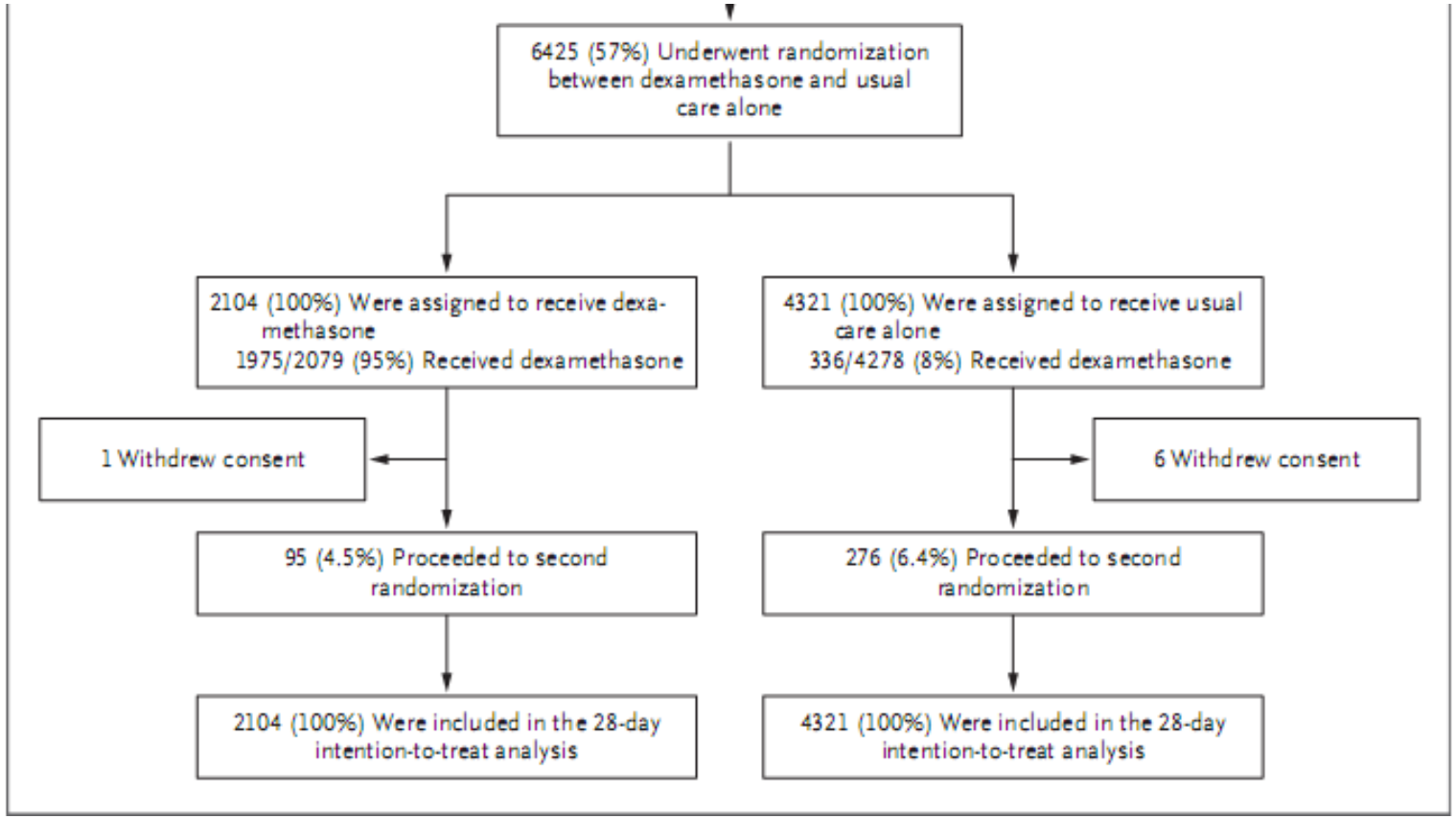
Tocilizumab data

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

The RECOVERY Collaborative Group*



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The affiliations of the members of the writing committee are listed in the Appendix. Address reprint requests to Drs. Horby and Landray at RECOVERY Central Coordinating Office, Richard Doll Bldg., Old Road Campus, Roosevelt Drive, Oxford OX3 7LF, United Kingdom, or at recoverytrial@ndph.ox.ac.uk.

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Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

