BREXIT: the impact on medical innovation and patients with Duchenne Muscular Dystrophy in the UK

SUMMARY INTRODUCTION

At a time when so many promising treatments are being developed for patients with Duchenne Muscular Dystrophy, Brexit threatens patient opportunity to access these new treatments in two ways: Firstly pharmaceutical companies have admitted that once the UK leaves the EU (and the shared regulatory body the European Medicines Agency), companies are unlikely to seek approval for new drugs in the UK as a priority, so patients could have to wait up to five years after medicines have been approved in Europe to see them approved here. Secondly if we are no longer able to remain part of the Europe’s extensive and well-funded research networks, it may be less likely that companies will come to the UK to run their clinical trials and patients will no longer be able to access potential therapies in a research setting.

This document highlights some of the major challenges Brexit poses to research and patient access to medicines.
WHAT DOES THE UK GET FROM THE EU?

The UK is a global leader in the field of rare disease and Duchenne research, and benefits hugely from being part of the EU.

FINANCIAL GAIN:

In four years, the three Universities leading Duchenne research, University College London (UCL), Imperial and Newcastle, between them received €219 MILLION in EU funding.

KNOWLEDGE GAIN:

Being part of the EU is about more than just the money, and EU grants are more than “just” the money. They offer the possibility for collaboration and international work which is essential for research, especially in rare diseases with small patient numbers spread across many countries.

In 2014 Duchenne UK co-funded a Phase 1 study of Vamorolone, a potential new treatment for DMD. The EU is funding the Phase 2 with a €6 million grant. The trial is being led by the team at Newcastle, and will have ten trial sites across the UK and Europe. European collaboration has allowed the trial to operate in the UK and several EU countries.

UK patients directly benefit from pharmaceutical companies selecting UK sites to conduct their clinical trials. Post Brexit, without direct harmonisation to the Clinical Trial Authorisation legislation (adoption by the MHRA), pharmaceutical companies may select other countries to conduct their clinical trials and patients in the UK will miss out on vital research opportunities.

OUR QUESTION: What will the government do to ensure continued access to collaborative funding streams and collaborative funding mechanisms for rare disease if we are forced to leave the European Union?
LOSING EU FUNDING – THE REAL IMPACT ON RESEARCH AND CLINICAL TRIALS

Leaving the EU will put access to future funding in jeopardy. Patients in the UK will suffer, as fewer clinical trials will be set up in the UK and research opportunities are closed off to them.

The very nature of rare disease, small patient populations geographically spread out with scarce and scattered resources and expertise, means it is uniquely placed to benefit from EU collaboration, crossing borders, uniting communities.

In 5 years, more than €22m has been invested in DMD research through the EU’s FP7 and Horizon 2020 programmes, which, in total, invest €150 billion in research and innovation. Patients are currently participating in potentially life-saving trials in the UK, because of EU funding.

The SKIP-NMD exon skipping trial received €5.6m from FP7. The positive results from Phase 1 and 2 of this trial have now led to a phase 3 trial (Essence) that has 39 participants.

IMMEDIATE CONSIDERATIONS:

Recruiting and funding clinical staff (Doctors nurses, physics, admin and clinical trial coordinators)

Many DMD trials are run by doctors from Europe because the current UK training path doesn’t incentivise or encourage doctors to specialise in neuromuscular disease.

Clinical trials

We need to ensure that industry continues to select UK trial sites by creating a central resource for industry – for example a central costing, streamlining the ethics / HRA process

OUR QUESTION: If doctors from Europe stop coming to the UK, how will the government ensure clinical trials are not jeopardised by a lack of qualified staff to run them?
EUROPEAN REFERENCE NETWORKS (ERN’S)

We have considerable professional rare disease expertise in the UK – our hospitals are amongst the finest in Europe. But the reality in rare diseases is that, no single country, however strong their health and research systems may be, will ever house all the expertise needed to properly diagnose, treat and care for patients. This is truly an area where cross-border collaboration is needed, and what ERNs offer is an unprecedented chance to network via a safe, secure, ethically-sound framework, in which the outcomes of inter-expert discussions readily translate into new learning and improvements in practice for all involved in that Network.

European Reference Networks (ERNs) are virtual networks involving healthcare providers across Europe. They aim to tackle complex or rare diseases and conditions that require highly specialised treatment and a concentration of knowledge and resources.

ERNs offer the potential to give patients and doctors across the EU access to the best expertise and timely exchange of life-saving knowledge, without having to travel to another country.

How the Neuromuscular ERN (EURO-NMD) helps patients?

EURO-NMD unites 61 of Europe’s leading Neuromuscular Diseases (NMD) clinical and research centres in 14 Member States and includes highly active patient organizations. More than 100,000 NMD patients are seen annually by the centres of which EURO-NMD is composed.

ERNs are formal networks which enable the creation of shared tools such as registries and biobanks, which are essential to build a better picture of the natural history of a disease, and to stimulate research. The impressive number of ERN responsibilities (from virtual care to clinical guidelines, diagnostics to registries, clinical research to integrated holistic care) unfortunately equates to a very broad range of activities from which our UK professionals and their patients now stand, in the worst case scenario, to be ‘cut off’.

