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Baricitinib reduces 30-day mortality in older adults with moderate-to-severe COVID-19 pneumonia

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Abstract

Background: Older adults are at the highest risk of severe disease and death due to COVID-19. Randomized data have shown that baricitinib improves outcomes in these patients, but focused stratified analyses of geriatric cohorts are lacking. Our objective was to analyze the efficacy of baricitinib in older adults with COVID-19 moderate-to-severe pneumonia.

Methods: This is a propensity score [PS]-matched retrospective cohort study. Patients from the COVID-AGE and Alba-Score cohorts, hospitalized for moderate-to-severe COVID-19 pneumonia, were categorized in two age brackets of age <70 years old (86 with baricitinib and 86 PS-matched controls) or ≥70 years old (78 on baricitinib and 78 PS-matched controls). Thirty-day mortality rates were analyzed with Kaplan–Meier and Cox proportional hazard models.

Justin Stebbing and Volker Martin Lauschke contributed equally to the work.

Results: Mean age was 79.1 for those ≥70 years and 58.9 for those <70. Exactly 29.6% were female. Treatment with baricitinib resulted in a significant reduction in death from any cause by 48% in patients aged 70 or older, an 18.5% reduction in 30-day absolute mortality risk (n/N: 16/78 [20.5%] baricitinib, 30/78 [38.5%] in PS-matched controls, $p < 0.001$) and a lower 30-day adjusted fatality rate (HR 0.21; 95% CI 0.09–0.47; $p < 0.001$). Beneficial effects on mortality were also observed in the age group <70 (8.1% reduction in 30-day absolute mortality risk; HR 0.14; 95% CI 0.03–0.64; $p = 0.011$).

Conclusions: Baricitinib is associated with an absolute mortality risk reduction of 18.5% in adults older than 70 years hospitalized with COVID-19 pneumonia.

KEYWORDS

baricitinib, COVID-19, mortality, older adults

INTRODUCTION

Advanced age is the most important risk factor for adverse outcomes and mortality in COVID-19 patients.[1,2] More than 50% of COVID-19 deaths occur in adults aged 70 years and older, despite the fact that the majority of SARS-CoV-2 infections are found in younger adults.[3] Case fatality rates are up to 22.7% among those aged 70–79 years old and between 22% and 38.1% in persons older than 80 years.[1,2,4–8]

Thus far, remdesivir, dexamethasone, or remdesivir plus baricitinib are the only Food and Drug Administration (FDA) approved drug for COVID-19 for adults.[9] Baricitinib received the Emergency Use Authorization from the FDA on November 19, 2020 in association with remdesivir in patients requiring supplemental oxygen, after revision of the Adaptive COVID-19 Treatment Trial 2 (ACTT-2).[10] More recently, the COV-BARRIER trial showed that baricitinib alone resulted in a significant reduction in death from any cause by 38% by day 28, the greatest risk reduction for any treatment observed thus far, although it did not meet statistical significance on the primary endpoint, progression to the first occurrence of noninvasive (NIMV) or invasive mechanical ventilation (IMV) or death.[11] However, little information is available for its use in older populations.

Baricitinib is a small molecule reversible Janus kinase (JAK) 1 and 2 inhibitor with suggested dual anti-cytokine and anti-viral activity against SARS-CoV-2 infection. It curtails excessive inflammatory signaling and blunts interferon-mediated induction of interferon response genes that include at least in some tissues the viral receptor angiotensin-converting enzyme 2 (ACE2).[12] In addition, baricitinib inhibits numb associated kinases that are directly involved in viral endocytosis.[13]

In our hospital, baricitinib has been largely used in patients with COVID-19 pneumonia, independent of age. Here, we present the results of the first 164 consecutive patients treated with baricitinib (78 with an age

Key Points

- Treatment with baricitinib results in a significant reduction ($p < 0.001$) in 30-day mortality from any cause in patients younger than 70 years by 54%, and by 48% in patients aged 70 or older.
- Treatment with baricitinib is associated with an 8.1% reduction in 30-day absolute mortality risk in patients younger than 70, and with an 18.5% reduction in 30-day absolute mortality risk in those aged 70 or older.
- Baricitinib is an effective treatment for older adults with moderate-to-severe COVID-19 pneumonia. Trials in this group are lacking.