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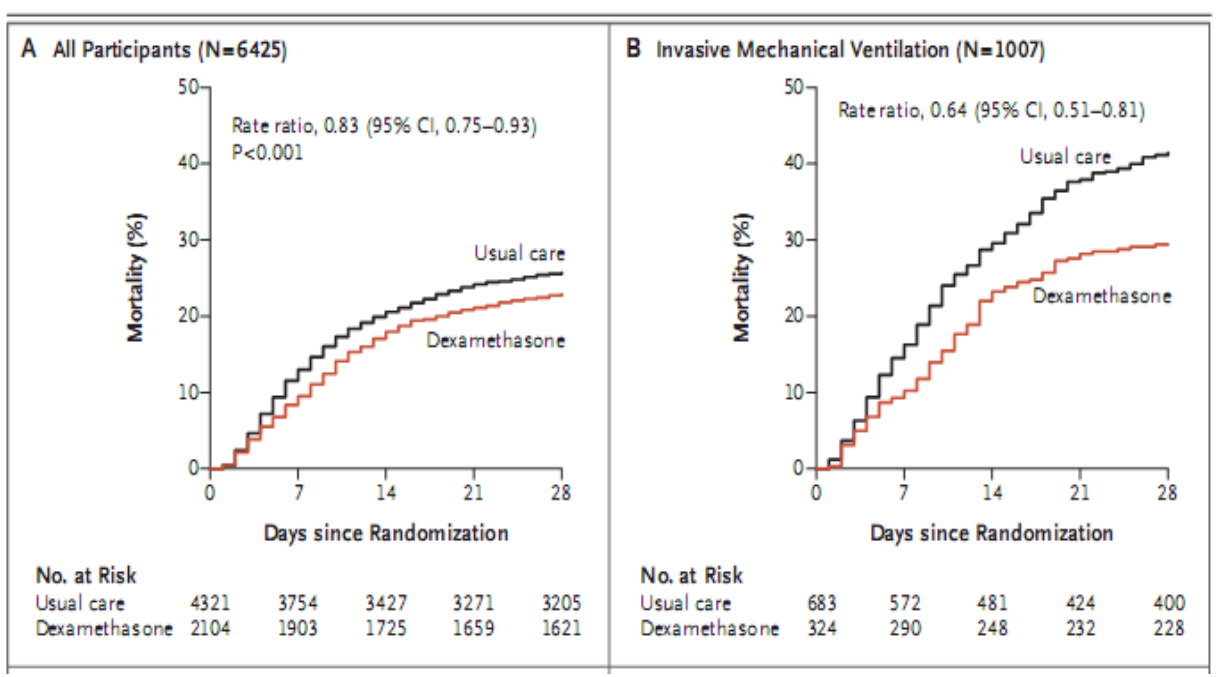

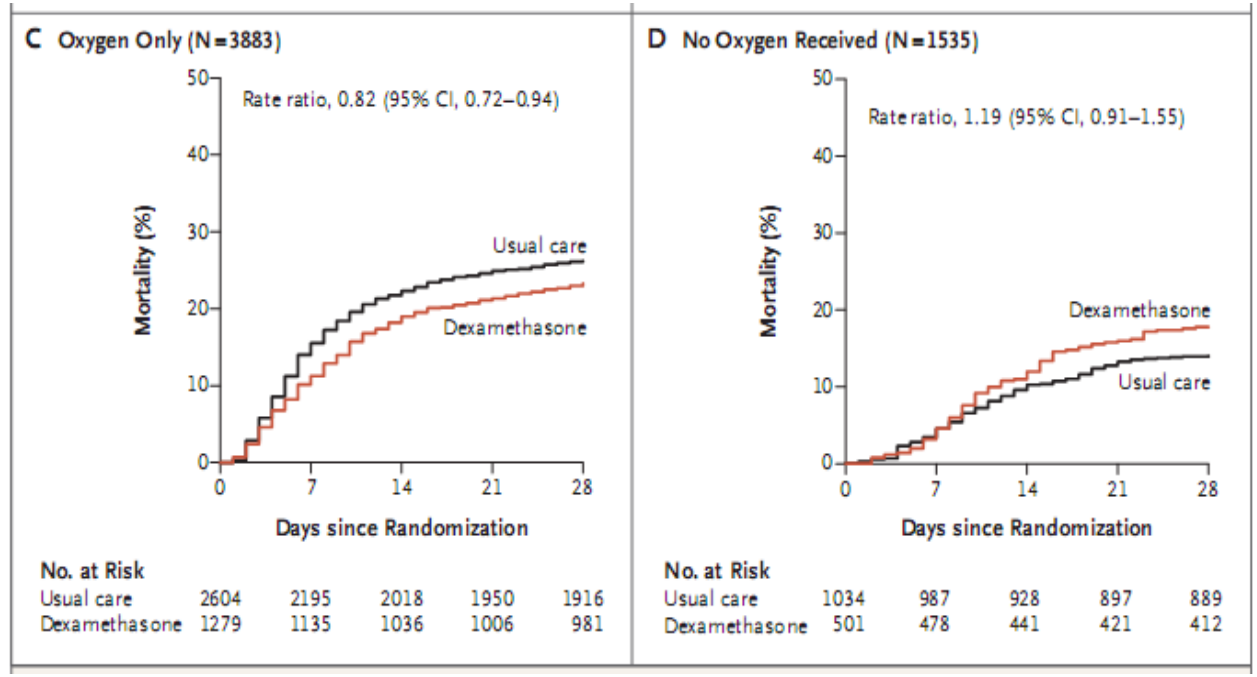

28 day death rate (Dexa vs SOC)

22.9% vs 25.7%

29.3% vs. 41.4%

23.3% vs. 26.2%

17.8% vs. 14.0%

The NEW ENGLAND JOURNAL of MEDICINE

This article was published on October 21, 2020, at NEJM.org.

