ADVANCED THERAPIES CONCEPT PAPER

Innovative Medicines Initiative

Response by Genetic Alliance UK, 25 July 2016

Introduction

Genetic Alliance UK is the UK charity working to improve the lives of patients and families affected by all types of genetic conditions. We are an alliance of over 180 patient organisations. Our aim is to ensure that high quality services, information and support are provided to all who need them. We actively support research and innovation across the field of genetic medicine.

In November 2015, Genetic Alliance UK held a multi-stakeholder workshop on how to improve patient access to advanced therapies such as gene or cell therapies. The workshop was attended by a broad range of stakeholders, including patient groups directly affected by the development of advanced therapies, academics and researchers working in the field of advanced therapies as well as key individuals in the regulatory and policy making landscape. This response draws on the information gathered through this process.

Genetic Alliance UK is a member of the Patients Network for Health and Medical Research (EGAN egan.eu), and has participated with other members of EGAN in a number of initiatives relating to the Advanced Therapy Medicinal Product (ATMP) Regulation. In this case though, since the experiences described here are so closely related to the UK, we have decided to respond as Genetic Alliance UK.

Responses

Have the key challenges that can be addressed through collaborative, public-private initiatives been properly identified?

We agree with the list of challenges which has been identified, but we would add two items.

First, availability of funding and support to SMEs to assist them in bringing a new product to phase one clinical trials. In the UK, research council funding for the development of advanced therapies is heavily front loaded. For example, in the 2010 Regenerative Medicine Portfolio, more than 90% of funding awards targeted or exploratory or pre-clinical research stages (A Strategy for UK Regenerative Medicine. Medical Research Council, published March 2012, available at: www.mrc.ac.uk/documents/pdf/a-strategy-for-uk-regenerative-medicine).

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However, unlike other therapeutics, the vast majority of work in the field of advanced therapies is carried out by hospitals, universities or smaller companies, which face a number of challenges accessing sufficient funding to bring a therapy to market. One such obstacle is the difficulty obtaining funding to run clinical trials, with the confounding factor that large pharmaceutical companies will only tend to buy products once they have successfully passed stage two trials.

Second, expansion of manufacturing capacity. In the UK there is effectively a bottleneck due to the limited capacity of the few sites capable of manufacturing advanced therapies for use in clinical trials. Researchers spoke of the challenges of accessing manufacturing "slots", and the difficulties of timing clinical trials so as to fit with this. Though annual surveys published by the Cell and Gene Therapy Catapult show the UK's GMP cell and gene therapy manufacturing resources growing year on year, this is not keeping up with the rapid growth in demand, which has a particularly negative impact on the translation of academic research into clinical trials.

Which of the proposed potential initiatives should be prioritised?

We would suggest that of the proposals, those most urgent and suited to the public-private partnership model are:

- Development of platform technologies such as a generic virus/vector system and universal allogeneic cell therapies.

The personalised nature of many existing advanced therapies has implications for their ability to be delivered at scale, and also means that these therapies are likely to be costly, due to higher R&D costs, higher manufacturing costs than for small molecule drug s and higher costs for clinical delivery. Researchers and patients therefore look to modular approaches using the same principal components in the hope that these will permit more efficient development and manufacture, and so reduce the overall preclinical and potentially clinical development activities.

- Provision of a precompetitive platform encouraging early interaction between researchers and regulators.

Though progress has been made in recent years on rationalising and simplifying the regulatory process, it remains a complex and confusing field. Developers of advanced therapies are predominantly hospitals, universities or SMEs, with very little experience of regulatory processes, and even less interest. They find themselves facing numerous overlapping bodies who may give conflicting decisions.

While early provision of scientific advice is potentially hugely valuable to developers, we are seeing in the UK ATMP sector that developers are not utilising the opportunities to engage with regulatory bodies that already exist. A key challenge is how to encourage developers to communicate with regulators such as the European Medicines Agency (EMA) earlier and more often than is common practice. It is not sufficient for the advice and support to be available, the EMA needs to proactively engage with developers and encourage them to consider their interactions with regulatory bodies as a conversation rather than a single hurdle to be overcome.

Attendees at our workshop spoke of researcher/developer interactions as being like "going to see the headmaster", reflecting a real fear of regulators that can exist, as well as a lack of

understanding of the process. A form of "light touch" regulation, involving informal, open discussions about how a product can be made to work, might alleviate some of the fears that innovators from small organisations might have, and help to encourage developers of advanced therapies to engage with both patient groups and regulatory bodies earlier and more often in the development pathway. It is worth remembering throughout that regulatory bodies are repositories of a great deal of expertise, not merely assessment centres. Developers and researchers should be encouraged to access this at a much earlier stage so that they have a clearer view of how to get products to patients, rather than just chasing the immediate goal of clinical trials.

- assessment of value of clinical data and its use for regulatory purposes

It emerged from our workshop that the biggest question to be answered regarding patient access to advanced therapies is how to bridge the gap to enable developers to take technologies from the hospital exemption/"specials" scheme to marketing authorisation in order to both address immediate clinical need, and gain a marketing authorisation to provide access for patients across the EU.

We understand that data collected from patient access under the "specials" scheme can be submitted to the Committee for Advanced Therapies as part of a marketing authorisation application, but that it is considered to have a much less robust evidence base than blinded clinical trials. This suggests that complacency about the level of patient access through these schemes may be short sighted.

- development of innovative reimbursement mechanisms suitable to ATMPs

Attendees at our workshop were very concerned about the issue of reimbursement. As yet no advanced therapy has gained routine commissioning in the UK, and this bottle neck is likely having repercussions at the earlier stages of the process. In other EU countries licensed therapies have been withdrawn from the market as they were not being reimbursed and were thus not commercially viable (MACI and Provenge), and this is impacting on willingness of research funders and industry to support early stage innovations.

An innovative approach to reimbursement is certainly necessary in the field of ATMPs. Our workshop attendees queried the approach (which potentially follows the regulatory approach) of treating them in the same way as traditional medicinal products. Perhaps if they could be considered in the same way that medical procedures are, as a single treatment with long term effects, then health services would be able to find a means to fund them. It is also worth considering possible fee incentives to reduce the financial impact of post-marketing obligations.

Are any areas missing?

Please see our answer to the first question.

What are the key European or national initiatives that IMI shall synergise with?

In the UK, relevant initiatives include the MHRA Innovation Office, the single point of contact for all the regulators involved in regenerative medicines, and the Cell and Gene Therapy Catapult, a not-for profit, independent centre which connects businesses with the UK's research and academic communities with the purpose of building the cell and gene therapy industry in the UK.

We also have a Regenerative Medicine Expert Group, which exists to develop an NHS regenerative medicine strategy so that the NHS is fully prepared to deliver these innovative treatments and also to assess the effect of regulation on the development of Regenerative Medicines in the UK.

At the European level, stakeholders report that they have found the Innovation Task Force and the SME Office (both at the European Medicines Agency) helpful. The PRIME (Priority Medicines) scheme has the potential to be very positive, but it is too early to judge as yet.