Why Does this Paper Matter

Baricitinib is associated with a 30-day mortality reduction in adults older than 70 years hospitalized with COVID-19 pneumonia. Absolute risk reduction is higher in this population than in propensity score-matched young adults. Baricitinib could be an effective treatment for older adults.

≥70 years and 86 with an age <70 years), and 164 matched controls who did not receive baricitinib.

METHODS

Patients from the COVID-AGE study (NCT04362943) and the Alba-Score project are included in the present manuscript. Both studies were conducted at the Complejo Hospitalario Universitario of Albacete between March 9, 2020, and July 7, 2020 in COVID-19 Units. Both cohorts together included the first 1470 consecutive patients with laboratory confirmed infection, as diagnosed by a positive SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) test by nasopharyngeal swab admitted to the hospital with moderate-to-severe or severe disease, but not requiring IMV/NIMV on admission. Both studies were approved by the local Ethics Review Committee (records 2020/04/039 and 2020/06/062).

Propensity score (PS)-matching was used to create the control group using patients who were not treated with baricitinib in the same period of time. Cases younger and older of 70 years were matched to 1:1 to a control patient, adjusted for age, sex, Charlson comorbidity index, and baseline Sat/FiO_2 ratio (oxygen saturation/inspired oxygen fraction), using the statistical package «MatchIt» (v4.0.2). No statistical differences were found for any variables included in the PS. Mortality reduction was analyzed with Kaplan–Meier and Cox proportional hazard models adjusted by age, sex, Charlson index of comorbidity, lymphocyte count, lactate dehydrogenase (LDH), alanine amino *transferase* (ALT), creatinine, $SatFiO_2$, need of NIMV/IMV during hospitalization, month of admission, and treatment with anakinra, tocilizumab, or corticosteroids. These three last medicines were the most common immunomodulators used in our hospital along with baricitinib. All analyses were performed using the statistical package "R".

RESULTS

Table 1 presents the baseline characteristics of the participants. One hundred and sixty-four participants (86 < 70 years old, 78 ≥ 70 years old) were treated with baricitinib, mean total dose of 17.6 mg (SD 10.2), for a mean number of 5.9 days of treatment, and were propensity-score matched with 164 participants without baricitinib. More patients in the baricitinib groups were also treated with tocilizumab, anakinra, and corticosteroids compared with those in the control groups. In addition, patients in the baricitinib groups more frequently required NIMV/IMV or intensive care unit (ICU) admissions, reflecting a higher disease severity. Despite this increased severity, both baricitinib groups presented lower mortality rates when compared with PS-matched controls.

Treatment with baricitinib resulted in a significant reduction ($p < 0.001$) in death from any cause in patients younger than 70 years by 54% (n/N: 6/86 [7.0%] baricitinib, 13/86 [15.1%] controls), and by 48% in patients aged 70 or older (n/N: 16/78 [20.5%] baricitinib, 30/78 [38.5%] controls). Treatment with baricitinib was associated with an 8.1% reduction in 30-day absolute mortality risk in patients younger than 70, and with an 18.5% reduction in 30-day absolute mortality risk in those aged 70 or older. Mean survival time until outcome for the four groups was 29.3 days (95% confidence interval [CI] 28.5–30.0) for <70 years old with baricitinib, 24.9 days (95% CI 22.4–27.4) for <70 years old without baricitinib, 26.5 days (95% CI 24.7–28.3) for ≥70 years old with baricitinib, 17.5 days (95% CI 14.3–20.7) for ≥70 years old without baricitinib (Log Rank 63.364; $p < 0.001$) (Figure 1).

Patients aged 70 or over on baricitinib presented a lower 30-day fatality rate than those without baricitinib (hazard ratio [HR] 0.21; 95% CI 0.09–0.47; $p < 0.001$), and similar results were found in those younger than 70 (HR 0.14; 95% CI 0.03–0.64; $p = 0.011$), adjusted by age, sex, comorbidity, lymphocyte count, LDH, ALT, creatinine, $SatFiO_2$, need of NIMV/IMV, month of admission, and treatment with anakinra, tocilizumab, or corticosteroids. Other variables with significance in the models were LDH, ALT, creatinine, $SatFiO_2$, and treatment with anakinra, only for the older sample. We did not observe serious adverse events that were directly attributed to baricitinib in our sample.