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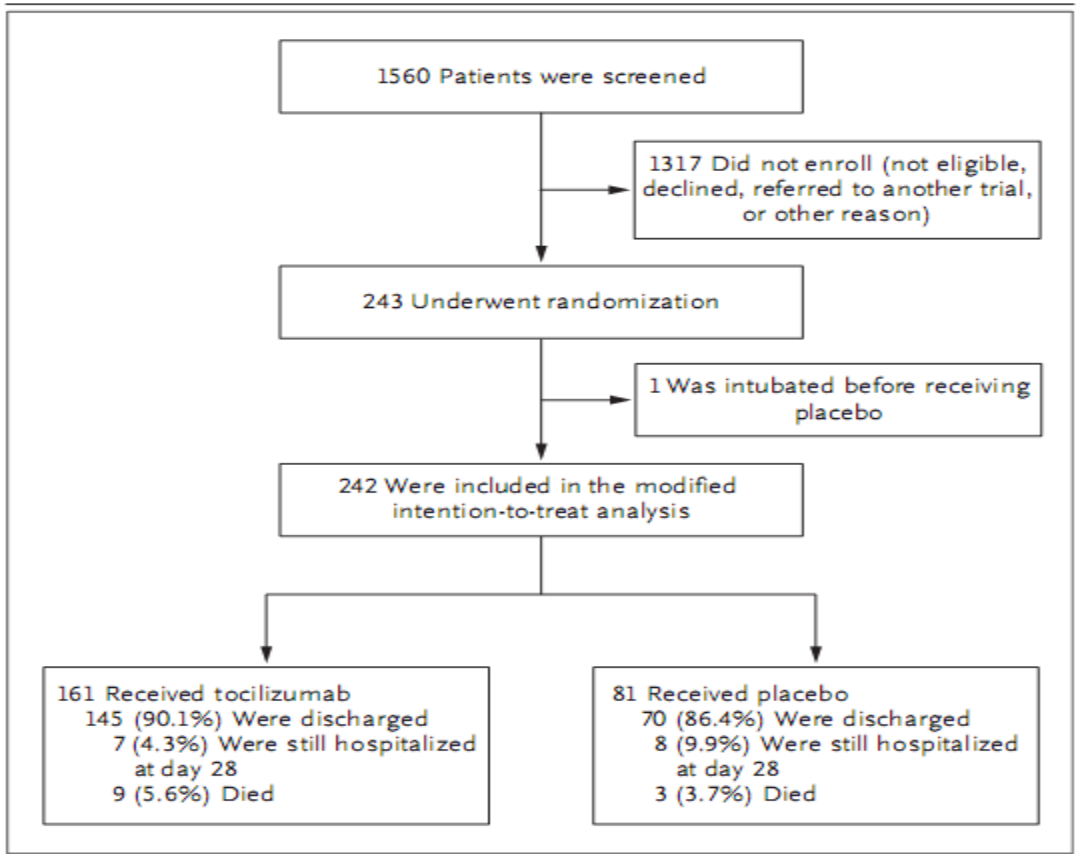
ORIGINAL ARTICLE

