**Appendix 6 (as submitted by the authors): Additional statistical analysis on ref. Zhou Q (doi: 10.1101/2020.04.06.20042580)**

## Background:

In this retrospective cohort study, 77 hospitalized COVID-19 patients with mixed severity illness received antiviral treatment with either interferon-α2b (IFN) (n=7), umifenovir (UMF) (n=24), or a combination of IFN plus UMF (n=46). The authors examined the association between time to viral clearance and treatment (IFN with or without UMF versus UMF alone) using Cox proportional hazards regression modelling, with age included as a covariate. However, the study only reported the Kaplan-Meier curves and the associated p value without relative estimates. Our judgement was that the more appropriate analysis would exclude the patients treated with IFN alone and focus on patients who received IFN plus UMF versus UMF. Because the study provided its original dataset as supplementary material, we were able to perform an optimal statistical analysis using original data.

## Methods

All patients eventually cleared the virus. As exact time to viral clearance were known for all patients (no partial data), we applied multiple linear regression analyses to explore associations of treatment (IFN plus UMF versus UMF alone) with two outcomes, time-to viral clearance and length of hospital stay. In evaluating the associations, the analysis adjusted for age, sex, comorbidity, and days from symptom onset to hospitalization. We report the adjusted mean differences and 95% confidence intervals in the outcomes between the treatment groups.

## Results

The patients treated with UMF alone were older [mean (SD) age 65 (13) vs 40 (14) years], and more had comorbidities [13 (54%) vs 7 (15%)] compared to the patients treated with interferon with UMF (Table 1). Median (IQR) days from symptom onset to hospital admission was higher in the UMF only patients [10 (4, 20) vs 7 (3, 10)]. On average, in the adjusted analysis, patients with UMF monotherapy took 4.6 days (95% CI: -0.5 to 9.6) longer time from symptom onset to viral clearance and stayed 4.4 days (95% CI: -1.5 to 10.3) longer in-hospital than patients treated with both IFN and UMF (Table 2).

Appendix to: Liu W, Zhou P, Chen K, et al. Efficacy and safety of antiviral treatment for COVID-19 from evidence in studies of SARS-CoV-2 and other acute viral infections: a systematic review and meta-analysis. *CMAJ* 2020. doi: 10.1503/cmaj.200647. 

**Table 1.** Baseline characteristics and health risk factors of COVID-19 patients

| | IFN with UMF | UMF only |
|---|---|---|
| N (%) | 46 (65.7) | 24 (34.3) |
| Age (years), mean ± SD | 40.4 ± 14.4 | 64.5 ± 13.2 |
| Male, N (%) | 20(43.5) | 11(45.8) |
| Comorbidities, N (%) | 7(15.2) | 13(54.2) |
| Days from symptom onset to hospital admission, median (IQR) | 6.5 (3.0, 10.0) | 10.0 (4.0, 20.0) |

[§]Hypertension, diabetes, COPD, chronic bronchitis, heart disease, cancer

**Table 2.** Comparisons of time-to viral clearance and length of hospital stay between COVID-19 patients treated with IFN plus UMF and UMF

| Outcome | IFN with UMF | UMF only | Adj. mean difference (95% CI) |
|---|---|---|---|
| Days from symptom onset to viral clearance | 24.30 (1.38) | 28.89 (1.88) | -4.60 (-9.64, 0.45) |
| In-hospital days[¥] | 18.99 (1.62) | 23.42 (2.18) | -4.43 (-10.31, 1.45) |

[¥]One patient remained in-hospital, thus length of hospital stay was not defined for that patient.
Data are presented as adjusted mean (SE), adjusted for age, sex, comorbidity, and days from symptom onset to hospitalization.