

**Appendix 3.** Intravenous Immunoglobulin (IVIG) Studies for COVID 19

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Hu H, et al.	Case report (China)	IVIG Methylprednisolone Norepinephrine Toracemide & furosemide Milrinone Sulbactam Pantoprazol	N/A	37y/o patient with pulmonary infection, enlarged heart, pleural effusion &(+) coronavirus nucleic acid test	Improvement in clinical status & laboratory parameters	The authors suggested that early glucocorticoid anti-inflammatory therapy & IVIG therapy may be of important value to this type of patient.	Published	<a href="https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa190/5807656">https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa190/5807656</a>
Zhao K, et al.	Case report (China)	IVIG Ganciclovir, Lopinavir/ritonavir, Moxifloxacin, Meropenem, Glutathione, Dexamethasone, Mecobalamin, Pantoprazole	N/A	66y/o with COVID-19 who developed acute myelitis	Clinical improvement, discharged for isolation & rehabilitation		Published	<a href="https://www.medrxiv.org/content/10.1101/2020.03.16.20035105v2">https://www.medrxiv.org/content/10.1101/2020.03.16.20035105v2</a>
Zhou Z, et al.	Prospective cohort study (China)	IVIG Moderate-dose corticosteroid	N/A	COVID-19 patients who failed low dose Corticosteroid (CS) (10)	Improvement in clinical status & laboratory parameters	All patients achieved significant improvement in terms of vital signs, blood work, & the APACHE II scores.	Published (Pre-print)	<a href="https://www.preprints.org/manuscript/202003.0065/v1">https://www.preprints.org/manuscript/202003.0065/v1</a>

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Shao Z, et al.	Retrospective cohort study (China)	IVIG Subgroups: <ul style="list-style-type: none"> <li>• IVIG &gt;15g/day</li> <li>• IVIG &lt;15g/day</li> <li>• IVIG given &gt;7 days</li> </ul> IVIG given ≤7 days	Standard care	Patients with COVID-19 ≥18y/o Subgroup: -Severe type -Critical type (325)	28-day & 60-day mortality	No improvement in 28-day and 60-day mortality -IVIG significantly decreased 28-day mortality in critical type patients -high dose IVIG (>15 g/d) significantly reduced 28-day & 60-day mortality -early use of IVIG (≤ 7d) significantly reduced the 60-day mortality	Published (Pre-print)	<a href="https://www.medrxiv.org/content/10.1101/2020.04.11.20061739v1.full.pdf">https://www.medrxiv.org/content/10.1101/2020.04.11.20061739v1.full.pdf</a>
Cao W, et al.	Case series (China)	IVIG	N/A	Patients with COVID 19, severe type 34 – 56y/o (3)	Improvement in clinical status & laboratory parameters	The 3 cases were successfully treated by high-dose IVIG at the early stage of clinical deterioration.	Published	<a href="https://academic.oup.com/ofid/article/7/3/ofaa102/5810740">https://academic.oup.com/ofid/article/7/3/ofaa102/5810740</a>

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Xie Y, et al.	Retrospective study (China)	IVIg < 48 hours after admission	IVIg > 48 hours after admission	COVID 19 with severe or critical illness (58)	28-day mortality	There was a statistically significant reduction in 28-day mortality between the two groups	Published	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7151471/pdf/main.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7151471/pdf/main.pdf</a>
Shi H, et al.	Case report (China)	Plasma exchange (PE) followed by IVIG	N/A	50y/o with laboratory-confirmed COVID-19 with respiratory failure, shock, persistent diarrhea despite conventional therapy	Improvement in clinical status & laboratory parameters after the 4th dose	Timely initiation of PE treatment followed by IVIG protected the patient from progressing to acute respiratory distress syndrome (ARDS) & multiple organ failure	Published	<a href="https://doi.org/10.1016/j.jantimicag.2020.105974">https://doi.org/10.1016/j.jantimicag.2020.105974</a>
Cui et al	Case report (China)	IVIg + Oseltamivir, Cefdinir, Lianhu Qingwen	N/A	35y/o male with Hemophilia A with pneumonia on CT scan	Clinical improvement	Asymptomatic with no increased bleeding events on follow-up	Published	<a href="https://onlinelibrary.wiley.com/doi/abs/10.1111/hae.14000">https://onlinelibrary.wiley.com/doi/abs/10.1111/hae.14000</a>
Moeinzadeh et al	Case report (Iran)	IVIg + methylprednisolone, Cyclophosphamide, HCQ, Plasmapheresis	N/A	25y/o male with glomerulonephritis, arthralgia and weakness	Improvement in clinical status & laboratory parameters	Discharged with no symptoms with stable creatinine level	Published	<a href="http://www.ijkd.org/index.php/ijkd/article/view/5537/1165">http://www.ijkd.org/index.php/ijkd/article/view/5537/1165</a>

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
LeVine S, et al.	Case report (Bhutan)	IVIG	N/A	76y/o immunocompromised with history of travel, developed GI symptoms & cough, RT-PCR (+); respiratory status deteriorated despite broad-spectrum antivirals, antibiotics, & intensive supportive care	Improvement in clinical status & laboratory parameters after the first dose		Published	<a href="https://doi.org/10.4269/ajtmh.20-0259">https://doi.org/10.4269/ajtmh.20-0259</a>
Patel et al	Case report (USA)	IVIG + azithromycin, HCQ, Tocilizumab, Remdesvir, Methylprednisolone, empiric antibiotics	N/A	12y/o female with severe respiratory failure and severe thrombocytopenia	Improvement in clinical status & laboratory parameters	Extubated and discharged improved	Published	<a href="http://pediatrics.aappublications.org/lookup/doi/10.1542/peds.2020-1437">http://pediatrics.aappublications.org/lookup/doi/10.1542/peds.2020-1437</a>
Li et al	Case report (USA)	IVIG + azithromycin, HCQ, Tocilizumab, Remdesvir, Methylprednisolone, empiric antibiotics	N/A	39/M with Evans syndrome	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16846">https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16846</a>

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Daneshpazh ooh et al	Case report (Iran)	IVIG + prednisolone, HCQ, Oseltamivir, Lopinavir/Ritonavir, Meropenem, Vancomycin, Ribavirin, Levofloxacin,	N/A	43y/o Male with mucous membrane pemphigoid on MMF and Prednisolone	Improvement in clinical status & laboratory parameters	IVIG mainly considered for his pemphigoid condition. Discharged with significant improvement and recovery of lymphopenia	Published	<a href="https://www.tandfonline.com/doi/full/10.1080/09546634.2020.1764472">https://www.tandfonline.com/doi/full/10.1080/09546634.2020.1764472</a>
Ahmed et al	Case series (UK)	IVIG	N/A	50/M with severe ITP; 49/F with bruises and gum bleeding, and severe ITP; 96/F with AF, IHD, CKD, pneumonia thrombocytopenia	Improvement in clinical status & laboratory parameters	Improvement in 2, and death in 1.	Published	<a href="https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16769">https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16769</a>
Scheidl et al	Case report (Germany)	IVIG	N/A	54/F with GBS	Improvement in clinical status & laboratory parameters	Recovery of neurologic condition	Published	<a href="https://onlinelibrary.wiley.com/doi/abs/10.1111/jns.12382">https://onlinelibrary.wiley.com/doi/abs/10.1111/jns.12382</a>
Anand et al	Case series (USA)	IVIG +Pred; one received HCQ and Ceftriaxone	N/A	90/F with dementia and MG, HPN; 42/F with hepatitis B and MG	Improvement in clinical status & laboratory parameters	Discharged improved	Published	<a href="https://onlinelibrary.wiley.com/doi/abs/10.1002/mus.26918">https://onlinelibrary.wiley.com/doi/abs/10.1002/mus.26918</a>

