

**Table 5. NEUROINFLAMMATION AND CYTOKINE-TARGETED INTERVENTIONS : Targeting JAK1/2**

Target	Drug	Main Indications	CT Number , Title, Study Protocol	Neurological Implications
<b>JAK1/2</b>	<b>Tofacitinib</b> Anti-Jak1 and -Jak3 Receptor Antibody	<ul style="list-style-type: none"> <li>• Psoriatic arthritis</li> <li>• Rheumatoid arthritis</li> <li>• Ulcerative colitis</li> </ul>	<b>NCT04415151</b> Tofacitinib for Treatment of Moderate COVID-19 (I-TOMIC) <b>Interventional Phase 2</b>	<p>Adoptive transfer of dendritic cells made tolerogenic ex vivo with tofacitinib dampened disease activity in an experimental model of MS (Zhou et al., 2016).</p> <p>Potential risks include occurrence of thromboembolic events and reactivation of latent viral infections (Scott et al., 2018).</p>
			<b>NCT04469114</b> Tofacitinib in Hospitalized Patients With COVID-19 Pneumonia <b>Interventional Phase 2</b>	
			<b>NCT04390061</b> TOFACitinib Plus Hydroxychloroquine vs Hydroxychloroquine in Patients With COVID-19 Interstitial Pneumonia (TOFACoV-2) <b>Interventional Phase 2</b>	
			<b>NCT04332042</b> TOFACitinib in SARS-CoV2 Pneumonia <b>Interventional Phase 2</b>	

Table 5 Continued (I)

Target	Drug	Main Indications	CT Number , Title, Study Protocol	Neurological Implications
<b>JAK1/2</b>	<b>Baricitinib</b> Anti-Jak1 and -Jak2 Receptor Antibody	• Rheumatoid arthritis	<b>NCT04340232</b> Safety and Efficacy of Baricitinib for COVID-19 <b>Interventional Phase 2/3</b>	Reverses HIV-associated neurocognitive disorders in animal models (Gavegnano et al., 2019). May induce thromboembolic events and promote new viral infections or the reactivation of latent infections (Scott et al., 2018).
			<b>NCT04421027</b> A Study of Baricitinib (LY3009104) in Participants With COVID-19 <b>Interventional Phase 3</b>	
			<b>NCT04358614</b> Baricitinib Therapy in COVID-19 <b>Interventional Phase 2/3</b>	
			<b>NCT04373044</b> Baricitinib, Placebo and Antiviral Therapy for the Treatment of Patients With Moderate and Severe COVID-19 <b>Interventional Phase 2</b>	
			<b>NCT04393051</b> Baricitinib Compared to Standard Therapy in Patients With COVID-19 <b>Interventional Phase 2</b>	
			<b>NCT04362943</b> Clinical-epidemiological Characterization of COVID-19 Disease in Hospitalized Older Adults <b>Observational</b>	
			<b>NCT04390464</b> mulTi-Arm Therapeutic Study in Pre-ICu Patients Admitted With Covid-19 - Repurposed Drugs (TACTIC-R) <b>Interventional Phase 4</b>	
			<b>NCT04401579</b> Adaptive COVID-19 Treatment Trial 2 (ACTT-2) <b>Interventional Phase 3</b>	
			<b>NCT04346147</b> Clinical Trial to Evaluate Efficacy of 3 Types of Treatment in Patients With Pneumonia by COVID-19 <b>Interventional Phase 2</b>	
			<b>NCT04321993</b> Treatment of Moderate to Severe Coronavirus Disease (COVID-19) in Hospitalized Patients <b>Interventional Phase 2</b>	
			<b>NCT04320277</b> Baricitinib in Symptomatic Patients Infected by COVID-19: an Open-label, Pilot Study <b>Interventional Phase 2/3</b>	
			<b>NCT04399798</b> Baricitinib for coRona Virus pnEumonia (COVID-19): a THERapeutic Trial <b>Interventional Phase 2/3</b>	

Table 5 Continued (II)

Target	Drug	Main Indications	CT Number , Title, Study Protocol	Neurological Implications
JAK1/2	Ruxolitinib Anti-Jak1 and -Jak2 Receptor Antibody	•Myelofibrosis	<b>NCT04348071</b> Safety and Efficacy of Ruxolitinib for COVID-19 <b>Interventional Phase 2/3</b>	<p>Ameliorates HIV-encephalitis in mice (Haile et al., 2016)</p> <p>Effective in a single patient with highly active <b>refractory NMO</b> (Hodecker et al., 2017).</p> <p>May induce thromboembolic events and promote new viral infections or the reactivation of latent infections (Scott et al., 2018).</p> <p>Fatal cases of JC polyomavirus encephalopathy and meningitis have been described in patients on chronic therapy with ruxolitinib (Ballesta et al., 2017; Reoma et al., 2019).</p>
			<b>NCT04414098</b> Ruxolitinib in the Treatment of Covid-19 <b>Interventional Phase 2</b>	
			<b>NCT04355793</b> Expanded Access Program of Ruxolitinib for the Emergency Treatment of Cytokine Storm From COVID-19 Infection <b>Expanded Access</b>	
			<b>NCT04377620</b> Assessment of Efficacy and Safety of Ruxolitinib in Participants With COVID-19-Associated ARDS Who Require Mechanical Ventilation (RUXCOVID-DEVENT) <b>Interventional Phase 3</b>	
			<b>NCT04334044</b> Treatment of SARS Caused by COVID-19 With Ruxolitinib <b>Interventional Phase 1/2</b>	
			<b>NCT04331665</b> Study of the Efficacy and Safety of Ruxolitinib to Treat COVID-19 Pneumonia <b>NA</b>	
			<b>NCT04337359</b> Ruxolitinib Managed Access Program (MAP) for Patients Diagnosed With Severe/Very Severe COVID-19 Illness <b>Expanded Access</b>	
			<b>NCT04361903</b> Ruxolitinib for the Treatment of Acute Respiratory Distress Syndrome in Patients With COVID-19 Infection (RESPIRE) <b>Observational</b>	
			<b>NCT04338958</b> Ruxolitinib in Covid-19 Patients With Defined Hyperinflammation (RuxCoFlam) <b>Interventional Phase 2</b>	
			NCT04374149 Therapeutic Plasma Exchange Alone or in Combination With Ruxolitinib in COVID-19 Associated CRS <b>Interventional Phase 2</b>	
			<b>NCT04348695</b> Study of Ruxolitinib Plus Simvastatin in the Prevention and Treatment of Respiratory Failure of COVID-19. (Ruxo-Sim-20) <b>Interventional Phase 2</b>	