Clinical trials and the challenge of regenerative medicine: do we need a new approach for cell therapy trials?

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Introduction

- In 2013 a House of Lords Science and Technology Committee report on Regenerative Medicine identified clinical trials as a key challenge for the translation of regenerative therapies in the UK.
- My research aims to address this by examining the role of trials in the innovation process. The main research objectives were:
  1. To characterise the UK cell therapy trials landscape;
  2. To identify the main challenges experienced in the day to day running of trials;
  3. To understand how trials fit in to the broader process of cell therapy innovation;
  4. To understand how the evidence generated by trials in used by cell therapy developers and regulators.

Main findings

1. There are less than 50 cell therapy trials currently underway in the UK, covering a broad range of clinical areas and split between immune-therapies, tissue regeneration and systemic therapeutic use.
2. The majority of trials are early-phase, investigator-led and publicly-funded.
3. There is no such thing as a 'typical' cell therapy trial – the landscape is very fragmented, and most trialists identify more closely with their clinical area than with 'cell therapy' or 'regenerative medicine'.
4. The main challenges experienced when running a trial are largely caused by financial constraints, the logistics of working with cells, the length of time required and coordinating the different disciplines involved.
5. Unlike drugs, cell therapies are complex interventions with multiple, interconnecting uncertainties. Many of these uncertainties can only be resolved by use in the clinic, a recursive process which conflicts with the phase model of drug trials, which imposes a linear innovation pathway.
6. Because of the complexity and novelty of cell therapies, regulators often lack expertise in the specifics of the treatment being regulated. This can be overcome by regulators adopting a collaborative, flexible and nuanced approach to evidence.

Conclusions and Recommendations

Although cell therapies are regulated as medicines, from a trials perspective they have more in common with complex interventions. This creates obstacles that have impeded innovation, however there are a number of actions that can be taken to address these issues, whilst also continuing to ensure robust regulation of these highly experimental treatments.

General recommendations

Predictability and consistency of regulation is important, so any changes (e.g. after leaving the EU) must be carefully considered and well communicated.

Cell therapies involve interconnected clinical and scientific uncertainties, so clinical research should be designed to address both.

Patient agency is problematic for cell therapy trials, so robust PPI is essential. Qualitative research should also be considered whenever possible.

'On-trial' evidence

Because cell therapy trials are so varied there is no trial design that is suitable for all trials.

Instead it would be useful to develop a 'basket of tools' for cell therapy trials, allowing trialists to select the most appropriate design for their circumstances.

Options that should be considered include adaptive and factorial designs, imbalanced randomisation and patient preference.

'Off-trial' evidence

The consent procedures and collection of outcome data for patients treated under hospital exemption currently falls outside of the clinical trials regulations.

A more systematic approach to hospital exemption, based on the IDEAL framework for surgical trials, would give patients greater protection.

The evidence generated could also supplement trials, particularly in the early stages of innovation or when randomisation is not possible.

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