Overwhelming infection, also called sepsis, is a major problem for the health community. It is the leading cause for admission to an Intensive Care Unit in the UK, accounting for about 30 per cent of all admissions. Despite advances in treatment around 40 per cent of such patients do not survive – more than breast and bowel cancer combined. It is an illness that can affect people of any age and patients can become critically ill very quickly. The NHS spends at least £700 million per year treating these patients on Intensive Care Units.

Sepsis can cause the patient’s blood pressure to fall dangerously, compromising blood flow to vital organs such as the liver and kidney. Conventionally, adrenaline-like drugs (Catecholamines) are used to support a patient’s blood pressure but they can have serious side effects for example, a heart attack.

Levosimendan is a new type of drug that improves the function of the heart in a different manner to the adrenaline-like drugs by opening the patient’s blood vessels. It has been extensively studied in patients with heart failure and is a licensed drug for this group of patients.

In patients with sepsis around half may develop impaired heart function and associated kidney failure, and Levosimendan has been shown to improve this, small studies have had promising results but none have been large enough to prove if it can help sepsis patients.

The LeoPARDS trial was carefully designed to try and identify whether using Levosimendan in patients with sepsis could produce important benefits by reducing multiple organ failure, which will then hopefully lead to better survival rates.

Patients being treated for sepsis on an Intensive Care Unit, and who had low blood pressure that required the use of adrenaline-like drugs to maintain it, were asked to take part. Half were randomly chosen to receive an additional infusion of Levosimendan whilst the other half received a dummy treatment, or placebo.
Outcomes and findings

In conclusion, in Intensive Care Unit patients with sepsis, the addition of Levosimendan to standard care did not improve organ function or increase survival rate.

Patients who received Levosimendan required more adrenaline-like drugs and were therefore still at risk of the serious side effects. Whilst Levosimendan is known to open blood vessels which might improve the blood supply to vital organs, higher doses of adrenaline-like drugs had to be given as opening blood vessels decreases blood pressure.

Patients who received Levosimendan were less likely to be successfully weaned from mechanical ventilation, and had more rapid heart rates (tachycardia) and a higher rate of irregular heart beats (supraventricular arrhythmia) than those who received the placebo.

Value to the NHS

Whilst Levosimendan did not demonstrate any patient benefit, the trial provided clear answers to important research questions. Knowing where a drug is and is not effective is important to give patients the best chance of recovery and reduce the risk of side-effects. It also saves precious NHS time and resources.

Levosimendan was not previously included in any UK clinical guidelines but NHS clinicians were beginning to use it to treat sepsis. The results of the trial are now included in the International Guidelines for Management of Severe Sepsis and Septic Shock 2017.

With Levosimendan costing several hundred pounds per day, this trial has saved the NHS a considerable amount of money.

The results of the trial highlighted the importance of controlling patients heart rates in sepsis, which may lead to damage of the heart and poor heart function.

The biological samples from this trial are now being used to develop a personalised medicine in sepsis platform, as part of an NIHR Research Professorship award.

Professor Gordon and his team are now working with colleagues in Birmingham to study the effects of beta-blockers in slowing down patient heart rates in sepsis.

Key publications:

- Study site: http://leopards-trial.org/
- The results were presented at the plenary “Hot Topic” session of the European Society of Intensive Care Medicine in Milan, in October 2016, and simultaneously published in the New England Journal of Medicine.