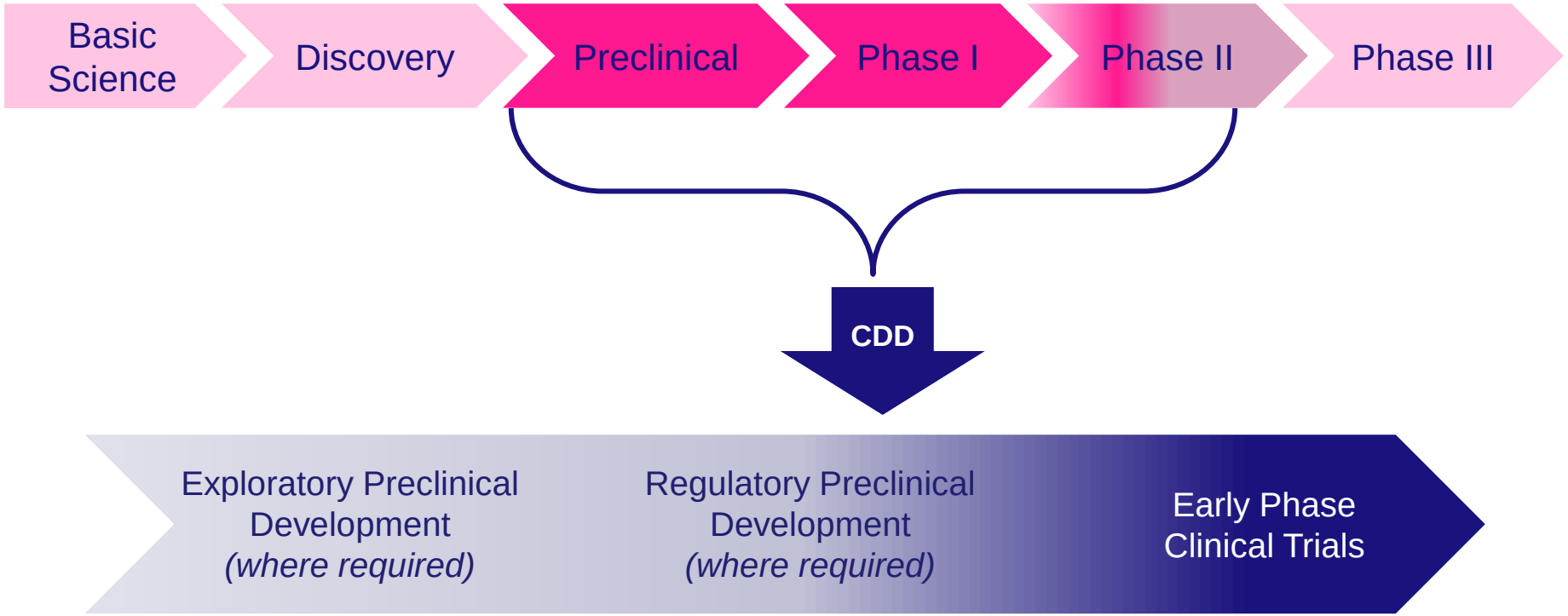
Managing Recruitment within CRUK's Centre for Drug Development

ECMC Meeting, 21st May 2015

Zoe Boylan, Combinations Alliance Manager (previously Clinical Study Manager, CDD)

