How can we deliver optimum benefits for patients? Maximising efficiency with a seamless phase ii/iii trial design

Society of Clinical Trials – 36th Annual Meeting

19 May 2015

Arlington, Virginia

Katie Neville[1], Lucy McParland[1], Walter Gregory[1], Jamie Oughton[1], Catherine Lowe[1], Emma Best[1], Fiona Collinson[1,2], Peter Hall[3], Timothy Eisen[4,5], Jenny Hewison[3], Janet Brown[6,2]

[1]Clinical Trials Research Unit, Leeds Institute of Clinical Trials Research, University of Leeds, Leeds, UK, [2]Leeds Teaching Hospitals, Leeds, UK, [3]University of Leeds, Leeds, UK, [4]Addenbrooke's Hospital, Cambridge, UK, [5]Cambridge University, Cambridge, UK, [6]University of Sheffield, Sheffield, UK,

This project is funded by the NIHR Health Technology Assessment Programme (project number 09/91/21). The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the HTA, NIHR, NHS or Department of Health. We are grateful for the support of the NCRI Renal Clinical Study Group.

ctru
Leeds Institute of Clinical Trials Research

NHS National Institute for Health Research Cancer Research Network

HTA

The University Of Sheffield.

NCRN

UNIVERSITY OF LEEDS

Overview

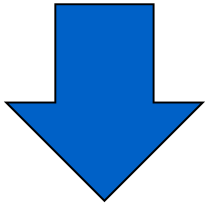
- STAR's multi-stage design & seamless transition
- areas for improvement on STAR
- benefits of multi-stage design
- recommendations for future multi-stage trials
- limitations of a multi-stage approach

The STAR trial

- randomised, controlled, UK, multi-centre, multi-stage (phase ii/iii)
- advanced renal cell carcinoma
- standard continuous treatment vs planned treatment breaks
- 1000 participants (210 in phase ii; 790 in phase iii)
- ~40 sites (16 in phase ii; 26 in phase iii)
- stop-go criteria at the end of phase ii, based on both:
  - recruitment
  - efficacy

Rationale for multi-stage design

- 1 versus 2 trials
- efficient transition between phases



- substantial time and cost savings
- research question answered earlier with fewer participants

STAR's multi-stage design

Pre-agreed and pre-planned

- **progression to phase iii (stop-go criteria)**
  - feasibility of recruitment
  - initial evidence of sufficient efficacy for the treatment break strategy
- **inclusion of phase ii participants in phase iii analysis**
  - possible due to continuity of trial design in phase ii and phase iii
- **uninterrupted recruitment at phase ii sites**

