BC CANCER
Provincial Health Services Authority

Headlines

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a newsletter for brain tumour patients and their families

winter 2020

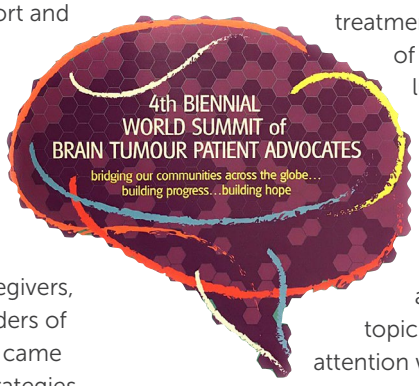
WORLD SUMMIT

International Brain Tumour Alliance (IBTA) 4th World Summit

By Yaron Butterfield

FROM OCTOBER 9-12, 2019, Rosemary Cashman, Nurse Practitioner at BC Cancer, and I attended the 4th Biennial International Brain Tumour Alliance (IBTA) World Summit in Bethesda, Maryland, US. IBTA was founded in 2005 as a dynamic worldwide community to advocate for the best treatments, information, support and quality of life for brain tumour patients and their families.

Two full days of the Summit were held at the National Institutes of Health, an internationally recognized medical research centre. Brain tumour patients and caregivers, researchers, clinicians and leaders of various brain cancer initiatives came together to share ideas and strategies to improve the care and well-being of those living with brain cancer. During the course of the Summit, I learned about the exceptional research occurring throughout the world that is focused on solving the problem of these deadly diseases. It was so inspiring to meet the people who do this work and to observe the passion that they bring to their efforts.



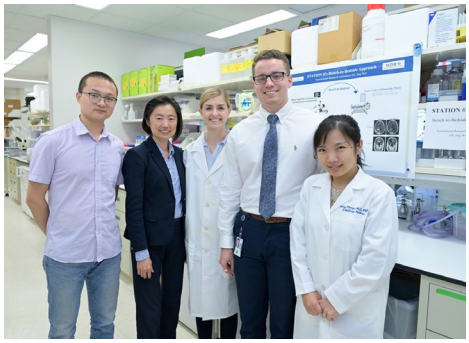
Talks ranged from brain tumour treatments and updates on research to discussions about patient perspectives. For example, we talked about quality of life, the outcomes that patients report, rehabilitation, returning to school and work after treatment and care mapping. I also learned about various brain tumour foundations around the world. Sadly, I heard how difficult access to treatment is in some parts of the world and how lucky I am to be living in Canada.

We discussed how patients can play a more active role in their treatment and healing. Another topic that caught my attention was the feeling of abandonment that some patients experience after their intense treatment ends. I definitely felt this after my treatment and now I can see that I would have benefitted from more support at that stage.

There were talks from parents of children with brain tumours who set up programs to support other families going through this hardship. As much as I've learned through my personal experience and through support groups about the effects of a brain tumour diagnosis on a family, I couldn't imagine how hard it would be to be the parent of a young child with brain cancer. It really hit me how brain cancer affects all aspects of life in so many different ways no matter where you live in the world. Each individual's path is unique, but we discussed strategies applicable to all. For me, just being with others who have been on the path I travelled was very meaningful.

In one of the question and answer periods, I offered a suggestion that was well received. I proposed that authors of

scientific research papers summarize their research for a lay audience. This would help patients and caregivers to better understand the research and close the gap between researchers and patients. It was clear that there is a need to expand the dialogue between those who treat brain cancer and those who are being treated.



We were also fortunate to get a tour of one of their neuro-oncology labs and were able to interact with researchers. It reminded me of our own labs at BC Cancer including our work in genomics at the Genome Science Centre (GSC). It made me proud

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Improvements in the classification system for brain tumours lead to better treatment for patients

By Dr. Brad Chaharyn
Resident doctor (PGY3) in Neuropathology
Vancouver General Hospital

UNDERSTANDING WHAT SORT OF tumour a person has is critically important in determining what type of treatment will be best to treat that tumour. The processes used to obtain a precise diagnosis can be complicated and expert neuropathologists play a critical role in diagnosis.