DISCUSSION

The main result of our study is that baricitinib is associated with a reduced mortality rate both in young and old patients hospitalized by COVID-19 pneumonia. The effect is lower in relative risk reduction (48% and 54% respectively) but more than double in absolute risk reduction (18.5% and 8.1% respectively) in the older adults' cohort, thus saving more lives in those older than 70 years. These results are in agreement with non-published data from the COV-BARRIER study, which show a significant reduction in 28-day mortality from any cause by 38%. However, results comparing young and old adults were not available. Because baricitinib is already recommended in clinical practice guidelines for the treatment of moderate–severe COVID-19 for adults of

TABLE 1 Baseline characteristics of the sample

		Age < 70		Age ≥ 70	
	Total sample ($n = 328$)	**Bari yes ($n = 86$)**	**Bari no ($n = 86$)**	**Bari yes ($n = 78$)**	**Bari no ($n = 78$)**
Age	68.5 (12.4)	58.6 (7.5)	59.2 (7.7)	79.2 (6.3)	79.1 (7.2)
Female sex	97 (29.6)	23 (26.7)	20 (23.3)	26 (33.3)	28 (35.9)
Institutionalization	31 (9.2)	0 (0.0)	4 (4.7)	10 (13.0)	16 (20.5)
Charlson Index	1.6 (2.0)	1.0 (1.7)	1.2 (1.7)	2.2 (2.2)	2.2 (2.2)
Hypertension	213 (64.9)	39 (45.3)	47 (54.7)	62 (79.5)	65 (83.3)
Diabetes	107 (32.6)	22 (25.6)	23 (26.7)	32 (41.0)	30 (38.5)
Obesity	75 (22.9)	20 (23.3)	22 (25.9)	13 (17.3)	20 (26.3)
SatFiO2	289 (129)	296 (137)	303 (133)	279 (118)	276 (127)
Lymphocyte count (/mcL)	901 (564)	903 (468)	903 (429)	926 (841)	871 (443)
Creatinine (mg/dl)	1.1 (0.6)	1.0 (0.6)	1.0 (0.5)	1.2 (0.5)	1.2 (0.7)
LDH (U/L)	396 (173)	442 (180)	362 (150)	387 (147)	391 (204)
ALT (U/L)	43 (45)	55 (53)	42 (38)	39 (53)	33 (29)
N days on baricitinib	5.9 (2.5)	6.1 (2.3)	-	5.7 (2.6)	-
Baricitinib total dose (mg)	17.6 (10.2)	20.6 (10.8)	-	14.3 (8.3)	-
Lopinavir/Ritonavir	267 (81.4)	70 (81.4)	72 (83.7)	67 (85.9)	58 (74.4)
Hydroxychloroquine	308 (93.9)	83 (96.5)	84 (97.7)	76 (97.4)	65 (83.3)
Tocilizumab	31 (9.5)	18 (20.9)	8 (9.3)	4 (5.1)	1 (1.3)
Anakinra	78 (23.8)	34 (39.5)	5 (5.8)	34 (43.6)	5 (6.4)
Corticosteroids	275 (83.8)	83 (96.5)	62 (72.1)	74 (94.9)	56 (71.8)
LWMH	322 (95.8)	85 (98.8)	83 (96.5)	77 (98.7)	69 (88.5)
NIMV/IMV	74 (22.6)	42 (48.8)	21 (24.4)	9 (11.5)	2 (2.6)
Critical care	70 (21.3)	41 (47.7)	21 (24.4)	6 (7.7)	2 (2.6)
Days of follow-up	14.1 (8.8)	18.4 (9.0)	11.0 (8.4)	17.7 (7.6)	9.3 (6.2)
Mortality	67 (19.9)	6 (7.0)	13 (15.1)	16 (20.5)	30 (38.5)

Note: All data are means (SD) or number of participants (%).

Abbreviations: LWMH, low-weight molecular heparin; NIMV/IMV, noninvasive mechanical ventilation or invasive mechanical ventilation; SatFiO2, Oxygen saturation/inspired oxygen fraction.

all ages including older adults, our results do not change current practice standards. However, our findings reinforce these current practice standards, mainly in older adult populations.

In our study, 97 (29.6%) participants received either tocilizumab or anakinra in the baricitinib groups, and more than 80% were also treated with corticosteroids. These figures are higher than in the control groups, likely reflecting greater disease severity and the increased use of all types of available drugs in the baricitinib groups. This finding aligns with the increased use of NIMV/IMV and critical care unit admissions in baricitinib groups. In the COV-BARRIER, standard of care included 79% of participants receiving corticosteroids and 19% receiving remdesivir, with some receiving both, and mortality reduction was more pronounced in patients receiving NIMV at baseline.[11] It may be plausible that in patients with more severe disease, with advanced age, or both, baricitinib may exhibit a better benefit profile.

