Behind the scenes of advanced therapies

Before a patient can receive an experimental gene or cell therapy in a clinical trial, regulators must answer a difficult question: is enough known about the treatment and its potential risks to justify testing it in humans? This is especially challenging for advanced therapy medicinal products (ATMPs), which, unlike traditional medicines, use living cells or genetic material to repair, replace or modify biological functions and may involve uncertainties regarding manufacturing, safety, and treatment effects. Some ATMPs are being developed for diseases such as cancer, genetic disorders and tissue damage, where conventional treatments may be limited or unavailable.

Before these advanced therapies can be authorised for administration in patients, regulators review clinical trial applications. They evaluate whether the product is sufficiently characterised, consistently manufactured and supported by adequate quality, non-clinical and clinical data. During this assessment, regulators frequently ask sponsors for clarifications or additional information regarding different scientific and regulatory aspects of the application. This project investigated which scientific and regulatory questions most frequently arose during the assessment of investigational ATMP clinical trial applications submitted between 2022 and 2025 where Sweden or Denmark acted as Reporting Member State (RMS).

To analyse these recurring assessment questions, the European Clinical Trials Information System (CTIS) was used. In the system, these questions, requests for clarification, and objections raised by regulators are called considerations. Consolidated Part I considerations from ATMP clinical trial applications were grouped into categories and analysed for recurring patterns. The analysis included 22 clinical trial applications and 907 considerations.

The results showed that quality and clinical considerations were the most common during assessment. Frequent quality-related considerations concerned product characterisation, manufacturing processes, materials, and control strategies, while clinical considerations mainly focused on trial population, safety and treatment strategy. The findings also showed that similar scientific and regulatory challenges often reappeared across several assessment areas, although viewed from different regulatory angles. The analysis also suggested that assessment patterns may differ depending on factors such as ATMP type, sponsor type, development stage and trial scope.

By examining recurring assessment patterns at an early stage of ATMP development, the study may contribute to a better understanding of the common scientific and regulatory challenges associated with investigational ATMPs. Earlier identification of such challenges at the clinical trial stage may help sponsors prepare more proactively for later stages of clinical development and future marketing authorisation applications.