**Supplementary Table 1. Studies included in the analysis**

| Study (First Name) | Country | N  | Intervention (N of patients) | Comparisons (N of Patients) | Details on agents included (or excluded) in the Standard of Care | CODE | Participants |
|--------------------|---------|----|-----------------------------|----------------------------|---------------------------------------------------------------|------|--------------|
| 1. Abbaspour Kasgari 2020 | IR      | 48 | 1. Sofosbuvir + Daclatasvir + Ribavirin N=24; 2. SoC N=24 | HydroxyChl + Lop/Rit, with or without ribavirin | SoC+ | NR |
| 2. Abd-Elsalam 2020a | EG      | 194| 1. HydroxyChl +SoC N=97; 2. SoC N=97 | Paracetamol, O2, fluids, antibiotic (cephalosporins), oseltamivir, and invasive mechanical ventilation with Hydrocort for severe cases | SoC+ | severe |
| 3. Abd-Elsalam 2020b | EG      | 191| 1. HydroxyChl +Zinco+ SoC N=96; 2 SoC N=95 | No details on SoC reported | SoC- | moderate, severe |
| 4. ACTIV-3/TICO USA, DK, SGP | 326 | 1. LY-CoV555 +SoC N= 169; 2. Placebo + SoC N= 157 | Remdes, O2 and glucocorticoids | SoC+; P | NR |
| 5. Ader 2021 | FR      | 604| 1. Lop/Rit N=150; 2. Lop/Rit + interferon beta 1a N= 150; 3. HydroxyChl N=151; 4. SoC N=152 | No details on SoC reported | SoC-; A+ | moderate, severe |
| 6. Agarwal 2020 (PLACID trial) | IN      | 464| 1. Plasma C +SoC N=235; 2. SoC N=229 | HydroxyChl, Remdes, Lop/Rit, Oseltamivir, broad-spectrum antibiotics, steroids, Tocilizumab and supportive therapy (O2 via nasal cannula, face mask, non-respiratory face mask; non-invasive or invasive mechanical ventilation | SoC+ | moderate |
| No. | Author Year | Country | No. of Patients | Treatment Details |
|-----|-------------|---------|----------------|------------------|
| 7. | Ahmed 2020 | BD      | 72             | 1. Ivermectin N=24; 2. Ivermectin + Doxycycline N=24; 3. Placebo N=24 | Placebo | P | NR |
| 8. | Alavi Darazam 2020 | IR      | 60             | 1. Interferon beta 1 a N=20; 2. Interferon beta 1 b N=20; 3. SoC | Lop/Rit + HydroxyChl (single dose) | SoC+ | moderate |
| 9. | AlQahtani 2020 | BRN     | 40             | 1. Plasma C N=20; 2. SoC N=20 | Paracetamol, antivirals, tocilizumab, antibiotics | SoC+ | moderate |
| 10. | Ansarin 2020 | IR      | 78             | 1. Bromesine hydrochloride N=39; 2. SoC N=39 | All patients received national COVID-19 treatment protocol and best practice guidelines and also the “HydroxyChl 200 mg/d for two weeks” in addition to supportive and symptomatic therapy. | SoC+ | moderate |
| 11. | Avendaño-Solà 2020 | E       | 81             | 1. Plasma C + SoC N=38; 2. SoC N=43 | No details on SoC reported | SoC- | moderate |
| 12. | Babalola 2021 | NG      | 62             | 1. Ivermectina (6mg) N=21; 2. Ivermectina (12mg) N=21; 3. Lop/Rit N=20 | No SoC | A+ | NR |
| 13. | Bajpai 2020 | IN      | 31             | 1. Plasma C N= 15; 2. Fresh frozen plasma N= 16 | No SoC | A+ | Severe |
| 14. | Balykova 2020 | RUS     | 200            | 1. Favipiravir N=100; 2. SoC N=100 | No details on SoC reported | SoC- | moderate |
| 15. | Beigel 2020 | USA, DK, UK, GR, DE, KR, MEX, ES, JP SGP | 1062 | 1. Remdes + SoC N=541; Placebo + SoC N=521 | No details on SoC reported | SoC-; P severe, moderate |
| 16. | Blum 2021 | BR      | 50             | 1. Nitazoxanide N=25; 2. Placebo N=25 | NO SoC | P | moderate |
| 17. | Brown 2020 | USA     | 85             | 1. HydroxyChl; 2. Azithro | NO SoC | A+ | NR |
|   | Author   | Country | Study ID | Study Design | Patients | Treatments | Outcome |
|---|----------|---------|----------|--------------|----------|------------|---------|
| 18. | Cadegiani 2020 | BR | 214 | 1. Proxalutamide + SoC N=114; 2. Placebo + SoC N=100 | Nitazoxanide, Azithro | SoC+; P | moderate |
| 19. | Cadegiani 2021 a | BR | 130 | 1. Dutasteride + SoC N=64; 2. Placebo+ SoC N=66 | Nitazoxanide, Azithro | SoC+; P | moderate |
| 20. | Cadegiani 2021 b | BR | 236 | 1. Proxalutamide + SoC N=171; 2. Placebo + SoC N=65 | Nitazoxanide, Azithro | SoC+; P | moderate |
| 21. | Cao B 2020 | CN | 199 | 1. Lop/Rit + SoC N=99; 2. SoC N=100 | Supplemental O2, noninvasive and invasive ventilation, antibiotic agents, vasopressor support, renal-replacement therapy, and extracorporeal membrane O2ation | SoC+ | severe |
| 22. | Cao Y 2020 | CN | 43 | 1. Ruxolitinib + SoC N=22; 2. SoC N=21 | Antiviral therapy, supplemental O2, non-invasive and invasive ventilation, corticosteroids, antibiotic agents, vasopressor support, renal replacement therapy and extracorporeal membrane O2ation (ECMO) +Placebo (100mg vitamin C) | SoC+; P | severe |
| 23. | Castillo 2020 | E | 76 | 1. Calcifediol N=50; 2. SoC N=26 | Hospital protocol: a combination of HydroxyChl and Azithro | SoC+ | moderate/severe |
