

FUNDING FOR RESEARCH INTO CANCERS WITH LOW SURVIVAL RATES

Submission by Dr Jonathon Parkinson on behalf of NSWOG (Neuro-oncology)

31st March 2017



Working together to lessen the impact of cancer

Senator Catryna Bilyk
Chair

Senator David Bushby
Deputy Chair

Dear Senators,

Please accept our submission as invited by the Select Committee into Funding for Research into Cancers with Low Survival Rates formed on 29th November 2016. Our group's specific interest is in the area of brain cancer, and we applaud the Committee's recognition within the terms of reference of this inquiry of the importance of research into brain cancer.

ABOUT US

The group which is currently known as the New South Wales Oncology Group (NSWOG) in Neuro-oncology was formed in October 2001 by a group of individuals interested in improving treatment of brain cancer patients in NSW. This group established regular meetings, and in 2004 were invited into the NSW Cancer Institute as a pre-existing group.

Achievements of NSWOG (Neuro-oncology) include patient education and support forums (on an annual or more frequent basis), production of support resources for patients, carers and professionals, as well as co-ordinating collaborative projects in epidemiology and clinical research.

At present the group meets in alternate months, with representatives from all aspects of neuro-oncology including clinicians (medical oncologists, radiation oncologists, neurosurgeons, neuropathologists and rehabilitation specialists), allied health professionals, research scientists, patient advocate group representatives and representatives of fundraising groups.

This submission will therefore focus on brain cancer, although many of the principles raised may be applicable to other cancers with low survival rates.

ABOUT BRAIN CANCER

The vast majority of brain cancers arise not from the nerve cells within the brain, but from those cells that surround the nerves, the glial cells. Unfortunately, the commonest type of brain cancer is that with the most aggressive clinical course, glioblastoma.

Advances in treatment of glioblastoma have been minimal over the past 40 years. In the late 1970s (*Walker et al 1978*) the utility of radiotherapy in their treatment was demonstrated; it was a further 30 years until survival was shown to improve with the addition of chemotherapy. Not only does the prognosis remain dismal even with optimal treatment (14.6 months' median survival, 25% 2 year survival (*Stupp et al 2005*)) but there has been very little advance in treatment since the above data was released over ten years ago.

Brain cancer remains the single biggest cause of cancer death in patients under 40 years of age. It is because of this that brain cancer results in more years lost per sufferer than any other cancer. This also has huge financial impact on both an individual and community level as frequently these people are taken in the years of their life during which they have maximum earning capacity.

As well as the financial impact of brain cancer, the very nature of brain cancer results on a much greater impact on the patient and their family than the majority of other cancers. Firstly, many patients' illness may declare itself by personality change, memory loss or some sort of neurological deficit (akin to a stroke) that may lead to a level of disability that requires extensive home help. Generally, patients have a craniotomy for initial diagnosis and treatment – because of this even those patients without an initial neurological deficit are unable to drive and usually therefore not work. Furthermore, standard treatment is usually in the form of radiotherapy administered on a daily basis Monday to Friday for a period of 6 weeks – again placing further burden on family or other supports for transportation. So within a few short months a family's entire life may be completely changed.

The very existence of this Senate Inquiry acknowledges the impact of brain cancer on the Australian community. Hopefully the above has served to reinforce the relevance of brain cancer.

ADDRESSING TERMS OF REFERENCE

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“the current National Health and Medical Research Council funding model, which favours funding for types of cancer that attract more non-government funding, and the need to ensure the funding model enables the provision of funding research into brain cancers and other low survival rate cancers;”

The NHMRC commonly supplies a great deal of funding for cancer research but typically delivers funding for projects into more common cancers. The Structural Review of NHMRC's Grant Program - Public Consultation released in July 2016 acknowledged that NHMRC peer reviewers are more likely to favour research into

the more common cancers, and also award established researchers with track records grants. These factors both work against brain cancer research as the relative lack of non-government funding available for brain cancer research provides a significant obstacle for researchers to establish themselves in the field.

B

“the obstacles to running clinical trials for brain cancers and other cancers with relatively lower rates of incidence, with regard to:

- i. funding models that could better support much-needed clinical trials, and*
- ii. funding support for campaigns designed to raise awareness of the need for further research, including clinical trials;”*

As stated above, brain cancer is relatively rare, however it has a disproportionate impact on the community. The low incidence however is a major impediment to effective research and clinical trials in brain cancer as the number of patients needed to show significant changes in outcome with changes in treatment are not easily obtained.

Current funding models, in particular the NHMRC funding grants, are often given to isolated projects. By funding participation of Australian bodies in multi-centre international trials the available resources for clinical research may be better utilised.

The Co-operative Trials Group in Neuro-Oncology (COGNO) has been established to further neuro-oncological research in Australia and as such has led to significant participation of Australian patients in international trials, as well as coordinating some such trials from within Australian centres. This group has a track record in establishing clinical trials in brain cancer within Australia and plays a vital role in “pooling” patients as well as disseminating information regarding available trials thereby optimising clinical trial participation across Australia.

