Department of Health & Social Care

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From the Chief Scientific Adviser,
Professor Lucy Chappell FMedSci

Cc
Chief Medical Officer for England, Professor Sir Chris Whitty
Chief Pharmaceutical Officer for England, David Webb

12 January 2024

Dear colleagues,

For hospitals and clinicians taking part in trials of influenza drugs.

Summary: randomising patients to existing trials with ethical review will strengthen our future knowledge base for treating influenza. We therefore ask that every effort is made to enrol patients admitted to hospital with influenza into the REMAP-CAP or RECOVERY trial.

On 14 December 2023, the Chief Medical Officer and Chief Pharmaceutical Officer (CEM/CMO/2023/003) advised that the influenza season had started and primary care clinicians may prescribe influenza drugs and that '*Hospital clinicians should continue to prescribe antiviral medicines for patients whose illness is confirmed or clinically suspected to be due to influenza, in accordance with UKHSA guidance for the treatment of complicated influenza*.' This is in the context of NICE guidance (published in 2009, reviewed in 2014) and UKHSA guidance (published in 2021) that includes treatment of individuals with influenza. As per the Chief Medical Officer's letter from January 2023, we want to emphasise why, **specifically for those hospitals and clinicians undertaking national trials** it is entirely in keeping with good clinical practice and our guidance to randomise.

Despite vaccination programmes and current treatment guidelines, influenza continues to be responsible for many deaths and is a major challenge facing the NHS most winters, including this one. There remains uncertainty, however, about how best to treat patients hospitalised due to influenza. For this reason, the DHSC and NIHR commissioned a national influenza platform trial (REMAP-CAP) to generate high quality evidence from a randomised controlled trial. The RECOVERY trial has also expanded to investigate treatments for influenza and the two studies are working together. REMAP-CAP and RECOVERY will investigate the following drugs initially: oseltamivir, baloxavir marboxil, and low dose corticosteroids.

To date, none of these antiviral treatments have been proven in randomised controlled trials to improve clinical outcomes for patients admitted to hospital for influenza. A meta-analysis of observational data suggested adults treated with neuraminidase inhibitors (e.g. oseltamivir) within two days of symptom onset may have reduced mortality but not if treated after two days (1). No effect in children was seen.

In routine clinical practice only 62% of patients admitted to hospital with influenza were given antiviral treatment (2). A recent survey showed that between 56% and 72% of UK

clinicians would use neuraminidase inhibitors for hospitalised patients with influenza, in part due to a perceived lack of evidence of effectiveness (3). Similarly, others have reported that most UK clinicians (89%) agreed that '*a randomised placebo-controlled trial to determine the clinical benefit and cost-effectiveness of neuraminidase inhibitors in adults admitted to hospital with suspected influenza infection should be conducted in the UK'* (4).

Therefore, there remains both clinical and collective uncertainty (equipoise) about the role of antiviral and steroid treatments for most patients hospitalised with influenza. During the COVID-19 pandemic, we demonstrated again the benefit of enrolling large numbers of patients into national and international trials when there is residual uncertainty about which treatments are effective or not. Whilst it is appropriate for those not taking part in national trials to continue to follow existing national guidance, the trials will strengthen the evidence base that underpins that guidance.

We therefore ask that every effort is made to enrol patients admitted to hospital with influenza into the REMAP-CAP or RECOVERY trial. It provides the option to evaluate new antivirals (baloxavir), as well as existing treatments (oseltamivir) where there is uncertainty, and the option of new treatments (steroids), all in an adaptive factorial design. This will help improve treatment in future years.

Treatment decisions should always be made on an individual patient basis. However, we encourage enrolment in REMAP-CAP or RECOVERY for patients who are admitted to hospital where that is possible and appropriate.

For more information about the trial please contact:
ukremap-cap@icnarc.org (for REMAP-CAP) or
recoverytrial@ndph.ox.ac.uk (for RECOVERY)

Yours sincerely

Prof. Lucy Chappell
DHSC Chief Scientific Adviser and NIHR Chief Executive Officer

References:

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