Implementation of the Australasian Teletrial Model: Lessons from practice

Supplement articles:

An Introduction to the Australasian Teletrial Model

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Steps for setting up a teletrial cluster

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Implementation of a Teletrial model in the Northern Cluster (North Queensland, Australia): A Case Study

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Appendix 1: Example Checklists To Establish A Teletrial Cluster For Sponsors And Sites

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About this supplement

The Australasian Tele-trial Model (ATM) involves the use of telehealth technology to conduct clinical trials at satellite sites. Under the direction of state governments, led by Queensland Health (QH) and the Clinical Oncology Society of Australia (COSA), a streamlined process for review, authorisation and conduct of the tele-trials model has been developed. Some state governments and cancer centres around the country have developed new standard operating procedures (SOPs) to incorporate tele-trials into routine practice. Queensland Health has undertaken reforms in governance and contract approval processes to facilitate its implementation in Queensland. Several pharmaceutical companies and trial groups have begun incorporating tele-trials into trial protocols to enhance rural and regional access to trials, access to rare cancer trials even within a metropolitan setting and overall rate of recruitment.

Several cancer centres around the country have begun embedding this model as part of their strategic and operational plans and several state departments of health have established steering committees to drive state-wide adoption. The National Mutual Acceptance (NMA) is currently coordinating the review and development of a standardised tele-trials subcontract with the outcome that the tele-trials subcontract will be adopted by Medicines Australia as a standard template to use with their suite of other standard clinical trial agreements.

This supplement covers various aspects of the concept of the Australasian Tele-trial Model and its implementation, to share our experiences with those who would like to adopt this model as part of their routine practice and to encourage more uptake across the nation thus placing the patient at the centre of healthcare.

An Introduction to the Australasian Tele-trial Model

What is the Tele-trial Model?

Tele-trials refers to the use of telehealth by clinical trial units (primary sites) to enable access by patients at remote sites (satellite site) to some or all aspects of clinical trials. The combination of the primary site and its satellites is referred to as a tele-trials cluster (Figure 1). Satellite sites can be either smaller regional and rural sites or larger metropolitan clinical trial units (refer to the COSA implementation guide[1]).