Efficacy of Tocilizumab in Patients Hospitalized with Covid-19

J.H. Stone, M.J. Frigault, N.J. Serling-Boyd, A.D. Fernandes, L. Harvey,

Moderate



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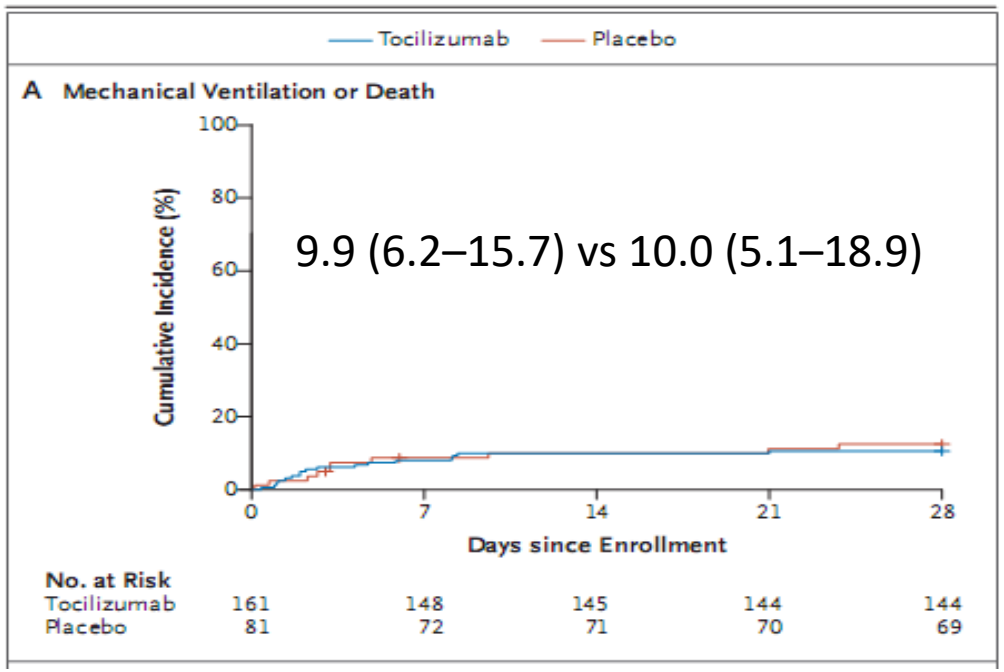
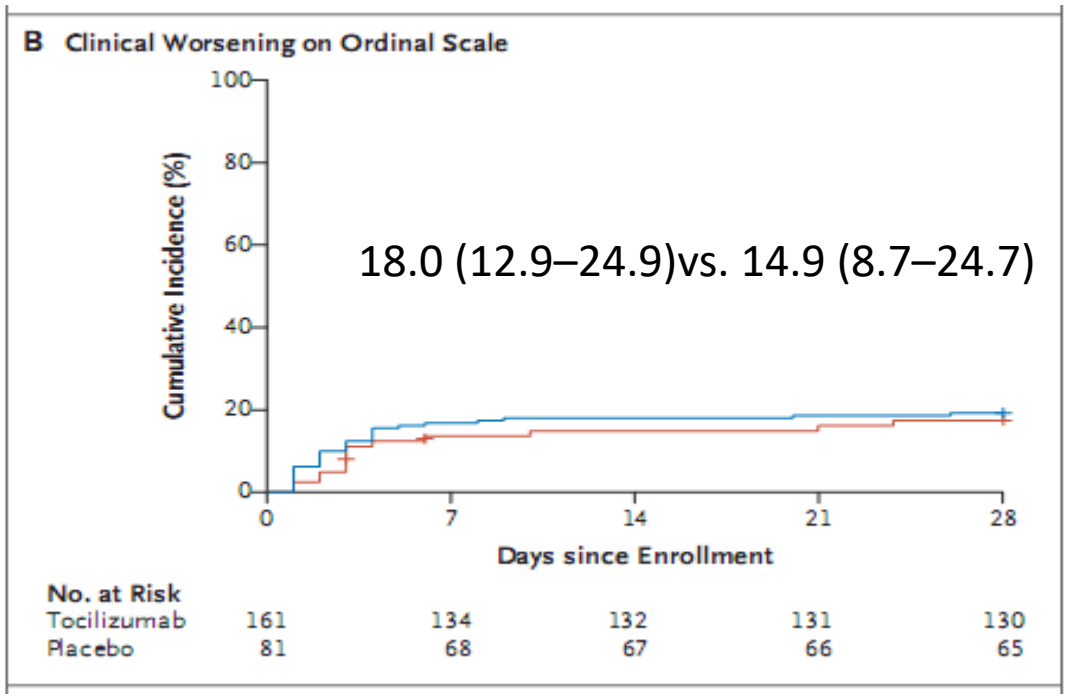
ORIGINAL ARTICLE

Efficacy of Tocilizumab in Patients Hospitalized with Covid-19



9.9 (6.2–15.7) vs 10.0 (5.1–18.9)



18.0 (12.9–24.9)vs. 14.9 (8.7–24.7)

14 day death rate: 4.4 (2.1–8.9) (MAB) vs. 1.3 (0.2–8.7) (placebo)

JAMA Internal Medicine | Original Investigation

Effect of Tocilizumab vs Standard Care on Clinical Worsening in Patients Hospitalized With COVID-19 Pneumonia
A Randomized Clinical Trial

Corresponding Author: Carlo Salvarani, MD, Unità Operativa di Reumatologia, Azienda USL-IRCCS di Reggio Emilia, Viale Risorgimento 80, 42100 Reggio Emilia, Italy (carlo.salvarani@ausl.re.it).

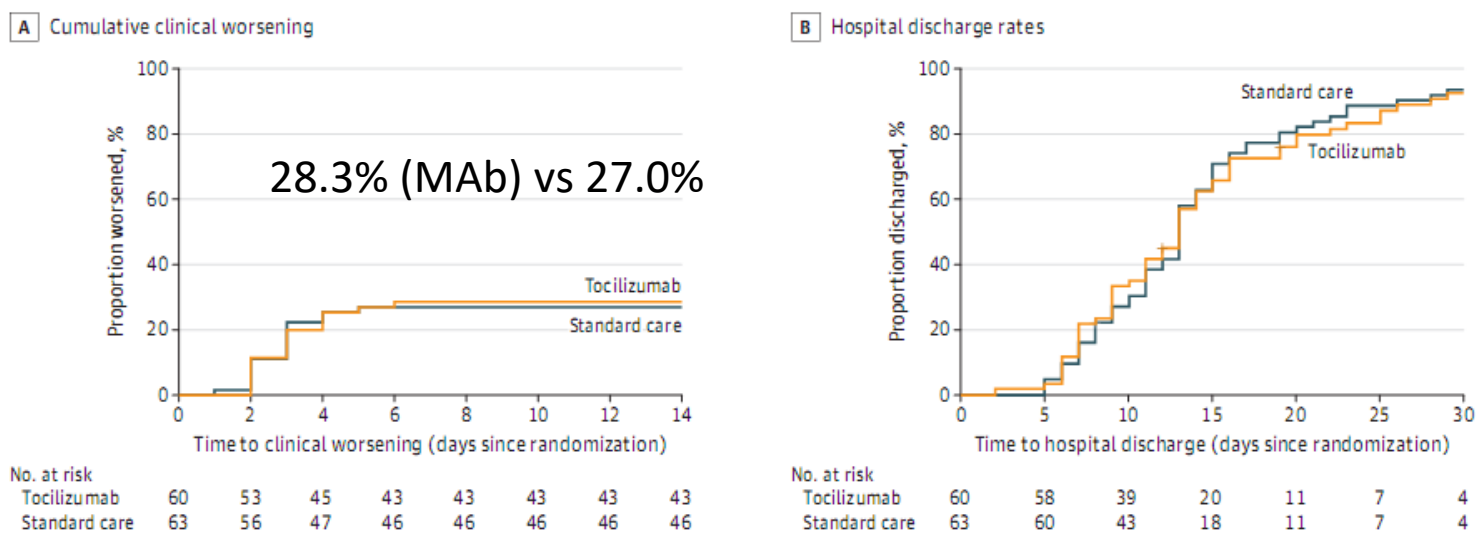
A total of 126 patients were randomized (60 to the tocilizumab group; 66 to the control group).