| 24. | Cavalcanti 2020 | BR | 667 | 1. HydroxyChl + Azithro + SoC N=217; 2. HydroxyChl + SoC N=221; 3. SoC N=229 | O2; antibiotics, corticosteroids, other immunomodulators (e.g., tocilizumab), other antivirals (e.g., oseltamivir for suspected influenza coinfection), as recommended by the attending physician. | SoC+ | mild, moderate |
| 25. | Chaccour 2021 USA | 24 | 1. Ivermectin N=12; 2. Placebo N=12 | No SoC | P | Mild |
| No. | Author Year | Country | Study Design | Groups | Interventions | Details | Severity |
|-----|-------------|---------|--------------|--------|---------------|---------|----------|
| 26. | Chen C 2020 | CN      | 236          | 1. Favipiravir + SoC N=116; 2. Umifenovir + SoC N=120 | Routine therapy but the details are No details on SoC reported. Other drugs were used for conventional therapy and symptomatic treatment to improve adverse reactions: Antibiotic, Antiviral drugs Glucocorticoid, Chinese herbal medicine, Psychotropic substances, Immunomodulator, Nutritional support | SoC+; A+ moderate/severe |
| 27. | Chen CP 2020 | TW      | 33           | 1. HydroxyChl N=21; 2. SoC N=12 | Ceftriaxone; or levofloxacin or moxifloxacin for subjects allergic to ceftriaxone or Azithro or according to physician discretion. Oseltamivir will be administered for 5 days to subjects presenting with concomitant influenza A or B infection. | SoC+ Mild, moderate |
| 28. | Chen J 2020 A | CN      | 30           | 1. HydroxyChl N=15; 2. HydroChloroq N=12; 3. SoC N=10 | O2 therapy, and symptomatic supportive treatment. Viral drugs such as alpha interferon nebulization, oral Lop/Rit (clepivir), etc., and antibacterial drugs are given if necessary. | SoC+; A+ moderate |
| 29. | Chen J 2020 B | CN      | 30           | 1. Darunavir/Cobicistat +SoC N=15; 2. SoC N=15 | Interferon alpha 2b and the standards of care according to the recommendations of the guidelines in China | SoC- moderate |
| No. | Author(s) Year | Country | Subjects | Interventions | Comments |
|-----|----------------|---------|----------|---------------|----------|
| 30. | Chen L 2020    | CN      | 67       | 1. Chloroq N=25; 2. HydroxyChl N=28; 3. SoC N=14 | Chinese diagnosis and treatment protocol for new coronavirus pneumonia (5th edition) |
|     |                |         |          |               | SoC-; A+ moderate |
| 31. | Chen Z 2020    | CN      | 62       | 1. HydroxyChl + SoC N=31; 2. SoC N=31 | O2 therapy, antiviral agents, antibacterial agents, and immunoglobulin, with or without corticosteroids |
|     |                |         |          |               | SoC+ moderate |
| 32. | Cheng LL 2020  | CN      | 200      | 1. Human Granulocyte Colony Stimulating Factor (rhG-CSF) + SoC N=100; 2. SoC N=100 | Supplemental O2, non-invasive ventilation, or intravenous antibiotics when indicated |
|     |                |         |          |               | SoC- moderate/severe |
| 33. | Chowdhury 2020 | BW      | 125      | 1. Ivermectin + Doxycycline N=63; 2. HydroxyChl + Azithro N=62 | No SC |
|     |                |         |          |               | A+ mild |
| 34. | Chowdhury 2021 | BW      | 606      | 1. Povidone iodine + symptomatic treatment N=303; 2. Lukewarm water (placebo) + symptomatic treatment N=303 | Placebo |
|     |                |         |          |               | P mild |
| 35. | CORIMUNO trial 2021 | FR | 116     | 1. Anakinra (interleukin 1 antagonist) + SoC N=59; 2. SoC N=57 | Usual care (antibiotic drugs, antiviral drugs, corticosteroids, vasopressor support, anticoagulants) was provided at the discretion of the site clinicians. |
|     |                |         |          |               | SoC- mild/moderate/severe/critical |
| 36. | Corral-Gudino 2020 | E      | 63       | 1. Corticosteroid (Metylprednisolone)+ SoC N=34; 2. SoC N=29 | Symptomatic treatment with paracetamol, O2 therapy, thrombosis prophylaxis with low molecular weight heparin and antibiotics for co-infections. Azithro, HydroxyChl and Lop/Rit |
|     |                |         |          |               | SoC+ severe |
| 37. | Dabbous 2020   | EG      | 100      | 1. Favipiravir N=50; 2. SoC N=50 | HydroxyChl + oseltamivir |
|     |                |         |          |               | SoC+ mild/moderate |
|   | Author                  | Country | Year | 1. Treatment | 2. Treatment | Comparator | Grade | Condition       |
|---|-------------------------|---------|------|--------------|--------------|------------|-------|-----------------|
| 38. | Dabbous 2021            | EG      | 96   | Favipiravir N=44; | Chloroq N=48 | No SoC     | A+    | mild / moderate |
| 39. | Davoudi-Monfared 2020  | IR      | 92   | Interferon β-1a + SoC N=46; | SoC N=46 | Hospital protocol: HydroxyChl + Lop/Rit or atazanavir/ritonavir for 7-10 days. Primary care, respiratory support, fluids, electrolytes, analgesics, antipyretics, corticosteroids and antibiotics have also been recommended in the hospital protocol if indicated. | SoC+ | mild /severe   |