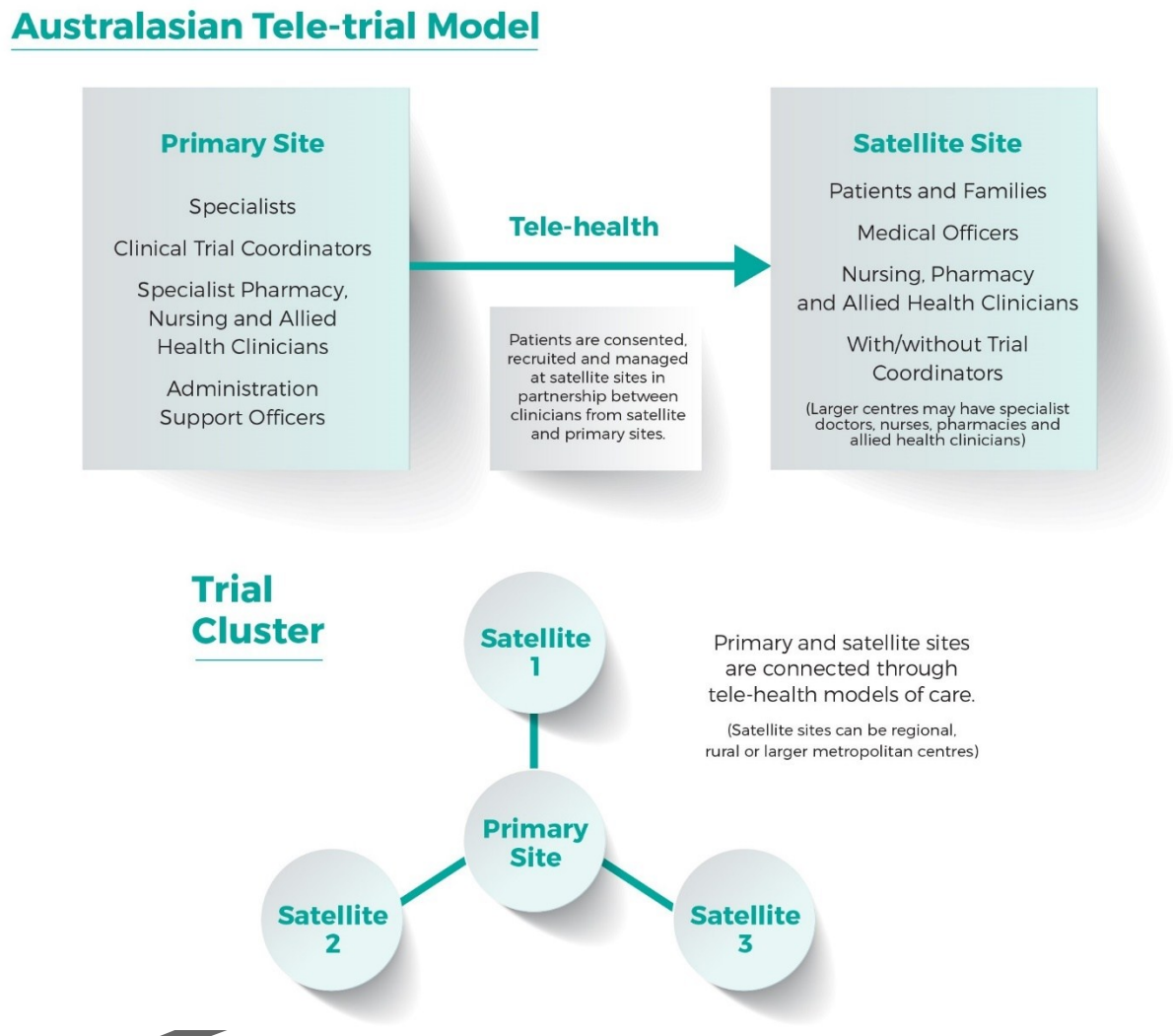

Figure 1: Teletrial model and teletrial clusters (source: COSA implementation guide)

In this model, a primary site takes overall responsibility for supervision and coordination of trial related matters for the cluster in collaboration with the satellite site staff and sponsor. Health professionals at primary sites and satellite sites work in collaboration where their roles and

responsibilities are formally agreed between sites and documented (for example in supervision plans, as detailed later). Depending on the satellite site capabilities and experience, some or all aspects of the trial operation can be delegated to the satellite site staff using delegation logs. Tele-trials is conceptually a simple idea: to increase recruitment and trial capacity by decentralising the processes of a clinical trial (consent, randomisation, delivery of investigational products, trial activity and potentially trial monitoring).

How does it differ from multisite trials?

Table 1 outlines the difference between multisite trials and tele-trials.

Table 1: Characteristics & comparisons of Multi-site trials and Tele-trials

	Multi-site trials	*Tele-trials*
Nature of site	Trials are conducted at multiple independent sites	Trials are conducted within clusters
Relationship between sites	Sites have no relationship with each other	Primary and satellite sites work in collaboration and are connected by telehealth for some or all aspects of the clinical trial
Trial coordination	At each site, trial coordination is the responsibility of the Principal Investigator (PI) with overall trial coordination across all sites performed by sponsors and Contract Research Organisations (CROs)	Within a cluster, trial coordination is the responsibility of the Principal Investigator at the primary site with contribution from satellite sites, sponsors and CROs.
Site of primary investigator (PI)	PIs are appointed at each site	PI at primary site and sub-Investigators at satellite sites work in collaboration
Regulatory processes	Governance and other regulatory approvals are performed separately by each site	This model paves the path for streamlining of approval processes, and minimisation of duplication due to collaborative nature of research governance officers within clusters

Purpose of the Tele-trial Model

Clinical trials are regarded as optimal management options as they introduce cutting-edge therapies in many fields of health care, especially in cancer care, prior to regulatory approval. Most cancer centres, as per international guidelines, embed clinical trials into their treatment algorithms.[2] This may mean that all cancer services (small or large) need to incorporate clinical trials as part of standard clinical practice. In addition, clinical trials help advance science and practice of health care by testing various processes and approaches. In terms of economy, participation in clinical trials generates revenue for the health system return on investment and jobs in trial related operations.[3]

It has been a priority for Australia for some time and significant investment has been made by all levels of government to increase clinical trial activity in all jurisdictions and to eventually become "business as usual".

