AUTUMN

STUDY SYNOPSIS

Title **AU**tologous **T**-regulatory cell tracking after Inf**U**sion in Autoi**M**mu**N**e Liver Disease patients
Study Design Single-centre, single-arm, feasibility pilot study (phase 0)
Objectives **Primary** – to determine whether autologous regulatory T cells (Tregs) migrate to the liver in patients with autoimmune hepatitis after leukapheresis, Tregs selection, indium labelling and reinfusion. **Secondary** – to assess the safety and tolerability of Tregs reinfusion as a potential future autologous cell therapy.
Outcome Measures **Primary:** • To quantify Indium-labelled Tregs at the liver at 4, 24 and 72 hours post reinfusion using a gamma camera scan to determine the overall distribution of indium-labelled Tregs. • To assess how the re-infused Tregs travel over time by performing Single Photon Emission Computed Tomography (SPECT-CT) at 24 hours post reinfusion. **Secondary:** • To monitor safety parameters from cell therapy infusion.
Patient Population Patients with non-cirrhotic/compensated cirrhosis Type-1 AIH
Sample Size 4 Autoimmune Hepatitis patients
Study Duration 24 months

INCLUSION AND EXCLUSION CRITERIA

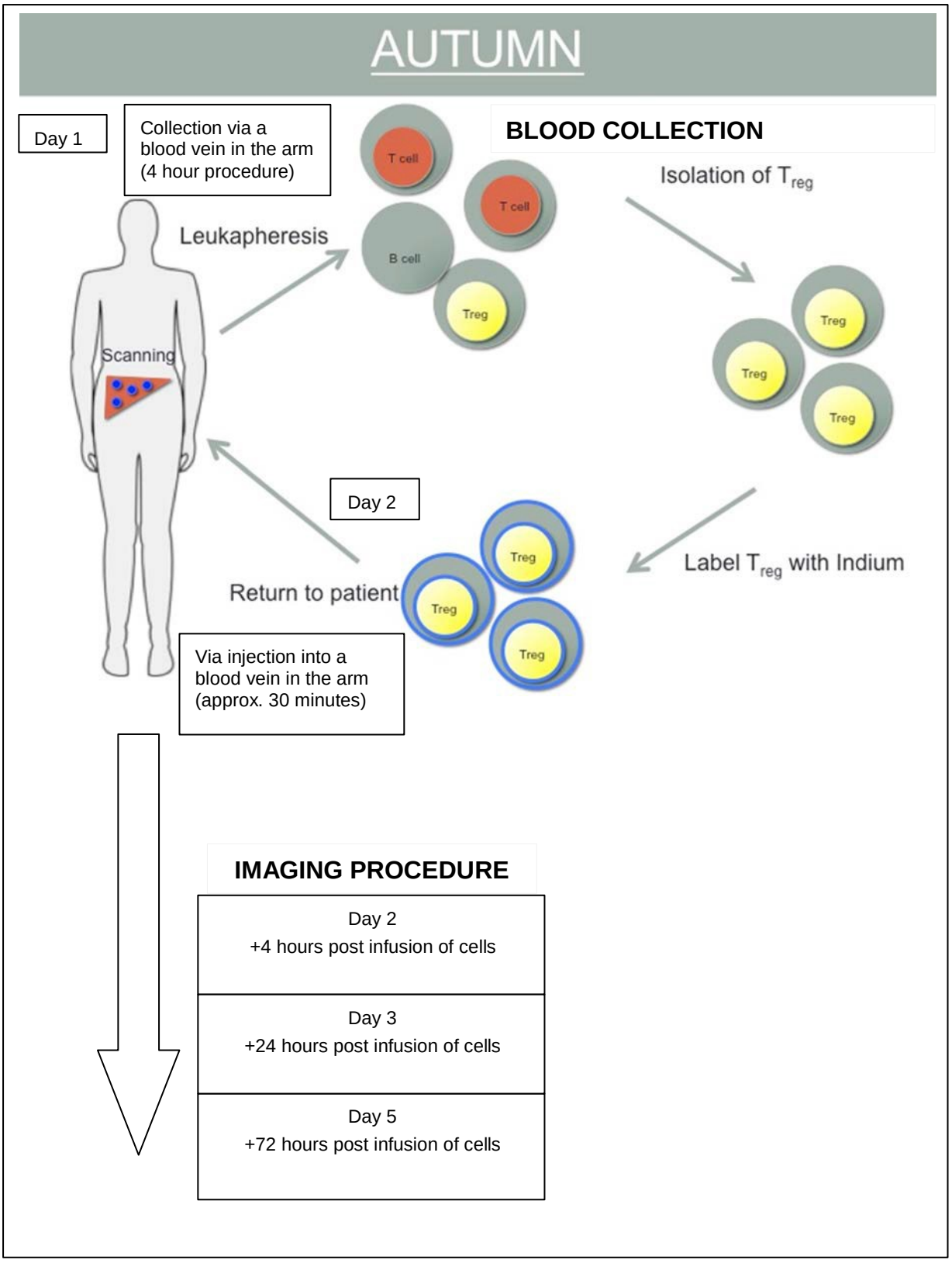
Inclusion Criteria

- Age ≥18 and <70 years at screening
- Diagnostic criteria for Autoimmune Hepatitis based on recommendations of the International Autoimmune Hepatitis Group (Appendix 1)
- Non-cirrhotic or compensated cirrhosis (Child Pugh Score <7)
- Leukocyte count ≥ 4 x 10^9/L
- World Health Organisation (WHO) performance status of 0 -1 (Appendix 2)
- Female subjects of childbearing potential must have a negative pregnancy test prior to starting study intervention. 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 ≤55 years of age with amenorrhea of any duration will be considered to be of childbearing potential
- All sexually active women of childbearing potential must agree to use a highly effective method of contraception from the Screening visit throughout the study period and for 99 days following Treg infusion. 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 period begins
- All sexually active males must agree to use reliable forms of contraception during the study and the 4 month follow up period
