

Models for Clinical Research: Cancer Trials Australia

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For discussion:

- Background to Cancer Trials Australia
- What we do well
- An increasing struggle
- Conclusions



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Cancer Trials Australia

- Member based organisation of Oncology Research Centres
 - Established in 2003 (CDCT 1993) by:
 - Austin Health
 - Melbourne Health
 - PMCC
 - Western Health
 - Ludwig Institute for Cancer Research
 - WEHI
- Board of Directors (6 Oncologists, 2 Independents)
- Not for profit company limited by guarantee
- New members – Bendigo Health, Border Medical Oncology, St. Vincent's Health



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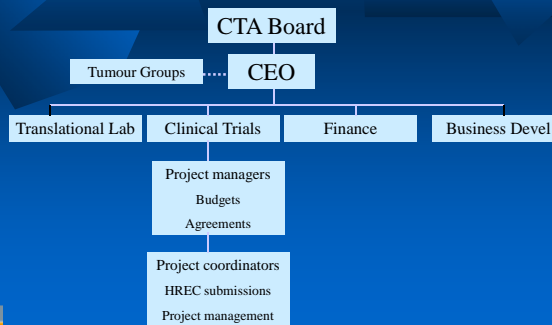
CTA Strengths

- Not for profit
- Large patient accrual base
- Strong basic science / preclinical
- Commitment to translational science
 - PET / Laboratory / Bio-informatics
- Early phase trials
- Collaborative structure
- Track record
- Single administrative hub
- Cost effectiveness

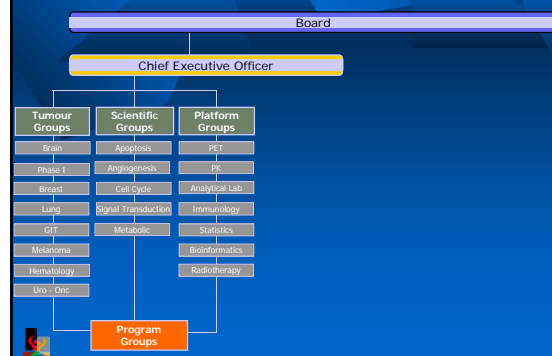


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Organisational Structure



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What does CTA do?

- Provides the administrative wherewithal for Sponsors and Investigators to open a clinical trial at a clinical site
- Provides project management in the ongoing administration of a clinical trial
- Provides a cadre of experienced Investigators to advise Sponsors about early Phase trial design including companion biological studies
- Provides a collaborative network through its Tumour Groups to advise Sponsors about Tumour specific studies
- Brings clinical trials to its Investigators
- Takes its Investigators to Sponsors



What else does CTA do?

- Provides a translational laboratory resource
- Provides access to additional platform technologies
- Provides preclinical expertise
- Initiates fundamental process change
 - Mutual acceptance
 - FTIH
 - Standard clinical trial agreement
- Promotes collaboration
- Promotes transparency
- Leading voice in clinical trial advocacy and process



Clinical Trial Project Management

- Selection of trials
- Legal Engagement
- Ethics submission and governance
- Co-ordination of "First Time in Humans" studies
- Project management
- Information systems
- Relationship with Tumour Groups

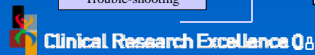


Clinical Project Management

- Sponsor contact, protocol development and review
- Budget development and review
- Clinical trial agreement
- HREC submission and approval
- Accrual monitoring
- Financial management
- Trouble-shooting



Clinical Project Manager:
 -dedicated project management for each trial
 -tracking & monitoring entire trial process
 -central point of contact for sponsors and investigators



Current trial portfolio

Phase	Accruing	Still open but closed to accrual
I	10	17
I/II	4	5
II	12	30
II/III	0	1
III	15	39
Other	4	5
Total	45	97



Some corporate highlights:

- Initiation of Mutual Acceptance program
- Initiation of Standard Trial agreement
- Initiation of FTIH protocol
- Active role of Tumour Groups (especially Phase I)
- Establishment of Associate Directors
- Appointment of a full-time CEO
- Membership expansion program
- ISO certification of the CTA laboratory
- Grant funding from VCA
- Support of the Clinical research in Oncology Training program



Challenges for CTA

- Large organisation
 - Keeping members happy and servicing their needs
 - Engage the scientists
 - Lack of expertise in particular areas
- Multi-centre HREC submissions
- Variable capacity
- Geographic isolation
- Increasing demands from Sponsors
- Increasing complexity of the clinical trial process
- Increasing cost of the clinical trial process
- Organisational change



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How do we do Cancer Clinical research in Australia?