While significant investment has been made to improve clinical trial capabilities in metropolitan settings by all stakeholders, even in metropolitan settings, rates of enrolment in clinical trials is lower than that what is expected according to international recommendations and benchmarks. For rural, regional and rare cancer patients, rate of enrolment to clinical trials is even lower.[4] Additionally the further molecular classification of cancers, even purportedly common cancers, has seen the potential trial participant pool contract. The common cancers are now being reclassified into smaller and smaller rare cancer populations (e.g. 3rd line ALK-translocated lung cancer patients are a rare cohort). Rapidly finding patients to recruit to a clinical trial is becoming more challenging.

Many regional and rural communities do not have clinical trial capabilities locally, mainly due to their reduced potential participant pool, and consequently are not chosen as trial sites by collaborative trial groups and industry sponsors. For patients, limited availability closer to home and cost and inconvenience of travel have been identified as main barriers to regional and rural participation in clinical trials.[5]

The Tele-trial Model takes advantage of the ability of telehealth technologies to connect smaller centres with larger centres in providing health services closer to home for patients and their families. It also allows sponsors to expand their trial catchment population without opening more trial sites.

Evidence for telehealth in cancer service delivery

Many centres around the world utilise telehealth models of care to provide cancer care for regional and rural patients, including initial consultations to end of life care [6, 7]. Several telechemotherapy models of care have been in operation including the Queensland Remote Chemotherapy Supervision (QReCS) model to provide chemotherapy services locally in small rural centres.[8] Literature on telehealth models of care report on positive patient and health professional acceptance and satisfaction, safety of chemotherapy delivery, and cost effectiveness.[7, 9-13] In addition, through peer support and additional training, rural capabilities have been enhanced to provide specialist care closer to home for rural and regional patients.[14,15] Several organisations and health disciplines have produced telehealth guidelines for health services and clinicians, including the Clinical Oncology Society of Australia (COSA) clinical practice guidelines for teleoncology.[16] Furthermore, governments have set up incentives to drive uptake of both telehealth and clinical trials participation. Recently, The Australian Commission on Safety and Quality in Health Care has included equity as an important aspect of research focus.[17]

Given the volume of evidence in literature supporting telehealth models of care and demonstrated rural and regional inequalities in access to clinical trials, the logical next step is the use of telehealth to enhance regional and rural access to clinical trials closer to home. Telehealth models of care connect towns, villages and people. They have been proven to facilitate access to safe and quality health care closer to home and require investment for implementation. As long as these models are constructed according to accepted governance and standards for safety and quality, they are safe and ready for use.

Australasian Tele-trial Model

COSA developed the Australasian Tele-trial Model (ATM) and national guide for implementation in 2016, in collaboration with Medicines Australia and its members, trial groups, state governments and research centres..

This model has been developed in consideration of the requirements for the proper conduct of clinical trials ensuring the protection of the rights and safety of trial participants and quality data for the demonstration of safe and efficacious cancer treatments.

Ethical and safe conduct of clinical trials using this model requires that the following aspects are considered and addressed by implementation plans: selection of satellite sites including their accreditation; identification of suitable clinical trials; workforce, roles, responsibilities and supervision plans; good clinical practice and trial related training; site initiation meetings and trial updates; technology and support; participant screening and recruitment; processes for obtaining participant consent, management and transport of medications; reporting of serious adverse events and patient reported outcomes; management of documentation; financial and regulatory considerations; and indemnity, insurance and clinical trial agreements.[1]

By connecting cancer centres and services within states and across state boundaries, this model may become a tool for creating an interconnected clinical trial system across Australia for not only cancer but for all disciplines.

Implementation of Australasian Tele-trial model

The first step in implementation of this model is for trial groups, sponsors and cancer centres to incorporate tele-trials into their routine business. Inclusion of tele-trials into organisational and governmental strategic and operational plans as a mechanism for addressing inequity of access to clinical trials for regional and rural patients may be an important enabler for sustainability. This will also ensure that additional resources are allocated for workforce, equipment and transport to address the unmet needs. Steps for setting up clusters for sponsors, and cancer centres are discussed further in this supplement.