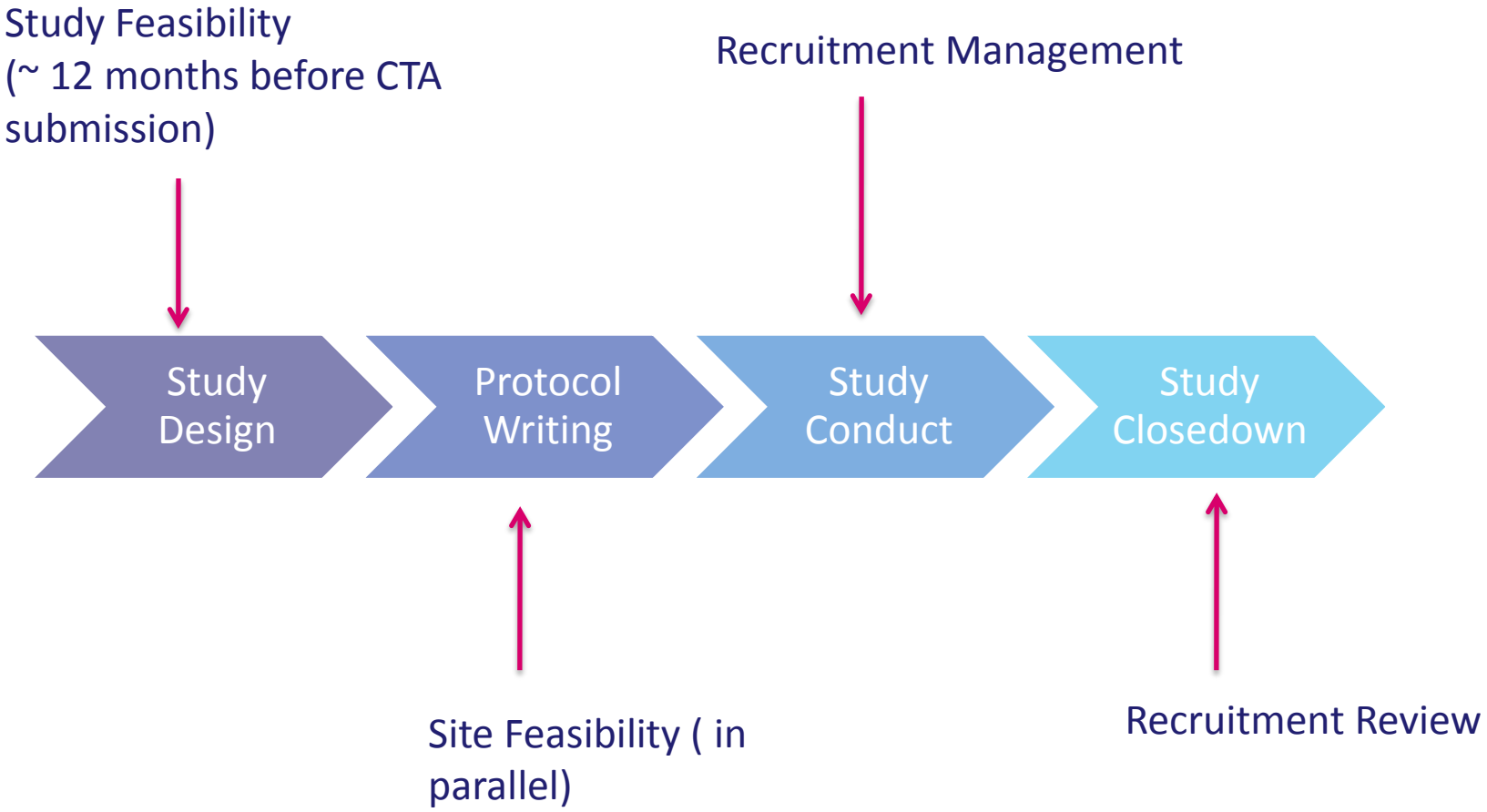
Introduction

CRUK CDD: What does the CDD do ?



CANCER RESEARCH UK | CENTRE FOR DRUG DEVELOPMENT

Recruitment Timeline: CDD sponsored trials



CANCER RESEARCH UK | CENTRE FOR DRUG DEVELOPMENT

Case Study: MVA-EBNA1/LMP2 vaccine

BACKGROUND

- Phase 1b study in Epstein Barr Virus positive nasopharyngeal (NPC) carcinoma patients.
  - Previously trialled in Phase 1a study.
- Rare cancer type & small patient population:
  - out of 1,200 EBV+ cancers diagnosed in 2011 in the UK a third were NPC (Parkin 2011).
- Primary objectives : Toxicity and Immunogenicity
- Maximum of 22 patients required
- 4 vaccinations given over 19 weeks, blood sampling up to 1 year.
- Open enrolment (not staggered – e.g dose escalation)
- Targeted 2 year recruitment period.
  - Decided early on, to match timelines of parallel study in Hong Kong
  - The phase 1a dose escalation study recruited 16 patients over 5 years.

"I'll eat my hat if MVA1b recruits a patient" *Head of portfolio and Project Management, CDD.*

CANCER RESEARCH UK | CENTRE FOR DRUG DEVELOPMENT

Study Feasibility

Study Design

Goal: Establish if the study can be conducted, in what timeframe, and become aware of barriers to recruitment.

Recruitment Questions:

- Does the patient population exist?
- How long to complete the study? / rough idea of number of sites needed.
- What will the key barriers to recruitment be: Competing studies, drugs due to be licensed soon, assessment complexity, study duration, attraction to patients.
- Is there initial interest in the study by the community?

