ALLG Operations Unit
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Improving the treatment and the lives of patients with blood cancers through clinical trial research

Submission to the 2017 Senate Inquiry: Funding for Research into Cancers with Low Survival Rates

The Australasian Leukaemia and Lymphoma (ALLG) is a not-for-profit clinical trial organisation that Sponsors Investigator Initiated clinical trials. ALLG is Australia's only cooperative clinical trial group offering investigator initiated trials across multiple hospital sites for patients with haematological malignancies.

The ALLG membership represents more than 700 haematologists, scientists, and clinical trial research staff across Australia and New Zealand. ALLG has a strong track record in the conduct of investigator initiated trials with 151 clinical trials over 44 years. In 2016 alone the ALLG had 16 clinical trials open to recruitment, recruited more than 250 patients in the year, published 8 trials in peer reviewed journals and supported its members to participate in 19 presentations of their clinical trial findings at local and international conferences.

The ALLG plans, designs, conducts, monitors and publishes investigator initiated clinical trials. Members facilitate generation of research ideas, concept development, reporting of trials in progress, updates of recent publications, and progress toward translation of research into evidence based standard of care practice for those with leukaemia, lymphoma and other haematological malignancies, including key diseases such as acute myeloid leukaemia (AML) and multiple myeloma with low survival rates.

The ALLG has considered the Senate's Select Committee Terms of Reference and contributes the following comments in regard to **the impact of health research funding models on the availability of funding for research into cancers with low survival rates**.

In the diagnosis and treatment of haematological malignancies a 'cancer with low survival rate' is a cancer generally defined as: a haematological malignancy in a patient over the age of 60 years, and/or a select haematological malignancy such as adult AML, high risk lymphoproliferative disease, and multiple myeloma according to certain definitions.

Our Australasian experience of low survival rate in haematological malignancy is comparable to global haematological malignancy statistics and outcomes.

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;***

<u>Current NHMRC model:</u>
The ALLG and its members have considerable experience with the National Health and Medical Research Council (NHMRC) funding model. The ALLG would concur with the position that the NHMRC funding model, as it stands currently, favours those cancers that attract more non-government funding.

The ALLG's experience is that the NHMRC has tended to favour clinical trials of randomised design. It is noteworthy that in our experience the cancers that tend to readily attract non-government funding are those that represent elements of:

- public "popularity" and prominence;
- commerciality i.e. where industry has a vested interest in a commercial pipeline; and
- potential commercialisation of intellectual property.

Accordingly, this funding model does not necessarily prioritise investigation into areas of unmet need, including orphan diseases and those with low survival rate.

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Need to fund research into brain and LSR cancer:

Is there a 'need' to ensure that funding models provision for funding research into brain cancers and other low survival rate cancers?

The ALLG would fully concur with the above statement. LSR cancers are a public health issue of equal and measureable importance compared to other more common or obvious cancers. On this basis, there is a need for a mechanism for funding for research into LSR cancers.

In regard to brain cancer more specifically, our concern is that one of the most common types of 'brain cancer' is Central Nervous System (CNS) Lymphoma, and this is a low survival rate disease. In a manner similar to others with a LSR cancer, those patients with CNS lymphoma confront challenging survivorship issues in their shortened life span i.e. those that do survive experience harrowing short and long term effects of surgery, chemotherapy, and radiotherapy.

Are there issues or impacts to funding just LSR cancers?

Yes, and whilst these should be dealt with separately, the achievements can be made through overcoming current clinical trial barriers (Table 1 below).

Adopting funding for only LSR cancers may be problematic since it ignores 'survivorship' issues in cured patients, and, similarly does not acknowledge the fact that 'poor players' exist within diseases that have otherwise good survival rates. For example, in Diffuse Large B-Cell Lymphoma (DLBCL) where a patient is effectively cured through initial treatment (long-term disease-free survival occurs in at least 50% of patients diagnosed) however is subject to experiences that compromise quality of life as their survivorship extends.

Therefore, regardless of the categorisation of LSR, cancer funding models need to focus toward follow-up and outcome measurements. ALLG believes that clinical trials offer an efficient and scalable solution to achieve this. Investment in clinical trials has continuous dividends; in the immediate, short and long-term.

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;

Obstacles to running clinical trials in LSR cancers:

The obstacles to running clinical trials in LSR's are varied, and some are shared in common with those that impact cancers of higher frequency and better survival rates.