In Queensland, the Health Innovation, Investment and Research Office (HIIRO) of Queensland Health, has recently released their Australian International Council for Harmonisation Good Clinical Practice (ICH-GCP) Standard Operating Procedures (SOPs), incorporating tele-trials. These SOPs are available for use by all stakeholders.[18] Contents of the SOPs were developed and finalised as part of national consultation based on the principles outlined in the COSA national guide and the results of the tele-trial pilots conducted in the Southern Cluster (Gold Coast with Hervey Bay); the Northern Cluster (Townsville with Cairns, Mackay and Mt Isa); the Victorian Comprehensive Cancer Centre (VCCC) collaborating with the Regional Trial Network (Peter MacCallum Cancer Centre, Bendigo Health and Border Medical Oncology Research Unit); and Orange/Dubbo clusters. In Queensland, this pilot was undertaken with the MonarchE protocol, involving an oral adjuvant breast cancer treatment, and gratefully sponsored by Eli Lilly. Further information on this implementation is presented in the case study. Orange/Dubbo clusters used the Australasian Gastro-Intestinal Trial Group's ASCOLT protocol (ACTRN12614000513617) and the VCCC cluster used their own investigator initiated thromboprophylaxis study (ACTRN12618000811202).

Opportunity for streamlining of regulatory processes at national and state levels

Regulatory processes related to conducting clinical trials are complex for sponsors, trial sites, approving officers and patients, due to the requirement for advanced safety monitoring and regulation to ensure the quality of clinical trials and confidentiality of trial participants. Current models of clinical trial management in Australia including all approval processes focus on management at individual sites even when the same trials are conducted at multiple sites. Whilst mutual recognition of ethics approval processes has somewhat streamlined the ethics processes, there are opportunities for reforms on governance and contractual processes to streamline tele-trials implementation. The current networked model approach including the Tele-trial Model offer new opportunities for this to occur.[4]

Establishment of clusters through the Tele-trial Model means that the primary site undertakes the coordinating role for all satellite sites. The primary site Research Governance Officer (RGO) can then approve the governance documentation on behalf of the cluster while the satellite sites retain autonomy regarding local issues including budget, logistics and workforce. Using the same principles, contracts can also be processed at cluster level using one of several possible approaches summarised below. In Queensland, QH is planning to include these processes using a Health Service Directive so that uniform processes and approaches are adopted across the state. This proposal also requires that the satellite RGOs waive the Site-Specific Assessment (SSA) approval fees given that most of the work has been performed by the primary site RGO.

For legal considerations, the most commonly used model is the tele-trial cluster sub-contract model developed in Queensland. In this model, a contract is negotiated between the primary site and the sponsor and the sub-contract is executed between the primary site and the satellite sites, with the main CTRA as an annexe to the sub-contract. The header agreement, that is, the main CTRA also

refers to the relationship with satellite sites via a special schedule condition (Schedule 1 of Medicines Australia CTRA).

St Vincent's Hospital, Sydney uses a vendor model to receive services from satellite sites. This model further expands on how vendors are used traditionally, such as for medical imaging and laboratory services. The model utilises external health facilities all over New South Wales to assist with obtaining the required clinical and safety data to ensure trial related decisions can be made in real time by the research team in Sydney despite a regional participant's location.

Steps for setting up a teletrial cluster

The supervision plan is a critical document to enable successful implementation of the Australasian Teletrial Model (ATM). The supervision plan which is developed in collaboration between the sponsor, primary and satellite site(s) articulates the roles and responsibilities of staff at primary and satellites conducting trials within a trial cluster. It provides the sponsor with the assurance that the satellites sites are appropriately clinically supervised and provides clarity for the primary and satellite sites about what is required to participate in the teletrial.

Supervision plan

The plan documents the roles and responsibilities of participating staff at the primary site and satellite site(s) and is tailored for each satellite site depending on their experience and capabilities within a cluster. It has been our experience that the plan evolves as the satellite sites gain confidence and acquire capabilities.

Example of items covered in supervision plans include the following:

1. Satellite site resources, including departments involved in the teletrial and staff availability
2. Aspects of how the sites will collaborate and communicate including what support will be provided by the primary site
3. Processes for and roles and responsibilities of trial related activities
4. Degree of supervision - this can range from direct supervision of trial related activity for a clinical trial naïve site through to delegated model for an established clinical trials site
5. Nature of cluster meetings - they include agenda, frequency and minutes. It is useful to maintain agenda and minutes for the Investigator Site File (ISF)
6. Training and training logs

Supervision of a satellite site occurs across the multi-disciplinary staff required to conduct a clinical trial at a site. The supervision plan documents how support is provided to all disciplines at a satellite site and where resources are not available how the primary site will address the deficit to ensure

that the required clinical trial activity is undertaken by suitably trained staff or completed by the primary site through the use of telehealth. Telehealth is used for some or all aspects of trial related activities depending on delegation.

An example of a supervision plan template is found at https://www.health.qld.gov.au/hiiro/html/regu/for_researcher/gcp,research-ethics-and-governance-standard-operating-procedures-sop .

