



Committee Secretary
Select Committee into Funding for Research into Cancers with Low Survival Rates
Department of the Senate
PO Box 6100,
Canberra ACT 2600
AUSTRALIA

31 March 2017

CanTeen Australia Submission to the Select Committee into Funding for Research into Cancers with Low Survival Rates

Dear Committee Secretary,

Thank you for the opportunity to make a submission to the Senate Select Committee into Funding for Research into Cancers with Low Survival Rates on behalf of CanTeen Australia. Our submission has been prepared with the support and endorsement of senior leaders in the Australian Research, Clinical Trials and Low Survival Cancer Advocacy sectors.

CanTeen is committed to advocating for, supporting and undertaking high-quality research and evaluation that enhances our knowledge, understanding and insight into young people impacted by cancer and identifying the most effective ways of treating and supporting them. We also focus on rapidly translating research findings into meaningful action and better access to appropriate care and support for these vulnerable young Australians.

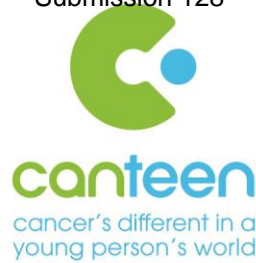
Young Australians diagnosed with cancer are impacted by a range of low survival and rare cancers, some of which have 5-year survival rates as low as 20%. In the wider Australian rare and low survival cancer context, it is clear that while critical foundational research to better understand rare and low survival cancers and develop treatments is needed, support for such research is currently sub-optimal.

Advances in treatment are hindered by complexities in conducting clinical trials for these populations, limiting opportunities to bring new treatments to market. Investment in research and implementation of early detection are also critically needed. Going forward, addressing these issues as well as the current lack of coordination in advocacy, strategy and investment in rare and low survival cancers will be vital drivers of improved outcomes.

I would be delighted to appear before the Committee at a public hearing to further elaborate on the issues presented in our submission should the opportunity be available.

Yours sincerely,

Peter Orchard
Chief Executive Officer
CanTeen Australia



Senate Select Committee into Funding for Research into Cancers with Low Survival Rates

On 29 November 2016, the Australian Federal Senate established a select committee to be known as the Select Committee into Funding for Research into Cancers with Low Survival Rates to inquire and report on the impact of health research funding models on the availability of funding for research into cancers with low survival rates. The committee terms of reference are as follows:

The impact of health research funding models on the availability of funding for research into cancers with low survival rates, with particular reference to:

- a) 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;
- 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;
- 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 and;
- d) other relevant matters.

Low Survival Cancers in Adolescents and Young Adults

Although overall survival rates are good for Adolescents and Young Adults (AYAs) at approximately 88%¹, this masks poorer outcomes seen in several high lethality cancers for this age group. Five-year survival for cancers such as Acute Myeloid and Acute Lymphoblastic Leukaemias and Brain and Bone cancers are still exceptionally low at between 61.3% and 65.6% with Sarcoma only slightly higher at 76.7%, with others such as Rhabdomyosarcoma and Lung and Adrenocortical Carcinomas having 5 Year survival rates well below 40%, and Hepatic Carcinoma only 20.6%¹⁻³.

Compared to paediatric and older adult populations, AYAs have experienced relatively poorer survival gains and reductions in mortality, in part driven by poorer access to clinical trials⁴. Embedding clinical research within standard paediatric care has been the single most important driver of the dramatic improvements in childhood cancer survival rates seen over the past 40 years. Compared with the approximately 45% of younger children with cancer in Australia who currently participate in potentially life-saving clinical trials⁵, AYA participation rates remain low at approximately 10%.

Strategies adopted in the UK aimed at increasing trial availability and access for AYA, which could be replicated in Australia, have seen participation rates of rise to 30% for 15-19 year olds and 14% for 20-25 year olds between 2005-2010⁶. These included increased awareness amongst healthcare professionals, patients and the public about research, initiation of trials with broader age limits allowing older AYAs to enrol and efficient approval processes facilitating initiation of new trials⁶.



The rarity of some cancers which disproportionately impact this age group is another reason for the poorer improvements in length of survival and mortality². Despite improvements in the diagnosis and treatment of common cancers that have resulted in dramatic reductions in mortality, early diagnosis programs for rare cancers have not improved over the last 20 years and diagnosis often remains slow, resulting in the cancer being diagnosed at a more advanced stage⁷.

In addition, rare cancer treatments have not advanced at the same pace as those for common cancers and it is likely that many patients with rare cancers are receiving suboptimal care; hence a rare cancer diagnosis is often accompanied by a very poor prognosis⁷. AYAs diagnosed with a rare cancer are significantly more likely to die from their disease, with these cancers being responsible for the majority of cancer-related deaths in this age group⁷. There is also evidence that AYA cancer has a distinct biology and responds differently to treatments that are otherwise successful in paediatric or older adult populations⁸.