Table 1: Obstacles to running clinical trials in LSR

OBSTACLE	IMPACT OF OBSTACLE	WAYS TO OVERCOME OBSTACLE
PEOPLE		
Patients: poor understanding of the benefits of clinical trials	Lack of awareness of clinical trials, therefore recruitment rate slow, answer to clinical trial question delayed.	General marketing and campaigns focussed to gain public interest in research and clinical trial participation
Clinicians: time poor.	Timely access to CT information, unfamiliar with available trials. Nihilistic approach due to prior experience with patients with 'dismal prognosis'	Funding for roles that provide initiatives to support clinical trial process at recruiting hospitals Encourage models that help public/private partnerships
Researchers: time and cost to develop and conduct trials	Diminished interest in research	Workforce supported to increase skills necessary for clinical trial concepts. Fund the essential coordination and data activities

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CLINICAL TRIAL		
Access to new beneficial treatments	Slows development of clinical trials whilst investigators wait for access to good drugs	Assistance to lobby industry – form networks of collaborations within the clinical trial sector Funding to purchase medications
Population feasibility	Small number of eligible participants with the LSR cancer	Funding to support Australia's international leadership role Funding to support Australia's participation in international trials Funding for the cross referral of patients to sites with active trials
Policy burdensome	Highly regulated environment, with many tasks being performed by those not necessarily skilled in specialist clinical trial processes	Empower researchers with education opportunities Support career growth for those working in clinical trial industry Seek opportunities to work in highly regulated environment with success
FUNDING		
Perceptions of industry impacting sustainable, compelling research	Not interested to fund small studies in Australia Small populations with orphan drugs No interest in funding studies that are off-patent but potentially re-purposable	Create opportunities for industry engagement where Australia can be promoted for clinical trial research
Cost of clinical trials	The significant funding required deters new ideas. The funding limits participation	Fund infrastructure that supports the regulated environment.

i. **Proposed funding models for clinical trials:**

Australia needs a publicly-funded program for LSR cancers, one which would focus efforts and support in order to address research questions that are of high public value and clear unmet need.

1. Fund trial groups directly

ALLG proposes that funding models are established equitably to Australia's clinical trial cooperative groups directly. Cancer cooperative trial groups add value, have the capacity to remove barriers, accelerate new research ideas and turn discoveries into new practices to improve outcomes of patients with LSR.

These Cancer Co-operative trial groups, already have member based networks and administrative support for receipt and reporting of funding. Moreover, there has been a highly successful long-standing Cancer Australia model of funding infrastructure support for all of the Cancer Co-operative trials groups including ALLG, and one which has succeeded on all its deliverables.

2. Establish a clinical trial participation Medicare rebate.

There is much conjecture around the costs to the public purse for undertaking investigator lead trials. Indeed, patients are otherwise treated as part of standard of care i.e. health care costs can be credited to regular care. On this basis the new intervention represents the only variation to the cost of care for these patients.

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3. Set goals, commit for the term of the clinical trial.

Clinical trials are relatively easy to run; the necessary guidance and framework exists and the research community full of innovative, intelligent ideas of high scientific merit. Unfortunately there is great hesitation from government and foundation partners to acknowledge that trial duration and timing are crucial. A quality clinical trial capable of producing highest impact evidence will need time and patience to complete. Whilst many things can be done to accelerate specific steps, time and process should not be trivialised. A funding opportunity put forward from the government needs to avoid penalising researchers who conduct trials with longer read out times, and, need to acknowledge the need to invest in the quality processes required to achieve quality research outcomes. For many LSR cancers clinical trials need a read out time of 5 years; otherwise the research will only ever continue to focus on immediate intervention impacts and fail to address the reasons why LSR cancers are still prevalent.

Furthermore, the opportunities in Australia provided by clinical trials can often be poorly optimised. Whilst government and industry continue to prioritise a narrow focus toward 'new drug discovery', there is little support for the compelling laboratory, psychosocial, and health economic research. Funding clinical trials for LSR cancers needs to commit to delivering across the breadth of research areas.

ii. **Proposed funding models for campaigns to raise awareness of clinical trials:**

It is fair to state that to date little has been done to advance a national campaign to promote clinical trials.
Some hospitals and research institutes have actioned small focussed campaigns usually targeted to overcome the barriers that clinicians encounter such as local awareness for local participation.