Steps for setting up the tele-trial cluster: for sponsors, primary sites and satellite sites

While the Australian ICH-GCP SOPs (including tele-trials) and the COSA ATM implementation guide outline safety and quality matters for clinical trials, and supervision plan templates articulate the roles and responsibilities of staff, the aim of this section is to outline the practical implementation of a teletrial cluster by listing the items that may need to be considered to ensure the smooth and efficient initiation of a teletrial cluster. The processes for sponsors, primary and satellite staff seem sequential, however many processes need to evolve concurrently among stakeholders. Table 2 gives an overview of the main steps for sponsors and Contract Research Organisations (CROs).

Table 2: Steps for sponsors and CROs

	Activities	*Comments*
1	Assessment of suitability of a protocol for teletrial model	Suitability of a protocol for teletrial model depends on capabilities of the satellite sites. This assessment is performed by the sponsor and primary site in partnership. Primary sites usually involve the satellites in this assessment as part of their initial discussions.
2	Site evaluation visits at satellite sites	Sponsors may wish to perform a site evaluation visit for the first trial as a mechanism for familiarising themselves with satellite site set up and staff. Consultation with CRO (if applicable) and quality advisors may be useful for monitoring purposes.
3	Addition of satellite sites to the central ethics notification and transfer of SSA form to the satellite sites	Most RGOs work collaboratively with satellite RGOs to expedite the approval processes. If the primary site RGO has approved an SSA form, satellite sites may only need to approve the true site-specific components. In this instance, satellite sites may be encouraged to not charge a governance processing fee.
4	Addition of satellites to CTN notification	If the Investigational Medicinal Product (IMP) is stored at the satellite site(s), it is necessary to make required notifications to add satellite site(s) to existing clinical trial notification (CTN). All satellite sites within a cluster

		are covered under the CTN registered with the Therapeutic Goods Administration (TGA).
5	Contracts and amendments	Contract processes are expected to evolve overtime and may vary between jurisdictions. One approach is to add the satellite site(s) as study sites to Schedule 1 of CTRA and add additional pharmacy costs according to the number of sites which will be in receipt of the Investigational Product (IP) in Schedule 2. Each site may require a new indemnity, and indemnities are added to Schedule 5 of CTRA.
6	Approval of supervision plans	Supervision plans are developed in collaboration between the clusters and sponsor. We find it useful to add "telehealth enabled trial activities" as an option even at sites that are fully capable and delegated all responsibilities. This option allows greater flexibility to access medical support within clusters.
7	Cluster Participant Information and Consent Form (PICF)	These are developed from the master PICF. It is useful to liaise with RGOs regarding details of submission of documents. Approval processes are likely to be streamlined in the future with maturity of the teletrial system.
8	Access to training and databases	Access to trial related and GCP training and electronic data capture (EDC) platform for the cluster should be provided.
9	Delegation and signature logs and training logs.	Usually the sponsor and CRA ensure that all staff conducting trial related activity at primary and satellite site(s) are on the delegation and signature logs; and have completed all training required and recorded on the training logs.
10	Site Initiation Visit (SIV) with the Teletrial cluster sites	Once the SIV is completed, satellites can receive the official letter to open the satellite site(s).

NB: Sponsors or CROs may also wish to conduct monitoring visits at satellites sites until confidence in data quality within the teletrial cluster model is established.

Table 3 gives an overview of the broad steps required for sites participating in the ATM. A more detailed example checklist is found in Appendix 1.

Table 3: Steps for primary sites

	Activities	*Comments*
1	Assessment of suitability of the clinical trial protocol for the Teletrial Model	Since the suitability of a protocol for ATM relies on capabilities of satellites, it may be useful to have

		information on resources, technology and workforce capabilities of the cluster sites.
2	Feasibility assessment.	The feasibility assessment is undertaken in collaboration with willing satellites. Given that the satellites may be small, it is important to agree on the estimated recruitment target for the cluster rather than assigning targets to individual sites.
3	Signing of CTRA Tele-Trials Subcontract with each satellite site.	Signed sub-contracts are submitted with RGO submission documents for sign off and approval.
4	Supervision plans	The supervision plan is developed in collaboration with each satellite site and is agreed by the sponsor. The supervision plan details all accountability and responsibilities of both primary and satellite site(s) as outlined in the Australian ICH GCP SOPs (including tele-trials) and the COSA Australasian Tele-Trial Model National Implementation Guide.
5	Submission of governance documents	The approach to this step may vary between jurisdictions. It is useful to liaise with RGOs regarding efficient processes for dealing with the documents and approval processes (Table 4).
6	Trial related and GCP training	The primary site may have to assist sponsor with satellite site training as required.
7	Completion of delegation and signature logs and training logs.	This applies to the primary site and satellite sites.
8	Site initiation visits	Site initiation can be conducted using telehealth or videoconferencing, once RGO approval is gained.

