TARGETING THE ELIMINATION OF BRAIN TUMOR INITIATING CELLS BY DISRUPTING THE PI3K PATHWAY

FINAL REPORT

STUDY SUMMARY
MAY 2011 – JULY 2013

July 22, 2013

This project is financially supported by

BRAIN TUMOUR FOUNDATION OF CANADA

STUDY CONTACTS

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Team Members: Dr Juliette Hukin
Dr. Sandra E. Dunn
Dr. Rod Rassekh
Dr. Abbas Fotovati
Dr. Christopher Dunham

Location: British Columbia Children's Hospital
University of British Columbia
Vancouver, BC, Canada

Study Coordinator: Mr. Ross Hengel
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Tel. (604) 875-2094
Fax. (604) 875-3109
E-mail: ash.singhal@cw.bc.ca

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Vancouver, BC V6H 3V4

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1. INTRODUCTION

Brain tumours are the most common type of solid tumour in children. The principal issue affecting survival is that brain tumours often recur, and in many instances children with malignant brain tumours have less than a 50% chance of surviving one year after their initial diagnosis. There is research suggesting that one reason why brain tumours are so difficult to treat is that a unique stem cell type, the brain tumour initiating cell (BTIC), makes the tumours drug and/or radiation resistant. One challenge with past research is that non-human (animal model) brain tumours are not necessarily representative of human brain tumours. Our study examines, using human pediatric brain tumour preparations, new treatment approaches with the goal of improving patient cure rates. If our study is successful, we plan to block a specific mechanism of growth of BTICs that we believe is responsible for the progression of those tumours. Once this mechanism is shut down, the cells will be deprived of necessary growth signals and they will die. We then plan to combine these inhibitors with classic agents used to treat brain tumours so that we are able to eliminate the cancer cells and improve cure rates.

Our overall goal is to produce a research platform which will allow the testing of treatment agents against human brain tumour cell cultures, and human brain tumour stem cells in particular. We hypothesise that BTIC's can be eliminated using agents that interfere with the PI3K pathway.

2. APPROVALS STATUS

The approval status for BC Children's Hospital (BCCH) is shown below in Table 1. The latest ethics approvals are also included in the appendices of this report.

Table 1. Study Approvals for BC Children's Hospital

Name of the Hospital	Date of Approval	Approval Expiry Date
BC Children's Hospital - Vancouver	May 13, 2010	May 13, 2011
BC Children's Hospital - Vancouver	March 8, 2011	March 8, 2012
BC Children's Hospital - Vancouver	February 14, 2012	February 13, 2013
BC Children's Hospital - Vancouver	January 25, 2013	January 25, 2014

3. IDENTIFYING STUDY PARTICIPANTS

The responsibility of patient identification and enrolment rest on the Clinical Research Coordinator, who monitors the operating room schedule and non-scheduled admissions to Pediatric Neurosurgery list for high-grade tumours. Figure 1 demonstrates the recruitment and identification process. The inclusion and exclusion criteria for eligible patients follow:

Inclusion Criteria
Pediatric patients (0-18 years) presenting to Neurosurgery for resection of the following brain tumour types will be eligible for participation in the BTIC study:

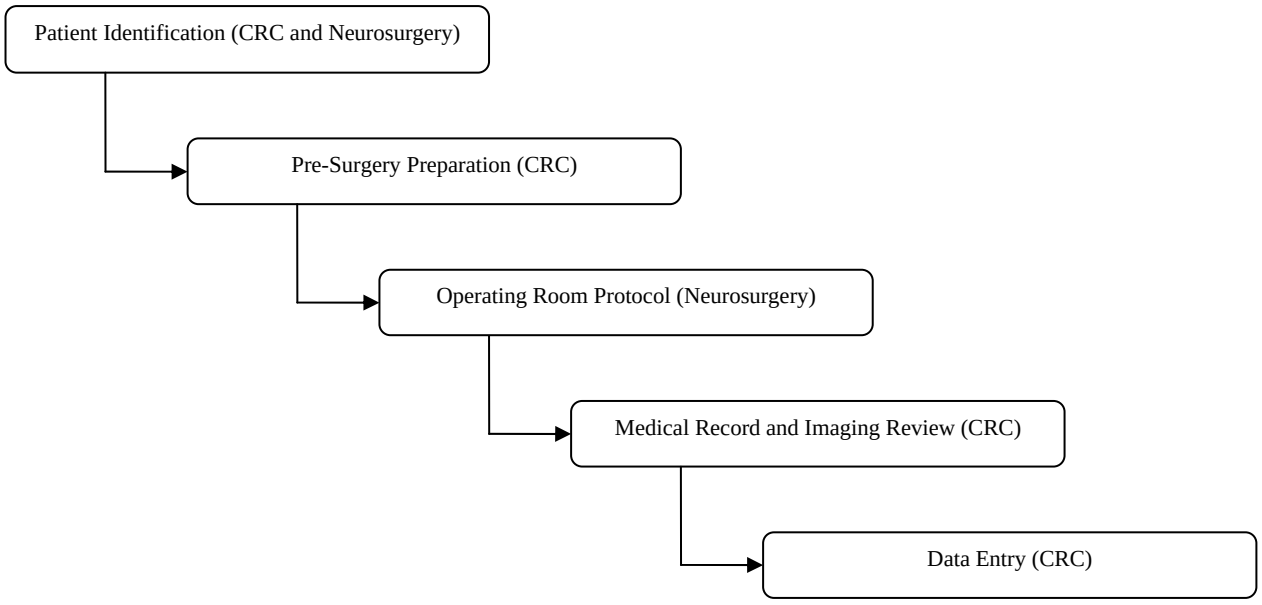
- Anaplastic Astrocytoma
- Malignant Germ Cell Tumor or Germinoma
- Glioblastoma
- Medullablastoma (PNET in Post Fossa)
- Ependymoma
- Anaplastic Pleomorphic Xanthoastrocytoma
- Atypical Teratoid Rhabdoid Tumor
- Other malignant tumor form