- **Sources of Information:**
  - Patient databases (eg: Pharma eTrack)
  - Potential Investigators/ Opinion Leaders:
    - Barriers to recruitment: how to overcome issues in Phase 1a study in the Phase 1b study design.
    - Feedback to minimise number of study visits, and allow blood tests to be done locally.
    - Reduce number of blood samples needed for immune analysis, based on results from Phase 1a
  - CI presented Phase 1a study results at Head & Neck Clinical Study Group (CSG)
    - Feedback on Phase 1b design obtained.
    - A list of interested centres was taken away from this meeting.
    - Later discussed referrals with CSG to participating centres

Site Feasibility : MVA-EBNA1/LMP2 vaccine

Protocol Writing

Goal: Establish an accurate study and site recruitment plan, by selection of the final sites.

Feasibility Questionnaire

(Sent to 14 sites)

- How many newly diagnosed NPC patients seen in the last: 2 years, year, and 3 months?, How many have bee entered into a clinical trial? , are undergoing treatment?
- Are NPC patients routinely tested for Epstein Barr Virus?
- Competing trials (now or anticipated during the study). How the studies are prioritised.
- Catchment area, referral system, and number of referrals expected.
- How will patients be identified and approached / by whom?
- Expected rate of screen failure and accrual, and reasons for these.
- Barriers to recruitment.

Feasibility Visit

(7 sites visited)

- Recruitment figures in more detail. Expected recruitment rate into the study.
- Asked to provide proof of where figures came from (either multi-disciplinary team list, patient database, or recruitment to similar studies).
- Note: **Pre-screening potential patient log** can be used (Not done in this study, but has been done in other studies
- Hospital catchment area, referral processes, networks, MDT frequency
- Understand how motivated site is, if they have the resourcing and infrastructure

CANCER RESEARCH UK | CENTRE FOR DRUG DEVELOPMENT

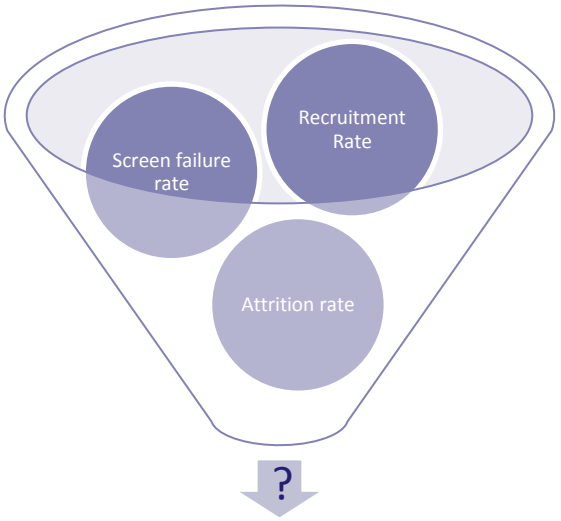
Site Feasibility: MVA-EBNA1/LMP2 vaccine

Protocol Writing

Goal: Establish an accurate study and site recruitment plan, by selection of the final sites.

Site Selection Summary:

- Newly diagnosed patient figures in last year were very low (all in single digits)
- None of the NPC patients had been entered trials in the last year.
- Routine testing for EBV was not common (3/ 7 sites tested as SOC)
- Some sites had participated in the Phase 1a study, so were aware of challenges. (eg high screen failure rate)
- Each site expected to recruit~ 2 patients per year.
- All 7 sites were selected to participate: uncertainties around if they would actually be able to recruit, and desire to avoid later lengthy set-up processes.
- Sites purposely spread across the country.



Number of sites

Back-up sites strategy:

- Identified during site feasibility, but that are only opened if recruitment falls behind a certain rate. (contained within initial CTA application).

CANCER RESEARCH UK | CENTRE FOR DRUG DEVELOPMENT

Recruitment Management: MVA-EBNA1/LMP2 vaccine

Study Conduct

Kick-Off Investigator Meeting

Goal: Maintain recruitment according to the study and site recruitment plans

- Attendance by Investigators, Research Nurses, Laboratory Staff.
- Training provided by CI, Study Nurse, Laboratory staff and CRUK.
  - Advantage of Chief investigator, Laboratory leads being able to answer all questions.
- Team felt this was instrumental in motivation, and generating enthusiasm of all parties involved in the trial.
  - The Chief Investigators dedication and belief in the study was engaging.
- Friendly competition in terms of recruitment was initiated.