Steps for satellite sites

The steps for satellites sites are similar to that of the primary sites. Depending on satellite site capabilities, primary sites may delegate some or all aspects of clinical trial conduct to the satellite site staff. Even when all activities are delegated to the satellites, primary sites are required to make sure the PI and the primary site maintain the oversight of the trial across the cluster. In addition to documenting the roles and responsibilities of cluster staff on mutually agreed supervision plans, regular cluster meetings are important forums for ensuring oversight and for providing support for satellite staff if required. In our experience, medical officers and trial nurses are in frequent contact among their peers outside of formal cluster meetings.

In relation to satellite site RGO approvals, it is often useful to involve the RGOs early in the process to identify agreed submission process and required documents (Table 4). In states where a streamlined cluster approval process is not in place, we encourage the satellite sites to lobby for expedited review process given that the trial was approved by the primary site RGO. Within some clusters, when the primary site RGO has approved the trial, satellite sites only focus on site specific matters such as contract and budgets.

Table 4: Example of submission of documents for RGO approvals

Submission of documents to RGOs and RGO approval by primary sites	**Submission documents and RGO approval by satellite sites**
Documents for primary site submission are:	*Prepare and submit documents for satellite site RGO approval including the documents received from the sponsor and primary site including:*
· PI signed letter to RGO · HREC Amendment approval letter · CTRA Teletrial subcontract for each satellite site · Supervision plan for each satellite site · CTRA Amendment · Teletrial Cluster Specific Patient Informed Consent Forms (Master PICFs do not need to be submitted to the Primary site RGO if the clinical trial is already approved at the primary site). RGO submission package and sponsor package sent to each of the satellite sites for satellite site RGO submission (pending receipt of approval letter from primary site RGO).	· Copy of primary site RGO Teletrial approval and acknowledgment · CTRA Amendment HREC approval, CTRA Teletrial Subcontract, Clinical Trial Notification, signed Supervision Plan, Cluster PICFs, current approved protocol, Investigator Brochure · Satellite site SSA form, indemnities, insurance etc. plus any other documentation required for RGO submission approval · Radiation safety letter · Patient diaries, thank you card and Quality of life questionnaires

Note: RGO approval processes are evolving overtime and may vary between jurisdictions.

Implementation of a Teletrial model in the Northern Cluster (North Queensland, Australia): A Case Study

Introduction

As part of the pilot project sponsored by the COSA Teletrial Consortium with matched funding from MTPConnect, QH seed funding and supported by the state-wide teletrial working group, a teletrial cluster was established in North Queensland. This section serves as a case study of implementation of the Teletrial Model within a cluster.

About the trial

The trial "A Randomized, Open-Label, Phase 3 Study of Abemaciclib Combined with Standard Adjuvant Endocrine Therapy Versus Standard Adjuvant Endocrine Therapy Alone in Patients with High Risk, Node Positive, Early Stage, Hormone Receptor Positive, Human Epidermal Receptor 2 Negative, Breast Cancer" known from here on as MonarchE was identified as a suitable trial for the Teletrial Model. This study aims to evaluate the safety and efficacy of abemaciclib in the study population.[19]

Establishing the teletrial cluster

In collaboration with COSA, a suitable trial was sought with an oral Investigational Medicinal Product (IMP) and a willing sponsor, keen to pilot the implementation of the Teletrial Model. During initial conversations undertaken with the Senior Clinical Development Liaison (Oncology and Diabetes) of Eli Lilly Australia and New Zealand, MonarchE was recognised as a suitable trial and Eli Lilly offered to sponsor its teletrial implementation.

