Centre of Research Excellence in
Pulmonary Fibrosis
PACT PF Australasian Clinical Trials

TELO-SCOPE Study

Trial title	The TELO-SCOPE Study: Attenuating Telomere Attrition with Danazol. Is there Scope to Dramatically Improve Health Outcomes for Adults and Children with Pulmonary Fibrosis.
Trial synopsis	Pulmonary fibrosis is a scarring lung disease that in its most common and severe form (Idiopathic Pulmonary Fibrosis (IPF)) causes progressive respiratory failure and premature death. The genetic origins of Pulmonary Fibrosis have been recently described, with the most common abnormalities being in telomere related genes. Telomeres act as protective caps at the ends of chromosomes – somewhat like the hard plastic at the end of a shoelace that prevents the shoelace from fraying. Telomere shortening is a normal ageing process, however in some people with pulmonary fibrosis this shortening occurs more rapidly due to specific genetic abnormalities in the machinery that controls telomere length. Up to 25% of people with pulmonary fibrosis may have abnormally short telomeres. While it is possible to measure the length of the telomere, it is not currently routinely incorporated in clinical practice. Danazol is a synthetic hormone which may increase telomere length. A small study of danazol in a group of patients with blood disease related to telomere shortening demonstrated stabilisation of lung function. The TELO-SCOPE study aims to evaluate the benefits and safety of danazol in patients with pulmonary fibrosis related to Short Telomeres. TELO-SCOPE is a randomised controlled trial (RCT), which means that the medication, danazol, is tested against a placebo so that we can be confident that it either works or does not work. By randomly assigning participants to either the danazol or placebo groups, makes sure that other factors (like age or gender) don't influence the results in any way. RCTs provide the strongest data to be sure whether or not a treatment works. This is a phase II trial – which means that we are testing the effectiveness and safety of danazol in people who have pulmonary fibrosis. Danazol has already been tested in other conditions.

Investigational medicinal product, comparator and randomisation	Danazol. Background antifibrotic therapy is allowed as drug pharmacokinetics do not predict interactions or additive hepatotoxicity, but these will be a key focus of the safety assessments.
Disease target	Any fibrotic lung disease
Sponsor	University of Queensland
Duration	12 months
Trial Status	Recruiting
Trial phase	Phase II
Key inclusion criteria	• Males and females aged >5 years, able to take capsules orally • Fibrosing interstitial pneumonia (Idiopathic PF, idiopathic non-specific interstitial pneumonia, chronic hypersensitivity pneumonitis, pleuroparenchymal fibroelastosis, unclassifiable interstitial lung disease (ILD)) diagnosed according to the current international guidelines. • Age-adjusted peripheral blood leukocyte telomere length ≤ 10th centile on Flow-FISH either at screening or previously established • FVC > 40% predicted • DLCOc > 25% predicted • If receiving background pirfenidone / nintedanib, stable dose for 28 days prior to screening • Able to understand and sign a written informed consent form (or legally authorised representative) • Agreement to use a medically approved form of non-hormonal contraception (if of child-bearing potential) (noting that oral contraceptives are advised not to be used concurrently with danazol)
Key exclusion criteria	• Actively or imminently listed for lung transplantation. • Undergone, awaiting, or likely to require bone marrow transplantation within 12 months. • Concurrent enrolment in another study. • Females with a positive pregnancy test at screening or currently breastfeeding. • Pelvic infection. • Past jaundice with oral contraceptives. • Undiagnosed abnormal genital bleeding. • Undiagnosed ovarian/uterine masses • Any history of malignancy likely to result in significant disability or likely to require significant medical or surgical intervention within the next 12 months. • History of androgen-dependent tumour.

	• Any condition other than PF that, in the opinion of the investigator, is likely to result in the death of the participant within the next 12 months. • History of end-stage liver disease or ALT or AST > 3 times the upper limit of normal. • History of end-stage kidney disease requiring dialysis. • Markedly impaired cardiac function. • Known increased risk of or history of thromboembolism (e.g. Factor V Leiden, Protein C or S deficiency). • Uncontrolled hypertension. • Uncontrolled lipoprotein disorder. • Poorly-controlled diabetes mellitus. • History of marked or persistent androgenic reaction to previous gonadal steroid therapy. • History of epilepsy induced or worsened by previous gonadal steroid therapy. • History of raised intracranial pressure. • Known intolerance to danazol. • Porphyria. • Use of any of the following agents within 28 days before screening: danazol or other androgen therapy, warfarin or other anticoagulant, carbamazepine, phenytoin, investigational therapy, cytotoxic therapy, tacrolimus, cyclosporine. • Professional singer due to potential for voice change. • Competitive athletes. • Prostate specific antigen (PSA) above the upper limit of normal (adult males only)
Number of participants sought	50
Lead site(s) in Australia	The Prince Charles Hospital (QLD)
Lead site(s) in New Zealand	N/A
Additional sites	• John Hunter Hospital (NSW) • Royal Prince Alfred Hospital (NSW) • The Alfred (VIC) • The Austin (VIC) • Fiona Stanley Hospital (WA)
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