

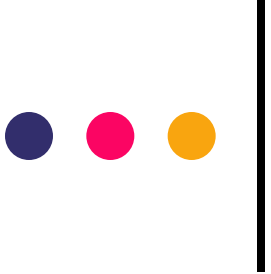


Clinical trials in childhood cancer

Maria Kirby

Oncologist

Women's and Children's Hospital,
Adelaide

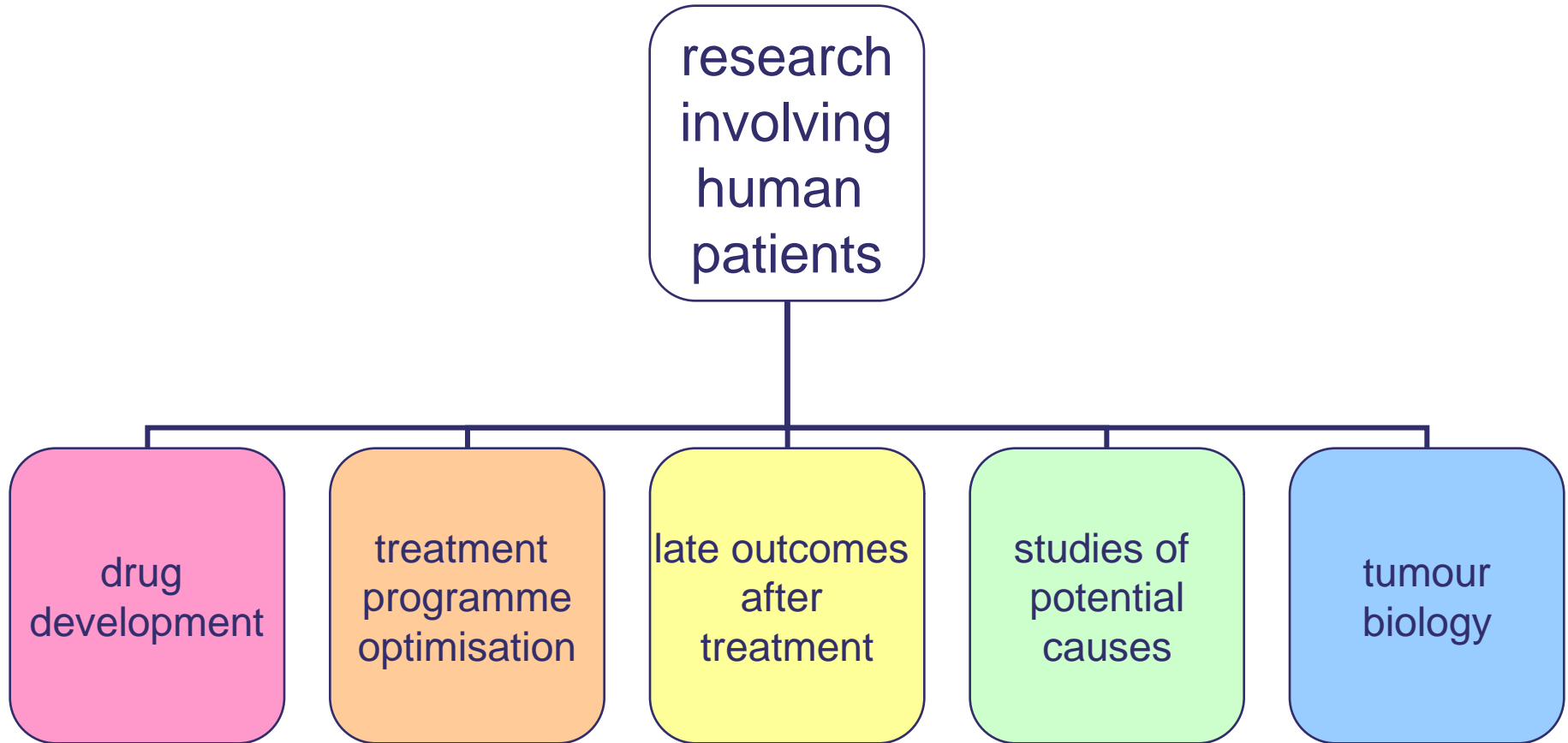


the WCH clinical trials programme

- participation in cooperative groups:
Children's Oncology Group
ACCT / ANZCHOG
SIOP Europe and soon BFM Europe
- 50-60 new patients per year
- currently about 45 active trials (some closed to new enrolments)
- currently about 200 active trial participants (some on more than one trial)