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Pfefferkorn et al	Case report (Germany)	IVIg and plasmapheresis	N/A	51/M with pneumonia and acute polyradiculoneuritis with locked-in syndrome	Clinical improvement	with some motor improvement but was still on MV	Published	<a href="http://link.springer.com/10.1007/s00415-020-09897-y">http://link.springer.com/10.1007/s00415-020-09897-y</a>
Delly et al	Case report (USA)	IVIg, Prednisone, HCQ also given AZT, Vancomycin, Cefepime	N/A	56/F with MG in crisis and CTD	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://linkinghub.elsevier.com/retrieve/pii/S0022510X20302240">https://linkinghub.elsevier.com/retrieve/pii/S0022510X20302240</a>
Su et al	Case report (USA)	IVIg, TMP-SMX	N/A	72/M with CAD, HPN, GBS and respiratory distress	Improvement in clinical status & laboratory parameters	still in the ICU	Published	<a href="https://onlinelibrary.wiley.com/doi/abs/10.1002/mus.26988">https://onlinelibrary.wiley.com/doi/abs/10.1002/mus.26988</a>
Bigaut et al	Case series (France)	IVIg	N/A	43/M with GBS; 70/F with GBS and respiratory failure	Clinical improvement	clinical improvement	Published	<a href="http://nn.neurology.org/lookup/doi/10.1212/NXI.0000000000000785">http://nn.neurology.org/lookup/doi/10.1212/NXI.0000000000000785</a>
Afshar et al	Case report (Iran)	IVIg, Meropenem, Levofloxacin, Linezolid, HCQ, Atazanavir, Methylprednisolone	N/A	39/F with respiratory distress	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://linkinghub.elsevier.com/retrieve/pii/S2211034820302923">https://linkinghub.elsevier.com/retrieve/pii/S2211034820302923</a>
Murt et al	Case report (Turkey)	IVIg and favipiravir	N/A	41/M with ITP	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.26138">https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.26138</a>
Author/ Study	Study design	Intervention	Comparator	Population	Primary	Results	Status	Source

Identifier					outcome			(hyperlink)
Assini et al	Case series (Italy)	IVIG + idrossichlorocline, Arbidol, ritonavir, and lopinavir; IVIG + HCQ, antiretroviral therapy, tocilizumab	N/A	55/M with GBS/MF; 60/M with GBS and pneumonia	Improvement in clinical status	with clinical improvement	Published	<a href="http://link.springer.com/10.1007/s10072-020-04484-5">http://link.springer.com/10.1007/s10072-020-04484-5</a>
Parsons et al	Case report (USA)	IVIG + high dose steroids	N/A	51/F with ADEM	Improvement in clinical status	with clinical improvement	Published	<a href="http://link.springer.com/10.1007/s00415-020-09951-9">http://link.springer.com/10.1007/s00415-020-09951-9</a>
Novi et al	Case report (Italy)	IVIG + high dose steroids	N/A	64/F with ADEM	Improvement in clinical status	with clinical improvement	Published	<a href="http://nn.neurology.org/lookup/doi/10.1212/NXI.00000000000000797">http://nn.neurology.org/lookup/doi/10.1212/NXI.00000000000000797</a>
Toubiana et al	Prospective observational (France)	IVIG or IVIG + Steroids	N/A	21 children and adolescents (3.7-16.6 y/o) with features of Kawasaki disease	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="http://www.bmj.com/lookup/doi/10.1136/bmj.m2094">http://www.bmj.com/lookup/doi/10.1136/bmj.m2094</a>
Ikuyama et al	Case report (Japan)	IVIG + Lopinavir/Ritonavir, Moxifloxacin, Piperacillin-Tazobactam, Peramivir, Vancomycin, Meropenem, Methylprednisolone	N/A	76/F with DM, HPN, and pneumonia, respiratory failure, renal failure	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://linkinghub.elsevier.com/retrieve/pii/S2213007120301714">https://linkinghub.elsevier.com/retrieve/pii/S2213007120301714</a>
Author/ Study	Study design	Intervention	Comparator	Population	Primary	Results	Status	Source

Identifier					outcome			(hyperlink)
Lorenzo-Villalba et al	Case series (France)	IVIg + Eltrombopag	N/A	66/M with ITP and HPN; 57/F with ITP, HPN, Hypothyroidism	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://www.ejcrim.com/index.php/EJCRIM/article/view/1702">https://www.ejcrim.com/index.php/EJCRIM/article/view/1702</a>
Pouletty et al	Cohort (France)	IVIg or IVIG + Steroids	N/A	15 of 16 pediatric patients with kawasaki disease	Improvement in clinical status & laboratory parameters	None died. All achieved inflammatory remission. 2 still with mild cardiac dysfunction.	Published	<a href="http://ard.bmj.com/lookup/doi/10.1136/annrheumdis-2020-217960">http://ard.bmj.com/lookup/doi/10.1136/annrheumdis-2020-217960</a>
Mohtadi et al	Case series (Iran)	IVIg or IVIG + Steroids; + HCQ antibiotics and antivirals	N/A	5 severe COVID-19 cases	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://linkinghub.elsevier.com/retrieve/pii/S0042682220300933">https://linkinghub.elsevier.com/retrieve/pii/S0042682220300933</a>
Webb et al	Case report (UK)	IVIg	N/A	57/M with HPN, Psoriasis, and GBS	Improvement in clinical status & laboratory parameters	with clinical improvement but still on MV	Published	<a href="http://casereports.bmj.com/lookup/doi/10.1136/bcr-2020-236182">http://casereports.bmj.com/lookup/doi/10.1136/bcr-2020-236182</a>
Virhammar et al	Case report (Sweden)	IVIg + plasma exchange; acyclovir	N/A	55/F with acute necrotizing encephalopathy	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="http://www.neurology.org/lookup/doi/10.1212/WNL.00000000010250">http://www.neurology.org/lookup/doi/10.1212/WNL.00000000010250</a>
Sokolovsky et al	Case report (USA)	IVIg + methylprednisolone and aspirin	N/A	36/F with Kawasaki-like multisystem inflammatory disease	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://linkinghub.elsevier.com/retrieve/pii/S0735675720305428">https://linkinghub.elsevier.com/retrieve/pii/S0735675720305428</a>
Author/ Study	Study design	Intervention	Comparator	Population	Primary	Results	Status	Source



