

# TDF/FTC FOR HIGH-RISK PATIENTS WITH COVID-19: THE PANCOVID RANDOMIZED CLINICAL TRIAL

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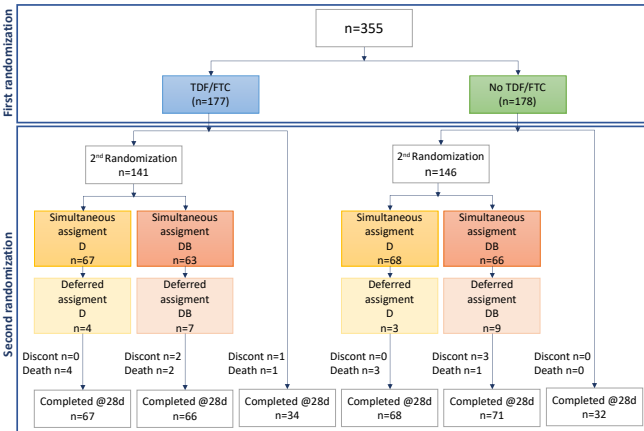
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## BACKGROUND

- Some in vitro, animal, and epidemiological data suggest that tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) might be an efficacious treatment for COVID-19.
- Baricitinib (B) added to dexamethasone (D) has demonstrated improvement in survival mostly in hospitalized COVID-19 patients requiring supplemental oxygen

## METHODS

- Multicenter open-label, pragmatic, RCT in 25 hospitals in Spain
- Inclusion criteria:
  - Confirmed SARS-CoV-2 infection detected by PCR or antigenic test
  - Creatinine clearance > 60 mL/min
  - Older than 60 years or younger if they had at least two comorbidities (hypertension, obesity, diabetes, cirrhosis, chronic neurologic disease, active cancer, cardiac insufficiency, ischemic cardiopathy or COPD).
- Exclusion criteria:
  - receiving steroids at immunosuppressive doses (15 mg/day in the 7 days prior to the onset of symptoms)
  - HIV infection
  - patients requiring a reservoir bag, mechanical ventilation or with acute respiratory distress criteria at the time of inclusion



\* 2<sup>nd</sup> randomization: At any moment during the trial, participants with room air O2 saturation <95% and at least one increased inflammatory biomarker.

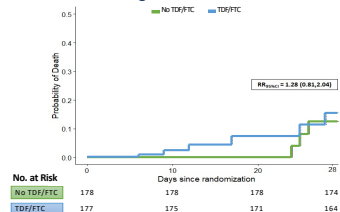
In this clinical trial of high-risk patients with COVID-19, **TDF/FTC did not improve disease outcomes**  
**Overall mortality was unexpectedly low**

## OUTCOMES

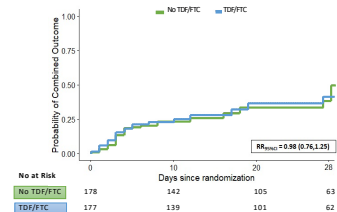
	TDF/FTC N=177	No TDF/FTC N=178	RR (95%CI)	p
<b>Primary outcome</b>				
28-day mortality, No. (%)	7 (4.0)	4 (2.2)	1.28 (0.81,2.04)	0.534
<b>Secondary Outcomes</b>				
Disease progression/critical care unit admission/28-day mortality (combined)	39 (22.0)	42 (23.6)	0.98 (0.76,1.25)	0.923
Disease Progression, No. (%)	39 (22.0)	42 (23.6)	0.98 (0.76,1.25)	0.923
Increase of O2 support	36 (35.6)	40 (37.7)	0.95 (0.71, 1.28)	0.867
Increase of steroid dose	19 (19.0)	19 (17.9)	1.04 (0.73,1.48)	0.985
Need for new medication	21 (21.0)	27 (25.5)	0.88 (0.61,1.25)	0.553
Mechanical Ventilation, No. (%)				
Non-invasive (BIPAP, CPAP, HFNC)	8 (4.5)	5 (2.8)	0.93 (1.35)	0.571
Invasive	8 (4.5)	13 (7.3)		
Days since 1 <sup>st</sup> randomization until death, median (IQR)	17.0 (10.5, 26.5)	25.5 (24.7, 34.7)	8.5 (-10.0,31.5)*	0.218
Days since 1 <sup>st</sup> randomization until discharge, median (IQR)	6.0 (4.0, 12.0)	7.0 (5.0, 14.0)	1.0 (-2.0,1.0)	0.369
Discharge ≤ 28 days, No. (%)	148 (89.7)	159 (91.9)	1.14 (0.81,1.60)*	0.606
Discharge > 28 days, No. (%)	17 (10.3)	14 (8.1)		

\*Median difference

Probability of Death At 28 Days In all Patients According to First Randomization



Probability of Disease Progression (Combined Outcome) According to First Randomization



**SAFETY:** Serious adverse events occurred in 6.18% / 5.65% of participants not treated/treated with TDF/FTC. Adverse events leading to TDF/FTC discontinuation occurred in 2.26%.

