murdoch children's research institute

www.acor-registry.org.au

Australian Cardio-Oncology Registry

Annual Report 2: 2019-20

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Australian Cardio-Oncology Registry

Summary

The Australian Cardio-Oncology Registry (ACOR) was created in 2018 to collect information about patients who have been exposed to cardiotoxic chemotherapies as part of their cancer treatment regimen. ACOR is a unique initiative to improve the cardiovascular health of paediatric, adolescent and young adult and adult cancer survivors. ACOR is a national study that includes 13 participating sites and will enrol 600 patients per year over a period of 3 years. This collaboration will address the following hypothesis and aims:

Hypothesis: The establishment of the registry and biobank will change the morbidity outcomes and ameliorate the burden of care on the health care system for paediatric and young adult patients with cardiovascular disease.

Aim 1: To expand Australia's first national cardio-oncology registry and biobank for paediatric, young adult and adult oncology patients that have been treated with cardiotoxic therapies.

Aim 2: To develop and implement national cardio-oncology guidelines and clinics, for the identification and management of cardiovascular disease in paediatric, adolescent/young adult and adult cancer survivors.

Aim 3: To include patient and patient families views through a Patient Advisory Group to improve patient care.

Aim 3: To determine (a) the cost and (b) short-term cost-effectiveness of the registry and cardio-oncology clinics, from a government and/or societal perspectives.

Introduction

Cancer survivors face an uncertain future. Each year, 80% of Australian children, adolescents and young adults and adults with cancer are cured. This dramatically improved survival rate comes at the cost of increased treatment related co-morbidities and there is a pressing clinical need to address this issue. Cardiovascular disease remains the main cause of health complications and premature death following cancer therapy. Whilst the risk of significant cardiovascular disease is known, and screening is recommended, up to 60% of childhood cancer survivors are lost-to follow up. Of the patients attending clinic, many survivors will have a diagnosable cardiac illness by the age of 29, approaching 40% by late adulthood.

The Australian Cardio-Oncology Registry (ACOR) is an established partnership of 13 tertiary paediatric, adult and academic institutes. The ACOR is supported by four philanthropic funding bodies; Kids Cancer Project, The Royal Australasian College of Physicians, The Royal Children's Hospital Foundation and HeartKids.

The ACOR Steering Committee is composed of 29 leading clinicians and scientists across cardiology and oncology, in both the paediatric and adult sectors. Thus, ACOR partners form a multi-disciplinary, nationwide network with the diverse expertise and skills required to effectively incorporate new evidence into policy and practice.

ACOR is building a comprehensive evidence foundation by prospectively recording data from all Australian paediatric, adolescent and young adult cancer patients exposed to cardiac toxic therapies. This evidence base will inform paediatric and young adult cardio-oncology guidelines, policies and position statements developed by the ACOR Steering Committee. Internationally,

cardio-oncology is emerging as an important sub-speciality to provide optimal care for patients following treatment. Therefore, ACOR will implement specialised cardio-oncology clinics to assess both the health and economic benefits of a dedicated centralised approach to managing cardiovascular health in cancer survivors in the era of immune and targeted and therapies. We are focused on the pharmacogenomics revolution and have created a national biobank to enable future studies into the pathogenesis of drug induced cardiovascular disease. Finally, a sophisticated health economics model will compare the current health burden and cost of care prior to, and following, introduction of the guidelines and clinics.

The ACOR has already formed a partnership across service providers, researchers and key philanthropic groups in both the cardiology and oncology sub-specialties. The ACOR will ensure there is effective integration of research evidence into health policy and service delivery for cancer therapeutic related cardiac disease. The ACOR and established Steering Committee will facilitate the implantation of guidelines and policy for ameliorating cardiovascular disease in paediatric and young adult cancer survivors. The Steering Committee will accept and facilitate funding and project applications at any time during the year to allow for timely, efficient collaborations to be fostered. Finally, the progress of research and release of guidelines or policy through ACOR, will be made available through the established ACOR website - www.acor-registry.com

Recruitment

As of to date, data for a total of 64 patients has been entered into the ACOR database. Currently, The Royal Children's Hospital, the Peter MacCallum Cancer Centre and the Women's and Children's in Adelaide, SA are enrolling patients into the registry. The Royal Melbourne Hospital, Monash Health, the Perth Children's Hospital, The Sydney Children's Network, the Royal Hobart Hospital and the John Hunter Children's Hospital are approved for the study and can welcome patients into the registry. Further 5 sites are in the process of getting research governance approval to commence recruitment.

ACOR study enrolment process

Eligibility

Any patients with a diagnosis of cancer who is exposed (or previously has been exposed) to cardiac toxic therapies.

Cardiac toxic therapies includes radiotherapy, anthracyclines, VEGF inhibitors, proteasomal inhibitors, tyrosine kinase inhibitors, immunotherapy, cyclophosphamide.