Identifier					outcome			(hyperlink)
Tiet and Alshaikh	Case report (UK)	IVIG	N/A	49/M with GBS	Improvement in clinical status	with clinical improvement	Published	<a href="http://casereports.bmj.com/lookup/doi/10.1136/bcr-2020-236536">http://casereports.bmj.com/lookup/doi/10.1136/bcr-2020-236536</a>
Artru et al	Case report (Switzerland)	IVIG + Dexamethasone, HCQ, Co-amoxiclav	N/A	38/M with obesity and ITP	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="http://casereports.bmj.com/lookup/doi/10.1136/bcr-2020-236815">http://casereports.bmj.com/lookup/doi/10.1136/bcr-2020-236815</a>
Revuz et al	Case series (France)	IVIG	N/A	57/F with pneumonia and ITP; 76/M with metastatic brochiolar adenoCA and ITP; 39/M with ITP	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7350967/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7350967/</a>
Bennett et al	Case report (USA)	IVIG and dexamethasone	N/A	73/F with HPN, hyperlipidemia, seasonal allergies, and ITP	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://www.cureus.com/articles/33674-immune-thrombocytopenia-purpura-secondary-to-covid-19">https://www.cureus.com/articles/33674-immune-thrombocytopenia-purpura-secondary-to-covid-19</a>
Deruelle et al	Case report (France)	IVIG and methylprednisolone, heparin	N/A	41/M with ARDS and ITP	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="http://link.springer.com/10.1007/s12185-020-02943-5">http://link.springer.com/10.1007/s12185-020-02943-5</a>
Klocperk et al	Case report (Czech Republic)	IVIG + methylprednisolone	N/A	8/F with PIMS-TS	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://www.frontiersin.org/article/10.3389/fimmu.2020.01665/full">https://www.frontiersin.org/article/10.3389/fimmu.2020.01665/full</a>
Author/ Study	Study design	Intervention	Comparator	Population	Primary	Results	Status	Source

Identifier					outcome			(hyperlink)
Abe et al	Case series (Japan)	IVIG, Tocilizumab; IVIG + favipiravir, tocilizumab	N/A	60/M with ESRD and severe pneumonia; 68/F with ESRD and severe pneumonia	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="http://link.springer.com/10.1007/s13730-020-00512-7">http://link.springer.com/10.1007/s13730-020-00512-7</a>
Ye et al	Case report (Italy)	IVIG + IFNa2b inhalation, Arbidol, Thymosin, lopinavir/ritonavir	N/A	72/F with CLL and severe pneumonia	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://www.frontiersin.org/article/10.3389/fonc.2020.01272/full">https://www.frontiersin.org/article/10.3389/fonc.2020.01272/full</a>
Rein et al	Case series (Israel)	IVIG + prednisone and pyridostigmine	N/A	38/F, 65/M and 42/F with MG;	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://linkinghub.elsevier.com/retrieve/pii/S0022510X20303907">https://linkinghub.elsevier.com/retrieve/pii/S0022510X20303907</a>
Hindilerden et al	Case report (Turkey)	IVIG + favipiravir, azithromycin, prednisolone	N/A	86/M with HPN, DM and severe pneumonia	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://www.frontiersin.org/article/10.3389/fmed.2020.00404/full">https://www.frontiersin.org/article/10.3389/fmed.2020.00404/full</a>
Raut et al	Case report (India)	IVIG + aspirin, azithromycin	N/A	5mo/M with incomplete KD	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://academic.oup.com/tropj/advance-article/doi/10.1093/tropj/fmaa047/5881351">https://academic.oup.com/tropj/advance-article/doi/10.1093/tropj/fmaa047/5881351</a>
Martincic et al	Case report (Slovenia)	IVIG + dexamethasone, lopinavir/ritonavir, HCQ, Piperacillin/tazobactam	N/A	48/M with DM, obesity, OSA and pneumonia and thrombocytopenia	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://linkinghub.elsevier.com/retrieve/pii/S1201971220306330">https://linkinghub.elsevier.com/retrieve/pii/S1201971220306330</a>
Author/ Study	Study design	Intervention	Comparator	Population	Primary	Results	Status	Source

Identifier					outcome			(hyperlink)
Gruber et al	Case series (USA)	7 received IVIG	N/A	8 children (median age of 11.5 y/o)	Improvement in clinical status & laboratory parameters	with clinical improvement	Pre-print	<a href="https://www.medrxiv.org/content/10.1101/2020.07.04.20142752v1">https://www.medrxiv.org/content/10.1101/2020.07.04.20142752v1</a>
Lee et al	Retrospective (USA)	20 received IVIG, 17 received steroids, 5 received anakinra	N/A	28 children with MIS-C (median 9y/o, range 1mo - 17y/o)	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="http://www.jci.org/articles/view/141113">http://www.jci.org/articles/view/141113</a>
Liu et al	Retrospective (Hong Kong)	61/109 received IVIG; 72/109 received steroids	N/A	109 confirmed COVID-19 cases (mean age 55y/o; range 22-94)	Improvement in clinical status & laboratory parameters	no significant effect on in-hospital survival in pts with ARDS	Published (Pre-print)	<a href="https://www.medrxiv.org/content/10.1101/2020.02.17.20024166v3">https://www.medrxiv.org/content/10.1101/2020.02.17.20024166v3</a>
Chen et al	Case report (China)	IVIG + dexamethasone	N/A	38/M with severe thrombocytopenia	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://linkinghub.elsevier.com/retrieve/pii/S2352302620301757">https://linkinghub.elsevier.com/retrieve/pii/S2352302620301757</a>
Zulfiqar et al	Case report (France)	IVIG + heparin, antibiotics, prednisolone, eltrombopag	N/A	65/F with HPN, autoimmune hypothyroidism and pneumonia, cerebral bleeding	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="http://www.nejm.org/doi/10.1056/NEJMc2010472">http://www.nejm.org/doi/10.1056/NEJMc2010472</a>
Bomhof et al	Case series (Netherlands)	IVIG + dexamethasone	N/A	59/M with stage IV NET, 66/F with HPN. Both with ITP.	Improvement in clinical status & laboratory parameters	with clinical improvement	Published	<a href="https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16850">https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16850</a>

