Guidance manual for phase II trial design in cancer

Sarah Brown

Principal Statistician

In collaboration with: Julia Brown, Walter Gregory, Chris Twelves, Marc Buyse, Max Parmar, Matt Seymour

Society for Clinical Trials
May 15 - 18, 2011

Vancouver, Canada

ctru

UNIVERSITY OF LEEDS

- **Background**
  - Many issues to consider in the design of phase II trials including trial aim, randomisation & endpoints
  - Literature discusses each of these points individually – no central resource
  - Multitude of designs available – how do we know which one to choose?
- **Aim**
  - Produce guidance on designing phase II trials to include:
    - key points for consideration
    - structured and systematic approach to trial design
    - detail on designs available

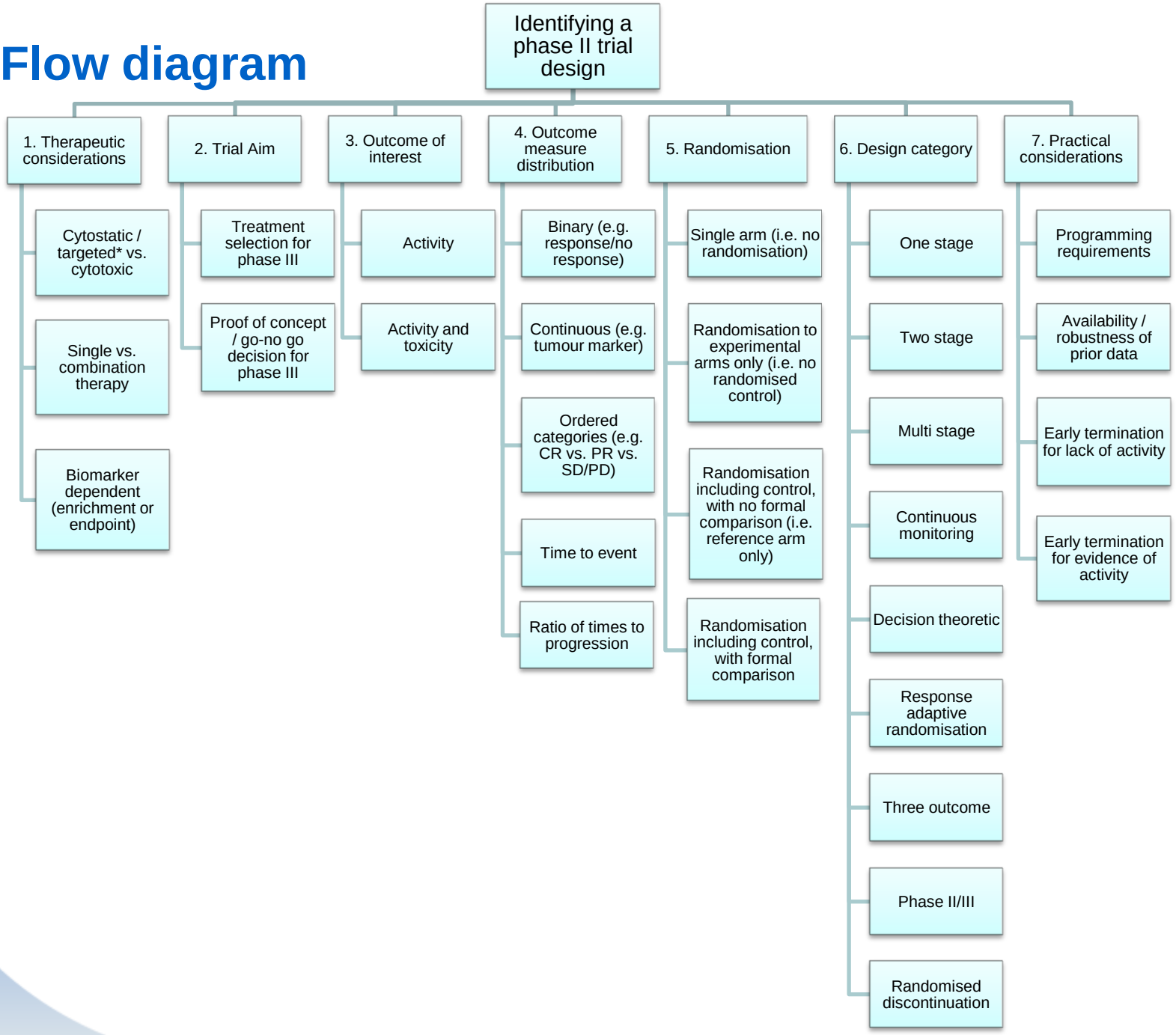
Methods

- Systematic review of phase II design methodology
- Identify designs that are easily implemented (n=121)
- Individual summary of each design identified
- Construct thought process for designing a trial
- Categorise and create library of designs

Guidance document – what is it?

- Practical tool to help researchers make informed decisions regarding phase II trial design
- Provides a thought process for clinicians and statisticians
- Flow diagram to aid decision process
- Detailed discussion on each of the points for consideration
- Identifies potential designs based on researcher-defined selection criteria – a bit like a dictionary!

Flow diagram



Points for consideration

- 1. Therapeutic considerations
  - Cytostatic / targeted vs. cytotoxic
  - Single vs. combination therapy
  - Biomarker dependent (enrichment of endpoint)

- Clinical input to inform decisions made later in the process

Points for consideration – to aid design selection (1)

- 2. Trial aim
  - Treatment selection for phase III
  - Proof of concept / go-no go decision for phase III
- 3. Outcome of interest
  - Activity
  - Activity and toxicity
- 4. Outcome measure distribution
  - Binary; Continuous; Ordered categories; Time to event; Ratio of times to progression

Points for consideration – to aid design selection (2)

- 5. Randomisation
  - Single arm
  - Randomisation to experimental arms only
  - Randomisation including control, no formal comparison
  - Randomisation including control, formal comparison
- 6. Design category
  - One stage; two stage; multi-stage; continuous monitoring; decision theoretic; response adaptive randomisation; continuous monitoring; phase II/III; randomised discontinuation

Points for consideration

- 7. Practical considerations
  - Programming requirements
  - Availability of data
  - Early termination

Conclusions / Points to note (1)

- Guidance focuses on practical elements of phase II design, offering a structured and systematic approach to identifying a phase II trial design in cancer
- It is intended to aid in design choices and to identify a range of possible designs, rather than being prescriptive
- Intended to facilitate clinician / statistician interaction

Conclusions / Points to note (2)

- Guidance remains a fluid document, which may be regularly updated with new designs and detail of additional resources for current designs
- As researchers use the manual and thought process to aid in design of phase II trials, it is hoped this will be reflected in the quality of publications in this area, and in readers' interpretation of phase II trial results
- Access document at http://ctru.leeds.ac.uk/phaseII
- Feedback facility available

Thank you

Email: s.brown@leeds.ac.uk
Website: http://ctru.leeds.ac.uk/phaseII