The classification of central nervous system (CNS) tumours has undergone rapid changes in the last two decades. This has come about from an explosion of knowledge in molecular diagnostics, a term used to describe the techniques used to analyse biological markers in an individual's genetic material. These techniques provide valuable information about cancer-specific alterations in proteins and DNA and RNA, which code for the amino acids that make up proteins.

In the past, pathologists looked at the appearance of cells alone in determining the type of tumour that was under the microscope. The study of the appearance of cells and tissues under a microscope is called histology. The new method of molecular diagnostics allows pathologists to better identify several CNS tumours based on distinct molecular characteristics of the tumour cells. These features also correspond to differences in the tumour's behaviour and the response of patients to treatment. Even tumour cells that look the same under the microscope can behave very differently from one another because of molecular characteristics that cannot be directly visualized.

The classification system that is used widely for brain tumours is the World Health Organization (WHO) system. This is updated regularly as advances in our understanding of tumour biology occur. The most recent WHO Classification of CNS Tumours was published in 2016. It introduced many of these molecular characteristics as criteria that pathologists can use to classify brain tumours, including gliomas.

The advances in classification of brain tumours come at a cost. Some of the new tests are expensive and time-consuming and some centers may not have access to the techniques or to staff with the ability to perform and interpret the tests.

At the time of the last classification publication in 2016, the International Society of Neuropathology (ISN) created the Consortium to Inform Molecular and Practical Approaches to CNS Tumour Taxonomy (which uses the acronym cIMPACT-NOW). cIMPACT-NOW provides a forum to evaluate and recommend proposed changes to future CNS tumour classifications. It has already published four updates since 2016.

The first update guided pathologists about how to classify tumours that either do not have molecular testing available (NOS, or "not otherwise specified") or do not fit into any of the current classifications for tumour cells (NEC, or "not elsewhere classified").

Other updates have clarified issues regarding specific diagnoses. One of the updates concerns a rare, very aggressive tumour that occurs in a particular location in the midline of the brain and has a mutation in a gene called H3 K27M. Other updates are relevant for the most common primary brain tumours affecting adults, the diffuse gliomas.

Diffuse gliomas include astrocytomas and oligodendrogliomas. The standard pathological investigation of a diffuse glioma involves microscopic examination of the tumour using laboratory tests involving a number of different staining techniques to highlight certain features of the cells. Molecular testing is also used, if needed. A cIMPACT update provided guidance about when to use these molecular tests. For example, in the case of diffuse gliomas with a mutation in an enzyme called isocitrate dehydrogenase (IDH), if a microscopic staining technique shows a specific pattern that is specific to an astrocytoma, a WHO 2016 diagnosis can be reached without the need for molecular testing.

cIMPACT updates have also provided molecular criteria to determine which low grade gliomas (meaning less aggressive by histology) will show a good response to treatment. Patients whose tumours have the IDH mutations tend to survive longer than those who do not. Tumours that do not have the IDH mutation (referred to as IDH –wildtype) were previously assumed to have exclusively poor outcomes. We now know that some IDH-wildtype tumours

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Gene/molecular change	Significance
IDH 1 and 2	Tumours that have a mutation in IDH 1 or 2 tend to behave better that those that do not have the mutation.
1p/19q	Deletion of segments of chromosomes 1 and 19 is used to diagnose an oligodendroglioma; a tumour with a good prognosis
ATRX	Presence or absence of this mutation helps distinguish between astrocytoma and oligodendroglioma
MGMT	When this gene is silenced or turned off in IDH-wildtype tumours, chemotherapy agents are more successful in treating the tumour
H3 K27M	A diagnostic molecular feature of diffuse midline glioma; a rare tumour with a poor prognosis

Improving outcomes through philanthropy

By Melissa Rottare, Communications Coordinator, BC Cancer Foundation

THE BC CANCER FOUNDATION is the fundraising partner of BC Cancer and the largest charitable funder of cancer research in British Columbia. Every dollar raised stays right here in B.C. to advance research and enhance care for families affected by the disease.

