	A Pilot Study of Systemic and Intrathecal Chemotherapy followed by Conformal Radiation for infants with Embryonal Intracranial Central Nervous System Tumors	+				+	+	+		
PBTC-002	A Phase I Study of SU5416 in Pediatric Patients With Recurrent or Progressive Poor Prognosis Brain Tumors	+	+	+	+				+	
PBTC-003	A Phase I Trial of Escalating Oral Doses of SCH 66336 in Pediatric Patients with Refractory or Recurrent Brain Tumors	+					+			
PBTC-004	A Phase I Study of Intrathecal Spartaject™-Busulfan in Children with Neoplastic Meningitis	+					+			
PBTC-005	A Phase I Trial of Temozolomide and O ⁶ -Benzylguanine in Pediatric Patients with Recurrent Brain Tumors	+					+			
PBTC-006	A Phase I/II Trial of STI571 in Children with Newly Diagnosed Poor Prognosis Brainstem Gliomas and Recurrent Intracranial Malignant Gliomas	+	+	+	+		+		+	
PBTC-007	A Phase I/II Trial of ZD1839 (Iressa™) and Radiation in Pediatric Patients Newly Diagnosed with Brain Stem Tumors or Incompletely Resected Supratentorial Malignant Gliomas with Phase II limited to Brain Stem Tumors	+	+	+					+	
PBTC-009	A Phase I Trial of GLIADEL® and O ⁶ -Benzylguanine in Pediatric Patients with Recurrent Malignant Gliomas	+	+	+	+					
PBTC-010	A Phase II Study of Oxaliplatin in Children with Recurrent or Refractory Medulloblastoma, Supratentorial Primitive Neuroectodermal Tumors and Atypical Teratoid Rhabdoid Tumors	+					+			
PBTC-011	A Phase I/II Trial of Intracerebral IL13-PE38QQR Infusions in Pediatric Patients with Recurrent Malignant Glioma	+								+
PBTC-012	A Phase I Study of Cilengitide (EMD 121974) in Children with Refractory Brain Tumors	+		+	+		+		+	
PBTC-013	A Phase I/II Study of a Recombinant Chimeric Protein Composed of Transforming Growth Factor (TGF)-α and a Mutated Form of the Pseudomonas Exotoxin Termed PE38 (TP-38) in Pediatric Patients with Recurrent or Progressive Supratentorial High Grade Gliomas	+								+

Table 7: PBTC Protocols [014-022]

Protocol	Trial	MR Brain	MR Diffusion	MR Perfusion	MR Spectroscopy	Cisternogram	MR Spine	Bone Scan	PET	CT
PBTC-014	A Phase I/II Trial of R115777 and Radiation in Pediatric Patients Newly Diagnosed Non-disseminated Intrinsic Diffuse Brainstem Gliomas	+	+	+			+		+	
PBTC-015	A Phase II Trial of 06-Benzylguanine and Temozolomide in Pediatric Patients with Recurrent or Progressive High-Grad Gliomas and Recurrent / Progressive Brainstem Tumors	+		+	+				+	
PBTC-016	A Phase I, Molecular Biology and Phase II Study of Lapatinib (GW572016) in Pediatric Patients with Recurrent or Refractory Medulloblastoma, Malignant Glioma or Ependymoma	+	+	+			+		+	
PBTC-017	A Phase I Study of CLORETAZINE™ (VNP40101M) in Children with Recurrent, Progressive or Refractory Primary Brain Tumors	+					+			
PBTC-018	A Phase I Trial of CC-5013 in Pediatric Patients with Recurrent or Refractory Primary CNS Tumors	+	+	+			+		+	
PBTC-019	A Phase I Pharmacokinetic Optimal Dosing Study of Intrathecal Topotecan for Children with Neoplastic Meningitis	+					+			
PBTC-020	A Phase 1 Clinical Trial of AZD2171 in children with Recurrent or Progressive Central Nervous System (CNS) Tumors	+	+	T1 permeability followed by T2*			+		+	
PBTC-021	A Phase I Trial of Capecitabine Rapidly Disintegrating Tablets and Concomitant Radiation Therapy in Children with Newly Diagnosed Brainstem Gliomas and High Grade Gliomas	+	+	+			+		+	
PBTC-022	Phase II study of Bevacizumab plus Irinotecan (Camptosar™) in Children with Recurrent, Progressive, or Refractory Malignant Gliomas, Diffuse/Intrinsic Brain Stem Gliomas, Medulloblastomas, Ependymomas and Low Grade Gliomas	+	+	T1 permeability followed by T2*			+		+	

Table 7: PBTC Protocols [023-032]