BCCH treats an average of 30 brain tumour patients annually, half of whom will present with a high-grade form described above. Thus, it is paramount that every eligible patient is identified and captured by the study coordinator to reach the study's target enrollment number.

Exclusion Criteria
Patients will be excluded from the study under the following conditions:

1. Specimen not capable of cultivating BTICs in the laboratory.
2. Contamination of specimen by external environment or poor sterile technique.
3. Resected tumor is adequate for clinical purposes, but insufficient for study; see ETHICAL CONSIDERATIONS, page 14).
4. Low-grade gliomas

Figure 1. Patient Screening and Recruitment



4. DEVELOPMENT OF STUDY DOCUMENTATION

4.1. Data Collection Forms

The BTIC Study began in May 2010. Since that time, a data collection form and a study database have been created to support and document the study subjects. The initial data collection form (DCF) contains the following information:

1. Demographics and Background
2. Tumour Characteristics
3. Surgery Procedure
4. Adjuvant Therapy

In addition, a DCF was designed for patients with recurrent tumours. This DCF contained information on the following:

1. Patient Background
2. Progression Characteristics
3. Progression Surgery and Post-op Characteristics
4. Adjuvant Therapy
5. Status at Last Follow-up

Once the DCFs are complete, data is entered into the study database, which is an excel database found at BCCH that contains all of the de-identified information as an electronic file for the purpose of data analysis.

4.2. Standard Operating Procedures

Included in the BTIC Study documents are the Standard Operating Procedures (SOPs), which contain instructions for the coordination, management and implementation of the BTIC Study at BC Children's Hospital. In addition to outlining the purpose and overall work process of the study, the SOPs provide a detailed description of the procedures, and serve as a guide and manual for the research staff.

The SOPs are included in the appendices of this report.