ALLG's view is that a campaign, should not only focus on LSR cancers, but should also centre around provision of general support for clinical trials more broadly.

Australia needs an inclusive approach to enable widespread uptake of, and participation in, clinical trials. ALLG would welcome being part of any national marketing strategy, one that targets a broad cross-section of stakeholders including researchers, patients, health care providers, not for profits, and industry.

Outcomes of any national campaign should:

- Increase actual clinical trial participation. (Recruitment is pivotal, representing the key measurable outcome)
- complement support of staff roles in recruiting centres
- actively promote a culture for clinical trial research

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;

ALLG suggest that the following proposed strategies be considered as real and tangible ways to improve survival rates, Table 2 below.

Table 2: Suggested strategies

Strategy to improve survival rates	How to implement it	Responsible persons
Fund clinical trial research that includes survival data as well as secondary endpoint data about QOL and laboratory research	Fund cancer clinical trial group research directly	Cancer Clinical Trial Group
Provide access for Australia's participation in global trials	Fund activities to create global connections, host research collaboration meetings for LSR cancers	Cancer Clinical Trial Group

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Create initiatives that support access to drugs that industry has declined to support A common ALLG example: Scientifically robust clinical trial concept, fully supported by members and international collaborators, however the drug company declines to supply drug because 'there are no plans to seek registration or reimbursement of the drug in the indication/disease', therefore the proposal is not progressed.	Fund, pressure, lobby. Provide funding programs for the access to drugs that are sufficiently robust for testing in the clinical trial setting, even though the area of disease research has no interest to the company that owns the drug.	Government to take a lead role
Enable sector collaboration private and public	Commence engagement with insurance companies, and private health care sector.	Government with the support of cancer cooperative trial groups.
Implement a national clinical trial uptake across public and private hospitals.	Create Key Performance Indicators for hospitals regarding clinical trial participation, uptake of their demographic of patients to clinical trials. Create a culture of positive benefit.	State government Hospitals

ALLG has actively pursued its own strategies; our example is Acute Myeloid Leukaemia and this is what we have done:

From the AMLM1 trial (1981) right through to current day AMLM21 trial the ALLG members have and continue to demonstrate incremental improvements in AML survival rates. Major practice changing findings of flagship trials such as the AMLM4, AMLM7, and AMLM12 have been published in the highest ranking journals, Journal of Clinical Oncology and Blood, to name a few. Despite the progressive improvements shown in these randomised trials, AML remains a LSR cancer.

As targeted therapy for multitudes of AML subtypes broadens the clinical trial landscape, we have recognised the importance of monitoring all aspects of AML. To achieve this, in 2012 the ALLG established a national clinical registry. The ALLG's National Blood Cancer Registry (NBCR) underpins ongoing research capability with patient consent, collection of specimens and molecular samples at the time of diagnosis, as well as the voluntary adherence to standard induction and consolidation regimens aligned to a new portfolio of AML clinical trials.

This modernised approach to adopt a national clinical registry as a platform to inform future trial designs will be pivotal to the success of the ALLG in an increasingly challenging clinical trial environment. The data collected in the NBCR transforms our knowledge of the survivorship issues, and can be a valued resource for government in the form of reliable data for such agency as Medicare, the PBAC, and TGA.

d. other relevant matters to cancers of low survival rates.

ACCESS: In Australia new drugs can be accessed via clinical trials. A clinical trial is the safe and effective way to deliver this access, thus ensuring all aspects of critical data for decision making is presented to the Pharmaceutical Benefits Advisory Committee for listing with the Pharmaceutical Benefits Scheme. Clinical trials sponsored by the ALLG (and other cancer co-operative groups) are designed to answer key clinical questions relevant to patient care in Australia; this is not always applicable to those trials sponsored by pharmaceutical industry. In Australia there is an ethics and regulatory framework for clinical trial conduct. Policy makers in ensuring their obligations to cancer patients should look to better support the Australian clinical trial environment as the key provider for access to evidence based research for Australians.
GEOGRAPHY: Proximity of trial participants to clinical trials including the treatment and follow-up of LSR cancers.
TYPE OF CANCER: Survival varies markedly by cancer type – stage and response to treatment. Inequalities of access to intervention strategies for prevention and treatment.