| 40. | Deftereos 2020_GRECCO Trial | GR      | 110  | Colchicine N=56; | SoC N=54 | No details on SoC reported | SoC- | NR             |
| 41. | Dequin 2020             | FR      | 149  | Corticosteroid (Hydrocortison) + SoC N=76; | Placebo + SoC N=73 | No details on SoC reported | SoC+P | Severe and critical |
| 42. | Duarte 2020             | RA      | 82   | Telmisartan +SoC N=41; | SoC N=41 | No details on SoC reported | SoC- | NR             |
| 43. | Dubée 2020              | FR      | 250  | HydroxyChl + SoC N=125; | Placebo + SoC N=125 | Concomitant treatment with Azithro, Lop/Rit, treatment with corticosteroids | SoC+ | Mild, moderate |
| 44. | Edalatifard 2020       | IR      | 68   | Methylprednisolone + SoC N=34; | SoC N=34 | HydroxyChl sulfate, Lopinavir, and Naproxen | SoC+ | severe         |
| 45. | Esquivel-Moynelo 2020  | C       | 79   | Interferon alfa 2b + interferon gamma + Lop/Rit + Chloroq N=41; | Interferon alfa 2b + Lop/Rit + Chloroq N=38 | No SC | A+    | mild-to-moderate |
| 46. | Feld 2020               | CA      | 60   | Perginterferon lambda N=30; | Placebo N=30 | No SC | P    | mild           |
| 47. | Furtado 2020           | BR      | 447  | HydroxyChl + Azithro N=237; | HydroxyChl N=210 | No SC | A+    | moderate/severe |
|   | Study          | Country | N.  | Treatments                                                                 | SoC          | SC   | Outcome   |
|---|----------------|----------|-----|----------------------------------------------------------------------------|--------------|------|-----------|
| 48. | Galan 2021    | E        | 168 | 1. HydroxyChl N=54; 2. Chloroq N=61; 3. Ivermectin N=53                  | No SC        |      | A+        |
|     |                |          |     |                                                                            |              |      | mild      |
| 49. | Gharbharan 2020 | NL       | 86  | 1. Plasma C + SoC N=43; 2. SoC N=43                                      | Depending on the hospital, off-label use of EMA-approved drugs (e.g., Chloroq, Azithro, Lop/Ritr, tocilizumab, anakinra) as treatment for COVID-19 was allowed in hospitals where this was part of the SC |      | SoC+      |
|     |                |          |     |                                                                            |              |      | moderate/critical |
| 50. | Ghandehari 2021 | USA      | 42  | 1. Progesterone + SoC N=18; 2. SoC N=22                                 | No details on SoC reported |      | SoC-      |
|     |                |          |     |                                                                            |              |      | moderate   |
| 51. | Garebaghi 2020 | IR       | 59  | 1. Immunoglobulin + SoC N=157; 2. Placebo + SoC N=155                  | All patients continued to receive initial treatments including methods including at least both one antiviral and one Chloroq-class drug |      | SoC+      |
|     |                |          |     |                                                                            |              |      | severe     |
| 52. | Gonzalez-Ochoa 2020 | MEX     | 312 | 1. Sulodexide; 2. Placebo                                               | No SoC       |      | P         |
|     |                |          |     |                                                                            |              |      | mild      |
| 53. | Gottlieb 2021 | USA      | 592 | 1. LY-CoV555 700mg N=101; 2. LY-CoV555 2800mg N=107; 3. LY-CoV555 7000mg N=101; 4. LY-CoV555 2800mg+Etesevimab 2800 N=112; 5. Placebo N=156 | No SoC       |      | P         |
|     |                |          |     |                                                                            |              |      | mild/moderate |
| 54. | Guvenmez 2020 | TR       | 24  | 1. Lincomycin N=12; 2. Azithro N=12                                       | No SoC       |      | A+        |
|     |                |          |     |                                                                            |              |      | moderate   |
|   | Study           | Country | Year | N | Treatment 1 and 2 | Clinical Condition | Treatment 3 | Outcome |
|---|----------------|---------|------|---|-------------------|---------------------|-------------|---------|
| 55. | Hashim 2020   | IR      | 2020 | 140 | Ivermectina + Doxiciclina N=70; SoC N=70 | All or some of the following, according to the clinical condition of each patient: Acetaminophen; Vitamin C; Vitamin D3; Azithro; O2 therapy/ C-Pap if needed; Dexamethazone or methylprednisolone, if needed | SoC+ | moderate/severe |
| 56. | Hermine 2020  | FR      | 2020 | 131 | Tocilizumab + SoC N=64; SoC N=67 | All patients received antibiotic agents, antiviral agents, corticosteroids, vasopressor support, anticoagulants | SoC+ | moderate/critical |