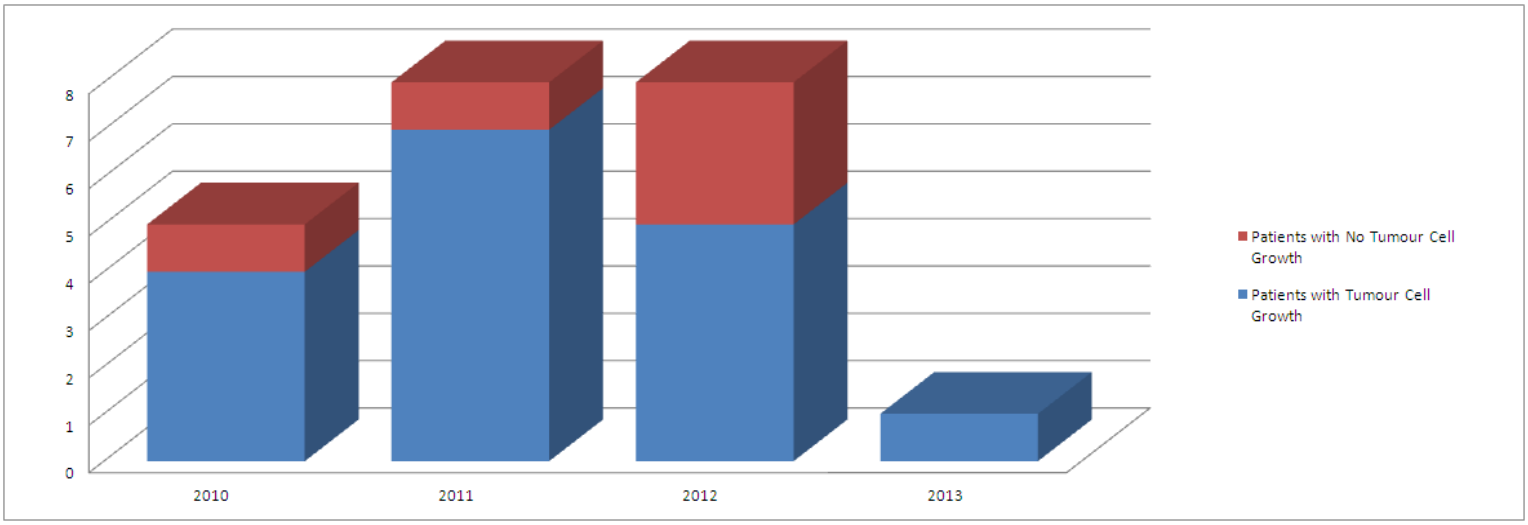
5. STUDY OVERVIEW

Study progression and enrolment have been stable since the beginning of the study. Currently, there are 22 subjects enrolled in the study. Moreover, one of these patients has required 2 subsequent surgeries for tumour relapse. Tumour samples from both of this patient's relapse surgeries were successfully collected into the study. Of all the eligible patients approached to participate in the study, only one family has declined enrolment. Thus, we have an excellent patient capture rate. Unfortunately, however, 5 subjects have been lost to study due to their tissue samples being unable to grow in the laboratory. At the beginning of the study, we expected an average cultivation rate of tumour samples in the lab to be around 85%. Factoring in the 5 uncultivated tumour samples, the study cultivation rate, this far, is 79%, which is in keeping with the expected cultivation rate. As demonstrated in Figure 2, recruitment rates can fluctuate over time. This year (2013) has had a particularly low number of high-grade brain tumours present to BCCH. Please see Figure 2 for more details about study enrolment.

The support from the Brain Tumour Foundation has been an indispensable resource in making this project successful over the last year. As mentioned earlier in this report, patient identification and enrolment is the most crucial step to the success of this project. The support provided by the Brain Tumour Foundation has allowed the Study Coordinator to successfully screen and approach 100% of families of children diagnosed with high-grade brain tumours. In our grant application, we expected to enrol between 8-10 patients. As expected, 8 patients presented to BCCH with high-grade tumours, with only one family declining participation in the study.

Unfortunately, because this is a long-term study, the findings of the study cannot be determined at this time. Work must continue to reach our target sample size and complete the data collection on all patients. At this time, there have been 2 abstracts and 1 manuscript submitted on information from the BTIC Study (see appendix 4 for more details). Additionally, the Brain Tumour Foundation will be mentioned as a key contributor in any future publications and presentations of the BTIC Study. We will be sure to forward any future publications and presentations to the Brain Tumour Foundation for consideration.

Figure 2. Patients Recruited Per Year



APPENDIX 1: Monthly Update

Monthly Update

Study Title: **Brain Tumor Initiating Cells (BTIC)**

PI: Dr. Singhal

Month ____June__ Year ___2013__	**No. of Subjects**	**Comment**
Eligible Subjects	0	
Subjects Approached	0	
Subjects Enrolled	0	

Enrolment # from the Study Start Up to Date	**No. of Subjects**	**Comment**
Eligible Subjects	23	
Subjects Approached	23	
Subjects Enrolled	22	
Subjects Lost to Study	5	
Subjects Withdrawn	0	

CRC: Ross Hengel

Date: July 5, 2013

APPENDIX 2: Standard Operating Procedures

NEUROSCIENCES PROGRAM

BTIC Study

Instructions for Coordination, Management and Implementation

Version 4: July 3, 2012

DOCUMENT CHANGE HISTORY

Version Number	Effective Date	Description of Revisions
Version 1	August 9, 2010	N/A
Version 2	November 15, 2010	Change to communication protocol
Version 3	March 8, 2011	Certificate of Approval – Renewal March 8, 2011
Version 4	July 3, 2012	New CRC, Study Renewal February 13, 2012

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INTRODUCTION AND PURPOSE

This documents serves as an introduction and guide for the management, coordination and implementation of the *BTIC STUDY*.

It describes the *BTIC STUDY*, its purpose, its overall work process and the established procedures within the *Neurosciences Program* of *British Columbia Children's Hospital*.

The purpose of this document is to provide a detailed description of the *BTIC STUDY* workflow, and to serve as a guide and manual for the *Neurosciences Program* research staff working on the *BTIC STUDY*.