**Appendix 4.** Convalescent Plasma (CP) Studies for COVID 19

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Duan K, et al	Case series (China)	CP	NA	Patients with severe COVID 19 (10)	Safety of CP transfusion; improvement of clinical symptoms & laboratory parameters within 3 days after CP transfusion	No serious adverse events; 10 patients improved in 1-3 days; reduced pulmonary lesion on CT; amelioration of routine blood tests & pulmonary function; Increase IgG & (-) SARS-CoV-2	Published (Pre-rpint)	<a href="https://www.pnas.org/content/pnas/117/17/9490.full.pdf">https://www.pnas.org/content/pnas/117/17/9490.full.pdf</a>
Shen C, et al.	Case series (China)	CP + anti-viral agents + Methylprednisolone ± IFN α 1b	NA	Critically ill patients with COVID 19 (5)	Before and after CP transfusion: -Changes in body temp. -Sequential Organ Failure Assessment (SOFA) score -PaO2/FiO2 -Viral load, serum ab titers, routine blood tests index -ventilatory/ ECMO support	After CP: -normal body temp. D3 -SOFA score decreased -PaO2/FiO2 improved D7 -CRP, procalcitonin & IL 6 decreased -ARDS resolved D12 -weaned ventilator D14 -discharged/ stable D37	Published	<a href="https://www.ncbi.nlm.nih.gov/pubmed/32219428">https://www.ncbi.nlm.nih.gov/pubmed/32219428</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)

Joyner M, et al.	Expanded Access, open label, cohort (US)	CP with higher antibody level transfused within 3 days from diagnosis	CP with lower antibody level transfused after 3 days from diagnosis	COVID 19 $\geq 18$ y/o (3,082)	7 & 30-day mortality	Lower mortality rates among those who received CP with higher antibody level & among those who received CP earlier	Published (Pre-print: Initial 3-month experience)	<a href="https://clinicaltrials.gov/ct2/show/NCT04338360">https://clinicaltrials.gov/ct2/show/NCT04338360</a>
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#### Appendix 5. Alpha-1 ( $\alpha 1$ ) Adrenergic Receptor Antagonist Study for COVID

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Konig MF, et al.	Retrospective cohorts	$\alpha 1$ -AR antagonists	Without $\alpha 1$ -AR antagonists	COVID 19 adults on $\alpha 1$ -AR antagonists 1 <sup>st</sup> cohort (13,125); 2 <sup>nd</sup> cohort (108,956)	Preventing poor outcomes resulting from pulmonary hyper-inflammatory responses	Support a clinical rationale in preventing severe COVID-19 & states of immune dysregulation	Published	<a href="https://www.medrxiv.org/content/10.1101/2020.04.02.20051565v2.full.pdf">https://www.medrxiv.org/content/10.1101/2020.04.02.20051565v2.full.pdf</a>

#### Appendix 6-A. Antiviral Agent Studies for COVID 19: Favipiravir

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Chen C, et al.	Randomized, open label parallel assignment (China)	Favipiravir	Arbidol	COVID 19 18 – 99y/o (239)	Clinical recovery rate	Favipiravir: : no significant improvement in clinical recovery rate compared to Arbidol.	Published	<a href="https://www.medrxiv.org/content/10.1101/2020.03.17.20037432v4.full.pdf">https://www.medrxiv.org/content/10.1101/2020.03.17.20037432v4.full.pdf</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)

Cai Q, et al.	Non randomized Open label (China)	Favipiravir	LPV/r	COVID 19 16-75y/o (59)	Viral clearance; radiologic improvement	Favipiravir group appeared to have faster viral clearance & better chest imaging change compared to LPV/r.	Published	<a href="https://doi.org/10.1016/j.eng.2020.03.007">https://doi.org/10.1016/j.eng.2020.03.007</a>
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**Appendix 6-B.** Antiviral Agent Studies for COVID 19: Lopinavir/Ritonavir (LPV/r)

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Cao B, et al.	Randomized, open label, parallel assignment (China)	LPV/r	Standard Care	Severe COVID 19 >18y/o (199)	Time to clinical improvement & detectable viral RNA	No difference in the time to: - clinical improvement - detectable viral RNA	Published	<a href="https://www.nature.com/doi/full/10.1056/NEJMoa2001282">https://www.nature.com/doi/full/10.1056/NEJMoa2001282</a>
Yuan, J, et al.	Retrospective descriptive (correlation) (China)	LPV/r + Ribavirin + IFN $\alpha$	LPV/r + IFN $\alpha$	Discharged COVID 19 7-39y/o (94)	Viral clearance & biochemical outcomes of discharge COVID 19	SARS COv-2 conversion time was correlated with length of hospital stay & decline in CK & LDH between 2 groups, suggesting benefit for COVID 19	Published	<a href="https://link.springer.com/article/10.1007%2Fs00011-020-01342-0">https://link.springer.com/article/10.1007%2Fs00011-020-01342-0</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)

Li Y, et al.	Randomized, open label parallel assignment (China)	LPV/r; Arbidol	Standard care	Mild-moderate COVID 19 18-80 y/o (86)	At D7 & 14: -average time of (+) to (-) conversion of SARS-CoV-2 nucleic acid -improvement in symptoms & chest CT	No difference in: 1. (+) to (-) conversion rate; 2. improvement in symptoms & chest CT; more patients on LPV/r progressed to severe/critical status	Published (Pre-print)	<a href="https://www.medrxiv.org/content/10.1101/2020.03.19.20038984v2.full.pdf+html">https://www.medrxiv.org/content/10.1101/2020.03.19.20038984v2.full.pdf+html</a>
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**Appendix 6-C.** Antiviral Agent Studies for COVID 19: Remdesivir

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Grein J, et al.	Cohort study (US, Japan, Europe, Canada)	Remdesivir	NA	Severe COVID 19 23 – 52y/o (53)	Clinical improvement	Improvement observed in 36 of 53 patients (68%).	Published	<a href="https://www.nejm.org/doi/full/10.1056/NEJMoa2007016">https://www.nejm.org/doi/full/10.1056/NEJMoa2007016</a>
Wang Y, et al.	Randomized, quadruple double blind, parallel assignment (China)	Remdesivir	Placebo	COVID 19 patients >18 y/o (237)	Time to clinical improvement	No significant benefits for remdesivir over standard care	Published	<a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31022-9/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31022-9/fulltext</a>
Goldman,JD et al (NCT04292899)	Randomized, open label, parallel assignment (USA)	Remdesivir	Standard care	COVID 19 patients > 12y/o (6,000)	Odds of ratio for Improvement on a 7-point Ordinal Scale on D14	No significant difference between a 5-day course and a 10-day course of remdesivir.	Published	<a href="https://www.nejm.org/doi/full/10.1056/NEJMoa2015301">https://www.nejm.org/doi/full/10.1056/NEJMoa2015301</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)

NCT04280705 (NIH)	Randomized, double blind, parallel assignment (USA)	Remdesivir	Placebo	COVID 19 patients 18 – 99 y/o (1,063)	% of subjects reporting each severity rating	31% had faster time to recovery than placebo; median time to recovery (11 days) than placebo (15 days); mortality rate (8.0%) than placebo (11.6%)	Published	<a href="https://www.nih.gov/news-events/news-releases/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19">https://www.nih.gov/news-events/news-releases/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19</a>
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**Appendix 6-D.** Antiviral Agent Studies for COVID 19: Ribavirin