| 57. | Hernandez-Cardenas 2021 | MEX | 2021 | 214 | HydroxyChl + SoC N=108; Placebo + SoC N=106 | Clarithromycin or Azithro; carbapenem; Oseltamivir; Lop/Rit; anticoagulants; corticosteroids (Methylprednisolone or Dexamethasone) | SoC+ | moderate |
| 58. | Ho 2021       | USA     | 2021 | 4313 | Corticosteroids N=574; SoC N=3739 | Adjuvant therapies, including tocilizumab and anticoagulants | SoC+ | moderate/severe |
| 59. | Huang 2020    | CN      | 2020 | 22  | Chloroq N=10; Lop/Rit N=12 | No SoC | A+ | moderate/severe |
| 60. | Huang Y-Q 2020 | CN | 2020 | 101 | Ribavirin plus Interferon α N=33; Ribavirin + Lop/Rit + Interferon α N=36; Lop/Rit + Interferon α N=32 | No SoC | A+ | moderate |
| 61. | Hung 2020     | CN      | 2020 | 127 | Lop/Rit + ribavirin + interferone β -1b + SoC N=86; Lop/Rit + SoC N=41 | O2 therapy; non-invasive ventilation; supportive ventilation; antibiotics; corticosteroids. | SoC+; A+ | moderate |
|   | Author          | Country | N  | Treatment 1                                         | Treatment 2                                      | SoC Description | SoC+ Description |
|---|-----------------|---------|----|----------------------------------------------------|-------------------------------------------------|-----------------|------------------|
|62.| Ivashchenko     | RU      | 60 | 1. Favipiravir (1600/600 mg) N=20; 2. Favipiravir (1800/800 mg) N=20; 3. SoC N=20 | No details on SoC reported | SoC- | moderate |
|63.| Jagannathn      | USA     | 120| 1. Peginterferon Lambda-1a (180mcg in single dose) N=60; 2. Placebo N=60 | No SoC | P |
|64.| Jamaati 2021    | IR      | 50 | 1. Dexamethasone +SoC N=25; 2. SoC N=25 | O2 support, fluid support, Lop/Ritr | SoC+ | moderate |
|65.| Jeronimo 2020   | BR      | 416| 1. Corticosteroid (Methylprednisolone) + SoC N=209; 2. Placebo + SoC N=207 | All patients received a combination of ceftriaxone plus a macrolide. All patients meeting ARDS criteria used pre-emptively intravenous ceftriaxone plus Azithro or clarithromycin | SoC+; P | moderate to critical |
|66.| Johnston 2021   | USA     | 231| 1. HydroxyChl + Azithro N=77; 2. HydroxyChl N=71; 3. Placebo-equivalent (ascorbic acid and folic acid) N=83 | No SoC | A+; P | moderate |
|67.| Joong 2021      | ROK     | 307| 1. CT-P59 40 mg/kg N=101; 2. CT-P59 80 mg/kg N=103; 3. Placebo N=103 | No SoC | P | mild-to-moderate |
|68.| Kalil 2020      | USA     | 103| 1. Remdes +Baricitinib N=515; 2. Placebo+Remdes N=518 SC | No SoC | A+; P | mild |
|69.| Kamran 2020     | PK      | 500| HydroxyChl + SoC N=349; 2. SoC N=151 | Vitamin C, vitamin D, zinc and tablet Paracetamol | SoC+ | mild |
|70.| Khamis 2020     | OM      | 89 | 1. Favipiravir + Interferon β 1b N=44; 2. HydroxyChl N= 44 | Standard care based on the national guidelines that had HydroxyChl | SoC+ | moderate/severe |
|71.| Kirti 2021      | IN      | 115| 1. Ivermectin + SoC N=55; 2. Placebo N=57 +SoC | No details on SoC reported | SoC-; P | mild-to-moderate |
| No. | Study | Country | No. | Treatment 1 | Treatment 2 | Comparator | No details on SoC reported | Description |
|-----|--------|---------|-----|-------------|-------------|-----------|---------------------------|-------------|
| 72. | Krolewicki 2020 | RA | 45 | 1. Ivermectin N=30; 2. SoC N=15 | No details on SoC reported | SoC- | mild-to-moderate |  |
| 73. | Kumar 2020 | IN | 32 | 1. Ivermectin + SoC N= 22; 2. SoC N=10 | O2, antibiotics, HydroxyChl, antivirals, steroids, low molecular weight heparin and vitamins | SoC+ | severe |  |
| 74. | Lanzoni 2021 | USA | 24 | 1. Umbilical cord mesenchymal stem cell (UCMSC) infusions + SoC N=12; 2. SoC N=12 | Best standard of care was provided in both groups following the current institutional COVID-19 guidelines. | SoC- | NR |  |
| 75. | Lemos 2020 | BR | 20 | 1. Enoxaparin N= 10; 2. Placebo N=72 | No details on SoC reported | SoC- | severe |  |
| 76. | Lenze 2020 | USA | 152 | 1. Fluvoxamine N=80; 2. Placebo N=72 | No SC | P | NR |  |
| 77. | Lescure 2021 | RA, BR, CA, RCH, FR, DE, IS, I, JA, RU, E | 416 | 1. Sarilumab 400 mg +SoC N=173; 2. Sarilumab 200 mg +SoC N=159; 3. Placebo +SoC N=84 | Clarithromycin or Azithro; carbapenem; Oseltamivir; Lop/Rit; anticoagulants; corticosteroids (Methylprednisolone or Dexamethasone) | SoC+; P | severe |  |
| 78. | Li C 2021 | CN | 94 | 1. genetically engineered recombinant super-compound interferon (rSIFN-co) + SoC N=46; 2. traditional interferon-alpha + SoC N=48 | Lop/Rit or umifenovir | SoC+ | moderate-to-severe |  |
| 79. | Li L 2020 | CN | 103 | 1. Plasma C N=52; 2. SoC N=51 | Support assistance for COVID-19, based primarily on China’s evolving national COVID-19 treatment guidelines and hospital practice. Possible treatments include antiviral drugs, antibacterial drugs, | SoC+ | Severe/critical |  |
steroids, human immunoglobulins, Chinese herbal medicines and other drugs.