DEFINITIONS AND ABBREVIATIONS

Some abbreviations used in this document are explained below:

AP	Anterioposterior (orientation used to calculate tumour volume)
BCCH	British Columbia Children's Hospital
BTIC	Brain Tumor Initiating Cell
CRC	Clinical Research Coordinator
CRF	Case Report Form
DCF	Data Collection Form
EHR	Electronic Health Record
ICF	Informed Consent Form
OR	Operating Room
PI	Principal Investigator
SOP	Standard Operating Procedures
XRT	Radiation Therapy (acronym)

STUDY IMPLEMENTATION

GENERAL STUDY INFORMATION

Study Title:	**BTIC STUDY**
Full Study Title:	**Targeting the Elimination of Brain Tumor Initiating Cells by Disrupting the PI3K Pathway**
Study PI:	Dr. Ash Singhal (Pediatric Neurosurgeon)
Co-investigators at BCCH site:	Dr. Juliette Hukin (Pediatric Neurologist), local 2121; Department: Oncology, K3-147 Dr. Rod Rassekh (Pediatric Oncologist), local 7878; Department: Oncology, Room A119B Dr. Christopher Dunham (Neuropathologist), local 3639; Department: Pathology, Room L218
Co-investigators at other sites:	Dr. Sandra Dunn (Molecular Biologist) Dr. Abbas Fotovati (Research Associate, Oncology)
Research Manager (RM):	Dr. Vesna Popovska, local 5157; Room K3-175
Research Coordinator:	Mr. Ross Hengel , local 7132; Room K3-167
Study Purpose:	The purpose of this study is to test the hypothesis that brain tumor initiating cells (BTICs), a stem cell line responsible for tumor resistance to drug and radiation therapy, can be eliminated using agents that interfere with the P13K pathway. This project will implement procedures for isolating and culturing primary BTICs using flow cytometry and immunostaining of CD133, a unique cell surface marker of BTIC cell lines. These cell lines will be treated with a library of P13K pathway inhibitors, and their effectiveness will be reflected by curbed BTIC proliferation and tumor growth, and will be quantified by reductions in neurosphere formation and decreases in CD133 expression. If successful, the results of this study may have applications towards creating novel treatments for brain tumor patients in the future.

PATIENT INCLUSION/EXCLUSION CRITERIA

Inclusion Criteria

Pediatric patients (0-18 years) presenting to Neurosurgery for resection of the following tumour types will be eligible for participation in the BTIC study:

- Anaplastic Astrocytoma
- Malignant Germ Cell Tumor or Germinoma
- Glioblastoma
- Medullablastoma (PNET in Post Fossa)
- Ependymoma
- Anaplastic Pleomorphic Xanthoastrocytoma
- Atypical Teratoid Rhabdoid Tumor
- Other malignant tumor form

BCCH treats an average of 30 brain tumour patients annually, half of whom will present with a high-grade form described above. Thus, it is important that every eligible patient is captured to reach the study's **target enrollment number** (n=10-15).

Exclusion Criteria

Patients will be excluded from the study under the following conditions:

1. Specimen not capable of cultivating BTICs in the laboratory.
2. Contamination of specimen by external environment or poor sterile technique.
3. Resected tumor is adequate for clinical purposes, but insufficient for study; see ETHICAL CONSIDERATIONS, page 14).
4. Low-grade gliomas

PROCEDURES

STUDY TEAM

The BTIC Study team at BC Children's Hospital consists of:

- PI and Co – investigators:
  Dr. Ash Singhal
  Dr. Juliette Hukin
  Dr. Rod Rassekh
  Dr. Christopher Dunham
- Research Manager: Dr. Vesna Popovska
- CRC: Mr. Ross Hengel

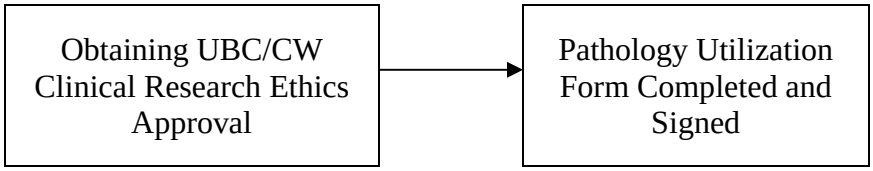
Applicable to all study staff:

The staff involved in this study is encouraged to read the *Standard Operating Procedures for Neurosciences Program Research* (hard copy provided in the CRC's office), and behave according to those procedures.

The staff involved in the study is also encouraged to familiarize themselves with the study protocol which is located on the U:\ Drive: \ Research Coordinator (personal drive to the CRC) and X:\ (shared drive): \ Neurosurgery Research \ BTIC protocol-May 10, 2010. A hard copy can be found in the CRC's office (Ross Hengel, Room K3-167) or in the Research Manager's office (Dr. Vesna Popovska, Room K3-175) in the BTIC Study file folder located in the second drawer of the grey filing cabinet.

