Nottingham Clinical Trials Unit
Applied Health Research Building
University of Nottingham
Room A17
Building 42
University Park
Nottingham, NG7 2RD
relief@nottingham.ac.uk

Dear RELIEF Study Sites/Teams,

Many thanks for your help and hard work going forwards on this critical asthma trial.

The trial PI Prof Harrison and I have recently received feedback from the trial coordinating team regarding concerns raised at SIVs by some sites regarding the recently licensed anti-inflammatory reliever therapy approach for mild asthma.

Some sites have indicated they are concerned that the increasing uptake of anti-inflammatory reliever therapy in local prescribing guidance means:

1) the trial is no longer required or
2) patients randomised to the comparator arm of the trial using ICS and SABA may somehow be disadvantaged compared to those prescribed anti-inflammatory reliever therapy.

We want to fully reassure you regarding these potential concerns.

Whilst anti-inflammatory reliever therapy is recommended by the Global Initiative for Asthma (GINA) as the 'preferred' reliever option for managing asthma of all severities, there are major evidence gaps and concerns about this approach of managing mild asthma in primary care that this trial seeks to address.

Firstly, some of the data on which GINA based this decision in mild asthma is inferred from patients with more severe asthma. Step 2 of the GINA treatment algorithm recommends ICS/formoterol as required either alone, or with low dose ICS maintenance treatment, even though the latter combination has never been studied in a clinical trial. It is possible that ICS maintenance plus ICS/formoterol as required may lead to the best asthma control overall (ICS for daily control and ICS/formoterol as required for exacerbations) but this approach needs to be evaluated. It is also worth highlighting that the use of ICS/formoterol as maintenance and reliever therapy (MART) has been recommended in GINA guidelines for 10 years for patients with moderate to severe asthma and yet less than 5% of the potential population in the UK are prescribed this treatment.

Secondly, many patients treated for asthma have no objective evidence of a diagnosis when formally evaluated. If these patients are switched to a combination of ICS/formoterol for symptom relief, there is a risk that they will use high doses of ICS/formoterol with no clinical benefit and risk of adverse effects. This potential risk needs to be evaluated in a pragmatic trial before creeping into clinical practice.

Thirdly, there is no economic evaluation of this new approach, which is particularly important because combination ICS/formoterol for symptom relief is considerably more expensive than SABAs. However, asthma exacerbations leading to unscheduled health care costs and admissions to hospital are the most expensive part of asthma care.

Lastly, there is a paucity of data on health care professionals' and patients' views on this fundamental change in asthma management. The SABA inhaler has been around for over 50 years, so many patients and doctors are likely to be reluctant to change. We need to understand the potential barriers and facilitators to change, if ICS/formoterol as required is going to be considered for routine health care. Hence, part of the RELIEF study is a detailed qualitative sub-study exploring the beliefs of patients and health care providers throughout the trial.

The overall aim of this trial is to determine the clinical benefit, cost effectiveness, physician and patient perspective of replacing SABA with an ICS/formoterol containing inhaler in patients with mild asthma, treated with low dose ICS, before anti-inflammatory reliever therapy without maintenance ICS creeps into UK clinical practice without us knowing the consequences. The RELIEF trial is therefore crucial work at a crucial time to determine the future management of mild asthma in the UK.

Thank you again for your support with this study and please contact the trial team if you have any further questions.

Matthew Martin

Deputy PI RELIEF Trial
Consultant Respiratory Physician
Nottingham University Hospitals NHS Trust