Tofacitinib for hospitalized acute severe Ulcerative colitis Management (the TRIUMPH study)

Inclusion Criteria

1. Adults ages 18 to 75 with ulcerative colitis (either known UC based on prior history with histological confirmation or new diagnosis)
2. Symptoms consistent with severe acute ulcerative colitis as defined by modified Truelove and Witts score (MTWSI) > 10 points
3. Primary non-response or secondary loss of response to anti-TNFα/anti-integrin therapies/anti-interleukin therapies OR immunomodulators OR non-response to minimum 3 days and maximum of 7 days of intravenous corticosteroids (intravenous at dose equivalent of prednisone 50mg daily / methylprednisolone 40mg daily).
    a. For patients using anti-TNFα or anti-integrin or anti-interleukin therapies, they must have been on a stable dose of one of the following:
        i. Adalimumab in the 14 days prior to screening
        ii. Golimumab in the 28 days prior to screening
        iii. Infliximab in the 28 days prior to screening
        iv. Vedolizumab in the 28 days prior to screening
        v. Ustekinumab in the 28 days prior to screening
    b. Persons on biologic therapy will have drug levels drawn during the time of hospitalization
4. Able to provide written informed consent
5. Treatment with concomitant corticosteroids or 5-ASA products is permitted, however patients will be placed on a corticosteroid weaning regimen after initiating study protocols. For patients using biologics or immunomodulators, these will be discontinued prior to initiation of tofacitinib.

Exclusion Criteria

- Enteric infection confirmed before inclusion into study by stool microscopy, culture, or histology (including Clostridum difficile, Campylobacter, Salmonella, Shigella, Cytomegalovirus, Human Immunodeficiency Virus, Epstein Bar Virus)
- Clinical signs of sepsis
- Patient has indication for surgery instead of medical rescue therapy (ex. toxic megacolon, massive exsanguination, or perforation)
- Positive blood (beta-HCG) pregnancy test or currently lactating, or women of childbearing potential not willing to use double barrier contraception for the duration of the active part of the study and for 4 weeks after the last dose of tofacitinib
- Participants will be sufficiently educated to ensure compliance with double barrier contraception prior to enrollment in the study
- Current malignancy
- Serious co-morbidity including but not limited to:
- Immunodeficiency
- Recent myocardial infarction or stroke (in the past month)
- History of heart, respiratory, renal, or hepatic failure
- Heart failure as defined as ejection fraction of <50% as determined by transthoracic echo
- Respiratory failure as defined as PaO2 <60mmHg
- Hepatic failure as defined as INR > 2.5 with total bilirubin >30
- Renal failure as defined as a creatinine clearance of 40ml/min (as estimated by the Cockroft-Gault equation)
- Infections such as abscess, opportunistic infection, or sepsis
- English not adequate in absence of local translation service
- Currently taking part in another clinical trial
- Treatment with tofacitinib in the 3 months prior to screening

- Use of strong CYP (3A4 or 2C19) inhibitors or inducers such as antifungals (ketoconazole, fluconazole), St John's wort or rifampin
- Patients will be told to avoid consumption of grapefruit juice