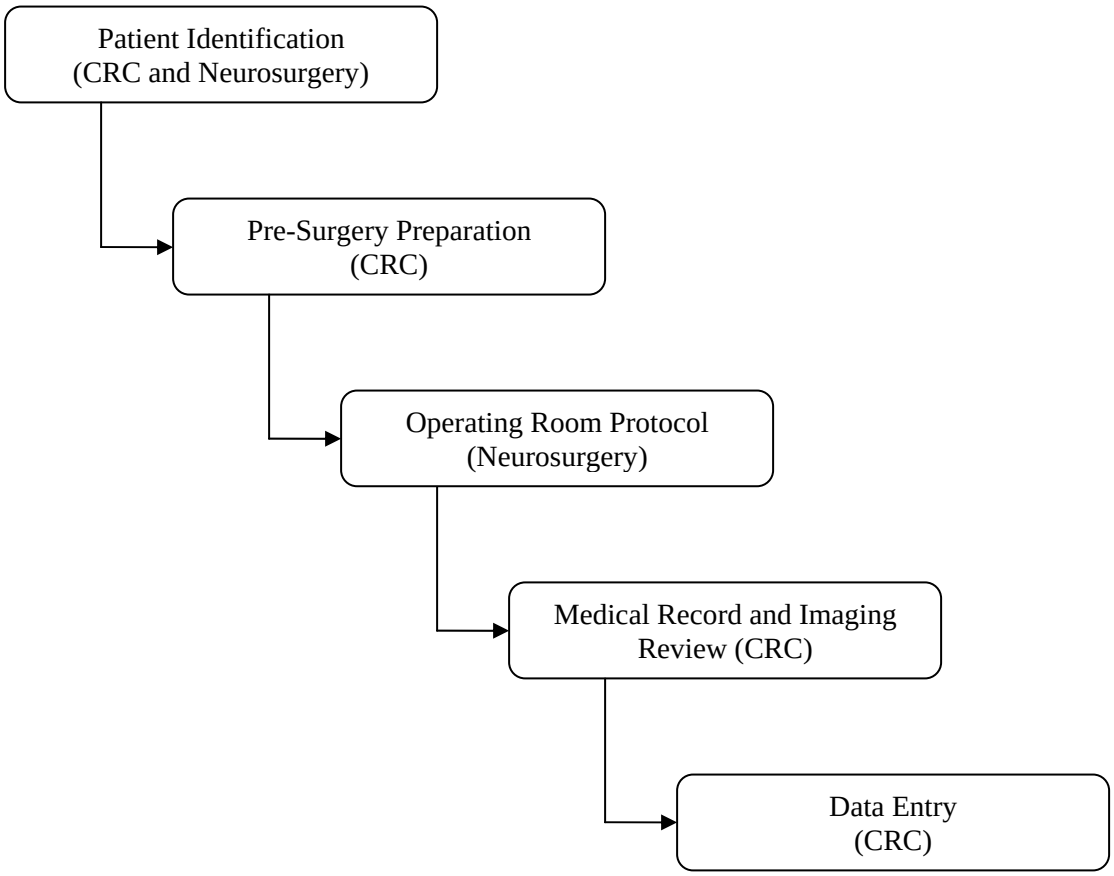
WORK FLOW DIAGRAM

Following study design by the PI, the **pre-approval** study implementation scheme takes place in the two phases diagramed below:



(RM) (CRC)

The **post-approval** on-site study implementation consists of the following phases:



OBTAINING CERTIFICATES OF APPROVAL

The Research Manager is responsible for obtaining ethics approvals from both the UBC/CW Research Ethics Boards. Adhering to the Neurosciences Research Program's Standard Operation Procedures and maintaining ethical renewals are also responsibilities of the research manager (table 1).

Originals and copies of the Certificates of Approval are filed by the RM and can be obtained from **Dr. Vesna Popovska's office; Room: K3-175; local: 5157**

- Ethics approvals are in both:
  - BTIC Ethics Folder in the 2nd drawer of filing cabinet or
  - Blue binder (Neurosurgery ethics approvals) on the top shelf above computer

- Electronic versions can be found under My Computer on the following drives:
  - U:\ All Current Studies \ BTIC Study \ Ethics
  - X:\ Neurosurgery \ Research \ BTIC study\Approvals

Table 1. Most recent ethics approvals

Certificate of Approval from UBC Clinical Research Ethics		
Date Obtained	Period Covered	
	From	To
May 13, 2010	February 14, 2012	February 14, 2013

Certificates of Approval from C&W Research Ethics Board		
Date Obtained	Period Covered	
	From	To
May 13, 2010	February 14, 2012	February 13, 2013

POST-APPROVAL STUDY IMPLEMENTATION

Patient Screening and Identification of Eligible Study Subjects

Patient screening for the BTIC study is performed by the CRC with the support of the pediatric neurosurgeons at BCCH. This task is the chief responsibility of the CRC, and is one of the most crucial steps to ensuring that all eligible study candidates have been considered.