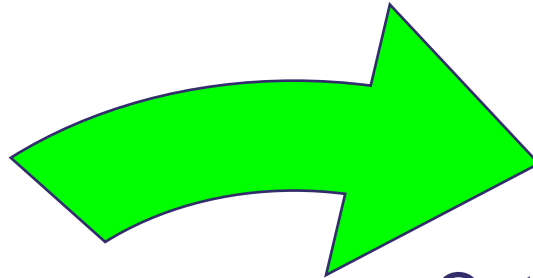
the spectrum of clinical trials



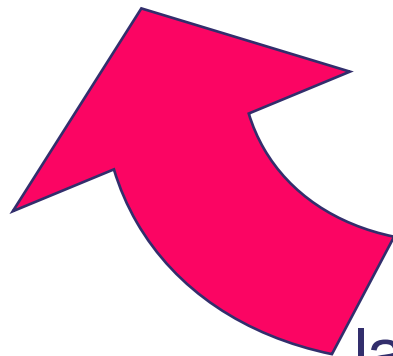


we need all trial types

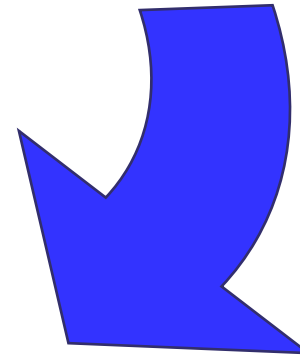
New drug
development



Optimise treatment
strategies

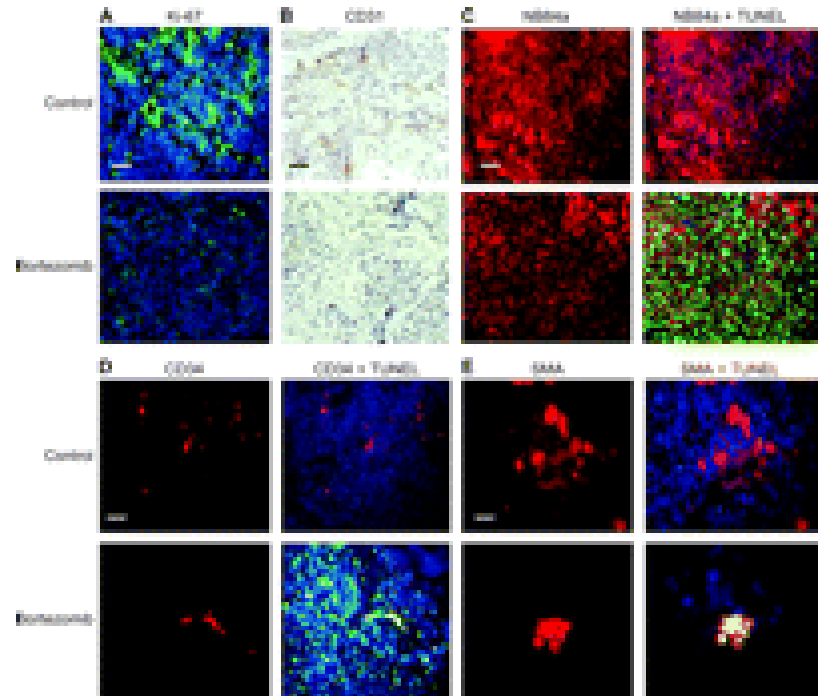


Link patient
information to
laboratory research
on tumours



drug development – pre clinical

- in vitro testing =
direct effect on
tumour cells in
laboratory



● ● ● | drug development – pre clinical

- in vivo testing =
toxicity,
effectiveness and
target drug levels in
animals





drug development: clinical

- Phase I:

 - focus on toxicity to determine optimal dose

- Phase II:

 - focus on effectiveness

- Phase III:

 - focus on integration into existing treatments



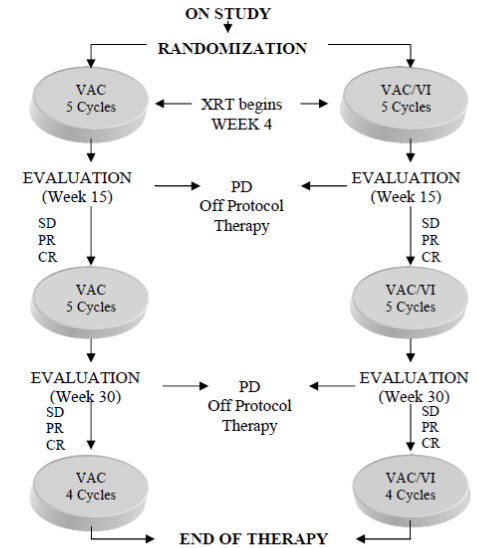
optimising treatment

- Phase III comparisons of two or more treatment programmes
- Refining patient classification to individualise treatment
- May try both approaches within the same study

optimising treatment

EXPERIMENTAL DESIGN SCHEMA

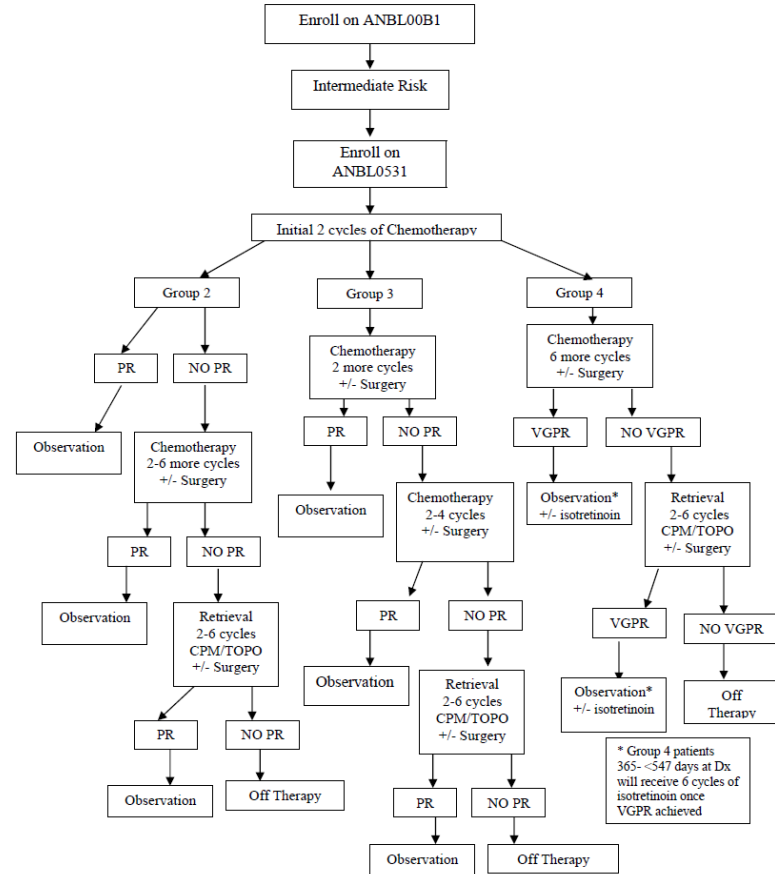
- Phase III comparisons of two or more treatment programmes



