IMI GETREAL: STAKEHOLDER VIEWS ON THE EARLY USE OF PRAGMATIC TRIALS DURING MEDICINE DEVELOPMENT TO SUPPORT ASSESSMENT OF NEW INTERVENTIONS

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INTRODUCTION

- Pragmatic clinical trials (PCTs) are randomized clinical trials that compare health interventions in patient populations in routine clinical practice
- To date, PCTs have been implemented before marketing authorization with the explicit purpose of supporting regulatory and health technology assessments
- The objectives of this work were to elicit a comprehensive stakeholder view on the acceptability of the early use (before marketing authorization) of PCTs for informing relative effectiveness of new medicines in regulatory assessments and health technology assessments

METHODS

- The pan-European IMI GetReal consortium conducted a workshop attended by key European and US stakeholders
- The workshop combined presentations, structured breakout sessions and plenary discussions
- The workshop captured stakeholders’ views on the acceptability and usefulness of PCTs, conducted before market authorization, for establishing the relative effectiveness of new drugs

RESULTS

When should early PCTs be considered?

- When efficacy is not predicted to match effectiveness: i.e. when randomised controlled trials (RCTs) do not demonstrate effectiveness in real life
- When comparators are used in a manner in the real world that can’t be replicated in RCTs: e.g. when a medicine is used off-label
- When wide variability in usual care makes it hard to define a single comparator

How strongly would results from pragmatic designs be accepted as evidence?

- Strengths generally relate to external validity, and weaknesses reflect lack of internal validity and difficulties with analyses
- Evidence from PCTs would be more acceptable for drugs with a known benefit/risk profile

How can we maximise the value and acceptability of PCTs?

- Develop guidelines on trial designs, evidence synthesis and best practice
- Upskill the pharmaceutical and public sectors on methods of evidence synthesis
- Develop a framework to determine where efficacy/effectiveness gap is expected

Conclusions

- PCTs are still very much in their infancy
- Questions remain on when pragmatic elements could add the most value, and on the timing of pragmatic trials in clinical development

References

1. IMI GetReal (www.imi-getreal.eu)

GetReal Case Studies: Capturing Stakeholder Perspectives

Aim

To develop a common understanding amongst healthcare decision makers and pharmaceutical R&D of the acceptability and usefulness of innovative development programmes which use real-world evidence to estimate the effectiveness of new medicines

Focus

Use of real-world evidence in an early setting (before marketing authorization)

Overall vision

For healthcare decision makers to have relevant evidence to assess effectiveness of new drugs when used in standard practice

How do we build on positive opportunities to use PCTs and address any barriers to acceptability?

- PCTs could allow enrolment of more patients than RCTs, including those who may otherwise be excluded from RCTs
- To demonstrate acceptability by patients in real practice and for confirming positioning of new treatment in treatment paradigms

How do we build on positive opportunities to use PCTs and address any barriers to acceptability?

- Explore innovative trial designs. For example, a hybrid PCT incorporating an ‘RCT population’ that could provide internal validity of the trial
- Characterise various options for PCTs, as these trials vary in their pragmatism. This could be done using the PRECIS tool\(^1\), which assesses the level of pragmatism of trials

Can we identify the factors that influence whether pragmatic trial data would be considered as ‘strong’ or ‘weak’ by decision makers?

- PCTs should not replace ‘standard’ RCTs, because decision-makers still require robust demonstration of treatment efficacy
- Robustness of long-term PCTs was questioned: randomisation can break down following treatment switching

How do we build on positive opportunities to use PCTs and address any barriers to acceptability?

- Best-practice guidelines on the use of early pragmatic designs will help guide the design of future PCTs. However they should not be so prescriptive that they stifle innovation
- Further collaborative efforts such as case studies will provide valuable insight in this respect