- (PaO2/FIO2) ratio between 200 and 300mm/Hg,
- an inflammatory phenotype defined by a temperature greater than 38 °C during the last 2 days, and CRP levels of 10mg/dL
- Patients were allowed to receive oxygen therapy with Venturi mask or high-flow nasal cannula with recorded and preset FIO2, but not invasive or noninvasive mechanical ventilation.

Moderate????

JAMA Intern Med. doi:10.1001/jamainternmed.2020.6615
Published online October 20, 2020.

Figure 2. Kaplan-Meier Estimates of Cumulative Clinical Worsening and Hospital Discharge



Kaplan-Meier estimates of cumulative clinical worsening (A) and hospital discharge (B).

Findings In this randomized clinical trial of 126 patients with a partial pressure of arterial oxygen to fraction of inspired oxygen (Pao_2/Fio_2) ratio between 200 and 300 mm Hg at enrollment, the rate of the primary clinical end point (clinical worsening) was not significantly different between the control group and the tocilizumab group.

Mortality at 14 days (1.7% vs 1.6%)

JAMA Internal Medicine | Original Investigation

Effect of Tocilizumab vs Usual Care in Adults Hospitalized With COVID-19 and Moderate or Severe Pneumonia
A Randomized Clinical Trial

Olivier Hermine, MD, PhD; Xavier Mariette, MD, PhD; Pierre-Louis Tharaux, MD, PhD; Matthieu Resche-Rigon, MD, PhD; Raphaël Porcher, PhD; Philippe Ravaud, MD, PhD; for the CORIMUNO-19 Collaborative Group

Corresponding author: Olivier Hermine, MD, PhD, Université de Paris, Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Necker, INSERM, Imagine Institute, 149-161 rue de Sèvres, Paris 75743, France (ohermine@gmail.com).

Figure 1. Study Flowchart[a]

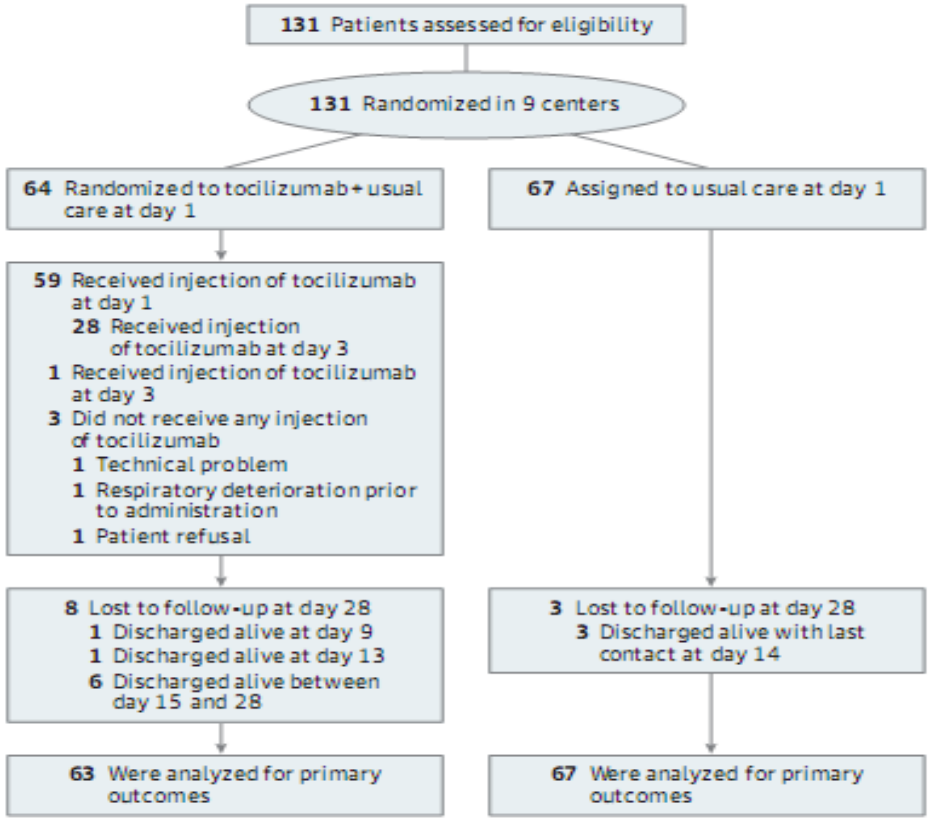


Table 2. Number of Patients With Noninvasive Ventilation or High-Flow Oxygen, Mechanical Ventilation, or Death

