A single arm, two-stage, multi-centre, phase II clinical trial investigating the safety and activity of the use of BTT1023, a human monoclonal antibody targeting vascular adhesion protein (VAP-1), in the treatment of patients with primary sclerosing cholangitis (PSC)

Inclusion and Exclusion Criteria

Inclusion criteria

Subjects must meet *all* of the following inclusion criteria to be eligible for participation in the clinical trial:

1. Males and females 18 - 75 years of age who are willing and able to provide informed, written consent and comply with all study requirements

2. Clinical diagnosis of PSC as evident by chronic cholestasis of more than six months duration with either a consistent MRI showing sclerosing cholangitis or a liver biopsy consistent with PSC in the absence of a documented alternative aetiology for sclerosing cholangitis

3. In those with concomitant Inflammatory Bowel Disease, clinical and colonoscopic evidence within the last year of stable disease, without findings of high grade dysplasia

4. In those on treatment with ursodeoxycholic acid (UDCA), therapy must be stable for at least 8 weeks and at a dose not greater than 20mg/kg/day. In those not on treatment with UDCA at the time of screening, a minimum of 8 weeks since the last dose of UDCA should be recorded

5. Serum ALP greater than 1.5 x upper limit of normal (ULN)

6. Stable serum ALP levels (levels must not change by more than 25% from Screening Visit 1 and Screening Visit 2)

7. Female subjects of childbearing potential must have a negative pregnancy test prior to starting study treatment. For the purposes of this study, a female subject of childbearing potential is a woman who has not had a hysterectomy, bilateral oophorectomy, or medically-documented ovarian failure. Women ≤ 50 years of age with amenorrhea of any duration will be considered to be of childbearing potential

8. All sexually active women of childbearing potential must agree to use two forms of highly effective method of contraception from the Screening Visit throughout the study period and for 99 days following the last dose of study drug. If using hormonal agents the same method must have been used for at least 1 month before study dosing and subjects must use a barrier method as the other form of contraception. Lactating women must agree to discontinue breast feeding before study investigational medicinal product administration

9. Men, if not vasectomised, must agree to use barrier contraception (condom plus spermicide) during heterosexual intercourse from screening through to study completion and for 99 days from the last dose of study investigational medicinal product

Exclusion criteria

Subjects who meet *any* of the following exclusion criteria are excluded from participating in the BUTEO trial.

1. Presence of documented secondary sclerosing cholangitis on prior clinical investigations.

2. Presence of alternative causes of liver disease, that are considered by the Investigator to be the predominant active liver injury at the time of screening, including viral hepatitis, alcoholic liver disease, non-alcoholic steatohepatitis, primary biliary cirrhosis. Patients with possible overlap syndrome with autoimmune hepatitis are excluded if the Investigator considers autoimmune hepatitis as the predominant liver injury.

3. AST and ALT >10 x ULN or bilirubin >3 x ULN or INR >1.3 in the absence of anti-coagulants

4. Serum creatinine >130µmol/L or platelet count <50 x 10^9/L

5. Any evidence of hepatic decompensation past or present, including ascites, episodes of hepatic encephalopathy or variceal bleeding

6. Recent cholangitis within last 90 days or ongoing need for prophylactic antibiotics

7. Pregnancy or breast feeding

8. Harmful alcohol consumption as evaluated by the Investigator

9. Flare in colitis activity within last 90 days requiring intensification of therapy beyond baseline maintenance treatment; use of oral prednisolone >10mg/day, biologics (i.e. monoclonal antibodies) and or hospitalisation for colitis within 90 days. Prior use of biologics is not a contraindication to screening

10. Diagnosed cholangiocarcinoma or high clinical suspicion of cholangiocarcinoma either clinically or by imaging

11. Concurrent malignancies or invasive cancers diagnosed within past 3 years except for adequately treated basal cell and squamous cell carcinoma of the skin and in situ carcinoma of the uterine cervix

12. Presence of a percutaneous drain or bile duct stent

13. Major surgical procedure within 30 days of screening

14. Prior organ transplantation

15. Known hypersensitivity to the investigational product or any of its formulation excipients

16. Unavailable for follow-up assessment or concern for subject's compliance

17. Participation in an investigational trial of a drug or device within 60 days of screening or 5 half-lives of the last dose of investigational drug, where the study drug half-life is greater than 12 days

18. Any other condition that in the opinion of the Investigator renders the subject a poor risk for