There will be two approaches to patient screening. The first approach involves the CRC identifying eligible patients through active surveillance of surgical appointments. This task is performed in the neurosurgery out-patient clinic (room K3-160) by examining the OR slate for upcoming brain tumour resection operations. The OR schedule, located adjacent to the unit clerk's work desk, lists surgeries scheduled during regular OR hours of operation (Tuesday and Friday) and does not take into account evening or weekend cases. Patients presenting to the OR for unscheduled tumor resections during the evening or weekend hours will be recruited by the attending on-call neurosurgeon. Once eligible patients are identified, the CRC will confirm their eligibility with the attending neurosurgeon, or Dr. Ash Singhal who is the principal investigator of the BTIC study.

The second method involves following-up with the neurosurgical team for patient referrals. The CRC will be responsible for sending monthly e-mail reminders to the neurosurgeons requesting that they refer any of their patients that match the inclusion criteria of the BTIC study (included in the email) to the CRC by providing the patient's name, date of birth and anticipated time/date of surgery. It is recommended that the CRC add this task to their outlook express calendar and save the e-mail message for use at later months.

Pre-Surgery Preparation

Obtaining Informed Consent

Upon identifying eligible patients for the BTIC study, the CRC will ask the attending Neurosurgeon to introduce him/her to the patient and the family. The CRC then explains the study to the family. If the parent or primary caregiver agrees to participate, the CRC will have them carefully read and sign the ICF. If the patient is 7 years of age or older and deemed competent, s/he signs an accompanying assent form. If the patient is 14 years of age or older, s/he signs the separate consent page on the consent form. Consent and assent forms for the BTIC study will be stored in pre-made study instructions packages (see below). After the consent/assent forms are signed, the CRC then proceeds to preparing the rest of the study team for specimen retrieval and transfer to Dr. Dunn's laboratory.

Team Preparation

Once informed consent has been obtained, the CRC will be responsible for contacting the Dunn laboratory and Drs. Dunham or Hendson with the approximate time/day of the patient's surgery at least 48 hours prior to the procedure (if possible). Early notification to both parties will ensure proper preparation for sample collection, and increase the likelihood of successful specimen transfer to the Dunn laboratory.

Prior to the surgery, the CRC will ensure that study specific instructions packages are stored in the "Neurosugery Research" slot in room #3R51 of the 3R ward. Each package contains the following items placed in a 9 x12 inch envelope:

- BTIC Study Instructions (*U:\Neurosurgery Research\BTIC Study\Study Package\BTIC Study Instructions.doc*)
- Study Consent Form (*U:\Neurosurgery Research\BTIC Study\Forms\Consent\BTIC Study Consent Form*)
- Study Assent Form (*U:\Neurosurgery Research\BTIC Study\Forms\Consent\BTIC Study Assent Form*)

- Pathology Study Utilization Form (*U:\Neurosurgery Research\BTIC Study\Forms\BTIC Requistion_revised September 23,2010.doc*)
    - With patient addressograph and specimen site, date of surgery, and time of BTIC specimen removal highlighted in green)
- The BTIC study Instructions and checklist labels will be affixed to the front of the envelope for easy recognition and consistency in following operating room protocol (*U:\Neurosurgery Research\BTIC Study\Study Package\Labels/Checklist 2.doc)*

The consent/assent forms are to be taken from these packages when obtaining informed consent. The BTIC study instructions envelope is then clipped to the front of the patient's surgical chart (located on the 3R ward) for the attending surgeon to consult when carrying out the study protocol.

Assigning the Patient ID

After the study team has been prepared for surgery, the CRC creates a *Patient Template* for the recruited patient. This serves as a reference sheet for the patient and includes the patient's name, MRN, date of birth, study identification and contact information.

Recruited patients will be assigned a study ID by Pathology to protect their confidentiality. The patient study ID will include the prefix "BT", followed by the patient's three digit enrollment number (i.e. the first enrolled patient=BT001, second enrolled patient=BT002). The Neuropathologist attending to the case will attach patient ID labels to the sterile specimen container and pathology study utilization to de-identify patient information. Study ID labels are stored in the BTIC study section of the Pathology Log (to be kept in L233 of the Shaugnessy Building, Department of Anatomical Pathology).

Surgical Protocol

In the event of an unscheduled evening or weekend procedure, the attending Neurosurgeon will obtain informed consent using the consent/assent forms provided in the BTIC study instructions packages. After removing the tumour sample, the OR nurse will contact the on-call neuropathologist. Sandy Dunn's lab will be notified by the on-call Neuropathologist (refer to call list protocol in study procedures) to prepare for sample pick-up. Neuropathologist to notify Ross Hengel of any new patients that underwent an evening/weekend surgery and relay the study # used.

Intra-operative procedures are provided in the study procedures manual (at the end of the study protocol) and study instructions sheet of the BTIC instructions package.