Protocol	Trial	MR Brain	MR Diffusion	MR Perfusion	MR Spectroscopy	Cister-nogram	MR Spine	Bone Scan	PET	CT
PBTC-023	A Phase I and Pharmacokinetic Study of Enzastaurin (LY317615) in Children and Adolescents with Refractory Primary CNS Tumors	+	+	T1 permeability followed by T2*			+			
PBTC-024	A Phase I Study of MK-0752 in Pediatric Patients with Recurrent or Refractory CNS Malignancies	+					+			
PBTC-025	A Phase I Pharmacokinetic and Safety Study in Children with Recurrent or Refractory Medulloblastoma to Identify a Pharmacokinetic Based Dose for GDC-0449 **	+					+			
PBTC-025B	A Phase I Pharmacokinetic and Safety Study in Children with Recurrent or Refractory Medulloblastoma to Identify a Pharmacokinetic Based Dose for GDC-0449	+					+			
PBTC-026	A Feasibility Study of SAHA combined with Isotretinoin and Chemotherapy in Infants with Embryonal Tumors of the Central Nervous System	+					+			
PBTC-027	A Phase I Study of ABT-888, an Oral Inhibitor of Poly(ADP-ribose) Polymerase and Temozolomide in Children with Recurrent/Refractory CNS Tumors	+					+			
PBTC-029	A Phase I and Pharmacokinetic Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	+	+				+			
PBTC-029B	A Phase 1 and Phase II Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	+	+				+			
PBTC-029C - Retreatment	A Phase 1 and Phase II Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	+	+				+			
PBTC-030	A Phase II Trial of Capecitabine Rapidly Disintegrating Tablets and Concomitant Radiation Therapy in Children with Newly Diagnosed Brainstem Gliomas *	+	+							
PBTC-031	A Phase I and Pharmacokinetic Trial of PTC299 in Pediatric Patients with Refractory or Recurrent CNS Tumors	+	+				+			
PBTC-032	A Phase II Clinical Trial Evaluating the Efficacy and Safety of GDC-0449 in Children with Recurrent or Refractory Medulloblastoma	+					+			

Table 7: PBTC Protocols [033-049]

Protocol	Trial	MR Brain	MR Diffusion	MR Perfusion	MR Spectroscopy	Cisternogram	MR Spine	Bone Scan	PET	CT
PBTC-033	A Phase I/II Study of ABT-888, an Oral Poly (ADP-ribose) Polymerase Inhibitor, and Concurrent Radiation Therapy, Followed by ABT-888 and Temozolomide, in Children with Newly Diagnosed Diffuse Pontine Gliomas (DIPG)	+	+	T1 permeability followed by T2*			+			
PBTC-036	A Molecular Biology and Phase II Study of Imetelstat (GRN163L) in Children with Recurrent High-Grade Glioma, Ependymoma, Medulloblastoma/Primitive Neuroectodermal Tumor and Diffuse Intrinsic Pontine Glioma	+	+				+			
PBTC-037	A phase I study of intratumoral/peritumoral herpes simplex virus-1 mutant HSV1716 in patients with refractory or recurrent high grade gliomas (HGG)	+	+	+	+				+	
PBTC-039	A Phase II study of Peginterferon alfa-2b (PEGIntron) for pediatric patients with unresectable or recurrent craniopharyngioma	+								
PBTC-041	A Phase I Trial of p28 (NSC745104), a Non-HDM2 mediated peptide inhibitor of p53 ubiquitination in pediatric patients with recurrent or progressive CNS tumors	+	+				+			
PBTC-042	Phase I study of CDK 4-6 inhibitor PD-0332991 in children with recurrent, progressive or refractory central nervous system tumors.	+					+			
PBTC-043	A Phase I Trial of Pomalidomide for children with recurrent, progressive or refractory CNS tumors	+	+				+			
PBTC-045	A Safety and Preliminary Efficacy trial of MK-3475 (pembrolizumab; anti-PD-1) in Children with recurrent, progressive or refractory high-grade gliomas (HGG) and DIPGs	+	+	+	+		+			
PBTC-047	Phase 1 Trial of Panobinostat in Children with Diffuse Intrinsic Pontine Glioma	+	+				+			
PBTC-048	Feasibility Trial of Optune for Children with Recurrent or Progressive Supratentorial High-Grade Glioma and Ependymoma	+	+				+			
PBTC-049	A Phase I study of Savolitinib in Recurrent, Progressive, or Refractory Medulloblastoma, High-Grade Glioma, Diffuse Intrinsic Pontine Glioma, and CNS tumors harboring MET aberrations	+	+				+			

Table 7: PBTC Protocols [050-060]

Protocol	Trial	MR Brain	MR Diffusion	MR Perfusion	MR Spectroscopy	Cister-nogram	MR Spine	Bone Scan	PET	CT
PBTC-050	A Phase I and Surgical Study of Ribociclib and Everolimus (RAD001) in Children with Recurrent or Refractory Malignant Brain Tumors	+					+			
PBTC-051	Phase I Study to Evaluate the Safety and Tolerability of the CD40 Agonistic Monoclonal Antibody APX005M in Pediatric Subjects with Recurrent/Refractory Brain Tumors and Newly Diagnosed Brain Stem Glioma	+					+			
PBT-053	A Pediatric Brain Tumor Consortium Phase I/ II and Surgical Study of CX-4945 in Patients with Recurrent SHH Medulloblastoma	+					+			
PBTC-055	Phase I/II trial of Dabrafenib, Trametinib, and Hydroxychloroquine (HCQ) for BRAF V600E-mutant or Trametinib and HCQ for BRAF fusion/duplication positive or NF1-associated recurrent or progressive gliomas in children and young adults	+	+				+			
PBTC-056	A Phase I study of the ADAM-01 inhibitor, INCB00789 in children with recurrent/progressive high-grade gliomas to target microenvironmental neuroligin-3	+	+				+			
PBTC-058	Phase 2 Study of Intraventricular Omburtamab-based Radioimmunotherapy for Pediatric Patients with Recurrent Medulloblastoma and Ependymoma	+	+				+		+	
PBTC-059	Phase 1 Trial of Autologous HER2-specific CAR T cells in Pediatric Patients with Refractory or Recurrent Ependymoma	+	+	+			+			
PBTC-060	A Pilot Study of Safety, Tolerability, and Immunological Effects of SurVaxM in Pediatric Patients with Progressive or Relapsed Medulloblastoma, High Grade Glioma, Ependymoma and Newly Diagnosed Diffuse Intrinsic Pontine Glioma	+	+	+			+			

* DTI

** MR of knee required