| Study | Year | Country | N | Treatment 1 | Treatment 2 | Intervention | Outcome |
|-------|------|---------|---|-------------|-------------|-------------|---------|
| Li T 2020 | CN | 18 | 1. Bromhexine Hydrochloride N=12; 2. SoC N=6 | Antiviral drugs, including arbidol hydrochloride granules (0.1g-0.2g tid) and recombinant human interferon α2b spray (0.083ml tid), | SoC+ | mild-to-moderate |
| Li Y 2020 | CN | 86 | 1. Lop/Rit (200mg) + SoC N=34; 2. Umifenovir (100mg) + SoC N=35; 3. SoC N=17 | Support assistance and O2 therapy | SoC- | mild-to-moderate |
| Libster 2020 | RA | 160 | 1. Plasma C N=80; 2. Placebo N=80 | No SoC | P | mild |
| Liesenborghs 2020 | B | 65 | 1. Itraconazole N=32; 2. SoC N=33 | No details on SoC reported | SoC- | NR |
| Lopes 2020 | BR | 75 | 1. Colchicine + SoC N= 37; 2. Placebo + SoC N=38 | 500 mg Azithro, 400 mg HydroxyChl twice daily for 2 days, then 400 mg once daily for 8 days, and unfractionated 5000 IU heparin three times daily until the end of hospitalization. Methylprednisolone 0.5 mg / kg / day for 5 days could be added if the need for supplemental O2 was 6 L / min or more | SoC+ | moderate/severe |
| Lopez-Medina 2021 | CO | 473 | 1. Ivermectin 300 μg/kg per day for 5 days N = 275; 2. Placebo N=198 | No SoC | P | moderate |
| 86. | Lou 2020   | CN | 30 | 1. Baloxavir + existing antiviral treatment N=10; 2: Favipiravir + existing antiviral treatment N=9; 3. existing antiviral treatment N=10 | Lop/Rit (400mg / 100mg, twice a day) or darunavir / cobicystate (800mg / 150mg, four times a day) and Umifenovir (200mg, three times a day). All in combination with inhaled interferon alpha (100,000 iu, tid or qid). | SoC+ moderate/severe |
| 87. | Maldonado 2020 | MEX | 54 | 1. Pentoxifylline N=36; 2. SoC N=18 | No details on SoC reported | SoC- NR |
| 88. | Mansour 2020 | BR | 30 | 1. Icatibant + SoC N=10; 2. Inhibitor of C1 esterase/kallikrein + SoC N=10 | 3. SoC N=10 | Upon medical decision, patients received antibiotics, antithrombotic therapy, O2 support, non-invasive and invasive mechanical ventilation, vasopressor drugs, stress doses of corticosteroids and renal support therapy | SoC+ severe |
| 89. | Mehboob 2020 | PK | 18 | 1. Aprepitant +dexamethasone N=8; 2. dexamethasone N=10 | No SoC | A+ moderate/severe/critical |
| 90. | Miller 2020 | USA | 30 | 1. Auxora (low supplemental O2 flow) + SoC N= 17; 2. Auxora (high supplemental O2 flow) + SoC N=3; 3. SoC N=9 | Antiviral agents, but investigational therapies and immunosuppressive medications were not permitted. At the discretion of the site investigators, patients treated with either Auxora or standard of care alone were able to receive Plasma C if they required invasive mechanical ventilation. | SoC+ severe |
| 91. | Mitjà 2020 | E | 293 | 1. HydroxyChl+ SoC N=136; 2. SoC N=157 | No details on SoC reported | SoC- mild |
| Study            | Country | Year | Participants | Treatment 1 | Treatment 2 | No. of Patients | No. of Control | Comparator | Case Severity |
|------------------|---------|------|--------------|-------------|-------------|----------------|----------------|------------|--------------|
| Mobarak 2021     | IR      | 2021 | 108          | 1. Sofosbuvir + Daclatasvir + SoC N=541; 2. Placebo + SoC N=542 | No details on SoC reported | SoC- | moderate/severe |
| Mohan 2021       | IN      | 2021 | 125          | 1. Ivermectin 24 mg single dose + SoC N=40; 2. Ivermectin 12 mg single dose + SoC N=40; 3. Placebo+SoC N=45 | No details on SoC reported | SoC- P | moderate |
| Monk 2020        | UK      | 2020 | 101          | 1. Interferon beta 1a N=50; 2. Placebo+SoC N=51 | No details on SoC reported | SoC- P | mild/moderate/severe |
| Morteza 2020     | IR      | 2020 | 180          | 1. Ivermectin (1 dose 200mcg/kg) N=30; 2. Ivermectin (3 doses 200mcg/kg) N=30; 3. Ivermectin (single dose 400mcg/kg) N=30; 4. Ivermectina (3 doses 400, 200, 200 mcg/kg) N=30; 5. SoC N=30; 6. SoC+Placebo N=30 | No details on SoC reported | SoC- P | mild/moderate/severe |
| Nojomi 2020      | IR      | 2020 | 100          | 1. Umifenovir plus HydroxyChl N=50; 2. Lop/Rit + HydroxyChl N=50 | No SoC | A+ | moderate/severe |
| Omrani 2020      | Q       | 2020 | 456          | 1. HydroxyChl + Azithro N=152; 2. HydroxyChl N=152; 3. Placebo N=152 | No SoC | A+ P | mild/asymptomatic |
| Rahmani 2020     | IR      | 2020 | 80           | 1. Interferon β-1b + SoC N=40; 2. SoC N=40 | Lop/Ritr (400/100 mg BD) or atazanavir/ritonavir (300/100 mg daily) plus HydroxyChl (400 mg BD in first day and then 200 mg BD) for 7–10 days. Other supportive cares such as fluid therapy, stress ulcer prophylaxis, | SoC+ | NR |
Deep vein thrombosis, treatment of electrolyte disorders and antibiotic therapy were considered according to the hospital protocols.