Variable	Tocilizumab (n = 63)	UC (n = 67)	Difference (95% CI)
Primary outcome by day 14, No.	15	24	
Cumulative incidence, % (95% CI)	24 (13 to 34)	36 (23 to 46)	−12 (−28 to 4)
First event, No.			
NIV/HFO	8	13	
MV	3	8	
Death/DNR order	4	3	
MV or death by day 14, No.			
% (95% CI)	17 (8 to 26)	27 (15 to 37)	−9 (−24 to 5)
First event, No.			
MV	5	14	
Death/DNR order	6	4	
Deaths			
Day 14, No.	7	6	
Survival, % (95% CI)	89 (81 to 97)	91 (84 to 98)	
Day 28, No.	7	8	
Survival, % (95% CI)	89 (81 to 97)	88 (80 to 96)	

JAMA Intern Med. doi:10.1001/jamainternmed.2020.6820
Published online October 20, 2020.

Meaning Tocilizumab may reduce the need for mechanical and noninvasive ventilation or death by day 14 but not mortality by day 28; further studies are necessary to confirm these preliminary results.

JAMA Internal Medicine | Original Investigation

Association Between Early Treatment With Tocilizumab and Mortality Among Critically Ill Patients With COVID-19

Shruti Gupta, MD, MPH; Wei Wang, PhD; Salim S. Hayek, MD; Lili Chan, MD, MSCR;

Corresponding Author: David E. Leaf, MD, MMSc, Division of Renal Medicine, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115 (deleaf@bwh.harvard.edu).

Figure 1. Study Cohort and Emulated Trial Flow

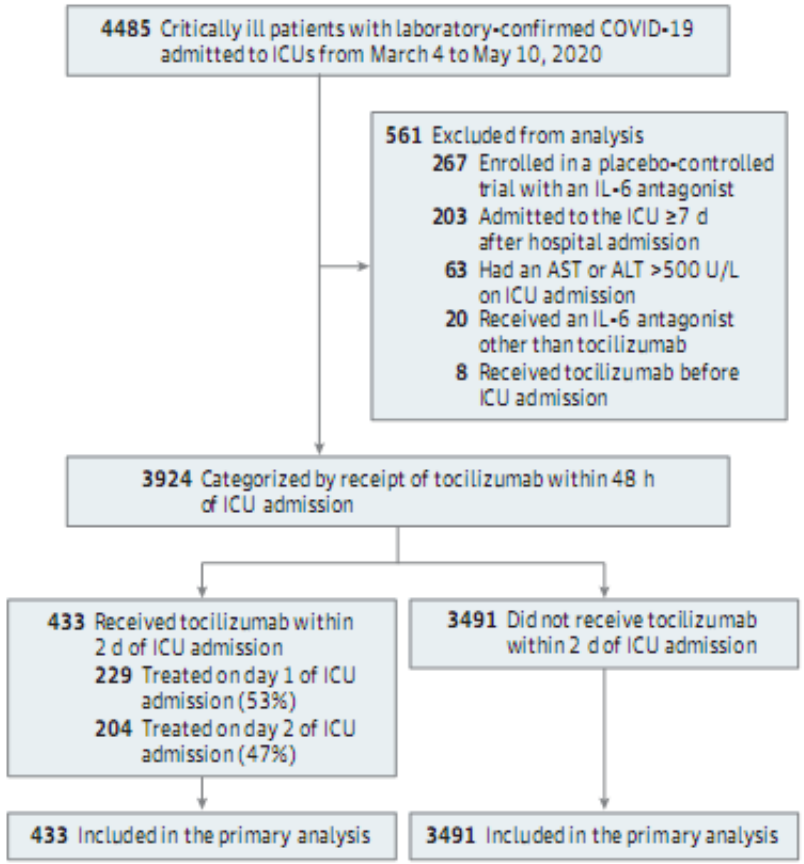
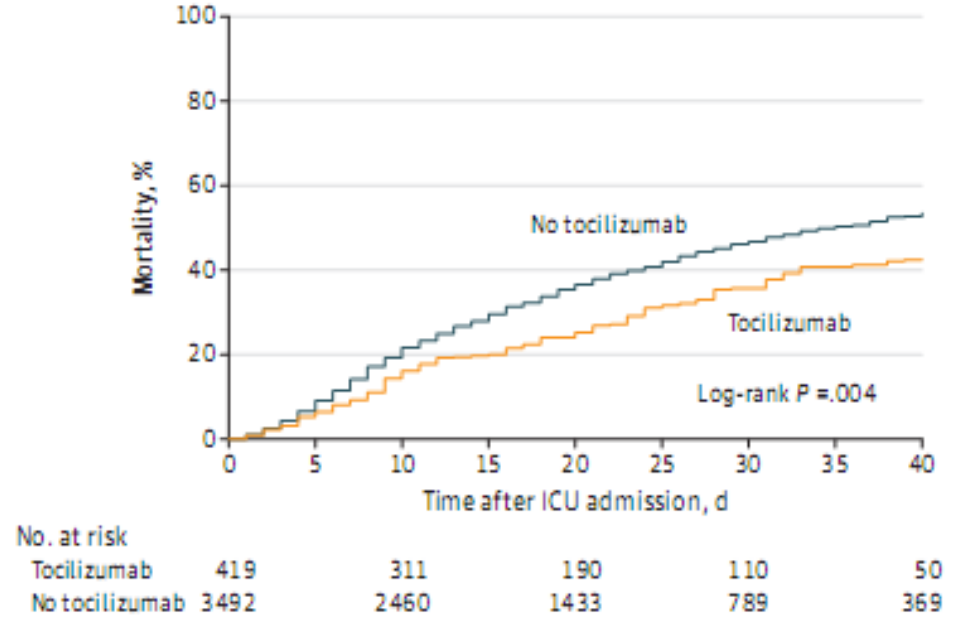


