Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

RCT-TCZ-COVID-19 Study Group
(the list was ordered by number of patients enrolled)

The following study group members were involved with the design and implementation of the study.

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eMethods

The trial was designed during the first two weeks of March 2020, by a multidisciplinary group at the Azienda USL-IRCCS of Reggio Emilia. The group included clinical specialists in Infectious Diseases (Giovanni Dolci, Marco Massari, Fabrizio Boni), Rheumatology (Carlo Salvarani), Respiratory Disease (Nicola Facciolongo), Pharmacology (Caterina Turrà), a group of statisticians (Silvio Cavuto, Luisa Savoldi, Luca Braglia) and clinical epidemiologists (Domenico Franco Merlo, Paolo Bruzzi and Massimo Costantini).

No funding was obtained for this study. The coordinator centre and all participating centres are using local resources to conduct the trial.
Roche provided the drug and its distribution to the centres.

GD, MC, CS and DFM drafted the first version of the manuscript. A second revision of the manuscript was performed by MM, NF, and FB. SC, PB, LS and LB contributed to the statistical section of the manuscript. CT revised the pharmacological section. The manuscript was revised and approved by all the authors, who agreed the submission for publication

eResults

Populations in study

1. **Randomised patients**: 126

2**. Population for Intention To Treat (ITT) analysis**: 123

Three patients withdrew consent to the study during the first week after randomisation:

ID-code	Arm	comments
010-004	Standard	withdrew consent day 6 (the PaO2/FiO2 was 318)
023-002	Standard	withdrew consent day 3 (the PaO2/FiO2 was 232)
023-003	Standard	withdrew consent day 2 (the PaO2/FiO2 was 281)

3. **Population for Per Protocol analysis: 113**

Two patients were excluded because they did not meet eligibility criteria:

ID-code	Arm	comments
006-001	Tocilizumab	in non-invasive ventilation at enrolment
021-002	Standard	Severe diverticulitis at enrolment

Eight patients were excluded because they received prohibited treatments or they did not receive the assigned treatment

ID-code	Arm	comments
001-006	Standard	Received Tocilizumab IV repeated after 12 hours on day 4 and Methylprednisolone (MPS) 40 mg daily for at least 10 days since day 4 (the PaO2/FiO2 on day 4 was 169)
028-002	Standard	Received Tocilizumab IV repeated after 12 hours on day 2 and MPS 160 mg daily for 3 days since day 2 and then 80 mg daily for 2 days (the PaO2/FiO2 on day 2 was 426)
016-001	Standard	Received Tocilizumab sub-Q day 2 (the PaO2/FiO2 was 192)
010-005	Standard	Received Canakinumab 600 mg on day 2 (the PaO2/FiO2 was 210)
012-001	Standard	Received MPS 40 mg daily for 3 days since day 5 (the PaO2/FiO2 was 229 on day 5)
017-002	Standard	Received MPS 40 mg day 9 and MPS 80 mg day 10 (the PaO2/FiO2 was 200)
011-002	Tocilizumab	Received dexamethasone since day 4 for at least a week (the PaO2/FiO2 was 144 followed by a second value of 159)
019-002	Tocilizumab	Did not receive Tocilizumab for the occurrence of gastro-intestinal bleeding just after randomisation

eTable 1. Clinical outcomes at 14 days according to subgroups

	Clinical worsening at 14 days				
	Tocilizumab		Standard		Rate Ratio (95% CI)
	N (%)		N (%)		
All patients (N=123)	17/60	28.3	17/63	27.0	1.1 (0.6 – 1.9)
Baseline C-reactive protein (N=123)					
< 5	5/14	35.7	4/24	16.7	2.2 (0.7 – 7.0)
5 - 9.9	4/13	30.8	6/20	30.0	1.0 (0.4 – 2.9)
10-14.9	6/20	30.0	4/11	36.4	1.0 (0.3 – 2.8)
≥ 15	2/13	15.4	3/8	37.5	0.4 (0.1 – 1.9)
Baseline LDH (N=111)					
< 250	3/13	23.1	4/11	36.4	0.6 (0.2 – 2.2)
250-499	7/22	31.8	6/27	22.2	1.6 (0.6 – 4.1)
≥ 500	6/21	28.6	4/17	23.5	1.2 (0.4 – 3.6)
Baseline D-Dimer (N=111)					
< 500	5/16	31.3	7/32	21.9	1.5 (0.6 – 4.1)
500-999	5/21	23.8	6/15	40.0	0.6 (0.2 – 1.7)
≥ 1000	3/16	18.8	2/11	18.2	1.0 (0.2 – 5.2)
Baseline Ferritin (N=105)					
< 300	3/12	25.0	2/10	20.0	1.4 (0.3 – 6.8)
300-599	5/10	50.0	2/21	9.5	5.3 (1.2 – 22.5)
≥ 600	5/27	18.5	11/25	44.0	0.4 (0.2 – 1.1)
Baseline IL-6 (N=99)					

< 30	1/14	7.1	1/24	4.2	1.9 (0.1 – 26.4)
30-79	5/19	26.3	6/19	31.6	0.9 (0.3 – 2.5)
≥ 80	7/14	50.0	5/9	55.6	0.8 (0.4 – 1.9)
Baseline PaO_2/FiO_2 (N=123)					
200-249	4/17	23.5	7/19	36.8	0.6 (0.2 – 1.8)
250-300	13/43	30.2	10/44	22.7	1.3 (0.6 – 2.7)

eTable 2. Clinical outcomes in the per protocol population

	Tocilizumab (N=57)	Standard (N=56)	Rate Ratio (95% CI)
Clinical worsening at 14 days	15 (26.3)	17 (30.4)	0.87 (0.48-1.56)
Overall events at 14 days			
admissions to ICU	5 (8.8)	5 (8.9)	0.98 (0.30-3.21)
deaths	1 (1.8)	1 (1.8)	0.98 (0.06-15.3)
discharges	34 (59.6)	32 (57.1)	1.04 (0.76-1.42)
Overall events at 30 days			
admissions to ICU	5 (8.8)	5 (8.9)	0.98 (0.30-3.21)
deaths	1 (1.8)	1 (1.8)	0.98 (0.06-15.3)
discharges	52 (91.2)	56 (91.1)	1.00 (0.89-1.12)

eFigure. Trend of the PaO_2/FiO_2 ratio and the lymphocytes count by arm (squares are mean values, vertical bars are 95%CI)