**OUR QUESTION:** Does the government have a plan to allow continued participation in ERNs? If not what is the alternative to ensuring rare disease patients do not suffer?
THE EUROPEAN MEDICINES AGENCY (EMA) - GATEWAY TO EUROPE

UK involvement in the EMA for the regulation of medicines, devices and other health technologies is absolutely vital. This must be secured in negotiations to avoid delays or harm to patients in the UK and EU, and an assurance of direct harmonisation and/or adoption must be in place. Particular notice should be given to the Orphan drug regulation and Advanced Therapeutics. Two areas that cannot be successfully delivered upon by one country in isolation. We also suggest that the current arrangements for the implementation period, whereby the MHRA will be unable to take part in the functioning of the EMA, are reviewed. A temporary hiatus in involvement could have a significant impact on any future cooperative relationship secured between the UK’s MHRA and the EMA. Any changes to the UK’s cooperation with the EMA, including during the relocation of the Agency’s headquarters from London to Amsterdam, should be monitored to ensure there are no delays in the ability of patients to access innovations; and to ensure the UK maintains its leadership in the life sciences. The EMA have already announced “a pause” in all work beyond essential services, which is delaying innovative initiatives from becoming reality.

The UK has been the leader in reviewing new drug application but after Brexit we will no longer have a substantial role and cannot act as rapporteur.

The EMA now requires all existing drugs assessors to transfer their personal knowledge of their specialist fields to counterparts in a European member state.

“Pharma always has extremely strategic plans in place for the launch sequence of bringing new drugs to market. If market access in the UK no longer guarantees entrance to the EU market, then it could be viewed as being a much less attractive place to launch from and indeed to invest in. The UK’s fragmented market access systems and reluctance to pay high prices could compound the situation making the UK a less attractive launch market and consequently less attractive as a place to do clinical trials.”

UK BioIndustry Association
Medical Centre Case Studies:

Great Ormond Street Hospital, London and the John Walton Muscular Dystrophy Research Centre, Newcastle

The UK is internationally renowned for DMD research, because of two leading academic and medical institutions in the UK: Great Ormond Street Hospital in London, and The John Walton Muscular Dystrophy Research Centre in Newcastle.

Great Ormond Street Hospital:

• At Great Ormond Street Hospital in London, none of the FOUR consultants working with Duchenne patients are originally from the UK.

• The Neuromuscular research team at GOSH has won TEN awards, and is currently running projects worth €6.9 million

John Walton Muscular Dystrophy Research Centre (JWMDRC):

• In Newcastle, 30% of the 90 staff members are from EU member states, providing vital care and research

• The JWMDRC has won THIRTEEN EU grants in 4 years. Newcastle University has received €80 million, with €10 million coming to the JWMDRC

“At least 3.5 million people in the UK are affected by rare diseases and benefit from EU funded research projects, European Reference Networks, from talented EU scientists and healthcare professionals that can freely move to the UK and from an open and outward looking scientific discussion. Even the idea of Brexit, no matter in what form, is already jeopardizing all of those fantastic achievements, penalizing UK universities, UK pharmaceutical industries and UK patients.”

Professor Volker Straub is Harold Macmillan Professor of Medicine for the Institute of Genetic Medicine at Newcastle University.
White dots = Staff from the EU
Grey dots = staff funded by EU on rare disease research
Visible = mainly students & staff from the NHS
Academic Case Study:

University College, London (UCL)

The Horizon 2020 grant is the EU’s biggest Research and Innovation funding scheme, with €79 billion of funding available over seven years (2014 to 2020). This programme is entirely meritocratic; due to the high standards of UK academia the UK has managed to secure large sums in the past years, essential for driving medical research.

In 2014 UCL’s success rates of winning grants, was four times the EU average

In 2015 UCL, together with Imperial College, received a total of €129 million in EU funding: That’s more than all the French National Research Centres together (1100 research units)

Industry-derived funding is also essential for developing and implementing new therapies, in particular for rare diseases. In EU countries progress has been accelerated through sharing of resources, knowledge, patient cohorts, and infrastructure in joined-up and integrated networks.

By breaking up the close research ties with EU partner states, the top performing UK academic institutions, who are a major motor for the development of new treatment approaches, risk losing out from EU financial support, networking capacity, access to early shared knowledge and access to comprehensive databases which are all indispensable assets for modern research.

The capacity of these academic institutions to take the lead in multi-national research networks, is an essential element of their attraction. Industry-derived funding is essential for developing and implementing new therapies, in particular for rare diseases.

“I believe Brexit, any form of Brexit with or without deal, will be not in the best interest of the English People. It will predictably be hugely damaging in economic and societal terms, and more particularly to Academia and Translational Medicine.”

Professor Thomas Voit is Director of the NIHR Great Ormond Street Hospital (GOSH) BRC, Professor and Honorary Consultant of Paediatrics at GOSH, and Vice-Dean for Enterprise at UCL’s Faculty of Population Health Sciences.
CONCLUSION

PRIORITY AREAS

Brexit has the very real potential to cut off our ability to access research opportunities with our colleagues and partners in Europe, with devastating repercussions on research and medical advances. Our priorities are aligned with the AMRC’s position and we ask for the following:

Priority areas

- Position the UK as an attractive destination for global research talent and expertise.
- Implement an aligned and compatible regulatory framework between the UK and the EU for medical research.
- Cooperate with the European Medicines Agency on EU regulatory frameworks and agreements for medicines and medical devices to ensure patients have timely access to new health innovations.
- Continue to participate in EU funding programmes and collaborative opportunities to progress the discovery and understanding of diseases and ill health.
- Ensure no disruption in the supply and trade of medicines and other health technologies from day one of the UK’s new relationship with the EU.

Questions to ask your MP to ask the government:

- How will the government ensure UK still has access to funding similar to EU grants?
- How will the government ensure the UK remains attractive for EU pharmaceuticals companies to both run clinical trials and to seek Marketing Authorisation and Reimbursement, if we are outside the EU’s regulatory framework?
- What can the government do to ensure that patients do not suffer if we are unable to remain a part of the regulatory framework of the EMA?
- How will the UK remain an open and attractive destination for EU citizens who are working in rare disease research?