

**Supplementary information**

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**Glucose-lowering treatments and COVID-19 mortality in T2DM**

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**Table 1: Current COVID-19 prospective trials on glucose-lowering treatment interventions in patients with T2DM**

Clinical trial number <sup>a</sup>	Placebo controlled	N	Inclusion criteria	Primary outcomes
<b>Drug tested: metformin</b>				
04510194	Yes	750	Non-hospitalized adults with SARS-CoV-2 infection	Decreased oxygenation (SO <sub>2</sub> ≤93% on home monitoring)
04625985	Yes	20	Hospitalized patients with COVID-19 patients and severe acute respiratory syndrome	Multiple primary outcomes (viral load, oxygen saturation, length of hospital stay among others)
04727424	Yes (metformin + 2 other ID)	2,724	Adults with SARS-CoV-2 positive PCR, flu-like symptoms lasting <7 days and enhancement factors (including age >50 years, chronic conditions)	Need for emergency care and observation for more than 6 hours due to the worsening of COVID-19
<b>Drug tested: pioglitazone</b>				
04604223	Yes	1,506	COVID-19 infection confirmed with PCR test and ≥1 COVID-19 symptoms	Multiple primary outcomes (hs-CRP level; composite outcome of mechanical ventilation, myocardial damage or death).
04535700	No	76	Confirmed diagnosis of COVID-19 or high clinical suspicion according to current criteria	Composite outcome: mechanical ventilation, ICU and/or death
04473274	No	20	Laboratory confirmed COVID-19 requiring hospitalization	Adverse events outcomes without attribution // attributable
<b>Drug tested: linagliptin</b>				
04542213	No, linagliptin + insulin vs insulin	70	Hospitalized patients with confirmed infection by SARS-CoV-2 and hyperglycaemia	Glucose levels during hospitalization
04371978	No, linagliptin + insulin vs insulin	100	Patients within 10 days of symptom onset or patients within 48 hours after laboratory diagnosis (SARS-CoV-2 PCR).	Clinical change as 2 points reduction in the WHO Ordinal Scale for Clinical Improvement of COVID-19
<b>Drug tested: dapagliflozine</b>				
04393246	No, dapagliflozine + 2 other ID vs SOC	1,407	Clinical picture strongly suggestive of COVID-19-related disease and risk count >3 or risk count ≥3 and radiographic severity score >3 <sup>b</sup>	Change in biomarkers associated with progression of COVID-19 // clinical status as assessed on 7-point ordinal scale
04350593	Yes	1,250	Hospitalized patients with respiratory manifestations of COVID-19 of any duration, without the need for mechanical ventilation	Prevention of COVID-19 complications or death: // Improving clinical recovery

<sup>a</sup>Actively-recruiting or completed trials registered on Clinicaltrial.gov (accessed on 13 April 2021); <sup>b</sup>Patients are given a risk count equal to the cumulative points received for specific risk criteria. COVID-19, coronavirus disease 2019; ID, investigation drug(s); SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SOC, standard of care; WHO, World Health Organization.