STAR's seamless transition

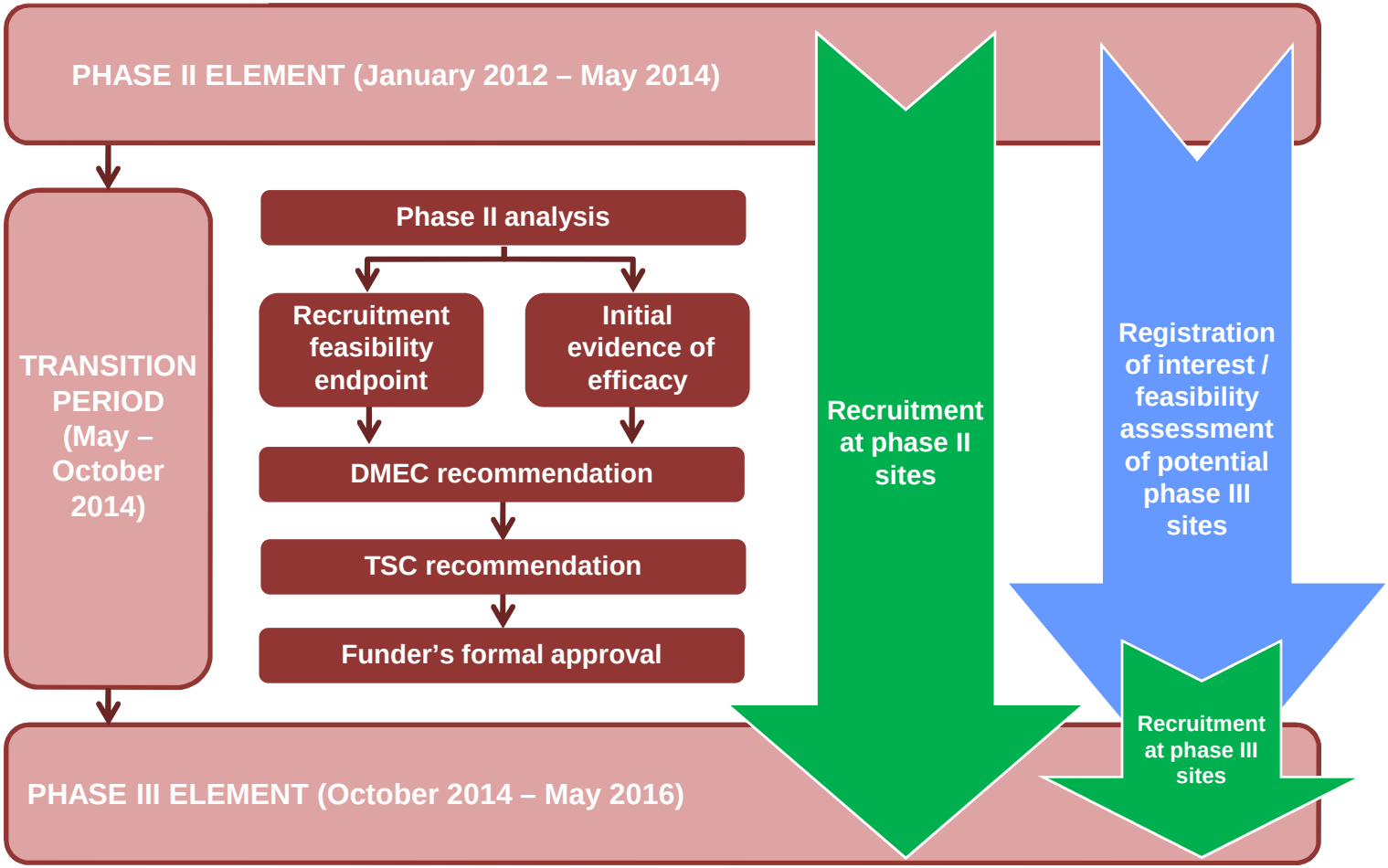
Transition period kept to a minimum

- **Advanced planning of phase iii sites' set-up**
  - establishing key contacts (e.g. PIs)
  - expressions of interest
  - formal feasibility

- **Efficient management**
  - funder pre-agreement to progress (upon steering committee approval)
  - efficient execution of interim analysis
  - timely oversight committee meetings

Phase II data lock: 01 May 2014
Phase II analysis: May-June 2014
Reports circulated: 26 June 2014
DMEC: 03 July 2014
TSC: 08 July 2014
Funder approval: 11 August 2014
1st Phase III site open: 16 October 2014

STAR's transition



ctru
Leeds Institute of Clinical Trials Research

UNIVERSITY OF LEEDS

STAR – room for improvement

Update to protocol and participant information sheet

Substantial amendment (updates referencing progression to phase iii)

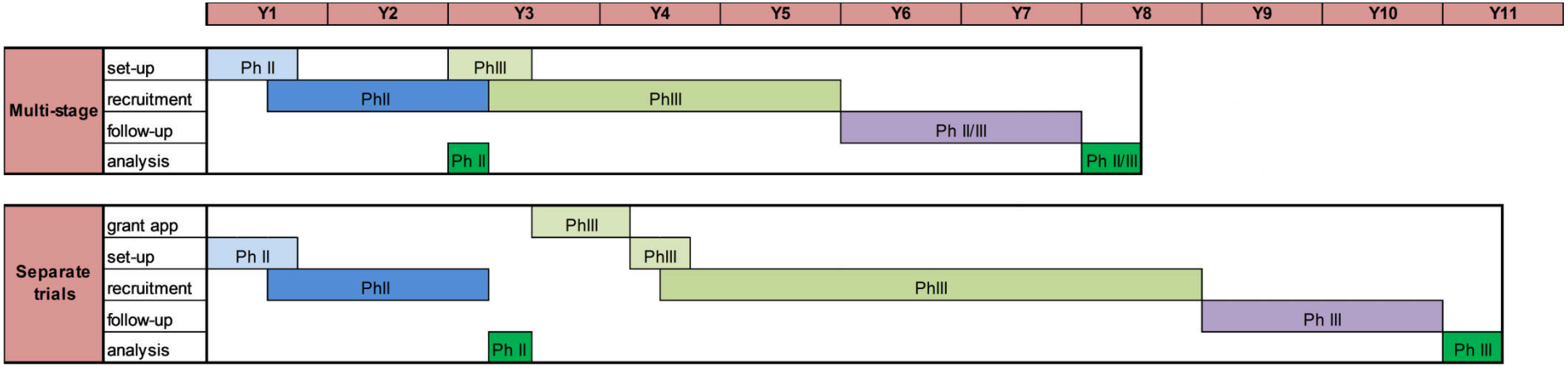
- careful wording of protocol and information sheet at outset

Lower recruitment rates during transition

Significant dip in recruitment at phase ii sites whilst waiting for approval to progress to phase iii

- effective communication with phase ii sites during transition

Benefits – What?



Time and cost savings!

