BARICITINIB FOR HIGH-RISK PATIENTS WITH COVID-19: THE PANCOVID RANDOMIZED TRIAL

#463

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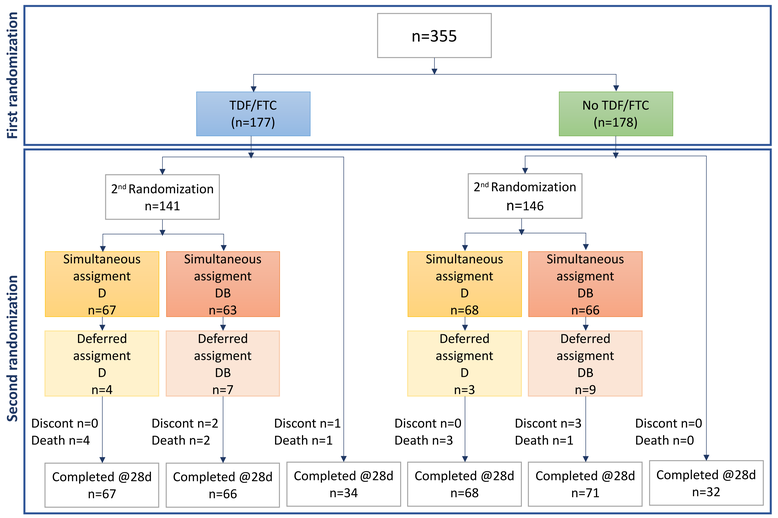
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BACKGROUND

- Recent studies suggest that baricitinib (B) added to dexamethasone (D) may reduce mortality in hospitalized COVID-19 patients requiring supplemental oxygen

METHODS

- Multicenter open-label, pragmatic, randomized clinical trial 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.
- Participants were initially randomized to receive or not TDF/FTC.
- 2nd randomization: At any moment, participants with room air O2 saturation <95% and at least one increased inflammatory biomarker biomarker could be randomized to receive dexamethasone or dexamethasone plus baricitinib.

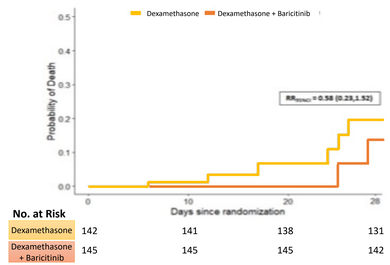


In this clinical trial of patients with COVID-19, all disease outcomes favored baricitinib added to dexamethasone

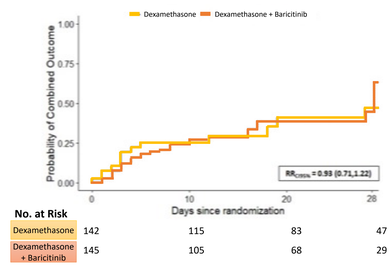
OUTCOMES	Dexamethasone + Baricitinib N=145	Dexamethasone N=142	RR (95%CI)	p
Primary outcome				
28-day mortality, No. (%)	3 (2.1)	7 (4.9)	0.58 (0.23,1.52)	0.318
Secondary Outcomes				
Disease progression/critical care unit admission/28-day mortality (combined)	36 (24.8)	39 (27.5)	0.93 (0.71,1.22)	0.708
Disease Progression, No. (%)	36 (24.8)	39 (27.5)	0.93 (0.71,1.22)	0.708
Increase of O2 support	34 (37.0)	36 (39.6)	0.95 (0.70, 1.28)	0.833
Increase of steroid dose	20 (21.7)	15 (16.7)	1.16 (0.84,1.62)	0.496
Need for new medication	22 (23.9)	21 (23.3)	1.01 (0.73,1.42)	1.000
Mechanical Ventilation, No. (%)				
Non-invasive (BIPAP, CPAP, HFNC)	3 (2.1)	8 (5.6)	0.76 (0.48,1.20)	0.362
Invasive	9 (6.2)	11 (7.7)		
Days since 1st randomization until death, median (IQR)	28.0 (26.5, 44.5)	24.0 (14.5, 25.5)	-4.0 (-49.0,1)*	0.110
Days since 1st randomization until discharge, median (IQR)	7.0 (5.0, 13.5)	7.0 (5.0, 12.0)	0.0 (-3.0,0.0)*	0.596
Discharge ≤ 28 days, No. (%)	131 (94.2)	121 (89.0)	0.67 (0.38,1.19)	0.173
Discharge > 28 days, No. (%)	8 (5.8)	15 (11.0)		

*Median difference

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



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



SAFETY: One hundred and eighty patients had at least one adverse event (60.6% in Dexamethasone group and 64.8% in Baricitinib plus Dexamethasone group). Twelve of them were serious adverse events, 6 in Dexamethasone group (4.2%) and other 6 in Baricitinib plus Dexamethasone group (4.1%).

