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.

Silvia Piantoni ,[1,2] **Enrico Colombo**,[3,4] **Roberto Furloni**,[3,4] **Laura Andreoli** ,[1,2] **Antonio Brucato** ,[5] **Massimo Imazio**,[6] **Paolo Airó** ,[1] **Mirko Scarsi**[3,4]

[1]Rheumatology and Clinical Immunology Unit, ASST Spedali Civili, Brescia, Italy
[2]Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[3]Internal Medicine Department, ASST Valcamonica, Esine (Brescia), Italy
[4]COVID Unit, ASST Valcamonica, Esine (Brescia), Italy
[5]Department of Biomedical and Clinical Sciences "Sacco", University of Milano, Ospedale Fatebenefratelli, Milano, Italy
[6]University Cardiology, A.O.U. Città della Salute e della Scienza di Torino, Torino, Italy

Correspondence to Dr Silvia Piantoni, Rheumatology and Clinical Immunology Unit, Department of Clinical and Experimental Sciences, ASST Spedali Civili and University of Brescia, Brescia, Italy; slv.piantoni@gmail.com

Handling editor Josef S Smolen

Twitter Silvia Piantoni @piantoni_silvia and Laura Andreoli @lauraandreoli80

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

PA and MS contributed equally.

PA and MS are joint senior authors.

To cite Piantoni S, Colombo E, Furloni R, *et al*. *Ann Rheum Dis* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/annrheumdis-2020-218806

Received 12 August 2020
Accepted 12 August 2020

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.

► http://dx.doi.org/10.1136/annrheumdis-2020-218759

Ann Rheum Dis 2020;**0**:1–2. doi:10.1136/annrheumdis-2020-218806

ORCID iDs
Silvia Piantoni http://orcid.org/0000-0003-0913-0197
Laura Andreoli http://orcid.org/0000-0002-9107-3218
Antonio Brucato http://orcid.org/0000-0002-7566-5600
Paolo Airó http://orcid.org/0000-0001-5241-1918

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