Pump-Priming Grant

Report

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Title: **Safety and efficacy of Tofacitinib in ameliorating ischaemia reperfusion injury and allograft pancreatitis in solid organ transplantation – a pilot study**

Objectives

Primary: To assess the safety and anti- inflammatory effect of Tofacitinib on allograft pancreatitis and ischaemia reperfusion, by measuring inflammatory markers in whole blood and assessing CT imaging using an oral dose of Tofacitinib 10mg BD for 7 days
Secondary: To quantify the level of inflammation observed following reperfusion of organs and identify what inflammatory pathways are being affected.
Tertiary: To assess any association of post- operative complications with administration of the drug. Clinical parameters which affect patient
experience and morbidity will also be measured

Method

This is a phase 2 single arm trial. A total of 21 simultaneous kidney and pancreas transplant (SPK) patients were recruited to have Tofacitinib administered at a dose of 10mg twice daily for 7 days starting on the day of transplantation. Data from 40 patients who had SPK transplant and were eligible but not recruited for various reasons collected and compared to the treatment group. All patients within the study received standard clinical care for SPK transplant.

Inflammatory markers were measured Serial during and after reperfusion of the pancreas and then once daily for the first 7 days post-surgery. All patients had post-operative day 5 computed tomography (CT) angiogram pancreas to look for evidence of pancreatitis. Clinical outcomes including reoperation, graft loss and length of stay were reported.

Results:

The incidence of AGP was 14.3% in the treatment group and 23% in the control group. A total of 5 (23.8%) were returned to operating room in the study group with only 2 (9.5%) operated on for pancreatitis related complications, compared to 16 (40%) return to operating room for various indications and 7 (17.5%) for pancreatitis in the control group. Early graft loss was reported as 3 (14.3%) and 2 (5%) in the study and control groups respectively. The median length of hospital stay, 11 (IQR 6) days in the treatment group and 11.5 (IQR 12) days in the control group. Serious adverse events occurred in 4 patients (incidence rate 0.19) in the study group and in 16 (incidence rate 0.40)

control group. One mortality reported in the control group and none in the intervention group.
Conclusion: Among patients received SPK transplant, Tofacitinib administration led to lower incidence of graft pancreatitis and reoperation. Tofacitinib is safe to administer in early post-transplant period.

Outputs (publications/presentations)

- Attached, draft of manuscript in preparation for publication

Next Steps (what is it leading to)

The results of this trial are encouraging, we are writing a protocol for multicentre, double blinded clinical trial to follow this safety study.