Foundational research is needed but support for research into low survival cancers is sub-optimal

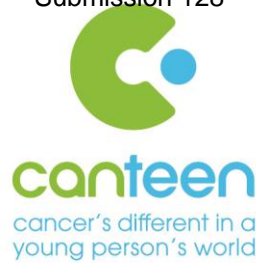
While the NHMRC currently takes multiple approaches to research and research infrastructure funding, they are all broadly geared towards areas with a substantial evidence base and individuals with a strong track record in the target area. They likewise favour short term projects and medical research with substantial existing infrastructure and collaborations. This is unlikely to favour low survival and rare cancers, where the evidence base is necessarily lacking and individuals are unlikely to have had an opportunity to establish the necessary track record to making funding likely.

Drugs for these types of cancers can be more expensive to develop than traditional cancer therapies as they often make use of cutting edge, targeted approaches and experimental delivery methods such as reprogrammed viruses and engineered nanoparticles. As some low survival cancers are also rare, targeted therapies for these can also have narrower applications than traditional chemotherapies, limiting opportunities to recoup investments. They are thus less likely to be attractive investment targets at early stages of development for the pharmaceutical industry without foundational investment from government bodies such as the National Health and Medical Research Council (NHMRC).

Substantial gains will be achieved through investment in research to better understand the mechanisms behind the poor outcomes seen in low survival cancers and how they can be addressed. Efforts also need to focus on making it easier for people with rare or low survival cancers to be part of large, international clinical trials. Facilitating trials of new applications of existing medicines in these cancers will also yield better outcomes by building an evidence-base that clinicians can call on when considering off-label prescription of existing therapies.

Action needed:

- Greater funding allocations for research into targetable genetic, protein, lipid or metabolic mechanisms for rare and low survival cancers
- Greater investment in symptom control research for rare and low survival cancers
- Greater willingness from funding bodies to fund studies that make use of novel designs that may be more economically, practically and ethically appropriate for low survival cancer populations (e.g. population / externally controlled studies)



- Greater investment in implementation and maintenance of biobanks and national minimum datasets for rare and low survival cancer populations facilitating future research
- Prioritisation of funding for rare cancers through the Medical Research Future Fund (MRFF).

Clinical trials complexities and approval requirements discourage drug development

Australian patients with rare and low survivability cancers currently have relatively poor access to world class clinical trials. This is in part due to Australia's complex clinical trials' environment which can vary considerably across neighbouring jurisdictions and between paediatric and adult clinical settings. Pharmaceutical companies can be reluctant to invest in the conduct of large-scale trials of promising new treatments for often small and widely dispersed patient populations given these complexities.

Meeting the challenge of carrying out trials in small populations will become increasingly critical as research into targeted agents advances and personalised medicines become the norm. With these developments, populations from which patients can be recruited will become narrower and traditional clinical trial models will become less and less relevant.

Conducting clinical trials in challenging populations such as those with rare or high lethality cancers can be time consuming and economically unattractive given the complex Australian clinical trials infrastructure and regulatory landscape and a lack of defined partnerships between the government and the pharmaceutical industry. Key issues which may discourage the establishment of domestically initiated studies or the inclusion of Australian sites in international trials for complex populations such as low survival cancers include:

- Complex economic, regulatory and legislative barriers leading to delays and additional costs for those initiating and conducting trials
- Inconsistent embedding of clinical trials in standard care, resulting in insufficient resources and research capacity being available within hospitals to administer trials
- Rare cancers and those with low survival offer a limited population base compared with other cancers
- Inconsistent age restrictions which can prevent some patients (e.g. adolescents and young adults or those over 65 years of age) from participating in trials in both paediatric and adult cancer treatment settings
- Randomised trial designs with the potential to receive a placebo or standard, less-effective treatment may be unethical with low survival cancer populations and may be less attractive to patients with low survival cancers, making them unlikely to enrol in such studies
- These diagnoses can be accompanied by rapid disease progression, making recruitment, treatment and data collection windows short and traditional late phase trials unlikely to be feasible.
- Capture and use of participation, treatment and outcome data could also be improved. Trial participation rates are challenging to measure as this data is not consistently or centrally recorded. This data could guide adjustment of recruitment strategies to ensure quick and efficient participant accrual.
- There are no support mechanisms or incentives to facilitate partnerships between the pharmaceutical industry and clinical investigators to encourage trials of new applications of existing medicines in the low survival cancer context. The evidence-base for off-label prescription of existing therapies is thus lacking and potential survival gains unknown. This can lead to erratic use of these drugs with little certainty regarding side effects, potential for patient suffering, and substantial out of pocket expense to patients and their families as this approach is rarely covered by government subsidies. This represents



a missed opportunity to gather much needed clinical data to drive evidence-based treatment innovations and improvements in patient outcomes.