Medical Record and Imaging Review

Once a pathology diagnosis is available (typically 2-3 days following tumour resection), the CRC will review the patient's health records and medical imaging to obtain the data needed to complete the *BTIC Case Report Form-DIAGNOSIS* located on the U:\Drive:\Neurosurgery Research\BTIC Study\Forms\Case Report Forms. There is a separate CRF (*Case Report Form-PROGRESSION)* to be completed for patients that have relapsed, as it requires additional information about the tumour progression since the initial surgery and any subsequent surgeries the patient received. The CRC may use iStentor or EVE (see *Orientation to Hospital Computer Programs*, U:\Drive\Neurosurgery Research\Training Resources) to access electronic patient health records, as well as the Neurosurgery charts (located in the office of the neurosurgery clinic) and Oncology charts (located in the Oncology/Haematology clinic on the far East wing of the main building on floor level).

Measuring AP, Transverse and Craniocaudal Dimensions to Calculate Tumour Volume (Diagnosis, Post-Surgery, Post-XRT, Post-Chemotherapy)

To calculate tumour volume, the CRC will review patients' medical images electronically to measure the anterioposterior (AP), transverse, and craniocaudal axes of the patient's

tumour. This **must** be done with the assistance of Neurooncologist Dr. Hukin to ensure that the measurements are accurate. Occasionally, these measurements will already be provided in the radiology report of the patient's medical images, and can be used to calculate the volume of the tumour at any of the given stages of treatment listed above. Therefore, it is best to check the radiology report first before contacting Dr. Hukin for assistance.

Adjuvant Therapy

Not all of the data required in the CRF will be available immediately or even soon after surgery. The adjuvant therapy section in particular contains many sections that cannot be completed until months or even a year following surgery. The CRC will have to wait at least one year after surgery to calculate tumour volume post-XRT (if applicable), due to the fact that maximum response to radiotherapy is observed within a year following the therapy completion date. Thus, a series of assessment scans will take place following completion of therapy to identify the best response of the tumour to radiotherapy. Although follow-up imaging takes place shortly after completion of chemotherapy treatment, many treatment regimens take a considerable length of time to complete, and calculating the best response of the tumour to chemotherapy (if applicable) may not be possible until several months following surgery.

Data Entry

Upon completion of the CRF, the CRC enters the data collected into the *BTIC database.xls* located on the U: Drive\Neurosurgery Research\BTIC Study. The spreadsheet workbook contains the following sheets:

- Patient Summary
- Diagnosis
- Progression 1
- Progression 2

Additional sheets may need to be added to the *BTIC database* if patients are enrolled with a third or higher progression order.

ETHICAL CONSIDERATIONS

It is the prerogative of the attending Neuropathologist to reject the use of any tumor specimen for the use of research if, after all samples are collected, there isn't an adequate amount of tissue available for clinical purposes. All study specimens sent for review by pathology must be accompanied by a completed **study requisition form** in order for the tissue to be transferred off-site to the Dunn laboratory following frozen section analysis.

APPENDIX 3: Ethics Approvals

CHILDREN'S & WOMEN'S HEALTH CENTRE OF BRITISH COLUMBIA
AN AGENCY OF THE PROVINCIAL HEALTH SERVICES AUTHORITY

UBC C&W Research Ethics Board
A2-136, 950 West 28th Avenue
Vancouver, BC V5Z 4H4
Tel: (604) 875-3103 Fax: (604) 875-2496
Email: cwreb@cw.bc.ca
Website: http://www.cfri.ca/research_support > Research Ethics

ETHICS CERTIFICATE OF DELEGATED APPROVAL: RENEWAL

PRINCIPAL INVESTIGATOR:	DEPARTMENT:	UBC C&W NUMBER:
Ash Singhal	UBC/Medicine, Faculty of/Surgery	H09-02812

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

Institution	Site
Children's and Women's Health Centre of BC (incl. Sunny Hill)	Child & Family Research Institute

Other locations where the research will be conducted:
N/A

CO-INVESTIGATOR(S):
Christopher Dunham
Juliette Hukin
Sandra E. Dunn
Abbas Fotovati
Rod Rassekh

SPONSORING AGENCIES:
- Brain Tumour Foundation of Canada - "Targeting the elimination of brain tumour initiating cells by disrupting the P13K pathway"
- Child & Family Research Institute - "Targeting the elimination of brain tumor initiating cells by disrupting the P13K pathway"

PROJECT TITLE:
Targeting the elimination of Brain Tumor Initiating Cells
by disrupting the PI3K pathway

REMINDER: The current UBC Children's and Women's approval for this study expires: January 25, 2014

APPROVAL DATE: January 25, 2013

CERTIFICATION:
In respect of clinical trials:
1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.
2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.
3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The Chair of the UBC Children's and Women's Research Ethics Board has reviewed the documentation for the above named project. The research study, as presented in the documentation, was found to be acceptable on ethical grounds for research involving human subjects and was approved for renewal by the UBC Children's and Women's Research Ethics Board.

