# BARICITINIB AND COVID-19

**This document may contain information not fully aligned with local requirements. Please see local labeling for approved or authorized indications and further information.**

## Baricitinib Use and Dosing in Renal Impairment

The recommended dose of BARI in patients being treated for COVID-19 with eGFR between 15-30 mL/min/1.73 $m^2$ is 2 mg once every 48 hours. BARI is not recommended for use in patients with eGFR of <15 mL/min/1.73 $m^2$.[1]

More information on dosing rationale is in Results in Severe Renal Impairment.

# BARICITINIB AVAILABLE CLINICAL DATA

## Pharmacokinetic Studies in Patients with Renal Impairment

Baricitinib exposure was evaluated in patients with mild, moderate, and severe renal impairment, including ESRD requiring hemodialysis, compared with healthy subjects with normal renal function.[1]

### *Results in Severe Renal Impairment*

Based on study data, severe renal impairment (eGFR 15 to <30 mL/min/1.73 $m^2$) is associated with an increase in the AUC by approximately 4-fold, with minimal impact on the $C_{max}$ (1.4-fold) of BARI.[1]

Therefore, a dose of 2 mg given every 48 hours in patients with severe renal impairment will produce a daily average exposure similar to that of a dose of 4 mg given daily in patients with normal renal function.[1]

### *Results in Hemodialysis*

The AUC ratio of BARI exposure relative to healthy subjects for patients receiving dialysis were

- 3.18 for ESRD with hemodialysis predose, and
- 2.41 for ESRD with hemodialysis postdose.[1]

These results suggest that BARI does appear to be dialyzable.[1]

## COV-BARRIER Treatment Trial

### *Clinical Trial Design*

COV-BARRIER is a phase 3, global, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of BARI in adult patients hospitalized due to COVID-19.[2]

Patients were randomized to treatment with either

- BARI 4 mg orally once daily + SOC (n=764), or
- placebo + SOC (n=761).[2]

Treatment was administered for up to 14 days or until discharge, whichever came first.[2]

The primary efficacy outcome was a composite percentage of participants who progressed to high-flow oxygen or non-invasive ventilation (OS6), invasive mechanical ventilation or ECMO (OS7), or death (OS8) by day 28.[2]

A key secondary outcome was all-cause mortality by day 28.[2]

If at screening, a patient was randomized to the treatment arm and had an eGFR between ≥30mL/min/1.73m$^2$ to <60 mL/min/1.73 m$^2$ , they received BARI 2 mg for the duration of the study.

### *COV-BARRIER Creatinine Clearance Calculation*

Per protocol, calculations were performed locally by the study site using the MDRD equation:

- For creatinine results reported in conventional units (mg/dL)
  - GFR (mL/min/1.73 m²) = 175 × (Scr) $^{-1.154}$ × (Age)$^{-0.203}$ × (0.742 if female) × (1.212 if African American)[1]

- For creatinine results reported in SI units (pmol/L)
  - GFR (mL/min/1.73 m²) = 175 × (Scr/88.4)$^{-1.154}$ × (Age)$^{-0.203}$ × (0.742 if female) × (1.212 if African American)[1]

### *COV-BARRIER Clinical Trial Exclusion Criteria*

Patients with an eGFR <30 mL/min/1.73 m$^2$ were excluded from the clinical trial.[3]

### *Efficacy and Safety in Patients With COVID-19 and Comorbid Renal Impairment in COV-BARRIER*

An analysis of the efficacy and safety of BARI in patients with COVID-19 and comorbid renal impairment has not been conducted.

The number of patients in the COV-BARRIER trial with COVID-19 and comorbid chronic kidney disease was

- 23/764 (3.0%) in the BARI treatment arm, and
- 18/761 (2.4%) in the placebo arm.[1]

## National Institute of Allergy and Infectious Diseases Adaptive COVID-19 Treatment Trial 2 (ACTT-2)

### *ACTT-2 Trial Design*

Eli Lilly and Company entered into an agreement with the NIAID, part of the NIH, to study BARI as an arm in NIAID's ACTT-2.[4]

This randomized, double-blind, placebo-controlled study investigated the efficacy and safety of BARI plus remdesivir in hospitalized adult patients with COVID-19. Study site locations were in North America as well as Europe and Asia.[4]

In ACTT-2, a total of 1033 patients were randomized 1:1 to

- BARI and IV remdesivir (N=515), or
- placebo and IV remdesivir (N=518).[4]

In this trial, BARI was administered as a 4-mg oral dose (given as two 2-mg tablets by mouth, or crushed and given through a nasogastric tube, if necessary) for the duration of hospitalization up to a 14-day total course of treatment.[4]

Primary outcome was time-to-recovery during the 28 days after enrollment. A key secondary outcome was clinical status at day 15 based on the eight-category ordinal scale developed by NIAID.[4]

### *ACTT-2 Creatinine Clearance Calculation*

Any automated calculation by the clinical laboratory or published formula for the calculation of creatinine clearance was acceptable. Per protocol, the study site was to select a formula to be used for all patients enrolled at the site for the duration of the study.[4]

### *ACTT-2 Clinical Trial Exclusion Criteria*

Patients with an eGFR <30 mL/min/1.73 $m^2$ or receiving hemodialysis or hemofiltration at time of screening were excluded from the clinical trial.[4]

### *Efficacy and Safety in Patients With COVID-19 and Comorbid Renal Impairment in ACTT-2*

An analysis of the efficacy and safety of BARI in patients with COVID-19 and comorbid renal impairment has not been conducted.[1]

The number of patients in ACTT-2 with COVID-19 and comorbid chronic kidney disease was

- 31/506 (6%) in the BARI + remdesivir group, and
- 33/501 (7%) in the placebo + remdesivir group.[1,4]

## REFERENCES


1. Data on file, Eli Lilly and Company and/or one of its subsidiaries.

2. Marconi VC, Ramanan AV, de Bono S, et al. Efficacy and safety of baricitinib for the treatment of hospitalized adults with COVID-19 (COV-BARRIER): a randomised, double-blind, parallel-group, placebo-controlled phase 3 trial. *Lancet Respir Med*. Published online September 1, 2021. https://doi.org/10.1016/S2213-2600(21)00331-3

3. A study of baricitinib (LY3009104) in participants with COVID-19 (COV-BARRIER). ClinicalTrials.gov identifier: NCT04421027. Updated June 9, 2021. Accessed June 14, 2021. https://www.clinicaltrials.gov/ct2/show/NCT04421027

4. Kalil AC, Patterson TF, Mehta AK, et al. Baricitinib plus remdesivir for hospitalized adults with covid-19. *N Engl J Med.* 2021;384(9):795-807. https://doi.org/10.1056/NEJMoa2031994


## GLOSSARY

ACTT-2 = Adaptive COVID-19 Treatment Trial 2

AUC = area under the concentration-time curve

BARI = baricitinib

$C_{max}$ = maximum concentration

COVID-19 = coronavirus disease 2019

ECMO = extracorporeal membrane oxygenation

eGFR = estimated glomerular filtration rate

ESRD = end-stage renal disease

IV = intravenous

NIAID = National Institute of Allergy and Infectious Diseases

NIH = National Institutes of Health