Corticosteroid Response and Gene Expression in Septic Shock (CRESS) Trial

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**Background** Septic shock is when severe infection leads to low blood pressure and organ failure. It is a life-threatening condition. Drugs called corticosteroids are often used in the sickest patients to try to improve blood pressure and outcomes for patients. Although we know that corticosteroids can shorten the duration of septic shock, their effect on patient survival rates is less clear. Some trials have shown a potential improvement with others showing no difference.

We have shown that patients with septic shock can be divided into two groups based on the patterns in which their genetic information is expressed in blood samples. These patterns have been called Sepsis Response Signatures or SRS. Normally patients with the first pattern (SRS1) of gene expression are at a higher risk of dying than those with the second (SRS2). This maybe because patients with the SRS1 pattern may have a weakened immune system and maybe less able to fight infection.

We have divided patients from a previous trial, where patients with septic shock were randomly allocated to get corticosteroids or a placebo, into SRS1 and 2 groups. Patients in both SRS groups had a shorter duration of septic shock if given corticosteroids. However, those in the SRS2 group, who normally have better survival, were more likely to die if they received corticosteroids than if they received placebo. Although corticosteroids may appear beneficial in all patients, by making shock improve more quickly, they may unintendendly cause harm to one group of patients.

These findings are from a small number of patients so need to be confirmed in a larger trial.

**Aim** To determine if patients with severe septic shock have improved survival if corticosteroids are given based on their SRS pattern compared to the standard approach of giving corticosteroids to all patients.

**Method** 1906 patients with severe septic shock will be randomly allocated to receive corticosteroids either using a ‘standard approach’ or an ‘SRS approach’. In the ‘standard approach’ corticosteroids will be given whatever the patient’s SRS pattern, as occurs now. In the ‘SRS approach’ treatment will be targeted. SRS1 patients will receive corticosteroids and SRS2 patients a placebo. This approach aims to target treatment to give most benefit and avoid possible harm. The doctors looking after the patients will not know the patients’ SRS group or which treatment approach they are receiving.

Patients’ SRS patterns will be determined by measuring seven genes. This will be done using a blood test analysed by a machine on the intensive care unit. This award will allow us to confirm the accuracy of this blood test to determine SRS groups.

We will compare survival rates between the ‘standard approach’ and the ‘SRS approach’. Rates of new infection, duration of shock and quality of life will also be recorded.

**Summary** This project will deliver the first trial to find out if targeting corticosteroid treatment is better than giving them to all severely ill patients. This type of “Personalised Medicine” study has been seen as a priority for critically ill patients.