## RESULTS

Baseline Characteristic	All patients * N=355	TDF/FTC N=177	No TDF/FTC N=178
Sex, Female, No. (%)	126 (35.5)	64 (36.2)	62 (34.8)
Age, median (IQR)	67.0 (62.0, 73.0)	68.0 (62.0, 74.0)	67.0 (62.2, 73.0)
>60 years, No. (%)	294 (82.8)	145 (81.5)	149 (84.2)
Time symptom onset to 1 <sup>st</sup> rand, median (IQR)	7.0 (5.0, 10.0)	8.0 (5.0, 10.0)	7.0 (5.0, 10.0)
>5 days, No. (%)	249 (70.1)	125 (70.6)	124 (69.7)
Comorbidities No. (%)			
None	82 (23.1)	37 (20.9)	45 (25.3)
One	105 (29.6)	55 (31.1)	50 (28.1)
Two or more	168 (47.3)	85 (48.0)	83 (46.6)
Hypertension	217 (61.1)	112 (63.3)	105 (59.0)
Diabetes	97 (27.3)	52 (29.4)	45 (25.3)
Obesity	57 (16.1)	27 (15.3)	30 (16.9)
O2 Saturation, median (IQR)	95.0 (94.0, 96.0)	95.0 (94.0, 96.0)	95.0 (94.0, 96.0)
O2 support, No. (%)			
None	133 (37.5)	65 (36.7)	68 (38.2)
Nasal prongs	214 (60.3)	108 (61.0)	106 (59.6)
Conventional Mask	3 (0.8)	2 (1.1)	1 (0.6)
High-flow device	4 (1.1)	1 (0.6)	3 (1.7)
Rebreathing mask	1 (0.3)	1 (0.6)	0 (0.0)
Inflammatory biomarkers, med (IQR)			
C Reactive Protein (mg/L)	61.7 (30.3, 107.5)	63.8 (30.7, 117.0)	58.4 (30.1, 96.9)
Lactate Dehydrogenase (U/L)	285.0 (232.5, 371.5)	299.0 (235.7, 374.7)	280.0 (232.0, 356.0)
D-Dimer (ng/mL)	406.0 (12.3, 650.0)	417.0 (9.9, 700.0)	380.0 (12.4, 590.7)
Interleukin-6 (pg/mL)	17.4 (6.8, 37.2)	20.0 (7.1, 36.1)	14.0 (6.8, 38.1)
Remdesivir prior/after 1 <sup>st</sup> rand, No. (%)	45 (12.7)	23 (12.9)	22 (12.4)
Anti-inflammatory treatment (2 <sup>nd</sup> randomization), No. (%)	287 (80.8)	141 (79.7)	146 (82.0)
Simultaneous with 1 <sup>st</sup> randomization			
Dexamethasone	135 (47.0)	67 (47.5)	68 (46.6)
Dexamethasone + Baricitinib	129 (44.9)	63 (44.7)	66 (45.2)
Deferred after 1 <sup>st</sup> randomization			
Dexamethasone	7 (2.4)	4 (2.8)	3 (2.1)
Dexamethasone + Baricitinib	16 (5.6)	7 (5.0)	9 (6.2)

\* Of these 355 patients, 7 were ambulatory, 4 were residents of long-term care facility and 344 were hospitalized.

## CONCLUSIONS

- The results of this randomized clinical trial exploring the efficacy of TDF/FTC for the treatment of patients with COVID-19 at high risk of disease progression do not suggest a beneficial effect of TDF/FTC although our estimate of its effect is imprecise.

## ADDITIONAL KEY INFORMATION

Complementary information: Abstract #463: "BARICITINIB FOR HIGH-RISK PATIENTS WITH COVID-19: THE PANCOVID RANDOMIZED TRIAL"

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