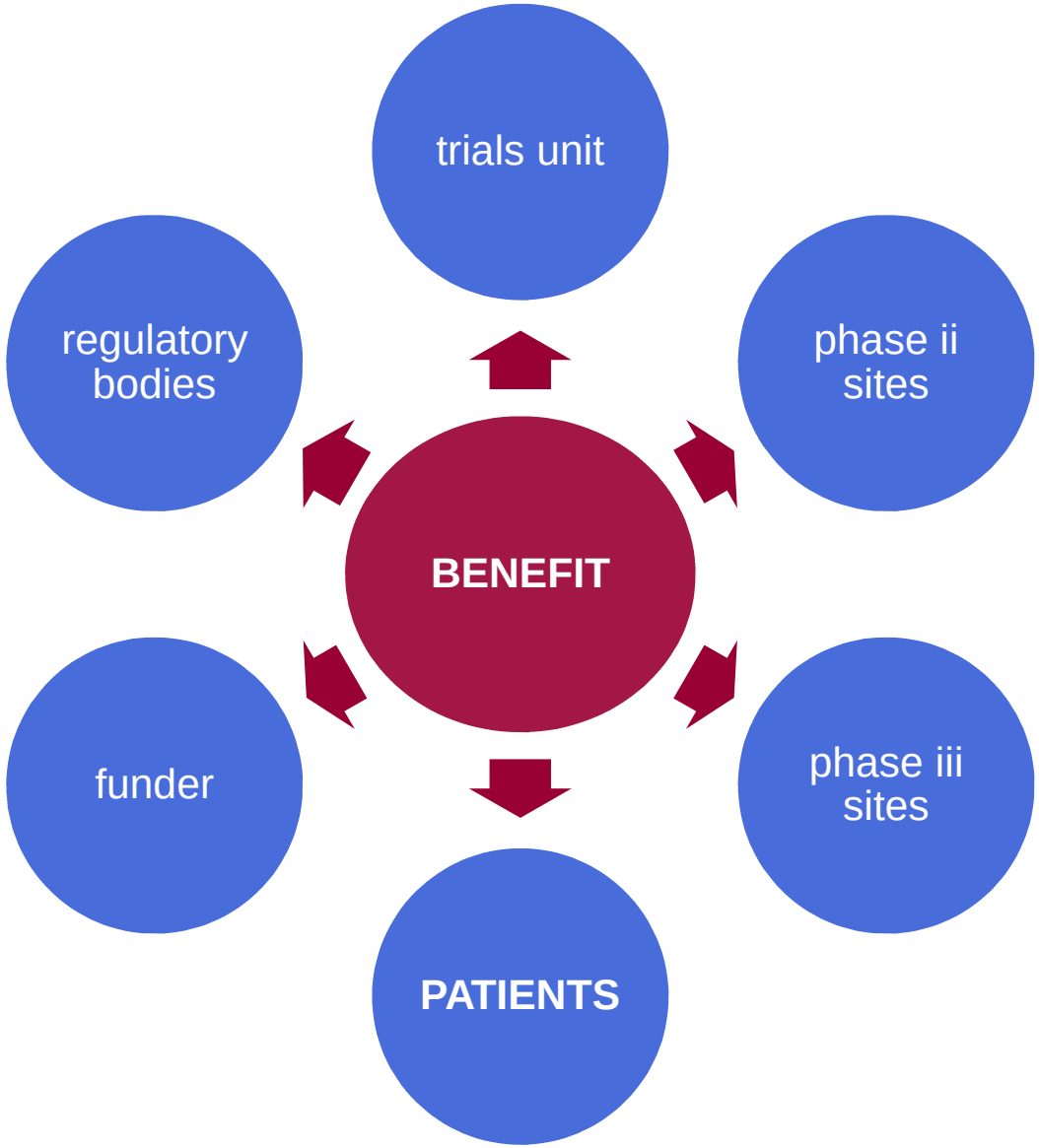
- no separate funding applications
- no separate regulatory / ethical approval process
- same trial documents / services
- concurrent trial stages
- reduced overall recruitment period

Estimated time-saving of 3 years

ctru
Leeds Institute of Clinical Trials Research

UNIVERSITY OF LEEDS

Benefits – Who?



Conclusion – Recommendations

Uninterrupted recruitment

- ensure recruitment continues during the transition period

Minimise the length of the transition period

- progress to phase iii upon approval of oversight committees

Communication strategy

- to current sites – maintains site engagement / recruitment momentum
- to new sites – provides a guide for estimated opening dates

Conclusion – Limitations

Scenarios where not beneficial

- stop-go criteria not easily / quickly measurable
- major changes to intervention, schedule, design between phases
- additional considerations (funding, etc)

Contact

Katie Neville
Senior Trial Coordinator
k.neville@leeds.ac.uk

Clinical Trials Research Unit
Leeds Institute of Clinical Trials Research
University of Leeds
Leeds
LS2 9JT
UK

ctru
Leeds Institute of Clinical Trials Research

UNIVERSITY OF LEEDS