Besides the two randomized clinical trials, baricitinib use in COVID-19 has been evaluated in several observational studies and has shown clinical benefits for different endpoints, including mortality reduction, shorter hospital stay, decreased incidence of ICU admission, reduced need for mechanical ventilation, and less need of supplementary oxygen at hospital discharge.[10,12,14–18] In addition, some of these studies showed a reduction in interleukin (IL) 6, IL-1β, tumor necrosis factor alpha (TNF-α), and D-dimer levels, and a reduction in viral load as possible mechanism implicated in the benefits of baricitinib. However, in none of the above studies age differences were analyzed.

Underlying mechanisms for adverse outcomes in older adults with COVID-19 may include endothelial

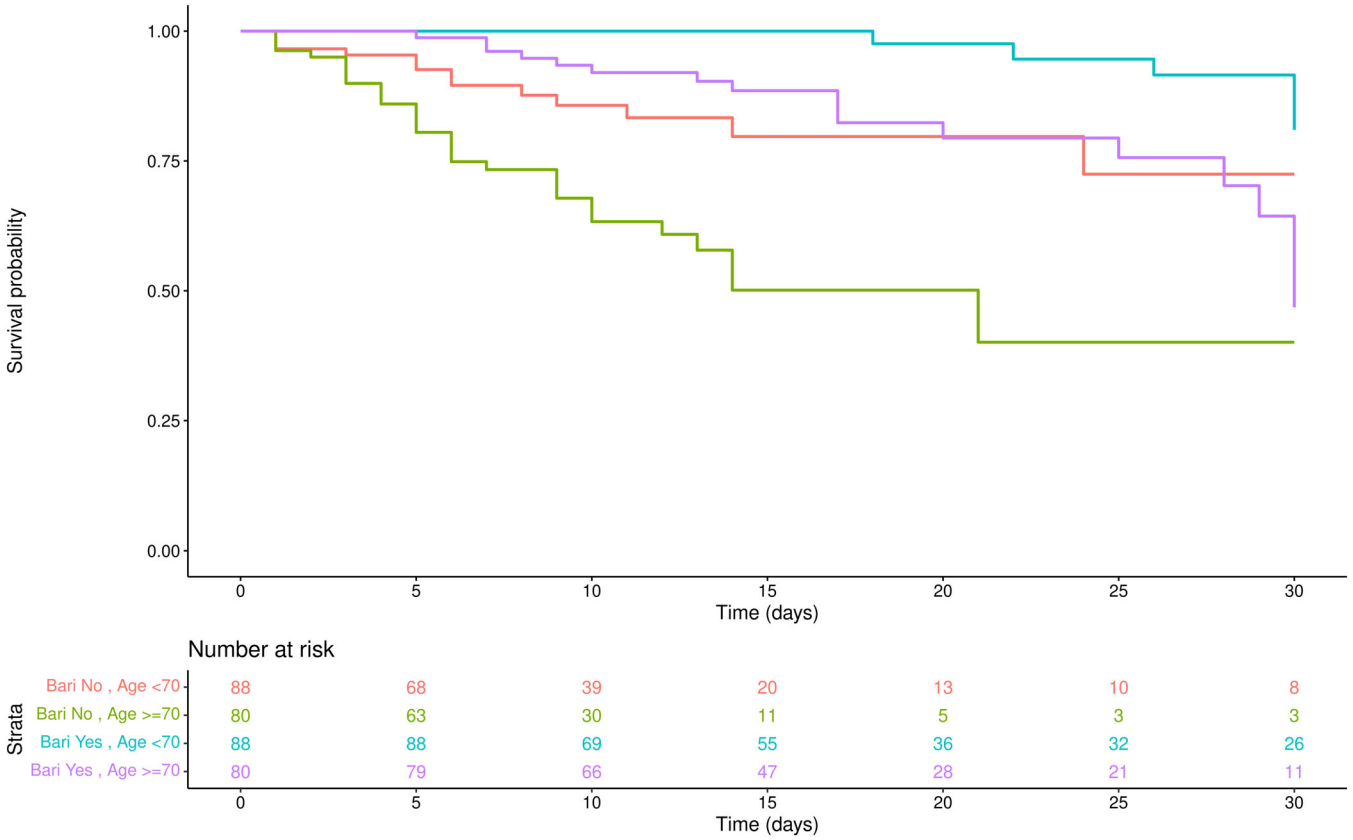

FIGURE 1 Thirty-day mortality and baricitinib treatment in patients hospitalized with COVID-19 pneumonia in those aged <70 years or ≥70 years old (Kaplan–Meier analysis)