Figure 2. Mortality in Tocilizumab-Treated vs Non-Tocilizumab–Treated Patients



A total of 1544 patients (39.3%) died, including 125 (28.9%) treated with tocilizumab and 1419 (40.6%) not treated with tocilizumab. In the primary analysis, during a median follow-up of 27 (IQR, 14-37) days, patients treated with tocilizumab had a lower risk of death compared with those not treated with tocilizumab (HR, 0.71; 95%CI, 0.56-0.92).

A Study to Evaluate the Efficacy and Safety of Itolizumab in Subjects Hospitalized With COVID-19 (EQUINOX)

ClinicalTrials.gov Identifier: NCT04605926

Recruitment Status : Not yet recruiting
First Posted : October 28, 2020

Brief Summary:

This is a randomized controlled trial to evaluate the efficacy and safety of **itolizumab** in subjects hospitalized with COVID-19.

Condition or disease	Intervention/treatment	Phase
Coronavirus	Biological: EQ001 Biological: EQ001 Placebo	Phase 3

Detailed Description:

This study will randomize up to 800 subjects in a 1:1 ratio; itolizumab vs. placebo. Subjects will receive either itolizumab or placebo administered intravenously on Day 1 and Day 8 with follow-up to Day 90. Two interim analyses of futility are planned. The first will take place when approximately 20% of the subjects have been evaluated for the primary endpoint, and the second will take place when approximately 50% of the subjects have been evaluated for the primary endpoint.

Study Design

Go to

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	800 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Masking Description:	The study will be blinded to all study staff that has direct access to the subjects and the sponsor.
Primary Purpose:	Treatment
Official Title:	A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of **Itolizumab** in Subjects Hospitalized With COVID-19
Estimated Study Start Date :	November 2020
Estimated Primary Completion Date :	April 2021
Estimated Study Completion Date :	June 2021

A Study to Evaluate the Efficacy and Safety of Itolizumab in Subjects Hospitalized With COVID-19 (EQUINOX)

Outcome Measures

Primary Outcome Measures :

1. Proportion of subjects who have recovered at Day 28. [Time Frame: Day 28]

   Proportion of subjects who have recovered at Day 28.

Secondary Outcome Measures :

1. Proportion of subjects deceased or requiring mechanical ventilation at Day 28. [Time Frame: Day 28]

   Proportion of subjects deceased or requiring mechanical ventilation at Day 28.

2. Proportion of subjects deceased at Day 28. [Time Frame: Day 28]

   Proportion of subjects deceased at Day 28.

A Study to Evaluate the Efficacy and Safety of Itolizumab in Subjects Hospitalized With COVID-19 (EQUINOX)

Other Outcome Measures:

1. Incidence of treatment-emergent adverse events (TEAEs). [Time Frame: Day 90]

   Number of participants with treatment-related adverse events as assessed by Common Terminology Criteria for Adverse Events (CTCAE)

2. Time to maximum **itolizumab** serum concentration, Tmax [Time Frame: Day 28]

   Time to maximum **itolizumab** serum concentration, Tmax

3. Maximum **itolizumab** serum drug concentration, Cmax [Time Frame: Day 28]

   Maximum **itolizumab** serum drug concentration, Cmax

4. Total **itolizumab** exposure across time, AUC (from zero to last) [Time Frame: Day 28]

   Total **itolizumab** exposure across time, AUC (from zero to last)

5. Inflammatory biomarkers [Time Frame: Day 28]

   Including but not limited to IL-1, IL-6, IL-17, TNF-α.