Across British Columbia, the generosity of donors has been a tremendous force in improving the outcomes for patients affected by brain cancer. Donations have provided funding for new technologies, lab equipment, and cutting-edge scientific research.

Whether it's through making a donation directly to support brain cancer research, organizing a fundraising event, fundraising in honour of a loved one, or taking part in the BC Cancer Foundation's annual Ride to Conquer Cancer, everyone can make an impact on the care of patients and families living with brain cancer.

Generous support for research initiatives of BC Cancer's neuro-oncology team will help bring new and improved therapies to the many British Columbians who are diagnosed with brain cancer each year. Here are two projects currently underway:

I. Rehabilitation for Brain Cancer Patients

Fatigue and difficulties with memory and thinking are commonly experienced by patients with brain tumours. Efforts are under way to implement a program using exercise and psychotherapy that is designed to address the needs of individuals with these problems. Researchers at BC Cancer, in collaboration with colleagues at the Watson Centre for Brain Health and the University of British Columbia, are seeking to test the feasibility of a rehabilitation program in individuals with a primary brain tumour. Because cognitive issues are a common side effect of all cancer treatments, this study also has the potential to improve the quality of life of people facing other types of cancer types, too. Funding is still needed to support this program.

II. Transforming Chemotherapy Delivery

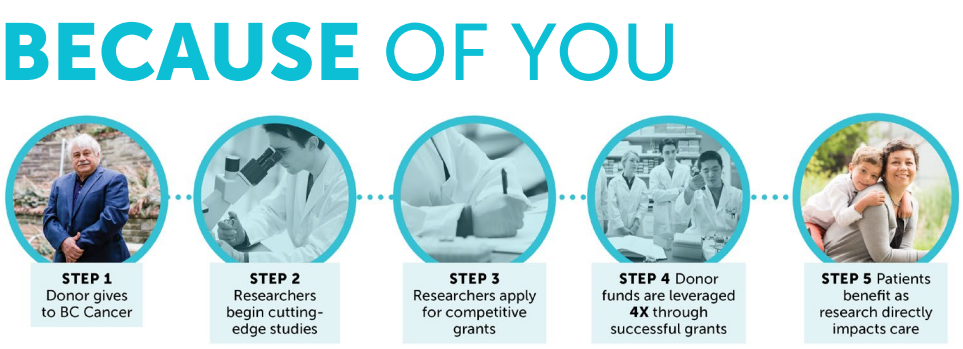
Glioblastoma multiforme (GBM) is difficult to treat because brain cancer cells are able to move quickly and infiltrate brain tissue. BC Cancer Senior Scientist Dr. Cathie Garnis is currently developing a hydrogel-based mesh that releases a special chemical designed to attract brain tumour cells and kill them with chemotherapy. Testing potential chemicals and delivery methods will bring this revolutionary new treatment one step closer to patients in the clinic.

Hope starts here

Whether it is through new drugs and delivery methods or innovations in support for patients and families, cutting-edge research holds the potential to transform daily life for British Columbians affected by brain cancer. With the help of our donors we hope to secure funding to hire a senior scientist who can lead the charge in advancing our understanding of these deadly diseases and develop a centre of excellence in brain tumour care and research.

To learn how you can support the latest breakthroughs in brain cancer research and care, please contact Vanessa Stevens at vanessa.stevens@bccancer.bc.ca or 604.707.5996.

For more information on the BC Cancer Foundation, visit www.bccancerfoundation.com



cIMPACT-NOW

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have a better prognosis. These tumours tend to occur in younger patients and have other identifiable and specific molecular changes.

Molecular diagnostics is becoming increasingly important in the diagnosis of CNS tumours. Knowledge in this field is expanding at such a rate that it is hard to keep current with the changes. cIMPACT-NOW was established to provide a source of continuing updates to guide pathologists as they await the next publication of the WHO classifications. It has been an invaluable resource for those who diagnose and treat tumours of the brain and spinal cord.

