Table 6. NEUROINFLAMMATION AND CYTOKINE-TARGETED INTERVENTIONS : Targeting GM-CSF				
Target	**Drug**	**Main Indications**	**CT Number , Title, Study Protocol**	**Neurological Implications**
GM-CSF	**Mavrilimumab** Anti-GM-CSF receptor alpha (GM-CSFRα) antibody	• Rheumatoid arthritis	**NCT04447469** Study of Mavrilimumab (KPL-301) in Participants Hospitalized With Severe Corona Virus Disease 2019 (COVID-19) Pneumonia and Hyper-inflammation **Interventional Phase 2**	No clinical data is available regarding the neurological implications of mavrilimumab treatment in humans; however, GM-CSF ko mice are protected from EAE (McQualter et al., 2001) whereas disease severity is increased in mice receiving the infusion of lymphocytes infected with adenoviruses carrying a GM-CSF transgene (Spath et al., 2017).
			NCT04492514 Mavrilimumab to Reduce Progression of Acute Respiratory Failure in COVID-19 Pneumonia and Systemic Hyper-inflation **Interventional Phase 2**	
			NCT04463004 Mavrilimumab to Reduce Progression of Acute Respiratory Failure in COVID-19 Pneumonia and Systemic Hyper-inflammation (Virginia) **Interventional Phase 2**	
			NCT04399980 Mavrilimumab to Reduce Progression of Acute Respiratory Failure in COVID-19 Pneumonia and Systemic Hyper-inflammation (Florida) **Interventional Phase 2**	
			NCT04397497 Mavrilimumab in Severe COVID-19 Pneumonia and Hyper-inflammation (COMBAT-19) (COMBAT-19) **Interventional Phase 2**	

Table 6. Continued				
Target	**Drug**	**Main Indications**	**CT Number , Title, Study Protocol**	**Neurological Implications**
GM-CSF	**Gimsilumab** Anti-GM-CSF antibody	• Rheumatoid arthritis	**NCT04351243** A Study to Assess the Efficacy and Safety of Gimsilumab in Subjects With Lung Injury or Acute Respiratory Distress Syndrome Secondary to COVID-19 (BREATHE) **Interventional Phase 2**	MOR103 (Otilimab), a monoclonal antibody that binds GM-CSF, has shown moderate beneficial effects in MS patients (Constantinescu et al., 2015). GM-CSF neutralization with lenzilumab, another monoclonal antibody which, similarly to gimsilumab, binds GM-CSF, reduces chimeric antigen receptor T (CAR-T) cell therapy-induced neurotoxicity (Sterner et al., 2019).
	Sargramostim Human recombinant GM-CSF	• Acute Myeloid Leukemia Following Chemotherapy • Autologous Peripheral Blood Progenitor Cell Mobilization and Bone Marrow Transplantation • Allogenic Bone Marrow Transplantation	**NCT04411680** Study of Sargramostim in Patients with COVID-19 **Interventional Phase 2** **NCT04326920** Sargramostim in Patients With Acute Hypoxic Respiratory Failure Due to COVID-19 (SARPAC) **Interventional Phase 2** **NCT04400929** Using GM-CSF as a Host Directed Therapeutic Against COVID-19 **Interventional Phase 2**	Recombinant GM-CSF protects from HSV-1 encephalitis (Tsuboi et al., 1998), reduces brain infarct size (Schabitz et al., 2008), ameliorates stab wound-induced brain injury in rats (Nishihara et al., 2011); is effective in experimental models of PD (Meuer et al., 2006; Kim et al., 2009). Improved motor function in a small cohort of **Parkinson** patients (Gendelman et al., 2017). Is neuroprotective in a mouse model of AD (Kiyota et al., 2018) and a clinical trial in AD patients (NCT01409915) has been completed (data not available yet).