Supplementary Table 1: Summary of current evidence on interventions mentioned in article for treating

spike protein related diseases

|  |  |  |  |
| --- | --- | --- | --- |
| Intervention | Trial Identifier for Treating Spike Protein Related Diseases | Status | Summary of evidence for spike protein diseases  (Covid-19, long covid, vaccine injury, vaccine response) |
| Caffeine |  |  | N/A |
| Spermidine | NCT05421546 | RECRUITING | N/A |
| Resveratrol | NCT04400890 | TERMINATED | Lower incidence of hospitalization [1].  Reduction in death for those receiving resveratrol with copper [2]. |
| Curcumin | NCT04912921 | COMPLETED | Decrease in inflammation in Covid-19 patients [3].  Combined curcumin/piperine treatment resulted in less severe Covid-19 symptoms [4] |
|  | NCT05150782 | NOT\_YET\_RECRUITING |  |
|  | NCT05130671 | COMPLETED |  |
|  | NCT04603690 | COMPLETED |  |
|  | NCT05037162 | COMPLETED |  |
|  | NCT04802382 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT05629975 | NOT\_YET\_RECRUITING |  |
| EGCG |  |  | Apparent positive effect on treatment outcome, but no controls[5]. |
| Rapamycin | NCT04948203 | RECRUITING |  |
| Resveratrol | See above |  | See above |
| Fisetin | NCT04771611 | COMPLETED | Reduce coronavirus mortality in aged mice[6] |
|  | NCT04476953 | ENROLLING\_BY\_INVITATION |  |
|  | NCT04537299 | ENROLLING\_BY\_INVITATION |  |
| Nicotinamide | NCT04751604 | COMPLETED | No statistically significant difference in full blood counts, lymphocyte counts or lymphocyte improvement rate [7,8] |
|  | NCT04818216 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT04604704 | COMPLETED |  |
|  | NCT05175768 | RECRUITING |  |
|  | NCT04910230 | COMPLETED |  |
|  | NCT04708340 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT05703074 | RECRUITING |  |
|  | NCT04809974 | RECRUITING |  |
| Melatonin | NCT05596617 | COMPLETED | Improvement in recovery rate, lower risk of hospitalization and death[9] |
|  | NCT04409522 | UNKNOWN |  |
|  | NCT04353128 | COMPLETED |  |
|  | NCT04568863 | COMPLETED |  |
|  | NCT04530539 | COMPLETED |  |
|  | NCT04470297 | UNKNOWN |  |
|  | NCT05318144 | COMPLETED |  |
|  | NCT04570254 | COMPLETED |  |
|  | NCT05670444 | COMPLETED |  |
| PQQ |  |  | Improves measures in a mouse model of COPD induced endothelial damage [10] |
| Cold Exposure |  |  | N/A |
| Exercise | 517 Studies for all spike protein related diseases  61 Studies for long covid or vaccine injury | Of 61 Studies, 11 completed | Improvement in cardiorespiratory fitness in long covid[11–13] |
| Nitric Oxide | NCT04421508 | TERMINATED | Reduced viral load in Covid-19 infection[14] |
|  | NCT03331445 | TERMINATED |  |
|  | NCT04306393 | COMPLETED |  |
|  | NCT05109611 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT04388683 | TERMINATED |  |
|  | NCT04460183 | COMPLETED |  |
|  | NCT04606407 | COMPLETED |  |
|  | NCT05430503 | COMPLETED |  |
|  | NCT04610554 | COMPLETED |  |
|  | NCT04312243 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT04728919 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT04397692 | TERMINATED |  |
|  | NCT05715788 | RECRUITING |  |
|  | NCT04476992 | COMPLETED |  |
|  | NCT04601077 | TERMINATED |  |
|  | NCT05012319 | RECRUITING |  |
|  | NCT05599919 | COMPLETED |  |
|  | NCT04383002 | COMPLETED |  |
|  | NCT04445246 | COMPLETED |  |
|  | NCT05715762 | RECRUITING |  |
|  | NCT04337918 | COMPLETED |  |
|  | NCT04338828 | TERMINATED |  |
|  | NCT04305457 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT05721144 | RECRUITING |  |
| Lipoic Acid | NCT05371288 | NOT\_YET\_RECRUITING | Lower mortality and lower rates of organ failure in severe Covid-19 [15] |
| Acetyl L-carnitine | NCT04623619 | UNKNOWN | Shorter time to recovery when combined with l-serine (serine), NAC, NR, and l-carnitine tartrate (LCAT, the salt form of l-carnitine) [16].  Those with higher carnitine levels due to genetics had significantly lower susceptibility to Covid-19[17]. |
| Nebivolol | NCT04631536 | ACTIVE\_NOT\_RECRUITING | Improves dyspnoea score and capillary blood volume in long covid [18] |
|  | NCT04467931 | COMPLETED |  |
| EGCG | NCT04446065 | UNKNOWN |  |
| Quercetin | NCT04468139 | UNKNOWN | Decreased risk of intensive care unit admission and hospitalization[19] |
|  | NCT05130671 | COMPLETED |  |
|  | NCT04578158 | COMPLETED |  |
|  | NCT04603690 | COMPLETED |  |
|  | NCT04536090 | NOT\_YET\_RECRUITING |  |