AND

Consenting to being included on the registry and sub studies OR have a legally acceptable representative capable of understanding the informed consent document and providing consent on the participants behalf.

ACOR is comprised of 4 arms- patients can opt into any of these arms at enrolment. The study arms are:

1) The registry study **2)** Biobanking **3)** Extended Cardiac Evaluation study (VIC only patients) **4)** MBS/PBS data linkage study.

Please see diagram 1 below, which shows the ACOR enrolment process.

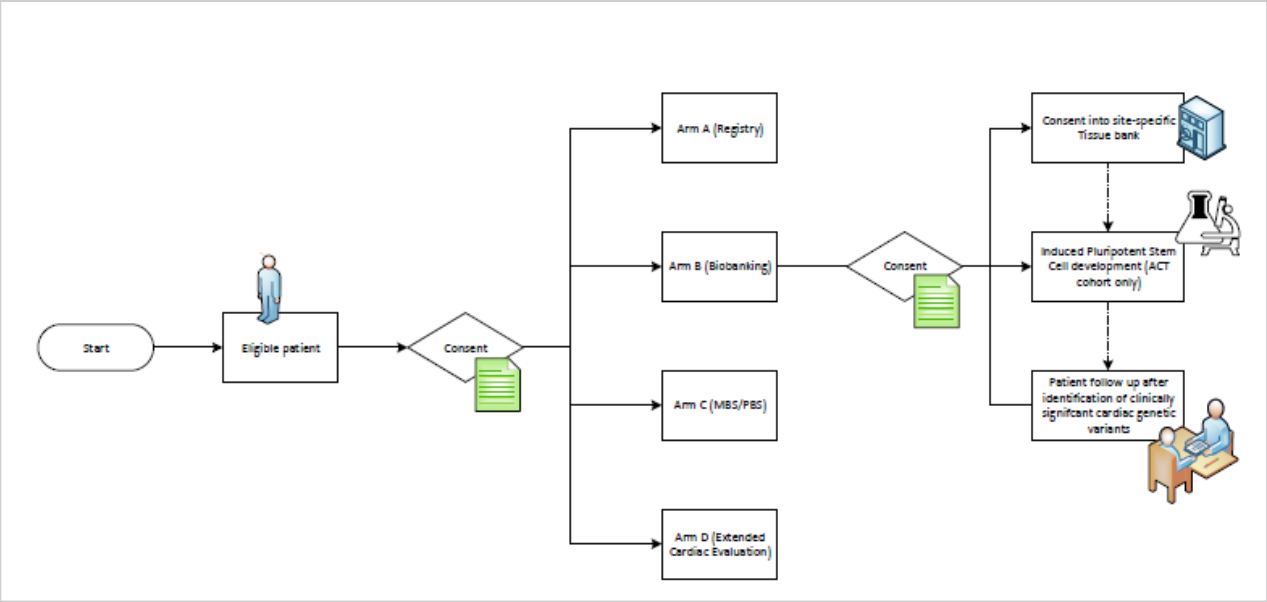

Diagram 1: ACOR patient enrolment flowchart

About our ACOR Participants

31 of the participants are male and 33 are female (see graph 2 below). The participants' main diagnosis is shown in Figure 2.

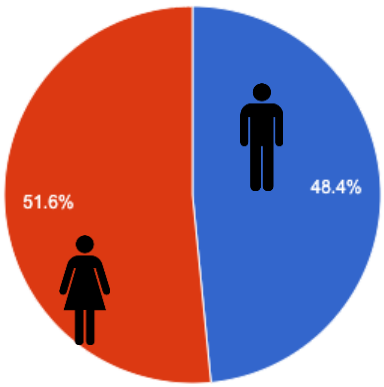

Figure 2: ACOR participants' gender

Participant's diagnosis at enrolment

The participants' main diagnosis is shown in Table 1. The main diagnosis is acute lymphoblastic leukaemia (ALL) (37,7%) followed by Acute myeloid leukaemia (AML).

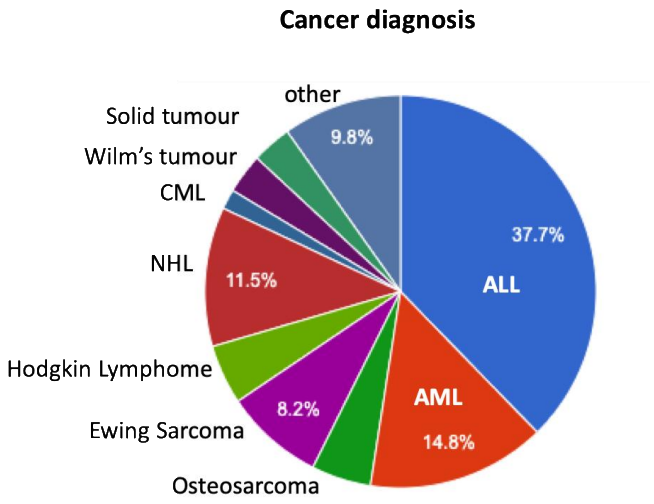

Figure 3: Main diagnosis

Enrolment cardiotoxic agent and cancer therapy related cardiac dysfunction

The most common administered agents were anthracyclines. They were administered to 54 out of 64 patients i.e. 82.8%. 10 patients have developed cancer therapy related cardiac dysfunction (CTRCD), of which 8 having been exposed to anthracyclines. Which resembles 15% of all patients that have been treated with Anthracyclines or 12.5% of all currently enrolled patients - see figure 4 and table 1 below.