Action needed:

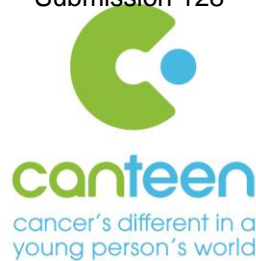
- National low survival cancer trials networks with strong international ties are needed to help reach and recruit patients impacted by high lethality cancers and ensure international trials are available in Australia
- These networks need to operate across multiple hospital boundaries (including across local health districts, public and private hospitals and adult and paediatric settings), assure rapid trial initiation, consistent, cost effective and timely ethics, governance and other relevant approvals, rapid and targeted access to patients and consistent monitoring processes and standards.
- Care of patients with rare or low survival cancers should be concentrated in centres of excellence with research and clinical trials embedded in clinical care (with commensurate resourcing of research and clinical trials support infrastructure in these settings)
- Funding is needed to establish these national networks and demonstrate their capabilities to attract industry investment and prove the value of this network based approach over direct approach to hospitals.
- Exploration and adoption of alternative trial models for low survival cancer populations as sufficient evidence for achieving approval and listing of new therapies on PBS for low survival cancers (e.g. one-person trials, adoption of surrogate endpoints, externally controlled trials using minimum datasets and biobanks to generate control data, basket-trials with broad inclusion criteria that seek to include those with rare cancers, and Bayesian adaptive trial designs)
- Minimise cost and regulatory barriers for hospitals to open trials for patients with rare or low survival cancers and establish incentives for clinicians to enrol these patients in appropriate clinical trials
- Establishment of support mechanisms and incentives for partnerships between the pharmaceutical industry and clinical investigators to conduct trials of new applications of existing medicines in the rare and low survival cancer context
- National capture and use of participation, treatment and outcome data to contribute to efforts to better understand low survival and rare cancers and identify effective treatment pathways

Investment in research and implementation of early detection is critical to improving outcomes

There is little investment into early detection research or implementation of professional development of community practitioners who triage patients who may have signs of low survival cancers. This is particularly critical for populations such as AYAs or those likely to experience rapid disease progression where cancer diagnoses often occur later than other populations, limiting treatment options and leading to poorer outcomes.

Action Needed:

- Investment in early detection tests and clinical protocols
- Investments in population-wide surveillance programs for more low survival cancers
- Development and implementation of training for community/primary health care professionals for early recognition low survival cancers
- Investment in public awareness campaigns to help support patient self-identification or warning signs of low survival cancers and self-efficacy to seek positive action from health care professionals



Greater coordination in advocacy, strategy and investment is needed

Efforts to raise awareness of cancers with low survivability fall almost exclusively to the not-for-profit sector or private individuals with an interest in, or impacted by, these illnesses.

The Australian government does not have a strategy to address low survivability cancers to guide investment via the NHMRC and MRFF or the setting of relevant government policy. Steps to address the need for a coherent strategy have been taken internationally (e.g. the 2012 Recalcitrant Cancer Research Act in the USA - <https://www.congress.gov/bill/112th-congress/house-bill/733>), which could guide Australian Efforts. Greater coordination of strategy, advocacy and research efforts would likely result in better outcomes for Australians impacted by low survivability cancers and a much stronger local research environment.

Action Needed:

- Establishment of a government supported taskforce for low survivability cancers, including representatives from not-for-profit advocacy and service delivery bodies, consumers, relevant government agencies, academics and industry representatives with a focus on the development of strategies to address low survivability cancers.
- Development of an advocacy and outreach strategy by the taskforce to include government, not-for-profit and medical/pharmaceutical industry engagement and advocacy (nationally and internationally) along with a public awareness strategy to build support for investment and awareness of warning signs (assist with early detection issue)
- Development of a research and investment strategy leveraging a mix of government (MRFF), industry and not-for-profit investment.
- Co-investment by the government and taskforce member organisations to sufficiently resource the activities of the taskforce and ensure sustainability

References

1. Deloitte Access Economics. *The economic cost of cancer in adolescents and young adults*. Sydney, Australia July 2016 2016.
2. Australian Institute of Health and Welfare. *Cancer in adolescents and young adults in Australia*. Cancer series No. 62. Cat. No. CAN 59. 62 ed. Canberra: AIHW; 2011.
3. Bleyer A. Latest estimates of survival rates of the 24 most common cancers in adolescent and young adult Americans. *Journal of Adolescent and Young Adult Oncology*. 2011;1(1):37-42.
4. Thomas DM, Seymour JF, O'Brien T, Sawyer SM, Ashley DM. Adolescent and young adult cancer: A revolution in evolution? *International Medicine Journal*. 2006;36:302-307.
5. Mitchell AE, Scarcella, D. L., Rigutto, G. L., Vicky J Thursfield, V. J., Giles, G. G., Sexton, M., Ashley, D. M. Cancer in adolescents and young adults: treatment and outcome in Victoria. *MJA*. 2004;180(19):59-62.
6. Teenage Cancer Trust. *Giving more young people with cancer the opportunity to take part in clinical trials: Discussion paper for Teenage Cancer Trust International Conference*. London, United Kingdom 2 July 2014 2014.
7. Rare Cancers Australia. *Just a little more time: Rare cancers update report*. Bowral, Australia: Rare Cancers Australia.; 16/03/2016 2016.
8. Bleyer A. Adolescent and young adult (AYA) cancers: distinct biology, different therapy? *Cancer Forum*. 2009;33(1).