

Table 1. NEUROINFLAMMATION AND CYTOKINE-TARGETED INTERVENTIONS : Targeting IL-1 β

Target	Drug	Main Indications	CT Number , Title, Study Protocol	Potential Neurological Implications
IL-1	Anakinra Anti-IL-1 β receptor antibody	<ul style="list-style-type: none"> • Rheumatoid Arthritis • Cryopyrin-Associated Periodic Syndromes 	<ul style="list-style-type: none"> • NCT04341584 • CORIMUNO-ANA: Trial Evaluating Efficacy Of Anakinra In Patients With Covid-19 Infection (CORIMUNO-ANA) • Interventional Phase 2 	<p>Beneficial effects have been observed in patients affected by stroke (Everett et al., 2020; Smith et al., 2018), epilepsy (Kenney-Jung et al., 2016), and neuromyelitis optica (NMO) as a complication of familial mediterranean fever (FMF) (Ozdogan et al., 2020).</p> <p>Potential risks may include facilitation of viral replication by highly cytopathic viruses such as the herpes simplex 1 (Sergeie et al., 2007) or the West Nile virus (Durrant et al., 2013).</p>
			<ul style="list-style-type: none"> • NCT04366232 • Efficacy of Intravenous Anakinra and Ruxolitinib During COVID-19 Inflammation (JAKINCOV) • Interventional Phase 2 	
			<ul style="list-style-type: none"> • NCT04443881 • Clinical Trial of the Use of Anakinra in Cytokine Storm Syndrome Secondary to Covid-19 (ANA-COVID-GEAS) (ANA-COVID-GEAS) • Interventional Phase 2/3 	
			<ul style="list-style-type: none"> • NCT04462757 • SCIL-1Ra in COVID-19 Feasibility & PK/PD • Interventional Phase 2 	
			<ul style="list-style-type: none"> • NCT04412291 • A Study in Patients With COVID-19 and Respiratory Distress Not Requiring Mechanical Ventilation, to Compare Standard-of-care With Anakinra and Tocilizumab Treatment The Immunomodulation-CoV Assessment (ImmCoVA) Study • Interventional Phase 2 	
			<ul style="list-style-type: none"> • NCT04424056 • A Trial Using ANAKINRA, TOCILIZUMAB Alone or in Association With RUXOLITINIB in Severe Stage 2b and 3 of COVID19-associated Disease (INFLAMMACOV) • Interventional Phase 3 	
			<ul style="list-style-type: none"> • NCT04364009 • Anakinra for COVID-19 Respiratory Symptoms (ANACONDA) • Interventional Phase 3 	

Table 1 Continued

Target	Drug	Main Indications	CT Number , Title, Study Protocol	Evidence for Neurological Implications
IL-1	Anakinra		NCT04357366 suPAR-guided Anakinra Treatment for Validation of the Risk and Management of Respiratory Failure by COVID-19 (SAVE) (SAVE) Interventional Phase 2	
			NCT04339712 Personalised Immunotherapy for SARS-CoV-2 (COVID-19) Associated With Organ Dysfunction (ESCAPE) Interventional Phase 2	
			NCT04324021 Efficacy and Safety of Emapalumab and Anakinra in Reducing Hyperinflammation and Respiratory Distress in Patients With COVID-19 Infection. Interventional Phase 2/3	
			NCT04362111 Early Identification and Treatment of Cytokine Storm Syndrome in Covid-19 Interventional Phase 3	
			NCT04408326 Efficacy and Safety of Angiotensin II Use in Coronavirus Disease(COVID)-19 Patients With Acute Respiratory Distress Syndrome (ACES) Observational	
			NCT04330638 Treatment of COVID-19 Patients With Anti-interleukin Drugs (COV-AID) Interventional Phase 2/3	
	Canakinumab Anti-IL-1 β antibody	<ul style="list-style-type: none"> Cryopyrin Associated Periodic Syndromes (CAPS) 	NCT04362813 Study of Efficacy and Safety of Canakinumab Treatment for CRS in Participants With COVID-19-induced Pneumonia (CAN-COVID) Interventional Phase 3	Beneficial effects have been observed in patients affected by drug-resistant epilepsy (DeSena et al., 2018), familial mediterranean fever and multiple sclerosis (Ozdogan et al., 2020). Reduced serious cardiovascular events in in patients with prior myocardial infarction (MI) and residual inflammatory risk (CANTOS trial; Everett et al., 2020).
			NCT04362813 Study of Efficacy and Safety of Canakinumab Treatment for CRS in Participants With COVID-19-induced Pneumonia (CAN-COVID) Interventional Phase 3	
			NCT04365153 Canakinumab in Covid-19 Cardiac Injury (The Three C Study) Interventional Phase 2	