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Hung IFN, et al.	Randomized, open-label, Parallel assignment (Hongkong)	LPV/r + Ribavirin + IFN β-1B	LPV/r	Hospitalized Patients with COVID 19 ≥18 y/o (127)	Time to negative NPS for SARS-Cov-2 viral RT-PCR	LPV/r + Ribavirin + IFN β1B were safe & superior to LPV/r in shortening virus shedding, alleviating symptoms & facilitating discharge of patients with mild to moderate COVID 19.	Published	<a href="https://clinicaltrials.gov/ct2/show/NCT04276688?cond=interferon+in+covid-19&amp;draw=2&amp;rank=11">https://clinicaltrials.gov/ct2/show/NCT04276688?cond=interferon+in+covid-19&amp;draw=2&amp;rank=11</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)



Yuan, J, et al.	Retrospective descriptive (correlation) (China)	LPV/r + Ribavirin + IFN $\alpha$	LPV/r + IFN $\alpha$	Discharged COVID 19 7-39y/o (94)	Viral clearance & biochemical outcomes of discharge COVID 19	SARS COv-2 conversion time was correlated with length of hospital stay & decline in CK & LDH between 2 groups, suggesting benefit for treatment	Published	<a href="https://link.springer.com/article/10.1007%2Fs00011-020-01342-0">https://link.springer.com/article/10.1007%2Fs00011-020-01342-0</a>
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**Appendix 6-E.** Antiviral Agent Studies for COVID: Umifenovir (Arbidol)

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Li L, et al.	Retrospective cohort (China)	Arbidol	LPV/r + IFN	COVID 19 >18y/o (111)	Viral clearance, radiologic improvement; O2 therapy requirement	Arbidol could enhance viral clearance, chest CT improvement & reduce demand for O2 therapy	Published	<a href="https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3542148">https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3542148</a>
Zhang J, et al.	Retrospective case control (China)	Arbidol	Oseltamivir	Family members (66) or health care workers w/o std respiratory protection (124) exposed to COVID-19	Occurrence of fever or respiratory symptoms within 24 days of exposure & confirmed by RT-PCR	Arbidol could reduce the infection risk	Published	<a href="http://www.chinaxiv.org/abs/202002.00065">http://www.chinaxiv.org/abs/202002.00065</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)

Zhu Z, et al.	Retrospective (China)	Arbidol	LPV/r	COVID 19 >18y/o (50)	Detection of viral load on day 7 and day 14	No difference in fever duration; arbidol group had shorter duration of (+) RNA test compared to LPV/r	Published	<a href="https://doi.org/10.1016/j.jinf.2020.03.060">https://doi.org/10.1016/j.jinf.2020.03.060</a>
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**Appendix 7. Azithromycin ± Hydroxychloroquine (HCQ) Studies for COVID 19**

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Geleris J et al	Observational, prospective (USA)	HCQ + Statin or ACEi or ARB or CS or Anticoagulant or Azithromycin or Remdesivir or Tocilizumab	Statin; ACEi or ARB; CS; Anticoagulant; Azithromycin; Remdesivir; Tocilizumab	Hospitalized COVID 19 Adults (1,376)	Intubation or Death	No significant association between HCQ use & intubation or death.	Published	<a href="https://www.nejm.org/doi/full/10.1056/NEJMoa2012410?query=RP">https://www.nejm.org/doi/full/10.1056/NEJMoa2012410?query=RP</a>
Gautret P, et al.	Non-randomized, open label, parallel assignment (France)	HCQ; HCQ + Azithromycin	Standard care	Hospitalized COVID 19 patients >12 y/o (36)	Viral clearance at D6 post inclusion	Viral clearance at D6: HCQ + Azithromycin (100%); HCQ (57%); Control (12.5%). Effect is reinforced by Azithromycin.	Published	<a href="https://www.sciencedirect.com/science/article/pii/S0924857920300996?via%3Dihub">https://www.sciencedirect.com/science/article/pii/S0924857920300996?via%3Dihub</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)

Lane J, et al	Cohort studies; self-controlled case series (Germany, Japan, Netherlands, Spain, UK, USA)	HCQ + Azithromycin	Sulfasalazine + Amoxicillin	Rheumatoid arthritis patients ≥18y/o (1,941,802)	Intention to treat & risk of SAEs associated with short-term use	Addition of Azithromycin: prolonged hospital stay - heart failure & cardiovascular mortality (synergistic effects on QT length)	Published (Pre-print)	<a href="https://doi.org/10.1101/2020.04.08.20054551">https://doi.org/10.1101/2020.04.08.20054551</a>
Gautret P, et al.	Observational, prospective (France)	HCQ + Azithromycin	NA	COVID-19 >18 y/o (80)	Disease progression, need for oxygen, ICU admission	Death (1); Discharge (81.25%); Virologic clearance on day 7 (83%); Mean length hospital stay (5 days); O2 therapy (12); Transferred to ICU (3) AE: nausea, vomiting, diarrhea	Published	<a href="https://www.sciencedirect.com/science/article/pii/S0924857920300996?via%3Dihub">https://www.sciencedirect.com/science/article/pii/S0924857920300996?via%3Dihub</a>
Chorin E, et al.	Observational retrospective (USA)	HCQ + Azithromycin	None	COVID-19 >18 y/o (84)	Change in QT interval	Prolonged QTc (11%)	Published (Pre-print)	<a href="https://doi.org/10.1101/2020.04.02.20047050">https://doi.org/10.1101/2020.04.02.20047050</a>
Molina JM, et al.	Observational, prospective (France)	HCQ + Azithromycin	NA	Severe COVID-19 Adults (11)	Virologic presence after D6-7 of treatment	(+) virus in NPS on D7 of treatment (8/10)	Published	<a href="https://doi.org/10.1016/j.medmal.2020.03.006">https://doi.org/10.1016/j.medmal.2020.03.006</a>

**Appendix 8.** Calcineurin Inhibitors Studies for COVID 19: Cyclosporin A, Tacrolimus

Author/ Study	Study design	Intervention	Comparator	Population	Primary	Results	Status	Source
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Identifier					outcome			(hyperlink)
Banerjee D, et al	Case series (United Kingdom)	Tacrolimus + Azathioprine + CS; Azathioprine + CS; Tacrolimus + MMF	NA	COVID-19 who underwent renal transplant 45 – 69y/o (7)	Effect of immune-suppressive therapy on COVID 19 patients undergoing renal transplant	Suggest to suspend kidney transplant during the pandemic for high-risk recipients with comorbidities	Published	<a href="https://www.kidney-international.org/article/S0085-2538(20)30361-6/fulltext">https://www.kidney-international.org/article/S0085-2538(20)30361-6/fulltext</a>
Ning L, et al.	Case report (China)	Cyclosporin + LPV/r + CS	NA	COVID 19 who underwent renal transplant 29y/o (1)	Clinical presentation, severity & outcome of COVID 19 with solid organ transplant	Clinical recovery with no significant complications	Published	<a href="https://onlinelibrary.wiley.com/doi/epdf/10.1111/ajt.15897">https://onlinelibrary.wiley.com/doi/epdf/10.1111/ajt.15897</a>
Bhoori S, et al.	Case series (Italy)	Cyclosporine; Tacrolimus	NA	COVID 19 post-liver transplant >65y/o (3)	Effects of immunosuppressive therapy on post liver transplant recipients	All 3 patients died who rapidly developed ARDS	Published	<a href="https://www.thelancet.com/pdfs/journals/lan/gas/PIIS2468-1253(20)30116-3.pdf">https://www.thelancet.com/pdfs/journals/lan/gas/PIIS2468-1253(20)30116-3.pdf</a>