dysfunction, chronic low-grade inflammatory phenotype a pro-coagulant state leading to thrombosis, dysregulated ACE2 activity enhancing viral entry to the cell and immunosenescence.[19–24] In this sense, drugs modulating these age-associated conditions, such as baricitinib, may be more suitable for older adults than for younger ones. In addition, baricitinib has been experimentally shown to reduce viral entry, helping the most compromised patients to reduce the viral load although this was not studied here.[12]

The characteristics of baricitinib are appropriate for older patients. It is a once-a-day oral medicine with a short half-life and benign safety profile, which is easy to titrate (only glomerular filtration rate <30 ml/min is a limitation but then the 2 mg dose can be used) and can be administered across layers of care. It has a low risk of drug–drug interactions and can be co-administered with most established COVID-19 treatments, such as glucocorticoids or LMWH with few to no drug–drug interactions. It is excreted largely unchanged and when used for a short duration, it is cheap compared, for example, with remdesivir. Its oral use and cost make it an informed choice in low-and-medium income countries.

Our study has several limitations. The first one could be a residual confounding or inadequate control of other explanatory factors for the difference in mortality, including obesity, immunocompromising conditions, or smoking, although we included all relevant clinical conditions that could be retrieved from medical charts under a retrospective methodology. We used the Charlson index for comorbidity control instead of individual clinical conditions in order to show a unique measure of comorbidity as a confounding risk factor for mortality. However, results using individual diseases or conditions were not significantly different. However, the main limitation is that our study is not a randomized clinical trial. We clearly describe that our data are retrospective, but the use of a PS-matching methodology, adjusting for relevant clinical variables, strengthens these results. Our data reinforce the evidence presented in the ACTT-2 and the COV-BARRIER trials, alongside other clinical studies.[10,12,14–18]

In conclusion, baricitinib is associated with a significantly reduced mortality rate in adults aged 70 years or older hospitalized by COVID-19 pneumonia. Baricitinib could be a good treatment in older adult populations with

severe COVID-19, and could also be of interest in long-term care facilities or in the community.

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CONFLICT OF INTEREST

All authors declare that there are no conflicts of interest, except. V.M.L. declares no conflict of interest according to the ICMJE Uniform Requirements but discloses the following financial relationship: CEO and shareholder of HepaPredict AB; co-founder and chairman of the board PersoMedix AB; consultancy work for Enginzyme AB. JS declares his conflict at: https://www.nature.com/onc/editors and none are relevant here.

AUTHOR CONTRIBUTIONS

Pedro Abizanda: Design of the work, data analysis and interpretation, drafting of the work, critically revision for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Juan María Calbo Mayo, Marta Mas Romero, Elisa Belén Cortés Zamora, María Teresa Tabernero Sahuquillo, Carlos Campayo Escolano, Alba Ochoa Serrano, Victoria Sánchez-Flor Alfaro, Rita López Bru, Cristina Gómez Ballesteros, David Caldevilla Bernardo, Francisco Javier Callejas González: Data acquisition, drafting of the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Luis Romero Rizos, Pedro Manuel Sánchez-Jurado, Ginés Sánchez-Nievas, Fernando Andrés-Pretel: Data analysis and interpretation, critically revision for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Volker Martin Lauschke, Justin Stebbing: Data interpretation, critically revision for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors had a role in writing the final manuscript and approved the final version.