- Patients who can give informed consent

Exclusion Criteria

- Post liver transplant or listed for liver transplantation
- Past surgical history of liver resection (including partial/hemi hepatectomy)
- Liver disease other than autoimmune related liver disease
- Positive for blood borne viruses Hepatitis B Virus (HBV), Hepatitis C Virus HCV), Human Immunodeficiency Virus (HIV), Human T-Lymphotropic Virus-1 (HTLV-1), HTLV-2 or syphilis
- Evidence of other active inflammatory disease or sepsis
- Pregnancy or breastfeeding
- Poor venous access
- Decompensated cirrhosis
- Clinically significant cardiovascular disease (ischaemic heart disease, heart failure)
- A history of any underlying previous malignancy
- Previous allergy to radio-contrast reagents
- Patients with metallic objects fitted to the body
- Any other physical or psychiatric disorder that may interfere with subject compliance, adequate informed consent, follow up or determine the causality of adverse events

DIAGRAM OF PATIENT PATHWAY



SCHEDULE OF EVENTS

Assessment	Screening	Day 1	Day 2	Day 3	Day 5	Week 2, 3, 4 Follow up	Week 6 & 8 Follow up	Week 12 Follow up	Week 16 Follow up
Obtain consent	**X**								
Assign registration number	**X**								
Patient admitted			**X**						
Leukapharesis		**X**							
Patient discharged				**X**					
T reg isolation		**X**							
Confirm eligibility	**X***								
T reg labelling			**X**						
T reg reinfusion			**X**						
Nuclear medicine imaging			**X (4 hrs post infusion)**	**X (24 hrs post infusion)**	**X (72 hrs post infusion)**				
SPECT-CT				**X**					
Fibroscan and Ultrasound scan	**X**								**X**
Standard Blood tests (Haematology and Biochemistry	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**

SCHEDULE OF EVENTS

Blood tests to assess immunological profile (inc. research samples)	X	X	X	X	X	X	X	X	X
Clinical assessment and physical examination	X	X	X	X	X	X	X	X	X
Vital signs and performance status	X	X	X	X	X	X	X	X	X
ECG	X	X	X	X	X	X	X	X	X
Adverse Event monitoring	X	X	X	X	X	X	X	X	X
Urine Pregnancy Test (female patients only)	X								
Concomitant Medications	X	X	X	X	X	X	X	X	X

***Eligibility will be confirmed upon analysis of screening procedures and before day 1 of study intervention**