**Appendix 9.** Corticosteroids (CS) Studies for COVID 19: Methylprednisolone

Author/ Study Identifier	Study design (Country)	Intervention	Comparator	Population (Sample size)	Primary outcome	Results	Status	Source (hyperlink)
Wang Y, et al.	Observational, retrospective (China)	Methylprednisolone	Standard care	Severe COVID 19 pneumonia (46)	Clinical & radiographic outcome of treatment w/ or w/o CS	Early short term & low dose CS: faster improvement	Published (Pre-print)	<a href="https://www.researchgate.net/publication/339892221">https://www.researchgate.net/publication/339892221</a>
Author/ Study Identifier	Study design (Country)	Intervention	Comparator	Population (Sample size)	Primary outcome	Results	Status	Source (hyperlink)
Zhou ZG, et	Case series	Methylpredni	NA	Patients with	Reversion of	Short-term	Published	<a href="https://www.p">https://www.p</a>

al	(China)	solone moderate dose + IVIG		COVID 19 who have failed low dose CS (10)	continued deterioration of COVID-19 patients.	mod-dose CS + IVIG is effective for reversing the continued deterioration of COVID-19 patients.	(Pre-print)	<a href="https://reprints.org/manuscript/202003.0065/v1">reprints.org/manuscript/202003.0065/v1</a>
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**Appendix 10. Hydroxychloroquine (HCQ) and Chloroquine (CQ) Studies for COVID 19**

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Zhaowei C, et al.	Randomized, Open label, parallel assignment (China)	HCQ	Standard care	COVID-19 with pneumonia >18 y/o (62)	Normalization of body temperature, cough relief, CT changes	Normal body temperature: HCQ (2.2 days); Cough relief HCQ (2.0 days); Progression to severe illness: HCQ (0); CT improvement: HCQ (25); Adverse effects with HCQ: rash (1), Headache (1)	Published (Pre-print)	<a href="https://doi.org/10.1101/2020.03.22.20040758">https://doi.org/10.1101/2020.03.22.20040758</a>
Chen J, et al.	Randomized,	HCQ	Standard	Patients with	Negative	No significant	Published	<a href="http://www.zju">http://www.zju</a>

	open label, parallel assignment (China)		care	COVID 19 (30)	conversion rate of COVID 19 nucleic acid in respiratory pharyngeal swab on D7 after randomization.	difference in (-) nucleic acid throat swab, median duration from admission to virus nucleic acid (-) conversion, median time for normal body temp & radiological progression in CT images		<a href="https://journals.com/med/EN/10.3785/j.issn.1008-9292.2020.03.03">journals.com/med/EN/10.3785/j.issn.1008-9292.2020.03.03</a>
Borba MG, et al.	Randomized double blind, quadruple; parallel assignment (Brazil)	CQ (high dosage)	CQ (low dosage) + placebo	COVID 19 ≥18y/o (440)	Mortality rate reduction of 50% by D28	High dose CQ + Azithromycin is not recommended for critically ill COVID 19: Lethality until Day 13 (39% in high vs 15% in low dose); QTc prolongation (18.9% high vs 11.1% low dose)	Published	<a href="https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2765499?utm_campaign=articlePDF%26utm_medium%3darticlePDFlink%26utm_source%3darticlePDF%26utm_content%3djamanetworkopen.2020.8857">https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2765499?utm_campaign=articlePDF%26utm_medium%3darticlePDFlink%26utm_source%3darticlePDF%26utm_content%3djamanetworkopen.2020.8857</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Mahévas M,	Observation-	HCQ in 1 <sup>st</sup> 48	Standard	COVID-19	Transfer to	Death or	Pre print	<a href="https://doi.org">https://doi.org</a>

et al.	al, retrospective (France)	hours after hospitalisation	care	pneumonia 18-80 y/o (181)	ICU within 7 days of inclusion and/or death from any cause	transfer to ICU: HCQ (20.2%) Non-HCQ (22.1%); Death in 7 days: HCQ (2.8%) Non-HCQ (4.6%); Harm w/ QTc prolongation (8), AV block (1), LBBB (1)	(Pre-print)	<a href="https://doi.org/10.1101/2020.04.10.20060699">/10.1101/2020.04.10.20060699</a>
Gao J, et al.	Randomized control, parallel assignment (China)	CQ	Standard care	COVID 19 (>100)	Clinical improvement	Reduced symptom duration; inhibited pneumonia exacerbation; improved lung function; virus (-) conversion; w/o severe side effects	Published	<a href="https://www.jstage.jst.go.jp/article/bst/14/1/14_2020_01047/article">https://www.jstage.jst.go.jp/article/bst/14/1/14_2020_01047/article</a>

**Appendix 11.** Interferons (IFNs) Studies for COVID 19: IFN- $\alpha$ , IFN- $\beta$

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Qiu et al.	Retrospective cohort study (China)	IFN $\alpha$ + LPV/r	NA	Mild-moderate COVID 19 0-16y/o (36)	Clinical presentation; diagnostic findings; therapy & outcome	Pneumonia improved at D4-10; (-) NPS after 10 days; 14 days admitted	Published	<a href="https://www.thelancet.com/action/showPdf?pii=S1473-3099(2020)2930198-5">https://www.thelancet.com/action/showPdf?pii=S1473-3099(2020)2930198-5</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)