|  | NCT04851821 | COMPLETED |  |
|  | NCT04622865 | RECRUITING |  |
|  | NCT04377789 | COMPLETED |  |
|  | NCT04844658 | COMPLETED |  |
|  | NCT05601180 | RECRUITING |  |
|  | NCT05037240 | COMPLETED |  |
|  | NCT04861298 | COMPLETED |  |
| Licorice extract | NCT04544605 | UNKNOWN | When combined with boswellic acid, significantly lowered time to recovery and mortality[20]  Multiple studies show positive effect [21,22] |
|  | NCT04553705 | COMPLETED |  |
|  | NCT05360004 | NOT\_YET\_RECRUITING |  |
|  | NCT04487964 | COMPLETED |  |
|  | NCT04846010 | UNKNOWN |  |
|  | NCT04790240 | UNKNOWN |  |
|  | NCT03348670 | ACTIVE\_NOT\_RECRUITING |  |
| cyanidin-3-glucoside | NCT05387252 | NOT\_YET\_RECRUITING | Suppression of inflammation from SARS-CoV-2 spike protein *in vitro* [23].  In vitro activity of a glucoside rich fruit extract (corozo) against SARS-CoV-2[24] |
|  | NCT04404218 | ACTIVE\_NOT\_RECRUITING |  |
| Methylene Blue | NCT05004805 | COMPLETED | Positive results on Covid-19 infection [25–27].  Patients (lacking controls) show improvement with methylene blue [27–31] |
|  | NCT04547127 | COMPLETED |  |
|  | NCT04416113 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT04619290 | UNKNOWN |  |
|  | NCT04635605 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT05003492 | NOT\_YET\_RECRUITING |  |
|  | NCT04370288 | UNKNOWN |  |
|  | NCT04376788 | UNKNOWN |  |
|  | NCT04933864 | COMPLETED |  |
|  | NCT05753878 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT04621123 | COMPLETED |  |
|  | NCT04615936 | COMPLETED |  |
| Vitamin C | 71 Studies for all spike protein related diseases  1 study for long Covid or vaccine injury |  | Decrease in severity but not statistically significant [32,33] |
| NAC | NCT04545008 | TERMINATED | Significant improvement [34,35] |
|  | NCT05258682 | NOT\_YET\_RECRUITING |  |
|  | NCT04570254 | COMPLETED |  |
|  | NCT04455243 | UNKNOWN |  |
|  | NCT05736887 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT05658549 | COMPLETED |  |
|  | NCT05220605 | COMPLETED |  |
|  | NCT04419025 | COMPLETED |  |
|  | NCT05504655 | COMPLETED |  |
|  | NCT05074121 | NOT\_YET\_RECRUITING |  |
|  | NCT04792021 | COMPLETED |  |
|  | NCT04928495 | UNKNOWN |  |
|  | NCT04370288 | UNKNOWN |  |
|  | NCT05371288 | NOT\_YET\_RECRUITING |  |
|  | NCT04374461 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT04666753 | COMPLETED |  |
|  | NCT04573153 | UNKNOWN |  |
|  | NCT04755972 | COMPLETED |  |
|  | NCT04900129 | COMPLETED |  |
|  | NCT04703036 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT04458298 | TERMINATED |  |
|  | NCT04466657 | WITHDRAWN |  |
|  | NCT04590274 | WITHDRAWN |  |
| Magnesium | NCT04716985 | ACTIVE\_NOT\_RECRUITING | Low magnesium associated with worse Covid-19 outcomes[36–41], including long covid[36].  Magnesium combined with Vitamin D and Vitamin B12 lessened need for oxygen support in older Covid-19 patients[42] |
|  | NCT04640168 | COMPLETED |  |
|  | NCT04973449 | COMPLETED |  |
|  | NCT05630339 | NOT\_YET\_RECRUITING |  |
|  | NCT04401579 | COMPLETED |  |
|  | NCT04621071 | COMPLETED |  |
|  | NCT04363606 | RECRUITING |  |
|  | NCT05226754 | RECRUITING |  |
|  | NCT05629975 | NOT\_YET\_RECRUITING |  |
|  | NCT04941703 | TERMINATED |  |
|  | NCT05057897 | TERMINATED |  |
|  | NCT04363216 | UNKNOWN |  |
|  | NCT05552625 | COMPLETED |  |
|  | NCT04357730 | COMPLETED |  |
|  | NCT05371288 | NOT\_YET\_RECRUITING |  |
|  | NCT04570462 | WITHDRAWN |  |
|  | NCT04864561 | COMPLETED |  |
|  | NCT05363410 | NOT\_YET\_RECRUITING |  |
|  | NCT04847518 | UNKNOWN |  |
|  | NCT05836402 | NOT\_YET\_RECRUITING |  |
|  | NCT05080244 | COMPLETED |  |
|  | NCT05290298 | COMPLETED |  |
|  | NCT04708340 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT04420676 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT05715944 | COMPLETED |  |
| Methylene Blue | See above |  | See above |
| PBM | NCT04418505 | UNKNOWN | PBM can reduce inflammation in animal models[43].  Improvement on pulmonary indices and faster recovery, less long covid after infection treated with PBM[44] |
|  | NCT04416113 | ACTIVE\_NOT\_RECRUITING |  |
|  | NCT05094726 | RECRUITING |
|  | NCT05258617 | TERMINATED |
|  | NCT04391712 | COMPLETED |
|  | NCT05760092 | RECRUITING |
|  | NCT04386694 | COMPLETED |
|  | NCT05857124 | NOT\_YET\_RECRUITING |
|  | NCT05430776 | RECRUITING |

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