Approved by one of:

Dr. Marc Levine, Chair **Dr. Caron Strahlendorf, Associate Chair**

CHILDREN'S & WOMEN'S HEALTH CENTRE OF BRITISH COLUMBIA

University of British Columbia – Children's & Women's Health Centre of BC
Research Ethics Board
(UBC C&W REB)

UBC C & W Research Ethics Board
Room A2-136
950 West 28th Avenue
Vancouver, B.C. V5Z 4H4
Tel: (604) 875-3103 Fax: (604) 875-2496
Email: reb@cw.bc.ca
Website: www.cfri.ca/Research Ethics
RISe: https://rise.ubc.ca

Jan 25 2013

C&W Institutional Certificate of Approval
-- RENEWAL --

PRINCIPAL INVESTIGATOR	DEPARTMENT	NUMBER
Singhal, Ash	Surgery	CW09-0268 / H09-02812

CO-INVESTIGATORS:
Hukin, Juliette; Dunn, Sandra E.; Fotovati, Abbas; Rassekh, Rod; Dunham, Christopher;

C&W DEPARTMENTS, PATIENT BASED PROGRAMS AND ADMINISTRATIVE JURISDICTIONS IMPACTED BY THIS STUDY:
Pathology and Laboratory Medicine; Records Management;

SPONSORING AGENCIES:
Child & Family Research Institute;

TITLE
Targeting the elimination of Brain Tumor Initiating Cells
by disrupting the PI3K pathway

TERMS OF RENEWAL	
Jan 25 2013 - Jan 24 2014	

CERTIFICATION:

Ethical approval has been granted for the above-referenced research project. I am pleased to inform you that all necessary hospital program/resource approvals and institutional agreements/contracts are now in place and that you have permission to begin your research.

_____

Dr. Stuart MacLeod
Vice President, Academic Liaison and Research Coordination,
Provincial Health Services Authority

This Certificate of Approval is valid for the above term provided there is no change in the research protocol

APPENDIX 4: Publications

Abstracts

Fotovati A, Radiloff D, Coute N, Triscott J, Chen J, Yip S, Louis D, Toyota B, Hukin J, Rassekh SR, Singhal A, Dunham C, and Dunn SE. The Y-Box binding protein-1 conveys temozolomide resistance by the inhibiting DNA damage response pathway through the polycomb repressor BMI-1. 2013 Pediatric Neuro-Oncology Basic and Translational Research Conference. Fort Lauderdale, Florida, May 2013. Platform presentation by S. Dunn.

Lee C, Triscott J, Foster C, Manoranjan B, Pambid MR, Fotovati A, Berns R, Venugopai C, O'Halloran K, Narendran A, Northcott P, Taylor MD, Singh SK, Singhal A, Rassekh R, Maxwell CA, Dunham C, and Dunn SE. Personalizing the treatment for medulloblastoma: Polo-Like Kinase 1 (PLK1) as a molecular target for the sonic hedgehog (SHH) subtype. 2013 Pediatric Neuro-Oncology Basic and Translational Research Conference. Fort Lauderdale, Florida, May 2013. Platform presentation by J. Triscott.

Manuscripts

Triscott J, Lee C, Foster C, Manoranjan B, Pambid MR, Berns R, Fotovati A, Venugopal C, O'Halloran K, Narendran A, Hawkins C, Ramaswamy V, Bouffet E, Taylor MD, Singhal A, Hukin J, Rassekh SR, Yip S, Northcott P, Singh SK, Dunham C, and Dunn SE**.** Personalizing the treatment for medulloblastoma: Polo-Like Kinase 1 (PLK1) as a molecular target for high-risk patients. Preparation for submission to Journal of Clinical Oncology.

APPENDIX 5: Finance Report

CHILDREN'S & WOMEN'S HEALTH CENTRE OF BRITISH COLUMBIA

RESEARCH INSTITUTE FINANCE
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Brain Tumor Foundation of Canada
620 Colborne St. Suite 301
London, ON N6B 3R9

Date: July 22, 2013

C&W Account No.#(s): CRG74190

Brain Tumour Fdn-P13K Pathways: Targeting the elimination of brain tumour initiating cells by disrupting the P13K pathway

STATEMENT OF EXPENDITURES

For the period May 30, 2012 to Jun 30, 2013

Opening Balance	
Funding received to date	24,900
Total funds available for expenditure	24,900
Expenditures	
Salary	24,900
Total expenditures	**24,900**
Unexpended amount	-

Dr Ash Singhal
Principal Investigator

Mike Gottenbos
Finance Manager
Child & Family Research Institute