Trial Innovation Network Expression of Interest:
OCTILIA

Study Title	A Phase 2, Randomized, Double-Blind, Placebo-Controlled Efficacy and Safety Study of Obinutuzumab in Subjects with Connective Tissue Disease-Related Interstitial Lung Disease.
Funding I/C	NHLBI
Study Description	OCTILIA is a phase 2, multicenter, randomized, double-blind, placebo controlled clinical trial designed to evaluate the efficacy and safety of administering obinutuzumab or placebo in patients with CTD-ILD on background mycophenolate over 24-weeks. We hypothesize that there will be an improvement in mean absolute change in FVC in mL over 24 weeks in the obinutuzumab (1000 mg IV on days 1 and 15) group compared to the placebo group. Efficacy will be evaluated through interval testing of pulmonary function tests. Other assessments include acute respiratory exacerbation, hospitalization, 6-minute walk distance, patient reported outcome measures, mortality and adverse events. Safety will be assessed by determining differences between the treatment arms for the rate of adverse events, serious adverse events, rates of acute exacerbation, hospitalization and all-cause mortality.
Study Design	The efficacy of obinutuzumab (1000 mg IV on days 1 and 15) compared to placebo will be tested for the mean absolute change in FVC in mL over 24 weeks. There are 2 arms drug and placebo. Randomization will occur at the EDC via the data center.
IRB	JHU sIRB
Coordinating Center	National Jewish Health
Study Length	5 years, 1 year planning
Study Enrollment #	100-105
Eligibility Criteria	**Inclusion Criteria** • Age 18-75 years; • A diagnosis of CTD, based on internationally accepted criteria; • screening forced vital capacity (FVC) <80% but ≥ 45% of the predicted value; • any ground glass opacity (GGO) on HRCT whether associated with reticulations (fibrosis) or not; and CTD within the previous 7 years. • On mycophenolate mofetil 3g/d for at least 12 weeks prior to screening **Exclusion Criteria** • Pre-bronchodilator FEV1/FVC < 0.7, pulmonary hypertension according to echocardiograpy (ECHO) or right heart catheterization (RHC) and judged by the investigator to be clinically significant and warranting drug therapy; • DLCO <40% predicted (30–39% predicted allowed if echocardiography and/or RHC failed to show evidence of pulmonary hypertension); • Emphysema >40% on HRCT • a single-breath diffusing capacity of the lung for carbon monoxide (DLCO) <40% predicted; • immunodeficiency syndromes (including hypogammaglobulinemia). • Suspected or proven untreated tuberculosis. • Active systemic infection, positive viral hepatitis, HIV, covid-19. • A history of known Hepatitis B infection with and without antiviral treatment history. • Unexplained neurological symptoms suggestive of progressive multifocal leukoencephalopathy. • evidence of significant airflow obstruction; • Leukopenia (WBC <4.0 ×103/µl) or thrombocytopenia (platelet count <150 ×103/µl); clinically significant anemia (<10.0 g/dl); • baseline liver function test (ALT, AST) or bilirubin >1.5 × upper normal limit; serum creatinine >2.0mg/dl; • uncontrolled congestive heart failure; • pregnancy (documented by urine pregnancy test) and/or breast feeding; • Receiving nintedinib or pirfenidone. • Treatment with anti-CD20 monoclonal antibody within 12 months from randomization.

		• Receiving systemic corticosteroids equivalent to prednisone ≥ 10 mg/day • Receiving cytotoxic, immunosuppressive, cytokine modulating, or receptor antagonist agents (including but not limited to methotrexate, azathioprine, cyclophosphamide, tocilizumab cyclosporine or other steroid sparing agent) within 4 weeks of screening (except mycophenolate mofetil).
Total # of Sites	18-24	
Site Requirements	<u>Study sites will need to have the following at their site to be considered:</u> • A dedicated research pharmacy to store and dispense the study medication • Access and ability to use the local laboratory(ies) for clinical testing (e.g., CBCC, CMP, QuantiFERON TB, HIV, Hepatitis, Covid-19 test, IgG) • Ability to collect, storage and ship whole blood tubes • Ability to electronically push HRCT images • Has a dedicated rheumatology and ILD clinic • Has a PFT lab and infusion site	
Site Investigator Qualifications	<u>Site Investigators should have the following:</u> • Be available for monitoring visits and attend study meetings • Available staff and coordinators to conduct the study • Be an ILD specialist or work in the ILD clinic, frequently see and manage ILD patients, or be a rheumatologist • Has dedicated clinic time or have a co-I with dedicated ILD clinic time	
Key Timeline Dates:	<u>The following dates are projections and subject to change:</u> **Site Selection Decisions**: July 2024 **Site Selection Notifications:** July 2024 **Enrollment begins:** June 2026 **Last Patient/Last Visit:** July 2030 **Study Closure:** July 2030	