

Why and how current EU-Regulations don't match the needs of regenerative medicine

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Can Harmonized Regulation Overcome Intra-European Differences? Insights from a European Phase III Stem Cell Trial

Author:

Christine Hauskeller

Examining how culture and the structure of society affect a clinical trial testing an autologous stem cell procedure, it became apparent how efforts to standardize regulations across the EU has advantages but also brings new challenges for regenerative medicines. Professor Hauskeller argues that academic research teams need access to a new system of support for solving these inevitable difficulties. The findings also provide reasons for re-considering how clinical trial norms can be adapted to suit the needs of regenerative medicine.



What questions & challenges are raised?

There are many claims that the current clinical trial (CT) process is in need of reform to meet the needs of developing regenerative medicine (RM) treatments. Issues such as scientific rigour, accessibility, public demand, financial incentives and moral implications have all contributed to calls for integrating more societal considerations. The EU has implemented the EU Tissue and Cells Directive and other policies to help standardise CTs, but differences in regional cultures and policies are not fully addressed and complicate CT implementation. Simple things such as language, trial insurance and post-clinical care provision can slow the process and increase the costs of a CT. In her recent publication, Professor Christine Hauskeller from the University of Exeter discusses how European legislation has affected a large multinational EU clinical trial with autologous cells. Professor Hauskeller has been accompanying the CT from its funding application in 2009 to present, and chronicled the many events and issues encountered. Details of this case study exemplify the need to establish centralised resources to support the complex logistics of European multinational trials in publicly funded research. Also, reforming the CT process should create avenues that support academic clinical research, the only actors that might bring autologous cell therapies into the clinic.

EU have largely focused on the scientific aspects of studying a treatment but should include cultural conditions as well. Many problems would be less pressing with better funding. A cheaper option might be a Europe-wide agency that helps academic teams with regulatory compliance in the face of cultural differences. But perhaps the structure of CTs themselves is problematic. Professor Hauskeller suggests that the many problems encountered in BAMI indicate that creating new routes to validate the safety and efficacy of RMs might be needed.

What insight & direction does this give for research policies?

The difficulties encountered by the BAMI CT highlight how establishing EU-wide policies may make the initial approval process easier and more rapid, but does little to address issues that arise from differences in culture and local regulations. Additionally, researchers in BAMI expressed concerns that the EU-wide policies hold all new cell therapies to the same rigorous standard, even those using the patient's own cells. This can stifle and discourage academic research and CTs with limited funds. Professor Hauskeller points out that some logistical issues encountered in the BAMI trial might be attributed to the fact that BAMI has been the first multinational EU stem cell trial run by clinician-scientists following the new regulatory regime. The experience gained by staff in the BAMI trial will be valuable for guiding and enacting changes to better facilitate future academic CTs. Many other issues were due to cultural differences and regional policies that cannot be harmonized. Professor Hauskeller states that policies adopted by the

What background and point are discussed?

Professor Hauskeller reports on a currently ongoing phase III clinical trial called 'BAMI' (an acronym for the full name). The CT is examining the benefits of collecting and implanting bone marrow stem cells from the patient into the heart after a heart attack. It is primarily funded by a European Commission grant and run by clinicians in 10 EU-countries. Professor Hauskeller and her research team collected observations from meetings, mini-surveys, and 30 extended interviews with BAMI staff. The issues that BAMI has encountered span many areas, including regulatory agency approvals, biological sample transportation, regulatory standards, differences in cultural environments, financing, staff retention and the study's time frame. A major problem was the implementation rules in new EU-wide regulations from 2010, after the trial had been planned. Only three of the six cell-processing laboratories the BAMI trial originally envisaged to use met the stricter requirements. Consequently, significant time and money had to be invested in regulation compliant transportation of patients' cells across borders. The new EU legislation standardizes CTs of RM, but other minor differences in practice, regulations and policies between different countries became a recurring obstacle. They include issues such as differences in after-hospital services provided, access and approval for specific drugs, staff certifications, ethical approval of consent forms and patient information sheets, language translations, and financial accountability (patient insurance). All these issues added costs, time and demands on staff. The CT started in 2011 with a 5-year timeline and is now expected to end in 2019. Lengthening the duration without additional funding has created subsequent issues with staff retention, the expiry of consumable standardized materials and equipment. The latter then required agency re-approval requests, which further delayed patient recruitment.