Northern Cluster

A cluster of four sites was established for this teletrial, including Townsville as the primary site; and Cairns, Mackay and Mount Isa as the satellite sites. The cluster services an area of 686,950km^2, with a population of approximately 684,000 in 2017. The trial was opened in September 2017 in Townsville, with the satellite sites following as per Table 5, after the approval processes previously outlined in this supplement. The satellite sites had a range of clinical trials experience and expertise, ranging from a dedicated oncology clinical trials unit with experience in trials, to a site with clinical trials experience in other settings (predominately surgical and intensive care) but little oncology trials experience, to a clinical trials naive site. The uniqueness of each site required a robust supervision plan to ensure the tele-trials processes were operationalised within each setting.

Table 5: Details, Capabilities and Resourcing of Satellite Sites in Northern Cluster Implementation

	Satellite Sites		
	Cairns	**Mackay**	**Mount Isa**
Approximate Distance from Primary Site (kms)	400	400	1000
Trial Opened	August 2018	September 2018	November 2018
Clinical Expertise Access	Extensive	Extensive	Limited. Fully operational oncology day unit, including level 7 oncology nurse. MO clinical services provided by Townsville through telehealth.
Clinical Trials experience and infrastructure	Extensive	Experienced in other settings, but limited experience in Oncology trials.	Clinical trials naïve.
Specific requirements for MonarchE tele-trials participation	Supervision plan with minimal oversight.	Supervision plan with minimal oversight. Some support provided given limited oncology trials experience.	Supervision plan with supervision by the primary site of most activities. Additional equipment was required including temperature loggers.
Staffing requirements	Sub-investigator with clinical trials unit support.	Sub-investigator with clinical trials unit support	Principal and SIs covered through Townville.

Observed Benefits

Under the model, after screening more than 25 patients across the cluster, 10 participants were randomised (5 in Townsville; 4 in Cairns, and 1 in Mackay). While this case study does not include formal evaluation or measures, the benefit of reduction in travel and time to the participating patients while allowing them access to participation in the trial was observed, thus increasing patient equity in trial accessibility. Eight satellite staff underwent GCP training and acquired trial

capabilities. Mackay and Mount Isa are in the process of commissioning isolators for compounding medications locally. Additionally, this model continues to strengthen the working relationships and capabilities amongst all sites and leads the way for future teletrial studies to be conducted within the Northern Cluster with Cairns and Mackay taking on the role of primary sites for some studies.

Enablers & Challenges

All four sites had prior experience providing services via telehealth. For Mt Isa, Townsville was the sole provider of services using teleoncology. Medical oncologists, nurses, pharmacists and administrative officers at the sites also had existing relationships at cluster level through joint tele-chemotherapy projects and educational sessions such as Far North Queensland post-American Society of Clinical Oncology meetings. Involvement of Queensland Health in the project enabled cluster level governance approval and contract processes. Common electronic medical records and treatment protocols made it easier to conduct monitoring evaluations.

With the satellite sites possessing differing capabilities and resourcing (Table 5), recognition of the different requirements of each site, with courtesy and respect was essential, with clear communication and expectations from all parties to ensure that potential was developed among all sites. Though budgets and allocation of funds are ongoing challenges, these aspects are expected to be streamlined through maturity of the cluster.

Future directions:

With the expected benefit of increased trial access without the travel burden, the patient perspective will be an important future research area. Furthermore, staff and resourcing evaluations will provide valuable information for future tele-trials. Further streamlining of clinical and approval processes at cluster level will of course make implementation smoother.

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Appendix 1: Example Checklists To Establish A Teletrial Cluster For Sponsors And Sites *(Courtesy of COSA and Queensland Health)*

Steps	Sponsors	Date Complete	Comments
1.	Sponsor and primary site consider the clinical trial protocol for suitability for the Teletrial model.		
2.	Conduct site evaluation visits at each satellite site if required. Consult with CRO (if applicable) and quality advisors for monitoring purposes.		
3.	Add satellites sites to the central ethics notification and transfer SSA form to satellite site(s). If IMP is stored at the satellite(s) make required notifications to add satellite site(s) to existing CTN. All satellite sites within a cluster are covered under the CTN registered with the TGA.		
4.	Amend CTRA to add the satellite site(s) as study sites to Schedule 1. and to add additional pharmacy costs according to the number of sites which will be in receipt of the Investigational Product (IP) in Schedule 2. Create a new indemnity per site. Indemnities are added to Schedule 3 of the subcontract.		
5.	Review and approve Supervision Plan developed between primary and satellite(s).		
6.	Develop a cluster PICF from the master PICF for the trial. Send Submission package including cluster PICF to Primary site to accompany the Primary site RGO submission package for satellite sites (satellite sites receive the complete submission package from sponsor and primary site combined).		
7.	Request access for all staff involved in the clinical trial at the primary and satellite site(s) to complete training in the clinical trial protocol. Ensure satellite sites have access to GCP training if required.		
8.	Sponsor and CRA check that all staff conducting trial related activity at primary and satellite site(s) are on delegation and signature logs and have completed all training required and this is entered on the training logs.		

