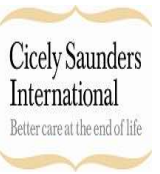


# Challenges of running an international multicentre trial of a pharmacological product during Brexit

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## Background

Trial opening and recruitment to an international randomised controlled trial (RCT) during Brexit has been challenging. The BETTER-B trial tests the clinical and cost-effectiveness of mirtazapine for chronic breathlessness in patients with Chronic Obstructive Pulmonary Disease (COPD) or Interstitial Lung Disease (ILD)

## Aim

To provide an overview of the challenges experienced in carrying out this RCT and the lessons learnt.

## Method

- The BETTER-B trial is an international, multicentre, Phase III double-blind, RCT, with centres in the UK, Ireland, Germany, Italy and Poland. Trial registration no. ISRCTN10487976.
- We collated information gathered from our partners and centres during trial set-up, opening and recruitment regarding the impact of Brexit.

## Results

- We had envisaged Brexit and proactively planned to mitigate it through a co-sponsorship agreement between King's College London (KCL) and University College Dublin (UCD). However, we could not include KCL as a co-sponsor to the Clinical Trial Authorisation (CTA) applications in Germany, Ireland, Poland and Italy.
- We resubmitted the CTA applications in these countries to designate KCL as having contractually outlined duties within the context of the global Covid-19 pandemic, leading to delays in receiving responses from regulators.
- Brexit further delayed trial opening due to the need for the submission of additional documentation because the investigational medicinal product (IMP) and matching placebo were manufactured in the UK.

## Results cont'd

- These challenges led to varied delays to trial opening in our European sites. Additional costs were incurred due to shipments of the IMP and placebo to the EU warehouse, storage and EU Qualified Person release of IMP batches.

## Conclusions

- As Brexit was still unraveling when we carried out this trial, the co-sponsors had very limited experience of the co-sponsorship model as well as the impact of Brexit on CTA applications.
- Brexit led to delays in trial opening and greater costs.

BETTER-B website: [www.betterbreathe.eu](http://www.betterbreathe.eu)

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Breathlessness is the feeling of being out of breath as your lungs work harder to draw in more oxygen. Persistent breathlessness is when this persists long-term, despite treatment of the underlying condition. It is a frightening symptom that leads to increased distress for patients, families and carers.

Research has shown it is often neglected or under-treated. Our international partners have worked to improve its visibility by growing the knowledge base for treatments which work to improve breathlessness self-management and quality of life, and those that don't.



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