The cIMPACT and WHO classification updates help pathologists to more accurately predict the clinical course of affected patients and allow oncologists to tailor treatments so that patients have the best possible outcomes.

References

1. David N. Louis, Hiroko Ohgaki, Otmar D. Wiestler, Webster K. Cavenee (Eds): WHO Classification of Tumours of the Central Nervous System (Revised 4th edition). IARC: Lyon 2016.

2. David N. Louis, et al. cIMPACT-NOW: a practical summary of diagnostic points from Round 1 updates. Brain Pathology. 2019 Jul;29(4):469-472.

BC Cancer Brain Tumour Clinical Trials 2020

By Dr. Brian Thiessen, Neuro-oncologist, BC Cancer – Vancouver

Clinical trials in brain cancer are critical for developing new treatments and establishing new standards of care for this challenging disease. Last year we opened a clinical trial for newly diagnosed glioblastoma patients with a novel agent, marizomib. Enrollment for that trial is ongoing, with many patients participating. We are pleased to be opening a new trial for patients with oligodendroglioma this year. The new trial is going to answer a major question in the management of this disease: which chemotherapy protocol is superior?

Studies in the past using older chemotherapy drugs have established in the last 6 years that using radiotherapy combined with PCV chemotherapy is associated with a longer survival over radiotherapy alone. PCV is a three drug combination therapy using procarbazine, lomustine (also called CCNU) and vincristine. In addition, studies in glioblastoma and astrocytoma have established that the combination of radiotherapy with a newer drug, temozolomide, is also superior to radiotherapy alone. Temozolomide has fewer side effects and is significantly better tolerated than PCV chemotherapy. The current study is designed to determine whether PCV or temozolomide leads to better outcomes for patients with oligodendroglioma when combined with radiotherapy.

The clinical trial is a phase 3 randomized open label study design. This means patients that enroll will receive radiotherapy and be randomly assigned by a computer to have the radiation combined with either PCV chemotherapy or temozolomide chemotherapy. Patients and care providers will not be "blinded" to the treatments since the two therapy arms are completely different schedules with completely different types of drugs. Close attention will be paid to side effects, treatment outcomes and quality of life to determine the best treatment option.

This study is currently open to all patients with grade 2 or 3 oligodendrogliomas where treatment with radiotherapy is deemed necessary by their oncologists. The hope is that we can finally answer which of the two chemotherapy options is better for patients with this disease. Since this is such a hotly debated topic amongst neuro-oncologists, the answer can't come soon enough.

Additionally we are hoping to open a new clinical trial for low grade gliomas after diagnosis by biopsy or surgical resection. This trial will study the value of an inhibitor (that is, a blocker) of mutated IDH (isocitrate dehydrogenase), which is found in 80% of low grade gliomas. IDH mutations are involved in the development of gliomas. The hope is that the new IDH inhibitor therapy will delay progression of these tumours and thereby also delay the need for radiotherapy and chemotherapy. Look to future issues of *Headlines* for more information on this trial as it moves forward.

For more information about clinical trials, see also Headlines Spring 07, Winter 16, Spring 16 and Winter 19 issues.

IBTA 4th World Summit

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of what we are doing in my home town of Vancouver and throughout Canada.

Meetings such as the Summit are an important way to open dialogue between patients, health care providers and researchers and to allow fruitful collaborations to occur.

IBTA is a great organization that raises awareness about brain tumours, advocates for patients and families and promotes international collaboration to improve the lives of those living with brain tumours.

For more information about IBTA see their website at http://theibta.org

You can also connect with IBTA by sending an email to chair@theibta.org and ask to be on their mailing list for updates on international research and advocacy efforts.

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For more information about how you can support enhanced patient care, patient information and brain tumour research, please contact Fatima Hassam, Associate Vice President, BC Cancer Foundation.
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If you would like to submit an article, ask a question, or serve on our patient and family editorial board, please contact Rosemary Cashman at rcashman@bccancer.bc.ca or 604 877 6072 (phone) 604 877 6180 (fax).