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Trials

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P-1
Abstract omitted

P-2
Some practical considerations in the design of multi-arm multi-stage designs

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Introduction: In the design of cancer clinical trials, one is often concerned with a number of options in the event that several treatments are of interest.
Methods: We explore in this work the distinct possibilities when four treatments are available, one acting as control and three as potentially efficacious alternatives. This design may be embedded within the context of multi-arm multi-stage (MAMS) trials where one may select a two- or three-stage design.
Potential Results: We explore the application of such designs, including trade-offs between potential gains in the number of patients with additional stages contrasted with patients "lost" due to practical considerations such as patients randomised in dropped arms while waiting for interim analyses and inspection by an Independent Data and Safety Committee. In addition, in cancer studies one may focus on the primary end-point using a time-to-event analysis or a binary outcome by looking at the probability of (potentially progression-free) survival at a specific, clinically meaningful, time point. The effect of such choices is extensively investigated.
Potential Relevance & Impact: We conclude with a discussion of the available software for MAMS designs and their advantages and disadvantages in terms of accuracy.

P-3
The UK plasma based Molecular profiling of Advanced breast cancer to inform Therapeutic CHoices (plasmaMATCH) Trial: A multiple parallel-cohort, phase IIa platform trial aiming to provide proof of principle efficacy for designated targeted therapies in patient subgroups identified through ctDNA screening (CRUK/15/010)

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Trials 2019, **20(Suppl 1):**P-3

Introduction: plasmaMATCH is a novel platform trial which assesses the potential of circulating tumour DNA (ctDNA) screening to direct targeted therapies in advanced breast cancer (ABC) patients. The trial recruited ahead of target and will report initial results within 3years of first patient first visit demonstrating efficiency of this design.
Methods: plasmaMATCH is an open-label, multi-centre phase IIa platform trial, consisting of a ctDNA screening component and five parallel treatment cohorts. Patients with an actionable mutation identified at ctDNA screening are invited to enter Cohorts A-D to receive a targeted treatment matched to the mutation identified (A: ESR1–extended-dose fulvestrant; B: HER2–neratinib+/-fulvestrant; C&D: AKT1 (or PTEN for Cohort D) –AZD5363+/-fulvestrant). Cohort E was added

PS4C

- O5

Abstract withdrawn

PS5A

- O1 When to do an external or internal pilot study: Findings from an interview study with research funders

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Introduction : A standalone external pilot explores the feasibility of performing a definitive RCT, with outcome data not routinely combined with data from the subsequent RCT. An internal pilot is designed and conducted as the first phase of an RCT, with outcome data included in the main analysis. When to perform an internal or external pilot is poorly understood. Qualitative work is needed to explore the views and perceptions of funders regarding how, when and why to choose an external or internal pilot study design.
Methods: Purposive sampling identified participants from UK funding panels including NIHR (HTA/RfPB/EME/PGfAR) CRUK, CSO and ARUK. Maximum variation sampling ensured inclusion of multiple characteristics, including chair/deputy chair/member positions on different funding panels and various methodological roles. Semi-structured interviews performed face-to-face or by telephone using a topic guide explored participants' views and practices of funding pilot work. Data analyses were conducted according to principles of thematic analysis, in an iterative and cyclical process as further interviews were conducted and until no new themes emerged or evolved.
Results: Of 27 participants contacted, 19(70%) consented and were interviewed in three iterative phases (mean duration 59minutes, range 30-88). Most participants agreed an external pilot design should be chosen when substantial uncertainty exists about one or more design parameters. Of these parameters, a stable, deliverable and acceptable intervention was perceived by most as essential for proceeding to a main trial. Some discussed how staged funding for external pilot studies progressing to a feasible main trial could improve efficiency and limit waste, through avoiding conduct of studies with little hope of main trial funding. Others felt an open ended funding strategy presented significant logistical difficulties, despite it's appeal.
Conclusion: Future work will focus on developing recommendations for when to do an external pilot, and establishing whether a flexible design model is possible.

PS5A

- O2 Exploring patient treatment preferences enhances trial recruitment, so why do trial recruiters often avoid doing it?

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Introduction: Patient treatment preferences are one of the most common preventable reasons for poor trial recruitment. Exploring treatment preferences during trial consultations entails eliciting and acknowledging the reasons for a patient's preference and providing information to balance treatment views. Doing so can improve informed consent, trial recruitment and retention. We examined how trial recruiters respond to treatment preferences during consultations and recruiters' views about exploring treatment preferences.
Methods: Transcribed audio-recordings of 128 trial consultations from 97 patients and semi-structured interviews with 53 trial recruiters (surgeons, oncologists, and nurses) from two multicentre trials (CONTRACT ISRCTN15830435; ROAM/EORTC-1308 ISRCTN71502099). Data analysis was thematic.
Results: Initially, few recruiters elicited treatment preferences but following training they increasingly did so. However, contrary to the training, recruiters' exploration and balancing of preferences tended to be asymmetrical - they particularly avoided exploring and balancing preferences when the patient's preference aligned with the recruiter's own preference. In one of the trials, this often resulted in the patient declining to participate. Recruiters spoke of being reluctant to explore and balance preferences and some attributed this to concerns about unduly influencing patients to participate. Some thought preference exploration would take too much time or would conflict with their clinical responsibilities to advise patients about treatments.
Discussion: Despite trial communication training, recruiters were hesitant to explore patient treatment preferences. Consequently, patients will often be relying on suboptimal information about treatments to inform their decisions about trials. Emphasising that preference exploration, regardless of the recruiter's own preference, is consistent with a supported and informed approach to decision-making could help to overcome recruiters' concerns. Evidence on the perspectives of patients on treatment preference exploration would inform recruiter training and practice. Trialists also need to consider the potential impact of recruiter biases on trial communication when designing future trials that compare markedly different treatments.

PS5A

- O3 Review of use of the Trials within Cohorts (TwiCs) design approach

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Introduction: Trials within Cohorts (TwiCs) is an innovative approach to the design and conduct of multiple randomised controlled trials (RCTs) (Relton et al, 2010). This approach utilises an observational cohort to recruit trial populations and obtain short and longer term outcomes. We describe what is currently known about the use of this design approach.
Methods: An extension of the 2010 Consolidated Standards of Reporting Trials (CONSORT) Statements for RCTs using cohorts and/or routinely collected health data is in development, supported by a scoping review that includes publications of methods or reports of protocols or results from RCTs using cohorts, registries, electronic health records and administrative databases. Data sources for this scoping review included Medline and Cochrane Methodology Register and were limited to English language.