- Individuals
- Hospital based
- Collaborations
- Cooperative groups
- Investigator led
- Sponsored



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What sponsors want

- Rapid accrual
- Rapid ethics approval
- Quality data

Some bonuses

- Innovation and value adding
- Cost-effectiveness



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What does Australia offer?

- Sophisticated health system
- High level medical/nursing care
- Moderate numbers of patients
- Enthusiasm for trials
- Clinical research expertise
- Platform technologies
- High level GCP
- High level IT
- Moderate cost



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What don't we offer?

- Large pt numbers
- Centralised HREC
- Proximity and time zones
- Low cost



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Cancer Drug Development

- 1345 cancer drugs in development (2002)
 - Pre-clinical 801
 - Phase I 205
 - Phase II 250
 - Phase III 76
- Estimated cost of developing a drug
 - USD897 million
- Clinical expenditure on a successful drug
 - USD175 million

Roberts et al. JCO 2003



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Cancer Drug Development

- IND → FDA approval = 10.8 years
- Cancer drug Phase III studies are the longest
- Cancer drugs have the second highest failure rate (of CNS)
- 280 drugs in Phase III clinical trials (75-94) → 29 received FDA approval

majority never reach FDA
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10 Essential Features of Successful Clinical Trial Management

1. Plan the therapeutic development path
2. Seek input from opinion leaders from the outset
3. Choose sites with experience, reliability and reputation
4. Use technology as a tool to clearly demonstrate endpoints
5. Negotiate the regulatory maze with a guide
6. Keep the HRECs informed
7. Utilise Investigators as partners in the process
8. Seek out dedicated research teams
9. Resource appropriately
10. Do it once and do it right

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Adapted from Kevin Lynch

How to do early phase trials?

- Understand what is required
- Regulatory and Administrative
 - Ethics and Consent
 - Protocol design
 - Trial Conduct
 - Evaluation of data
 - Reporting of data
 - Drug development strategy

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How to do early phase trials?

- Understand the difficulties
- Red-tape / paper work
 - Few drugs are winners
 - Additional work-load
 - Frustration with
 - Companies
 - Ethics committees
 - Hospitals
 - Trial staff
 - Yourself

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New drug development

- High risk
- Expensive
- Tension btw science and the market
- Requires pragmatism not idealism
- Requires broad range of expertise
 - Preclinical
 - Regulatory
 - Toxicology
 - Clinical

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Sources of new drugs

- Big pharma pipelines
- Big pharma pipelines
- Big pharma pipelines
- Australian biotech
- NCI
- International biotech

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The glory days of cancer clinical trials

- Plenty of money from sponsors
- Limited claim for hospital services
- Little oversight
- No questions asked
- Funded studies subsidised unfunded studies

Now...

- It's all about budgets....
 - Sponsors want a detailed budget
 - Hospital services have implemented fees
 - Protocol review fees
 - Establishment fees
 - Management fees
 - Service fees
 - Everyone wants a slice of the pie
- Significantly less discretionary monies
 - Unfunded studies are no longer feasible

The old paradigm is dead

- Single institutions rarely have sufficient:
 - tumour specific clinical expertise
 - accrual prospects
 - broad scientific expertise
 - platform technologies
- Collaborations can provide flexibility and a breadth of capability

Conclusions

- Clinical Trial Medicine is good medicine
- Early phase trials are difficult
- Early phase trials are exciting
- Winners are uncommon
- Most business is personal
- We live or die through collaboration
- Equity and transparency are critical
- The sum has to be greater than its parts