RESULTS

Baseline Characteristic	All patients N=287	Dexamethasone + Baricitinib N=145	Dexamethasone N=142
Sex, Female, No. (%)	99 (34.5)	51 (35.2)	48 (33.8)
Age, median (IQR)	67.0 (62.0, 74.0)	68.0 (63.0, 75.0)	67.0 (61.0, 72.7)
≤60 years, No. (%)	61 (17.2)	23 (15.9)	30 (21.1)
>60 years, No. (%)	294 (82.8)	122 (84.1)	112 (78.9)
Time symptom onset to 2nd random, median (IQR)	7.0 (5.0, 10.0)	8.0 (5.0, 11.0)	7.0 (5.0, 9.7)
>5 days, No. (%)	204 (71.1)	108 (74.5)	96 (67.6)
Time from 1st to 2nd randomization (excluding simultaneous randomization), median (IQR)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	2.00(1.0, 2.5)
Comorbidities No. (%)			
None	76 (26.5)	43 (29.7)	33 (23.2)
One	83 (28.9)	44 (30.3)	39 (27.5)
Two or more	128 (44.6)	58 (40.0)	70 (49.3)
Diabetes	85 (29.6)	37 (25.5)	48 (33.8)
Hypertension	165 (57.5)	78 (53.8)	87 (61.3)
Obesity	54 (18.8)	27 (18.6)	27 (19.0)
O2 Saturation, median (IQR)	95.0 (94.0, 96.0)	95.0 (94.0, 96.0)	95.0 (93.0, 96.0)
O2 support, No. (%)			
None	74 (25.8)	42 (29.0)	32 (22.5)
Nasal prongs	205 (71.4)	99 (68.3)	106 (74.6)
Conventional Mask	3 (1.0)	3 (2.1)	0 (0.0)
High-flow device	4 (1.4)	1 (0.7)	3 (2.1)
Rebreathing mask	1 (0.3)	0 (0.0)	1 (0.7)
Inflammatory biomarkers, med (IQR)			
C Reactive Protein (mg/L)	66.70 (33.6, 113.7)	68.1 (33.8, 113.6)	65.3 (33.6, 113.6)
Lactate Dehydrogenase (UI/L)	304.0 (242.0, 378.0)	303.5 (238.5, 371.7)	305.0 (247.0, 379.0)
D-Dimer (ng/mL)	417.5 (15.4, 655.5)	430.0 (35.0, 665.0)	410.0 (9.4, 640.0)
Interleukin-6 (pg/mL)	17.7 (6.5, 37.3)	19.2 (7.8, 43.4)	12.0 (6.0, 29.9)
Remdesivir prior to/at 1st randomization, No. (%)	44 (15.3)	22 (15.2)	22 (15.5)
TDF/FTC prior to/at 2nd randomization, No. (%)	141 (49.1)	71 (48.9)	70 (49.3)

CONCLUSIONS

- The results of this clinical trial of high-risk patients with COVID-19 all disease outcomes favored baricitinib added to dexamethasone, but differences did not reach statistical significance.
- Overall mortality was unexpectedly low.

ADDITIONAL KEY INFORMATION

Complementary information: Abstract #460: "TDF/FTC FOR HIGH-RISK PATIENTS WITH COVID-19: THE PANCOVID RANDOMIZED CLINICAL TRIAL"

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Funding: By grant COV20/00023 from Instituto de Salud Carlos III (ISCIII), Minister of Innovation and Science of Spain. Co-funded by European Regional Development Fund/European Social Fund "A way to make Europe"/"Investing in your future".
Baricitinib have been provided by Eli Lilly.
Tenofovir/emtricitabine have been partially provided by Teva.