- Site staff discussed which patients they could identify:
  - Patients in-remission eligible
- Agreement to translate PIS into Chinese

Generation of positivity around the trial

CANCER RESEARCH UK | CENTRE FOR DRUG DEVELOPMENT

Recruitment Management: MVA-EBNA1/LMP2 vaccine

Study Conduct

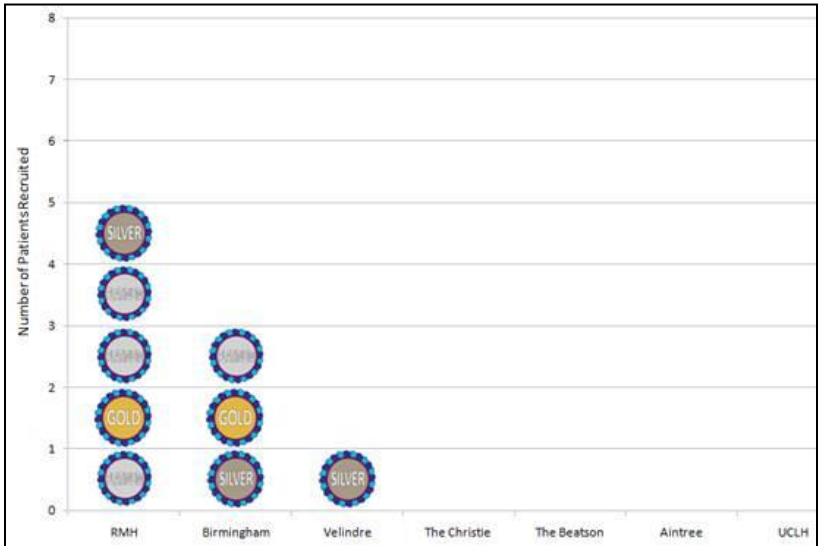
Goal: Maintain recruitment according to the study and site recruitment plans

Set the Site recruitment plan: Written document outlining Site recruitment targets. To be discussed, finalised and agreed at the study initiation, with contingency plans should the targets not be met.

- Monthly Newsletters: with league tables in terms of recruitment.
  - Encouraged competition and sustained motivation.
  - Recognition each month, of hard work and commitment of site staff.
  - Site level newsletters to their networks about the trial.
    - Including info sheet for clinicians.

Like the format of the newsletter, well done to everyone (and especially to those singled out for special mention!) – *Principal Investigator*

- Recruitment Awards: per patient awards were introduced:



CANCER RESEARCH UK | CENTRE FOR DRUG DEVELOPMENT

Example Contingency Plan:

Study Conduct

Milestone	Contingency 1	Contingency 2
Recruitment on Track	CRA to meet with PI every 2nd Visit	Screening log to provided at each visit for CRA to review
Three month period within which slot available and no patients recruited at site	PI to hold a meeting at site to discuss recruitment	Meeting to be held by Sponsor including all PIs to discuss recruitment
Six month period within which slot is available and site don't recruit	Sponsor to consider opening a new site	Sponsor to consider early site close-down after discussion with the site.

Contingencies can also be site specific. For Example:

- Extend the patient catchment area to Preston and North Wales (The Christie)
- Seek referrals from other hospitals such as Brighton Hospital. (RMH)

Study Close-down: MVA-EBNA1/LMP2 vaccine

Study Closedown

Goal: Evaluate success of recruitment plan and lessons learnt for the future

Questions:

- Did study and site recruitment match original predictions?

Target: 2 Years	**Actual**: 18 months (saving 6 months)
Initial Sites: 7	**Actual Sites**: 5* (two were not opened, as when agreements were finalised, all the slots had been reserved by other sites)

- Which sites were realistic in their predictions? All sites met their target of 2 patients a year (4 exceeded them)

- Which contingency strategies worked well? None implemented, although these were implemented prior to trial opening based on lessons learnt from Phase 1a study.

- Was the screen failure rate as anticipated? Yes, as was discovered in the Phase 1a
  - 53 patients screened(15- declined entry, too many blood tests/visits, 7- due to prior treatments, 3 EBV negative, all others – various reasons) = 22 entered.

THANK YOU!

CANCER RESEARCH UK

cruk.org

CENTRE FOR DRUG DEVELOPMENT , CANCER RESEARCH UK

Zoe Boylan (nee Backholer)
Combinations Alliance Manager
Tel: 020 3469 6992
Zoe.Backholer@cancer.org.uk