6. Pharmacodynamic markers [Time Frame: Day 28]

   sCD6, sALCAM

Treatment of COVID-19 patients with the anti-CD6 antibody itolizumab

Table 3. Predictive values of triglycerides, aspartate aminotransferase (AST), D-dimer, interleukin 6 (IL-6), absolute leucocyte count (ALC), neutrophils, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) associated with COVID-19 severity or mortality according to ROC analysis

	Area	Sig.	95% CI		Sensitivity	Specificity	Cut-off
Severity							
Triglycerides	0.756	0.003	0.617	0.896	78.6%	65%	1.24 mmol L^{-1}
AST	0.858	0.000	0.749	0.966	82.8%	85%	20.5 IU L^{-1}
D-Dimer	0.783	0.009	0.603	0.964	80%	78.6%	1.35 µg mL^{-1}
IL-6	0.828	0.002	0.683	0.973	71.4%	73.9%	27.4 pg mL^{-1}
ALC	0.838	0.000	0.740	0.936	82.9%	70.8%	6.55 × 10^9 L^{-1}
Neutrophils	0.840	0.000	0.735	0.945	94.7%	70.8%	4.34 × 10^9 L^{-1}
NLR	0.799	0.000	0.685	0.913	70.6%	82.6%	4.91
PLR	0.673	0.029	0.524	0.823	75.8%	69.6%	135.0
Mortality							
AST	0.802	0.000	0.667	0.937	83.3%	71%	22.1 IU L^{-1}
D-Dimer	0.742	0.035	0.515	0.969	80%	63.2%	1.35 µg mL^{-1}
IL-6	0.770	0.033	0.527	1.000	71.4%	73.9%	53.4 pg mL^{-1}
ALC	0.727	0.003	0.592	0.863	72.7%	65.1%	7.60 × 10^9 L^{-1}
Neutrophils	0.765	0.001	0.636	0.895	81.0%	65.9%	5.57 × 10^9 L^{-1}
NLR	0.894	0.000	0.804	0.984	82.4%	85.0%	8.85
PLR	0.711	0.014	0.556	0.866	81.3%	60%	146.2

Treatment of COVID-19 patients with the anti-CD6 antibody itolizumab

Table 4. Univariate logistic regression analysis

		Death Odds ratio	IC 95%	
Generals	Age (> 65)	1.680	0.601	4.697
	Time between symptoms and itolizumab (>7)	5.625	1.862	16.989
	Neurological symptoms	4.778	1.076	21.224
Comorbidities	Hypertension	0.613	0.220	1.709
	Diabetes mellitus	2.024	0.712	5.753
	Cardiovascular disease	1.813	0.644	5.102
	COPD	0.952	0.216	4.197
	Cancer	2.000	0.264	15.163
	Chronic renal disease	4.778	1.076	21.224
	Asthma	1.583	0.478	5.246
	Obesity	1.500	0.307	7.326
	Nutrition deficit	0.327	0.066	1.634
Baseline laboratory biomarkers	AST (> 22.1 IU L^{-1})	10.500	2.462	44.78
	D-dimer (> 1.35 μg mL^{-1})	6.857	1.124	41.827
	ALC (> 7.60 × 10^9 L^{-1})	4.978	1.610	15.387
	Neutrophils (> 5.57 × 10^9 L^{-1})	8.196	2.311	29.073
	NLR (> 8.85)	26.444	5.788	120.819
	PLR (> 146.2)	6.500	1.594	26.511
	IL-6 (> 53.4 pg mL^{-1})	7.083	1.075	46.478

The highlighted variables are significantly associated with higher odds of death.

Immunity & Ageing

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Saavedra *et al. Immunity & Ageing* (2020) 17:34
https://doi.org/10.1186/s12979-020-00207-8

Immunity & Ageing

RESEARCH Open Access

An anti-CD6 monoclonal antibody (itolizumab) reduces circulating IL-6 in severe COVID-19 elderly patients

Danay Saavedra[1*], Ana Laura Añé-Kourí[2], Naivy Sánchez[3], Lázaro Manuel Filgueira[4], Julio Betancourt[4], Carlos Herrera[4], Leniel Manso[4], Elibet Chávez[5], Armando Caballero[4], Carlos Hidalgo[3], Geydi Lorenzo[1], Meylan Cepeda[1], Carmen Valenzuela[1], Mayra Ramos[1], Kalet León[1], Zaima Mazorra[1] and Tania Crombet[1]

Clinical & Translational Immunology

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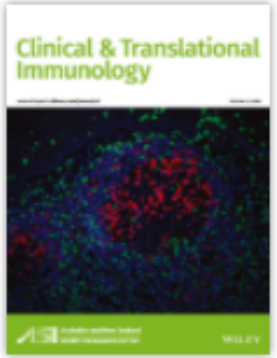

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ORIGINAL ARTICLE

Treatment of COVID-19 patients with the anti-CD6 antibody itolizumab

Armando Caballero[1], Lázaro M Filgueira[2], Julio Betancourt[2], Naivy Sánchez[2], Carlos Hidalgo[2], Alberto Ramírez[3], Alejandro Martinez[3], Rolando E Despaigne[4], Alberto Escalona[5], Henrry Diaz[6], Elio Meriño[6], Lilia M Ortega[7], Ulises Castillo[8], Mayra Ramos[9], Danay Saavedra[9], Yanelda García[9], Geydi Lorenzo[9], Meylán Cepeda[9], Maylén Arencibia[9], Leticia Cabrera[9], Milagros Domecq[9], Daymys Estévez[9], Carmen Valenzuela[9], Patricia Lorenzo[9], Lizet Sánchez[9], Zaima Mazorra[9], Kalet León[10] & Tania Crombet[9]

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Gerontology

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Gerontology

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Use of a Humanized Anti-CD6 Monoclonal Antibody (Itolizumab) in Elderly Patients with Moderate COVID-19

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