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REFERENCES

1. Lloyd-Sherlock PG, Kalache A, McKee M, Derbyshire J, Geffen L, Casas FG. WHO must prioritise the needs of older people in its response to the covid-19 pandemic. *BMJ*. 2020;368:m1164.
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China. Summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323:1239-1242.
3. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA*. 2020;323:1775-1776.
4. WHO–China Joint Mission. Report of the WHO-China Joint Mission on Corona Virus Disease 2019 (COVID-19) (pdf); 2020. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf. Accessed April 25, 2021.
5. Geriatric Medicine Research Collaborative. Age and frailty are independently associated with increased COVID-19 mortality and increased care needs in survivors: results of an international multi-centre study. Geriatric Medicine Research Collaborative. *Age Ageing*. 2021;50:617-630.
6. Centers for Disease Control and Prevention. Severe outcomes among patients with coronavirus disease 2019 (COVID-19)—United States, February 12–March 16, 2020; 2020. https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e2.htm. Accessed April 25, 2021.
7. Bonanad C, García-Blas S, Tarazona-Santabalbina F, et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. *J Am Med Dir Assoc*. 2020;21:915-918.
8. Lee JY, Kim HA, Huh K, et al. Risk factors for mortality and respiratory support in elderly patients hospitalized with COVID-19 in Korea. *J Korean Med Sci*. 2020;35:e223.
9. U.S. Food & Drug Administration. FDA combating COVID-19 with therapeutics; 2021. https://www.fda.gov/media/136832/download. Accessed April 25, 2021.
10. Kalil AC, Patterson TF, Mehta AK, et al. Baricitinib plus Remdesivir for hospitalized adults with Covid-19. *N Engl J Med*. 2021;384:795-807.
11. Lilly Investors News Release. Lilly and Incyte announce results from the Phase 3 COV-BARRIER study of baricitinib in hospitalized COVID-19 patients; 2021. https://investor.lilly.com/news-releases/news-release-details/lilly-and-incyte-announce-results-phase-3-cov-barrier-study. Accessed 2021 April 25.

12. Stebbing J, Sánchez-Nievas G, Falcone M, et al. JAK inhibition reduces SARS-CoV-2 liver infectivity and modulates inflammatory responses to reduce morbidity and mortality. *Sci Adv*. 2020;7:eabe4724.
13. Stebbing J, Krishnan V, de Bono S, et al. Mechanism of baricitinib supports artificial intelligence-predicted testing in COVID-19 patients. *EMBO Mol Med*. 2020;12:e12697.
14. Cantini F, Niccoli L, Nannini C, et al. Beneficial impact of Baricitinib in COVID-19 moderate pneumonia; multicentre study. *J Infect*. 2020;81:647-649.
15. Bronte V, Ugel S, Tinazzi E, et al. Baricitinib restrains the immune dysregulation in patients with severe COVID-19. *J Clin Invest*. 2020;130:6409-6416.
16. Rodriguez-Garcia JL, Sanchez-Nievas G, Arevalo J, García-Gómez C, Jiménez-Vizuete JM, Martínez-Alfaro E. Baricitinib improves respiratory function in patients treated with corticosteroids for SARS-CoV-2 pneumonia: an observational cohort study. *Rheumatology (Oxford)*. 2021;60:399-407.
17. Titanji BK, Farley MM, Mehta A, et al. Use of Baricitinib in patients with moderate and severe COVID-19. *Clin Infect Dis*. 2021;72:1247-1250.
18. Rosas J, Pasquau Liaño F, Llombart Cantó M, et al. Experience with the use of Baricitinib and tocilizumab monotherapy or combined, in patients with interstitial pneumonia secondary to coronavirus COVID19: a real-world study. *Reumatol Clin*. 2020;S1699-258X(20)30271-0.
19. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet*. 2020;395:1417-1418.
20. Smeda M, Chlopicki S. Endothelial barrier integrity in COVID-19-dependent hyperinflammation: does the protective facet of platelet function matter? *Cardiovasc Res*. 2020;116:e118-e121.
21. Schouten LR, van Kaam AH, Kohse F, et al. Age-dependent differences in pulmonary host responses in ARDS: a prospective observational cohort study. *Ann Intensive Care*. 2019;9:55.
22. Mueller AL, McNamara MS, Sinclair DA. Why does COVID-19 disproportionately affect older people? *Aging (Albany NY)*. 2020;12:9959-9981.
23. Pinto BGG, Oliveira AER, Singh Y, et al. ACE2 expression is increased in the lungs of patients with comorbidities associated with severe COVID-19. *J Infect Dis*. 2020;222:556-563.
24. Fan X, Wang Y, Sun K, et al. Polymorphisms of ACE2 gene are associated with essential hypertension and antihypertensive effects of captopril in women. *Clin Pharmacol Ther*. 2007;82:187-196.

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