Zhou Q e al.	Non-randomized, retrospective (China)	IFN $\alpha$ -2B + Arbidol	IFN $\alpha$ -2B; Arbidol	COVID 19 Adults (77)	Clinical improvement	IFN- $\alpha$ 2b + arbidol reduced the duration of (+) SARS Cov-2 on NPS & of elevated IL-6 & CRP	Published	<a href="https://www.medrxiv.org/content/10.1101/2020.04.06.20042580v1.full.pdf+html">https://www.medrxiv.org/content/10.1101/2020.04.06.20042580v1.full.pdf+html</a>
Hung IFN, et al.	Randomized, open-label, parallel assignment (Hongkong)	LPV/r + Ribavirin + IFN $\beta$ -1B	LPV/r	Hospitalized Patients with COVID 19 $\geq$ 18 y/o (127)	Time to negative NPS for SARS-Cov-2 viral RT-PCR	LPV/r + Ribavirin + IFN $\beta$ 1B were safe & superior to LPV/r in shortening virus shedding, alleviating symptoms & facilitating discharge of patients with mild to moderate COVID 19.	Published	<a href="https://clinicaltrials.gov/ct2/show/NCT04276688?cond=interferon+in+covid-19&amp;draw=2&amp;rank=11">https://clinicaltrials.gov/ct2/show/NCT04276688?cond=interferon+in+covid-19&amp;draw=2&amp;rank=11</a>
Huang YQ, et al.	Randomized, open labeled,	Ribavirin + IFN- $\alpha$	LPV/r + IFN- $\alpha$ ; Ribavirin + LPV/r + IFN- $\alpha$	Mild to moderate COVID-19 18–65 y/o (101)	Difference in the interval from baseline to (-) NPS SARS-CoV-2 nucleic acid	No significant differences among the three regimens in terms of antiviral effectiveness in patients with mild to moderate COVID-19.	Published	<a href="file:///C:/Users/Vicky/Downloads/fphar-11-01071%20(1).pdf">file:///C:/Users/Vicky/Downloads/fphar-11-01071%20(1).pdf</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)



Monfared ED, et al.	Randomized, open label, Parallel assignment (Iran)	IFN $\beta$ -1a	Standard care	COVID-19 $\geq$ 18 y/o (42)	Time to reach clinical response	No change in the time to reach clinical response; increased discharge rates on D14 & decreased 28-day mortality in treatment group. IFN significantly improved survival if given early.	Published	<a href="https://aac.asm.org/content/aac/early/2020/07/08/AAC.01061-20.full.pdf">https://aac.asm.org/content/aac/early/2020/07/08/AAC.01061-20.full.pdf</a>
Dastan F, et al.	Prospective non-controlled (Iran)	IFN- $\beta$ -1a	NA	COVID-19 $\geq$ 18 y/o (20)	Symptoms remission	Significant decrease in viral clearance in 10 days; imaging studies with significant recovery after 14 days in all patients; no deaths or significant adverse drug reactions	Published	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7275997/pdf/main.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7275997/pdf/main.pdf</a>

**Appendix 12-A.** Targeted Monoclonal Antibody Studies for COVID 19: Anti-IL1: Anakinra

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Franzetti M, et al.	Case report (Italy)	Anakinra with Remdesivir	N/A	57-year old man with severe COVID-19 who refused ventilatory support	Improvement in clinical & laboratory parameters	Potential role of anakinra in treatment of respiratory dysfunction in COVID-19	Published	<a href="https://www.sciencedirect.com/science/article/pii/S120197122030357X">https://www.sciencedirect.com/science/article/pii/S120197122030357X</a>
Filocamo G, et al.	Case report (Italy)	Anakinra	N/A	50-year old man with COVID-19 who developed hepatic involvement	Improvement in clinical and laboratory parameters	The patient improved but developed bacteremia; anakinra is effective and safe.	Published	<a href="https://www.sciencedirect.com/science/article/pii/S1201971220303337">https://www.sciencedirect.com/science/article/pii/S1201971220303337</a>
Karadeniz H, et al.	Case report (Turkey)	Anakinra	N/A	33-year-old male affected by COVID-19 complicated by pericarditis	Clinical and laboratory improvement after unsuccessful colchicine and indomethacin therapy	Anakinra is an effective and reliable option in COVID-19-associated pericarditis	Published	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7391046/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7391046/</a>
Cauchois R, et al.	Prospective cohort (USA)	Anakinra	Standard care (10)	COVID-19 pneumonia in patients with a positive PCR (12)	Clinical improvement	Significant clinical improvement consisting of the NEWS score at day 5 (p<0.01)	Published	<a href="https://www.pnas.org/content/early/2020/07/21/2009017117">https://www.pnas.org/content/early/2020/07/21/2009017117</a>
Gonzalez-Garcia A, et al.	Case report (Spain)	Anakinra	N/A	47-y/o man with COVID-19, asthma & intolerance to CS	Clinical improvement	High dose SC anakinra had no safety problems.	Published	<a href="https://academic.oup.com/rheumatology/article/59/8/2171/5860797">https://academic.oup.com/rheumatology/article/59/8/2171/5860797</a>
Author/ Study	Study design	Intervention	Comparator	Population	Primary	Results	Status	Source

Identifier					outcome			(hyperlink)
Dimopoulos G, et al.	Case series (Greece)	Anakinra	N/A	COVID-19 patients with secondary hemophagocytic lymphohistiocytosis (8)	Severe respiratory failure leading to mechanical ventilation and death	All patients had improvement in their respiratory function at the end of treatment (7 days) but 3 patients later died of refractory shock (mortality still lower than historical series of patients with sHLH in sepsis)	Published	<a href="https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(20)30289-4?returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1931312820302894%3Fshowall%3Dtrue">https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(20)30289-4?returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1931312820302894%3Fshowall%3Dtrue</a>
Huet T, et al.	Retrospective cohort study (France)	Anakinra	Standard of care using historical control (44)	COVID-19 patients >18 y/o with severe COVID-19-related bilateral pneumonia (52)	Need for admission to the ICU with invasive mechanical ventilation or death	Need for invasive mechanical ventilation or death occurred in 13 (25%) of 52 patients in the anakinra group compared with 32 (73%) of 44 patients in the historical group (HR 0.22 [95% CI 0.11–0.41; p<0.0001)	Published	<a href="https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30164-8/fulltext">https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30164-8/fulltext</a>
Author/ Study	Study design	Intervention	Comparator	Population	Primary	Results	Status	Source

Identifier					outcome			(hyperlink)
Navarro-Millan I, et al.	Retrospective case series (USA)	Anakinra	N/A	Patients with COVID-19, AHRF, and signs and symptoms of CSS (14)	Prevention of mechanical ventilation (MV)	8 of 14 patients treated with early initiation of anakinra did not require MV or avoided recurrent MV; 3 patients with late-initiation of anakinra required MV; 3 patients who did not receive anakinra required MV	Published	<a href="https://doi.org/10.1002/art.41422">https://doi.org/10.1002/art.41422</a>
Figuro-Pérez L, et al.	Case report (Spain)	Anakinra	N/A	51 y/o man with COVID 19, COPD, liver cirrhosis & rectal CA refractory to antiviral & anti-IL-6	Clinical improvement	The patient had clinical improvement in 48 hours	Published	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7298486/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7298486/</a>
Pontali E, et al.	Case series (Italy)	Anakinra	N/A	COVID-19 patients (5)	Resolution of systemic inflammation and improvement in respiratory parameters	All 5 patients experienced rapid resolution of systemic Inflammation & remarkably improved in respiratory parameters	Published	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7211718/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7211718/</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)