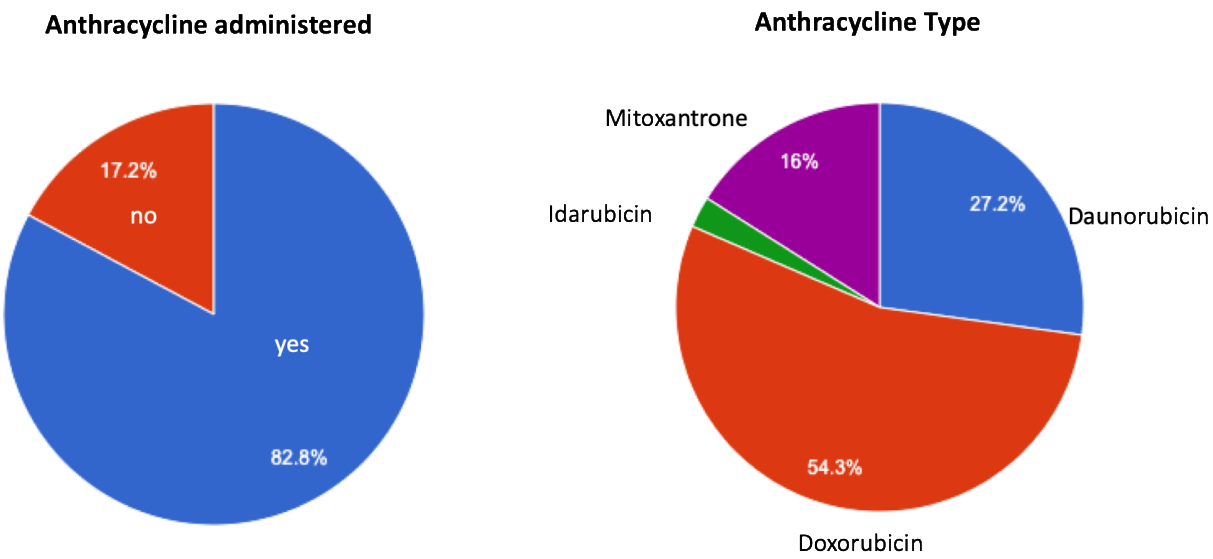

Figure 4: Anthracycline administered and Anthracycline type

Cardiotoxic chemotherapeutic agent at enrolment	No of participants who were administered agent	CTRCD
Anthracycline	53	8
Immunotherapy -Checkpoint inhibitor	10	
Tyrosine Kinase Inhibitor	7	

Table 1: Enrolment cardiotoxic agent and CTRCD

ACOR biobanking

Patients are enrolled into the biobanking study arm prospectively. Enrolled and consented patients have a one-off peripheral blood draw (4-12ml). However if the patient is unable to give blood the following samples will be collected instead; a saliva sample, urine saliva sample and a small amount of bone marrow (collected as part of clinical care) will be collected. Participating sites are expected to store samples in on-site tissue banks however if this is not possible the samples can be transferred to the Murdoch Children's Research Institute for storage. Please contact the National Coordinator at acor@mcri.edu.au to discuss.

Once patients are identified to exhibit CTRCD their samples are transferred to the Murdoch Children's Research Institute (MCRI) for DNA/RNA extraction and whole exome sequencing (WES) to identify variants placing them at risk of CTRCD. To date all 64 patients have been bio banked into the MCRI tissue bank.

56 of these samples have been Sanger sequenced, and are currently curated and validated for variants that pre-dispose patients to CTRCD by the Victorian Clinical Genetics Services (VCGS). Also

39 historic samples including those from the pilot study ACTive have been sequenced as part of ACOR by AGRF.

External Cardiac Evaluation arm

The extended cardiac evaluation (ECE) study is a radiological study arm of the ACOR, whose aim is to accurately define myocardial changes and cardiac reserve using cardiac MRI, VO2 max testing and echocardiographic strain analysis. Currently 45 patients between the ages of 3-21 have been consented into the ECE study.

Register your interest to be part of ACOR

If you are interested or know someone who is interested in being a participating site please contact:

ACOR National Coordinator via email at acor@mcri.edu.au

Or via telephone on: 03 9936 6033

We look forward to hearing from you.