| Study | Country | Inclusion N | Treatment | Details |
|-------|---------|-------------|-----------|---------|
| 99. Ramakrishnan 2021 | UK | 146 | 1. Inhaled budesonide N=73; 2. SoC N=73 | Paracetamol, or nonsteroidal anti-inflammatory (such as aspirin and ibuprofen) and honey for symptoms of cough. |
| 100. Ranjbar 2021 | IR | 86 | 1. Methylprednisolone (2mg/kg/day) + SoC N=44; 2. Dexamethasone (6mg/kg/day) + SoC N=42 | No details on SoC reported |
| 101. Rashad 2021 | EG | 306 | 1. Azithro 500 mg/24 h for 7 days N=107; 2. Clarithromycin 500 /12 h for 7 days N=99; 3. SoC N=99 | Symptomatic treatment for control of fever and cough |
| Study | Country | N | Interventions | Outcomes |
|-------|---------|---|--------------|----------|
| 102.  | Ray 2020 | IN | 80 | Plasma C N=40; SoC N=40 | HydroxyChl, Azithro, Ivermectin and Doxycyclin; O2 therapy as per requirement; corticosteroids; therapeutic anticoagulation using either low molecular weight heparin or unfractionated heparin; appropriate broad-spectrum antibiotic therapy reservoir, high flow nasal cannula (HFNC) or in some cases mechanical ventilation (MV) were deployed. 1 patient in the SOC arm received Tocilizumab, none in the CPT arm. 13 patients in the SOC arm and 11 patients in the CPT arm received Remdes. |
| 103.  | RECOVERY | UK | 4716 | HydroxyCh + SoC N015611561; Dexamethasone +SOC N= 2104; Lop/Rit +SoC N= 1616; Azythro + SoC N= 5182; Tocilizumab +SoC N= 2022 | No details on SoC reported | Severe |

Horby 2020
Horby 2020
Horby 2020
Horby 2020
Horby 2021
| ID   | Study          | Country | N  | Treatment 1                                                                 | Treatment 2                                                                 | Outcome 1                                      | Outcome 2                             |
|------|----------------|---------|----|------------------------------------------------|----------------------------------------------------------------------------|-----------------------------------------------|----------------------------------------|
| 104. | REMAP CAP Angola 2020 Gordon 2020 | Europe; AU; NZ | 403 | 1. Hydrocortisone (fixed dose 50 / 100mg every 6 hours) + SoC N=143; 1. Tocilizumab N=353; 2. Hydrocortisone at the time of shock 50 / 100mg every 6 hours + SoC N=152; 3. No hydrocortisone + SoC N=108 2. Sarilumab N=48; 3. SoC N=402 | No details on SoC reported, the majority of patients (80%) glucocorticoids | SoC-; A+                              |
| 105. | Ren 2020       | CN      | 20 | 1. Azvudina+ SoC N=10; 2. SoC N=10 | Standard antiviral drugs: interferon alpha, kaletra + ribavirin + interferon alpha; kaletra + ribavirin; Chloroq and HydroxyChl. Symptomatic treatment: antibiotic therapy and traditional Chinese medicine | SoC+ mild/moderate                          |
| 106. | Rocco 2020     | BR      | 475 | 1. Nitazoxanide N=238; 2. Placebo N=237 | No SoC                                                                 | P mild/moderate                             |
| 107. | Rosas 2020     | CA, DK, FR, DE, IT, NL, E, UK USA | 452 | 1. Tocilizumab (8 mg/kg infusion, maximum 800 mg) + SoC N=301; 2. Placebo + SoC N=151 | Antiviral treatment, low-dose steroids, Plasma C, supportive care.       | SoC+ P severe                             |
| 108. | Ruzhentsova 2020 | RUS     | 168 | 1. Favipiravir (1800 mg BID on day 1, followed by 800 mg BID for up to 9 days) N=112; 2. SoC N=56 | Umifenovir + intranasal interferon alpha-2b, or HydroxyChl for up to 10 days | SoC+ mild/moderate                        |
| 109. | Sadeghi 2020   | IR      | 70 | 1. Sofosbuvir/daclatasvir (400mg/60mg) N=35; 2. SoC N=35 | HydroxyChl 200mg twice daily with or without Lop/Ritr 200mg/50mg twice daily. | SoC+ moderate/severe                      |
|   | Authors 2020     | Country   | N  | 1. Intervention                                      | 2. SoC N= | Supportive care and other treatments               | SoC     | Severity   |
|---|-----------------|-----------|----|-----------------------------------------------------|-----------|---------------------------------------------------|---------|------------|
|110| Sakoulas 2020   | USA       | 34 | 1. Intravenous Immunoglobulin with 40 mg methylprednisolone N=17 | 2. SoC N=17 | Glucocorticoids, Plasma C, and Remdes or other treatments not included in the trial. | SoC+    | moderate/severe |
|111| Salama 2020     | USA, MEX, EAK, ZA, PE, BR | 388 | 1. Tocilizumab (IV 8mg/kg massimo 800mg+SoC N=259) | 2. Placebo+SoC N=129 | No details on SoC reported | SoC-    | severe |