9.	Sponsor and the CRA conduct the Site Initiation Visit with the Teletrial cluster sites including all confirmed satellites and once completed the official letter to open the satellite site(s) is sent.		

Steps	**Primary Site**	**Date Complete**	**Comments**
1.	Determine the suitability of the clinical trial protocol for the Teletrial Model in collaboration with the sponsor.		
2.	Collaborate with satellite sites to assess their willingness and capacity to participate in the Teletrial cluster and complete the feasibility assessment. Assist sponsor with satellite site evaluation visits as required.		
3.	Provide the sponsor with all contact details, finance information and addresses including the e-mail address of satellites for the transfer of the online SSA form.		
4.	Sign a CTRA Tele-trials Subcontract with each satellite site. This is submitted with RGO submission documents for Chief Executive sign off and approval. (It is recommended that a first draft of the subcontract be provided to the sponsor for feedback prior to sign off).		
5.	Develop a mutually agreed Supervision Plan in collaboration with each satellite site and ensure these are approved by the sponsor. The supervision plan details all accountability and responsibilities of both primary and satellite site(s) as outlined in the Australian ICH GCP SOPs (including tele-trials) and the COSA Australasian Teletrial Model National Implementation Guide. The Supervision Plan will outline the matrix of responsibilities for all trial activity.		

6.	Submit all documentation to primary site RGO for approval to open the clinical trial at the primary site. Primary site RGO will acknowledge all other documents submitted to assist the satellite RGO with their approval. Documents for primary site submission are: • PI signed letter to RGO • HREC Amendment approval letter • CTRA Teletrial subcontract for each satellite site • Supervision plan for each satellite site • CTRA Amendment x 3 copies • Teletrial Cluster Specific Patient Informed Consent Forms (Master PICFs do not need to be submitted to the Primary site RGO if the clinical trial is already approved at the primary site).		
	Send RGO submission package and sponsor package to each of the satellite sites for satellite site RGO submission (pending receipt of approval letter from primary site RGO).		
7.	Participate in all protocol related training and assist Sponsor with satellite site training as required.		
8.	Ensure all staff conducting trial related activity at primary site are recorded in delegation and signature logs and have completed all training required.		
9.	Primary site receives notification from the sponsor when the trial is officially open. Participate in Site Initiation for all sites within the Teletrial cluster. Site initiation can be conducted using telehealth or videoconferencing.		

Steps	**Satellite Site**	**Date Complete**	**Comments**
1.	Review proposed Clinical Trial Protocol for suitability for site participation in the proposed teletrial cluster.		
2.	Participate in feasibility assessment with primary site and site evaluation visit with the sponsor.		
3.	Complete online SSA form once transferred from the sponsor and complete all required documentation such as FDA forms, privacy consents etc. as required by the sponsor.		
4.	Review and sign CTRA subcontract with the primary site.		

5.	Develop the Supervision Plan in collaboration with the primary site.		
6.	Prepare and submit documents for satellite site RGO approval including the documents received from the sponsor and primary site including: • Copy of primary site RGO Teletrial approval and acknowledgment • CTRA Amendment HREC approval, CTRA Teletrial Subcontract, Clinical Trial Notification, signed Supervision Plan, Cluster PICFs, current approved protocol, Investigator Brochure • Satellite site SSA form, indemnities, insurance etc plus any other documentation required for RGO submission approval • Radiation safety letter • All patient Diaries, Thank you cards, Quality of life Questionnaires		
7.	Complete all required training for working in clinical trials as required by the sponsor and complete training for the specific protocol/ clinical trial once the CTRA amendment is approved by ethics.		
8.	Ensure all staff conducting trial related activity at satellite site are on delegation and signature log and have completed all training required and entered on the training log.		
9.	Once RGO approval is gained, attend Site Initiation Visit organised by primary site. The clinical trial can now commence at the satellite site. It is recommended that close supervision occur for the informed consent visit and subsequent patient activity/treatment visits for the first patient until the primary site and satellite site are confident that the satellite site is fully supported to conduct trial activity.		

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