VAC = Vincristine, Dactinomycin, Cyclophosphamide
VI = Vincristine, Irinotecan

optimising treatment

EXPERIMENTAL DESIGN SCHEMA

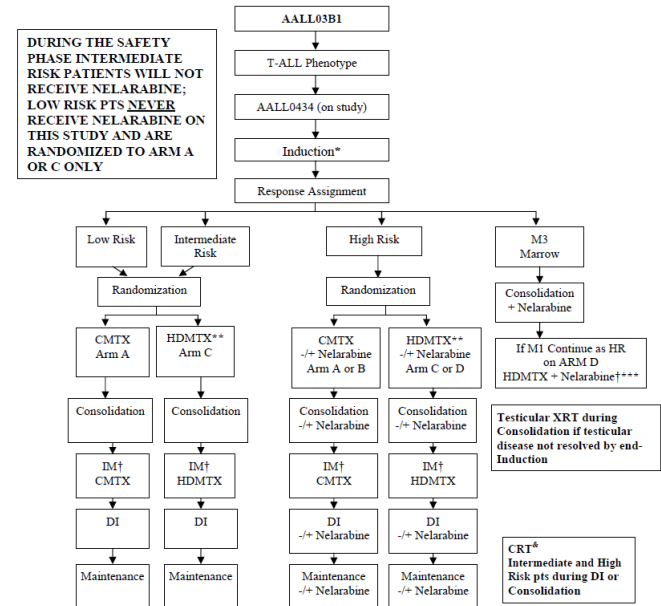


- Refining patient classification to individualise treatment

optimising treatment

- May try both approaches within the same study

EXPERIMENTAL DESIGN SCHEMA: SAFETY PHASE



* Induction evaluation = Day 8 BMA; if not M1 then repeat on Day 15.
Evaluation of BMA and MRD on Day 29.

** Patients with CNS3 and/or testicular disease at Dx will be assigned to HDMTX arms

*** Patient may also be taken off study for alternate therapy, including BMT

† Patients must be M1 at end-Consolidation to continue on therapy

RER = M1 marrow on Day 8 and < 0.1% MRD on Day 29 OR

M2/M3 marrow on Day 8 and M1 marrow on Day 15 and < 0.1% MRD on Day 29.

SER = M2/M3 on Day 15 OR positive MRD on Day 29.

Low Risk = NCI SR by age & WBC count; RER, M1 on Day 15 and MRD < 0.1% on Day 29; CNS 1 status; and no testicular disease at diagnosis.

Intermediate Risk = RER or SER with MRD < 1% on Day 29; any CNS status.

High Risk = M2 at end of Induction or MRD ≥ 1% on Day 29; any CNS status.

The safety phase ends when the 1st 20 High Risk pts to receive Nelarabine have been evaluated per Section 10.2.



late outcomes of treatment

- studies of groups of people who have all previously had similar treatment
 - what happens and how often?
- studies of people selected for having a particular type of problem
 - why did these people get the problem and can we predict or prevent it?



studies of potential causes

- potential environmental factors
- potential genetic factors
- can we:
 - prevent cancers?
 - detect them earlier? (and does this help?)

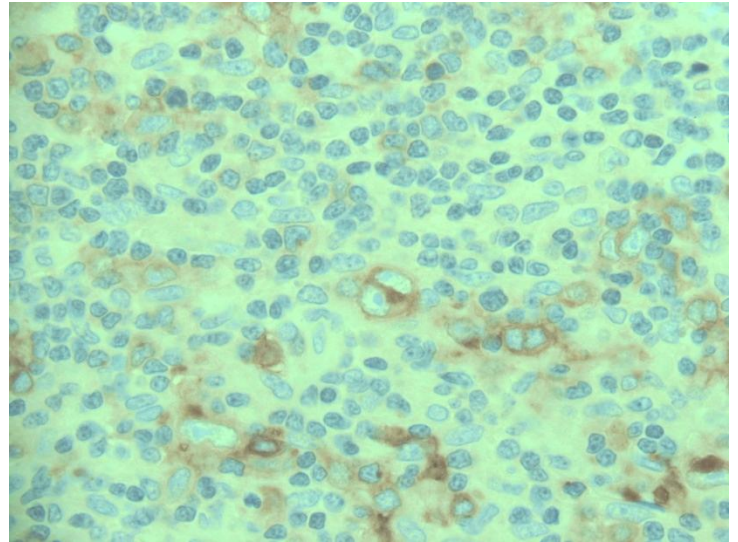


tumour biology

- link research on tumour samples and normal tissue to information about the patients who donated the samples
- identify:
 - targets for new drugs
 - new risk stratification tools
- save left over tumour tissue for future research