|112| Salvarani 2020  | I         | 126 | 1. Tocilizumab N=60 | 2. SoC N= 66 | Supportive care following the treatment protocols of each center including HydroxyChl, heparin and LMWH, antiretrovirals (darunavir/cobicistat, darunavir/ritonavir, or Lop/Ritr; Azithro | SoC+    | severe |
|113| Sekhavati 2020  | IR        | 111 | 1. Azythro + Lop/Rit + HydroxyChl N=56 | 2. Lop/Rit + HydroxyChl N=55 | No SC | A+        | NR       |
|114| Self 2020       | USA       | 479 | 1. HydroxyChl + SoC N=242 | 2. Placebo + SoC N=237 | During Hospitalization: antivirals (open label HydroxyChl, Remdes, others); immunomodulator (corticosteroids, tocilizumab, other); antibacterial (Azithro); Plasma C | SoC+    | severe |
|115| Shi 2020        | CN        | 101 | 1. Umbilical cord_ mesenchymal stem cells (hUC-MSC) + SoC N=66 | Placebo + SoC N=35 | No details on SoC reported | SoC-    | severe |
| ID  | Study          | Country/Region | Total  | Treatment 1                                      | Treatment 2                                      | Comparator  | Outcomes       |
|-----|----------------|----------------|--------|------------------------------------------------|------------------------------------------------|-------------|----------------|
| 116 | Shu 2020       | CN             | 41     | 1. Umbilical cord mesenchymal stem cells (hUC-MSC) + SoC N=12; | 2. SoC N=29 O2; antiviral agents (abidor/oseltamivir), antibiotic agents (moxifloxacin is taken orally; glucocorticoid therapy (1–2 mg/kg, less than a week). | SoC+         | mild/moderate/severe |
| 117 | Simonovic 2020 | RA             | 334    | 1. Plasma C N=228;                                | 2. SoC N=106 Antiviral agents, glucocorticoids, or both | SoC+; P     | severe          |
| 118 | Soin 2021      | IN             | 180    | 1. Tocilizumab + SoC N= 90;                       | 2. SoC N= 90 Remdes + corticosteroids            | SoC+         | moderate/severe |
| 119 | Solaymani-Dodaran 2021 | IR        | 380    | 1. Favipiravir (1.6 gr loading, 1.8 gr daily) + SoC N= 193; | 2. Lop/Rit (800/200 mg daily) + SoC N= 187 HydroxyChl 200 mg twice a day for 1 week | SoC+; A+     | moderate/severe |
| 120 | Spinner 2020   | USA, Europe, Asia. | 596    | 1. Remdes 5 days +SoC N=197; 2. Remdes 10 days +SoC N=199; | 3 SoC N=200 No details on SoC reported | SoC-         | moderate        |
| 121 | Stone 2020     | USA            | 243    | 1. Tocilizumab +SoC N=161;                        | 2. Placebo+SoC N=82 No details on SoC reported | SoC-; P     | moderate/severe |
| 122 | Tabarsi 2020   | IR             | 84     | Immunoglobulin 400 mg/Kg daily for three doses. Premedication: 500 mg Acetaminophen, 100 mg Hydrocort, and 25 mg Diphenhydramine 30 min before the injection N=52; | SoC N=32 O2 and fluid support, Lop/Ritr (200/50 mg, Hetero labs), two tablets twice a day, and HydroxyChl (Tehran-Daru) 200 mg two times daily. | SoC+         | severe          |
| 123 | Tang W 2020    | CN             | 150    | HydroxyChl (1200mg for 3 days, followed by 800mg) +SoC N=75; | SoC N=75 Lop/Ritr, oseltamivir, entecavir, antibiotics, glucocorticoid | SoC+         | mild/moderate/severe |
| Study | Author      | Country | N  | Group 1                                      | Group 2                                      | Description                                                                 | Severity |
|-------|-------------|---------|----|---------------------------------------------|---------------------------------------------|------------------------------------------------------------------------------|----------|
| 124.  | Tang X 2021 | CN      | 86 | Methylprednisolone + SoC N=43;              | No Methylprednisolone + SoC N=43            | standard therapy of COVID-19 according to the Chinese Diagnosis and Treatment Plan for COVID-19 (trial version 6) | moderate/severe |
| 125.  | Tardiff 2021| CA      | 448| Colchicine N=2235;                         | Placebo N=2253                              | No SoC                                                                       | P        |
| 126.  | Toloian 2021| IR      | 100| Bromhexine 8 mg four times a day + SoC N=48;| SoC N=52                                    | Lop/Rit and interferon beta-1a                                              | SoC+     |
