Anti-inflammatory action of colchicine in hospitalised patients with COVID-19. Response to: 'Colchicine treatment in community healthcare setting to prevent severe COVID-19' by Della-Torre *et al*

We thank Della-Torre *et al* for their interest on our report on the retrospective, case-control observational study with colchicine in patients hospitalised for severe COVID-19,[1] and for rising the really crucial issue of the timing of the therapeutic intervention with anti-inflammatory therapies in this disease.[2]

Our observations should be interpreted in the scenario of the uncontrolled epidemic that, during March and April 2020, overwhelmed the health system in Lombardy, Italy, with rapid shortage of intensive care unit beds. As pointed out by the authors in other papers, after this period, the severity of the COVID-19 progressively decreased, in parallel with the exhaustion of the epidemic.[3 4] The COVID-19 related mortality observed in our study (27.5% in the overall cohort of 262 consecutive cases; 36.4% in the standard of care group, and 15.8% in patients treated with colchicine), although much higher than that observed in the previous first reports from China, was very similar to those reported by the group of Della-Torre himself[4–8] (for a comment: see[9]) and by others[10 11] who described patients hospitalised for COVID-19 in Lombardy during this period of time, and cannot therefore be considered unexpected.

The intervals (mean (SD)) between the onset of respiratory symptoms (cough and/or dyspnoea), or of spiking fever, and the start of therapy with colchicine in our patients were of 7 (5) and 7 (6) days, respectively. Notably, the interval was not shorter in patients who survived after treatment, as compared with those who died (respiratory symptoms: 7 (5) vs 8 (4) ; p=0.3; fever: 8 (6) vs 6 (6) : p=0.3, respectively).

In their interesting study, Della-Torre *et al* reported the efficacy of colchicine treatment in nine domiciliary patients with COVID-19, in which this drug was started after a shorter interval of symptoms (3–5 days of fever)[12]; they observed rapid defervescence within 3 days in all nine patients, suggesting that the drug might be effective in dampening the rise of the inflammatory response in its first phases. Our experience in hospitalised patients (table 1) might support this hypothesis. In fact, we observed a marked decrease of the C-reactive protein (CRP) serum levels, and an improvement of the PaO_2/FiO_2 ratio after 6 days of treatment with colchicine, whereas in patients treated with standard of care only, the CRP remained highly elevated and PaO_2/FiO_2 ratio worsened. A trend for the reduction of serum ferritin was also observed in the colchicine group, and not in the control group. The longer half-life of ferritin (30 hours)[13] might account for the less clear evidence of this results.

The rationale for, and the potential advantages of the use of colchicine in COVID-19 were recently elucidated by others and us.[14 15] These few first observational studies seem to lend support to this approach. We agree that the use in the settings of outpatients appears very promising. Only controlled randomised trial will demonstrate the real utility of colchicine in the care of COVID-19, and the optimal time of therapeutic intervention.

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Table 1 Comparison of clinical and laboratory features at baseline and after 6 days of therapy in patients treated with standard-of-care (SoC) or colchicine plus (+) SoC

	SoC			Colchicine + SoC		
Features	Day 0	Day 6	P value*	Day 0	Day 6	P value*
C-reactive protein (mg/L)	112 (83)	114 (100)	0.75	159 (53)	42 (53)	<0.0001
Ferritin (ng/mL)	1129 (1105)	1313 (974)	0.76	1987 (1983)	1185 (1011)	0.36
Neutrophil count (cell/µL)	5844 (3786)	7428 (2875)	0.51	6859 (4070)	7665 (3674)	0.20
Lymphocyte count (cell/µL)	1016 (660)	883 (498)	0.92	921 (427)	983 (406)	0.21
PaO_2/FiO_2 (mm Hg/%)	245 (106)	215 (128)	0.04	177 (81)	201 (103)	0.005

Data are expressed as the mean (SD).
*Wilcoxon signed-rank test.

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REFERENCES

1 Scarsi M, Piantoni S, Colombo E, *et al*. Association between treatment with colchicine and improved survival in a single-centre cohort of adult hospitalised patients with COVID-19 pneumonia and acute respiratory distress syndrome. *Ann Rheum Dis* 2020;79:1286–9.
2 Della-Torre E, Ramirez G, Dagna L, *et al*. Colchicine treatment in community healthcare setting to prevent severe COVID-19. *Ann Rheum Dis* 2022;81:e198.
3 Della-Torre E, Campochiaro C, Cavalli G, *et al*. Targeting IL-1, IL-6 or GM-CSF in COVID-19. Response to: 'More evidences on which biologic and which pathway is key in severe-critical COVID-19 pneumonia' by Ferraccioli. *Ann Rheum Dis* 2022;81:e158.
4 Ciceri F, Castagna A, Rovere-Querini P, *et al*. Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy. *Clin Immunol* 2020;217:108509.
5 Della-Torre E, Campochiaro C, Cavalli G, *et al*. Interleukin-6 blockade with sarilumab in severe COVID-19 pneumonia with systemic hyperinflammation: an open-label cohort study. *Ann Rheum Dis* 2020;79:1277–85.
6 Campochiaro C, Della-Torre E, Cavalli G, *et al*. Efficacy and safety of tocilizumab in severe COVID-19 patients: a single-centre retrospective cohort study. *Eur J Intern Med* 2020;76:43–9.
7 Cavalli G, De Luca G, Campochiaro C, *et al*. Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study. *Lancet Rheumatol* 2020;2:e325–31.
8 De Luca G, Cavalli G, Campochiaro C, *et al*. Gm-Csf blockade with mavrilimumab in severe COVID-19 pneumonia and systemic hyperinflammation: a single-centre, prospective cohort study. *Lancet Rheumatol* 2020;2:e465–73.
9 Ferraccioli G. More evidences on which biologic and which pathway is key in severe-critical COVID-19 pneumonia. *Ann Rheum Dis* 2022;81:e157.
10 Capra R, De Rossi N, Mattioli F, *et al*. Impact of low dose tocilizumab on mortality rate in patients with COVID-19 related pneumonia. *Eur J Intern Med* 2020;76:31–5.
11 Grasselli G, Zangrillo A, Zanella A, *et al*. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. *JAMA* 2020;323:1574–81.
12 Della-Torre E, Della-Torre F, Kusanovic M, *et al*. Treating COVID-19 with colchicine in community healthcare setting. *Clinical Immunology* 2020;217:108490.
13 Cullis JO, Fitzsimons EJ, Griffiths WJH, *et al*. Investigation and management of a raised serum ferritin. *Br J Haematol* 2018;181:331–40.
14 Piantoni S, Patroni A, Toniati P, *et al*. Why not to use colchicine in COVID-19? an oldanti-inflammatory drug for a novel auto-inflammatory disease. *Rheumatology* 2020;59:1769–70.
15 Piantoni S, Colombo E, Airò P, *et al*. The rationale for the use of colchicine in COVID-19: comments on the letter by Cumhur Cure M et al. *Clin Rheumatol* 2020;39:2489–90.