tumour biology

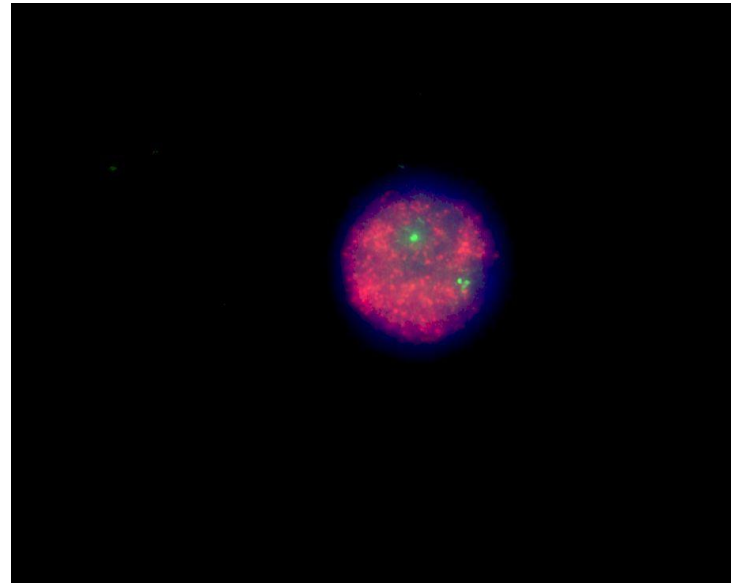
- targets for new drugs





tumour biology

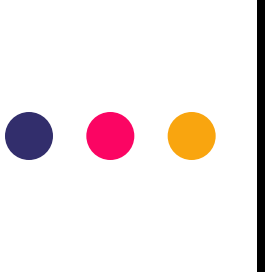
- new risk stratification tools





extra challenges in children

- each type and subtype of cancer is rare
- success rates are already fairly high for many cancers
- drug development is a commercial endeavour
- international regulatory challenges
- too young to consent for themselves so extra protection needed
- randomisation is very challenging for families and clinicians



but trials are really
important...

- overall, children participating in cancer trials have slightly better outcomes than children receiving the same treatment without trial participation (discipline and quality control?)
- almost everything we know about childhood cancer was learned from clinical trials



the sample size problem

- 160 children in Australia with acute lymphoblastic leukaemia per year
- total calculated sample size for current generation of COG ALL studies = 9500
- to answer these questions using just Australian patients:
59.3 years to accrue!



Children's Oncology Group

- Most children's cancer centres in USA, Canada, Australia, New Zealand and some in Europe
- Huge collaborative group –
about 9500 trial enrolments each year
about 140 trials currently open to accrual
about 23,000 patient reports per month!
- Funding mainly through US National Cancer Institute, with important supplementation from charitable donations
- Scale enables:
rapid answers to important questions in more common cancers
ability to study rarer problems in reasonable timeframe



ACCT

- Australian cooperative group for early phase trials
- aims to give appropriate Australian children access to new drugs in development
- a subgroup of ANZCHOG
- all national children's cancer units involved
- ACCT acts as intermediary between hospitals and drug companies –
 - simplifies contracts and funding
 - centralised ethics material preparation
 - increases chance of successful recruitment



the way forward...

- more national and international collaboration
- more tumour biology research
- more tumour and normal tissue banking for future research
- funding for childhood cancer research independent of pharmaceutical industry
- practical support at hospital level to enable trial participation