Cavalli G, et al.	Retrospective cohort study (Italy)	Anakinra	Standard treatment (16)	COVID-19 patients >18 y/o with moderate to severe ARDS	Survival	At D21: survival was 90% in the high-dose anakinra group & 56% in the standard treatment group. Treatment with low dose anakinra was stopped after 7 days due to paucity of effects in CRP & clinical status.	Published	<a href="https://doi.org/10.1016/S2665-9913(20)30127-2">https://doi.org/10.1016/S2665-9913(20)30127-2</a>
Day JW, et al.	Case series (United Kingdom)	Anakinra	N/A	three patients with acute leukaemia and confirmed or suspected COVID-19 pneumonia with a life-threatening hyper-inflammatory syndrome	Clinical improvement	IL-1 blockade with anakinra was safe and resulted in clinical improvement in patients with acute leukemia	Published	<a href="https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.16873">https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.16873</a>
Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)

Aouba A, et al.	Prospective case series (France)	Anakinra	N/A	Moderate to severe COVID-19 pneumonia at high risk of worsening >18 y/o (9)	Avoidance of mechanical ventilation	1 patient developed acute respiratory failure after 1 dose; the 8 other patients had good clinical & biologic outcomes	Published	<a href="https://ard.bmj.com/content/annrheumdis/early/2020/05/05/annrheumdis-2020-217706.full.pdf">https://ard.bmj.com/content/annrheumdis/early/2020/05/05/annrheumdis-2020-217706.full.pdf</a>
Langer-Gould, et al.	Retrospective cohort study (USA)	Anakinra	Tocilizumab	COVID 19 treated with at least 1 dose of tocilizumab or anakinra to treat cytokine storm (93)	Treatment failure (death) & treatment response	The risk of death was lower in anakinra group than tocilizumab group; % of anakinra treatment responders was higher; this difference did not reach statistical significance	Published (Pre-print)	<a href="https://pubmed.ncbi.nlm.nih.gov/32768693/">https://pubmed.ncbi.nlm.nih.gov/32768693/</a>

**Appendix 12-B.** Targeted Monoclonal Antibody Studies for COVID 19: Anti-IL-6: Tocilizumab

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Sciascia S et al.	Prospective open label, single-arm (Italy)	Tocilizumab	NA	Severe COVID 19 50 -74y/o (63)	Improvement in clinical & laboratory parameters	Associated w/ increased likelihood of survival within 6 days of treatment	Published	<a href="https://www.clinexprheumatol.org/article.asp?a=15723">https://www.clinexprheumatol.org/article.asp?a=15723</a>
Author/ Study	Study design	Intervention	Comparator	Population	Primary	Results	Status	Source

Identifier					outcome			(hyperlink)
Xu et al.	Observational, prospective (China)	Tocilizumab + LPR + Methylprednisolone	NA	Severe or critical COVID-19 (21)	Normalization of body temperature, O2 sat & improvement in CT scan findings	After day 1 of Tocilizumab: normal temperature; improved SpO <sub>2</sub> & resolution of lung opacities	Published	<a href="http://www.chinaxiv.org/abs/202003.00026">http://www.chinaxiv.org/abs/202003.00026</a>

**Appendix 12-C. Targeted Monoclonal Antibody Studies for COVID 19: JAK 1 and 2 Inhibitors: Baricitinib**

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Sodani P, et al.	Case report (Italy)	Baricitinib + Tocilizumab + Remdesivir + HCQ	NA	COVID 19 pneumonia with follicular non-Hodgkin lymphoma in remission 50 y/o male	NA	Successful recovery	Published	<a href="https://reader.elsevier.com/reader/sd/pii/S2213007120302574?token=87453CD0C3FAE748CE67E0967BE784314E2A36DE085896543F3CDF4981A1A128AB74BAE11C21A16C1ED8D76D8B814E14">https://reader.elsevier.com/reader/sd/pii/S2213007120302574?token=87453CD0C3FAE748CE67E0967BE784314E2A36DE085896543F3CDF4981A1A128AB74BAE11C21A16C1ED8D76D8B814E14</a>
Cantini F, et al.	Non-randomized, open label, cross over assignment (Italy)	Baricitinib	Standard care	COVID 19 with pneumonia 18 – 85y/o (12)	Safety of Baricitinib combined with LPV/r in terms of adverse events incidence rate	Both at week 1 & week 2, Baricitinib therapy significantly improved clinical & laboratory parameters, none required ICU support, & majority were discharged.	Published (Pre-print)	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7177073/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7177073/</a>

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Caputo SL, et al.	Case report (Italy)	Baricitinib + LPV/r + HCQ	LPV + HCQ	Mild – moderate COVID 19 87 y/o wife, 90 y/o husband, 59 y/o son	NA	The wife given Baricitinib recovered while the husband and son not given Baricitinib died	Published	<a href="https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.26033">https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.26033</a>
Titanji BK, et al.	Non-controlled Retrospective cohort (USA)	Baricitinib + HCQ	NA	Moderate – severe COVID 19 (15)	Recovered; not recovered; died	12 (73.3%) recovered with no fever, decreased inflammatory markers & need for O2; 3 (13.3%) died with secondary bacterial or fungal infections.	Published (Pre-print)	<a href="https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1210/5892909">https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1210/5892909</a>
Cingolani A, et al.	Case report (Italy)	Baricitinib	NA	COVID 19 ARDS with incomplete response to standard care & Sarilumab 71 y/o male	NA	Significant decreased serum IL6 levels & clinical/ radiologic improvement after 2 weeks treatment with Baricitinib	Published	<a href="https://link.springer.com/content/pdf/10.1007/s15010-020-01476-7.pdf">https://link.springer.com/content/pdf/10.1007/s15010-020-01476-7.pdf</a>



**Appendix 13.** H2 Receptor Blocker Studies for COVID 19: Famotidine

Author/ Study Identifier	Study design	Intervention	Comparator	Population	Primary outcome	Results	Status	Source (hyperlink)
Janowitz T, et al	Case series (USA)	Famotidine	NA	COVID 19 20 - 70y/o (10)	COVID 19 symptom scores	Suggested high dose oral famotidine is well tolerated & associated with improved outcomes	Published	<a href="https://gut.bmj.com/content/early/2020/06/10/gutjnl-2020-321852">https://gut.bmj.com/content/early/2020/06/10/gutjnl-2020-321852</a>
Freedberg DE, et al	Retrospective cohort (USA)	Famotidine	Standard care	COVID 19 ≥18y/o (1620)	Composite of death or endotracheal intubation	famotidine use was associated with a reduced risk of clinical deterioration leading to intubation or death	Published	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7242191/pdf/main.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7242191/pdf/main.pdf</a>
Cheung KS, et al	Retrospective cohort (Hong Kong)	Famotidine	Standard care	COVID 19 ≥18y/o (952)	Severe disease	Did not support any association between famotidine & COVID-19 severity	Published (Pre-print)	<a href="https://www.gastrojournal.org/article/S0016-5085(20)34940-4/pdf">https://www.gastrojournal.org/article/S0016-5085(20)34940-4/pdf</a>