Clinical trial participation across Australia is also hampered by the poor centralisation of neuro-oncological services. Development of a smaller number of more specialised neuro-oncological centres would ensure more focused centres increase patient numbers so as to maximise recruitment to clinical trials, both local and international.

Traditional study design has also resulted in long delays between new technology being devised and implemented into clinical practice. Adaptive trial design, such as employed in the GBM-AGILE project (<https://www.curebraincancer.org.au/page/175/about-gbm-agile>) are likely to help improve prognosis for brain cancer however adequate resources are imperative for progress.

Regarding awareness of the need for clinical trials, the biggest impediment to raising awareness is the poor prognosis of brain cancer. Many patients with other cancers, most notably breast cancer, survive their illness and are able to advocate for the cancer they have been afflicted with. The universally poor prognosis of brain cancer contrasts this. Furthermore, aside from the dire psychological effects of losing a loved one to brain cancer, the exhaustive process of treatment as described above means many touched by brain cancer no longer have the psychological or financial resources to contribute to the cause.

C

“the low survival rate for brain cancers, lack of significant improvement in survival rates, and strategies that could be implemented to improve survival rates”

As stated above, the commonest form of brain cancer is unfortunately the most aggressive. Glioblastoma currently has a median survival of approximately 14.6 months. More disturbingly is the lack of improvement in survival over the past 40 years or so – with data from the late 70s putting the median survival at 9 months (*Walker et al 1978*). This is in clear contrast to other cancers including breast cancer, prostate cancer, lung cancer and melanoma.

Prevention of brain cancer is, in contrast many cancers, almost impossible. The cause(s) are still unknown. By raising public awareness of early detection in the case of breast and prostate cancers or of prevention in lung and melanoma cancers, significant reductions in the impact of these cancers have been made. Unfortunately, in the instance of brain cancer no such impact has been made. Brain cancer remains the most common cause of cancer death in Australians below the age of 40 and subsequently has the greatest impact on the Australian society in terms of average years of life lost.

There however has been some recognition of subtleties in diagnosis of brain cancer that have offered some hope for ongoing treatment. Using modern molecular techniques distinct subtypes of what has previously been grouped into one heterogeneous group (glioblastoma) have been identified. Data from The Cancer Genome Atlas (TCGA) have shown the existence of four molecularly distinct subgroups of glioblastoma (proneural, neural, classical and mesenchymal); this is important to the patient as it allows them to better understand their own disease and its likely course; to the treating team as it may alter the treatment offered; but the true value of this data lies in the ability for researchers to investigate the fundamental causes of this disease (or diseases) and ultimately offer a cure.

At present detailed characterisation of individual patient tumours is available only in a research setting. While common genetic alterations such as mutations in the IDH gene are routinely tested as part of pathology, further analysis is not made available for the vast majority of patients – clearly limiting the ability of the treating team to potentially tailor treatment to that is best for the patient. The correlation of this is that this may alter survival rates adversely.

New technologies such as establishing patient-derived cell lines from individual patients' tumours at the time of surgery, and then testing these tumours for their response to various chemotherapy agents in the laboratory are changing the way we can tailor treatments. This may present the opportunity to administer only drugs that the patient's tumour is likely to respond to, avoiding potentially dangerous side effects. But such a process is labour intensive, requires costly laboratory research and at present has not undergone the necessary detailed scientific investigation to become commonplace in patient treatment.

Without a doubt the strategy which is likely to have the greatest impact on survival rates in brain cancer is improved research funding. Only through increased resources will investigation of the causes of brain cancer ultimately provide effective treatment options and potentially universal cure. This process is likely to take some years however it is must remain the ultimate goal.

In the interim, a number of measures may result in improved survival from brain cancer.

1. Increase availability of molecular markers that could potentially result in tailoring of treatment and improve survival at the individual level.
2. Adaptation of novel research / clinical trial design to promote rapid translation of research findings into clinical practice.
3. Expand care co-ordination services to allow brain cancer sufferers access to optimal treatment as well as provide psychosocial support for their families and carers (see below).

D

“other relevant matters.”

Care co-ordination

As detailed above the impact of brain cancer on a patient and their family is profound. Effects of ongoing treatment can continue to have significant impact throughout the course of a patient’s illness from diagnosis until death. Monitoring is usually through regular MRI scans which need to be arranged. Other complications of brain cancer such as epilepsy, electrolyte disturbances and side effects of medication such as corticosteroids need to be managed.

Cancer patients are therefore best cared for under a model of care co-ordination. Care co-ordinators are usually nurses, with additional sub-specialist training that provides them with the knowledge of specific complications sufferers of each particular cancer may encounter. At present there are very few dedicated brain cancer care co-ordinators in NSW and indeed Australia-wide. Indirectly, through suboptimal management of complications there is a negative impact on the survival of patients with brain cancer.

Attention to this inadequately addressed area of patient care is likely to result in an almost instant improvement in overall patient survival.

Yours faithfully,

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Chair NSWOG (Neuro-oncology)