| 127.  | Tomazini 2020| BR     | 299| Dexamethasone (20mg intravenously once daily for 5 days, followed by 10 mg intravenously once daily for additional 5 days or until ICU discharge, whichever occurred first N=151; | SoC N=148                                    | No details on SoC reported                                                  | SoC-     |
| 128.  | Tornling 2021| SE     | 106| Oral angiotensin II type 2 receptor agonist C21 + SoC N=51; | Placebo+SoC N=55                            | antibiotics and antiviral compounds (Remdes in 67.0%), with no major differences between the treatment groups | SoC+; P  |
| 129.  | Udwadia 2020| IN      | 150| Favipiravir +SoC N=75;                      | SoC N=75                                     | Antipyretics, cough suppressants, antibiotics, and vitamins                  | SoC+     |
| 130.  | Ulrich 2020 | USA     | 128| HydroxyChl + SoC N=67;                      | Placebo + SoC N=61                           | No details on SoC reported                                                   | SoC-; P  |
| 131.  | Veiga 2021  | BR      | 129| Tocilizumab + SoC N=65;                     | SoC N=64                                     | HydroxyChl, Azithro, corticosteroids, and antibiotics                        | SoC+     |
| 132.  | Vlaar 2020  | NL      | 30 | Anti-C5a antibody (IFX-1) + SoC N=15;       | SoCN=15                                      | No details on SoC reported                                                   | SoC-     |
| 133.  | Wang 2020   | CN      | 237| Remdes + SoC N=158;                        | Placebo+SoC N=79                             | Lop/Rit; Antibiotics; Corticosteroids                                         | SoC+; P  |

SoC: Standard of Care; P: Placebo.
|   | Study | Country | N | Intervention 1 | Intervention 2 | SoC | SoC Details |
|---|-------|---------|---|----------------|----------------|-----|-------------|
| 134. | Wang D 2020 | CN | 65 | Tocilizumab + SoC N=33 | SoC N=32 | No details on SoC reported | moderate/severe |
| 135. | Wang M 2020 | CN | 50 | Leflunomide plus Interferon α-2a N=26 | SoC N=24 | SoC N=32 | A+ | NR |
| 136. | Weinreich 2021 | USA | 269 | REGN-COV2 at a dose of 2.4 g N=92; 2, REGN-COV2 at a dose of 8.0 g N=90; Placebo N=93 | No SoC | No SoC | P | mild |
| 137. | WHO-Solidarity trial | WHO countries | 142 | Remdes +SoC N=2750; HydroxyChl + SoC N=954; Lop/Rit + SoC N=1411; Interferon β-1a + SoC N=2063; | SoC N=2725; SoC N=909; SoC N=1380; SoC N=2064 | No details on SoC reported | SoC-; A+ | mild/moderate/severe |
| 138. | Wu 2020 | CN | 52 | Triazavirin (moderate: 250 mg orally 3 times / day; severe / critical: 250 mg orally 4 / day) + SoC N=26 | Placebo + SoC N=26 | Antibiotics, Antiviral drugs, Interferon, Arbidol, Ribavirin, Lopinavir, HydroxyChl, Antifungal drugs, Chinese medicine therapy | SoC+; P | moderate/severe/critical |
| 139. | Yadollahzadeh 2021 | IR | 112 | Sofosbuvir + Daclatasvir N= 58; Lop/Rit N= 54 | No SoC | Standard Care as per the Egyptian Ministry of Health (MOH) protocol: HydroxyChl multivitamin and zinc supplements with vitamin C and D. Other drugs were given according to each patient clinical condition and included: analgesic-antipyretic, cough mixtures, Parenteral antibiotics, heparin/low |
| 140. | Yakoot 2020 | EG | 89 | Sofosbuvir plus Daclastavir + SoC N=44; SoC N=45 | | SoC+ | mild, moderate, severe |
molecular weight heparin/or novel oral anticoagulants, conservative IV fluid management if indicated and O2 therapy, up to mechanical ventilation as needed.

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|---|---|---|---|---|
| 141. Youssef 2021 | USA | 196 | 1. Aviptadil (Vasoactive Intestinal Peptide) + SoC N=131 vs 2. Placebo+ SoC N=65 | No details on SoC reported | SoC- moderate |
| 142. Zarychanski-2021 | CA | 108 | 1. Heparin + SoC N=532; 2. Pharmacological thromboprophylaxis + SoC N=557 | No details on SoC reported | SoC- severe |
| 143. Zhao 2020 | CN | 26 | 1. Favipiravir (1600mg day 1 then 600mg) + Tocilizumab (4-8mg/kg) N=14; 2. Favipiravir (1600mg day 1 then 600mg) N=7; 3. Tocilizumab (4-8mg/kg) N=5 | No SoC | A+ moderate/severe/critical |
| 144. Zheng 2020 | CN | 89 | 1. Novaferon (40 mg) N=30; 2. n=30 Novaferon (40 mg) + Lop/Rit (200/50mg) N=30; 3. Lop/Rit (200/50mg) N=29 | No SoC | A+ moderate/severe |

HydroxyChloroquine= HydroxyChl; Lopinavir/ritonavir= Lop/Rit; Remdesivir= Remd; Convalescent plasma = Plasma C; Azithromycine= Azithro; Favipavir= Favi; Tocilizumab= Toci; Chloroquine= Chloroq; Colchicine= Colchi; Ivermectine= Iver; Ribavirine= Riba; Methylprednisolone= Methylpredni
