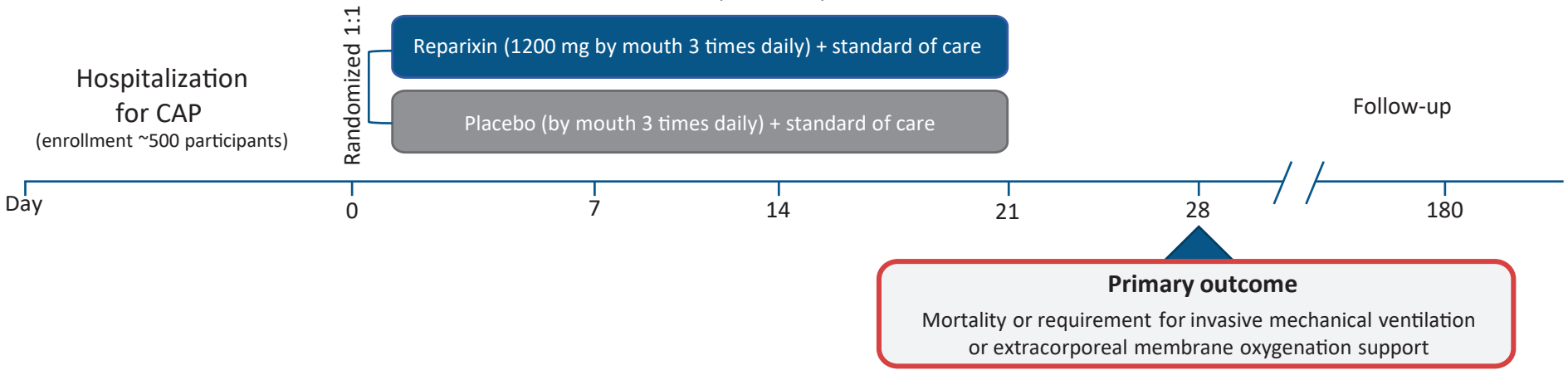
REPAVID-22 IS NOW ENROLLING AT YOUR HOSPITAL

ATTENTION: Are you caring for patients hospitalized with community-acquired pneumonia (CAP) who require oxygen support?

A phase 3, multinational, randomized, double-blind, placebo-controlled trial (NCT05254990)[1] is ongoing at your hospital to evaluate the efficacy and safety of oral reparixin as an add-on therapy to the standard of care to limit disease progression in adults hospitalized with CAP



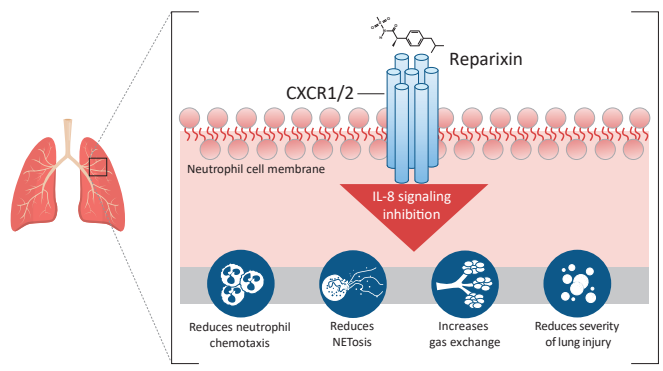
TARGET PATIENT POPULATION

- Hospitalized adults (aged ≥18 years)
- Clinically suspected viral or bacterial CAP within 72 hours of hospital admission
  - ≥1 of the following signs/symptoms: dyspnea, cough, purulent sputum, crackles (rales), or rhonchi
  - Body temperature >38°C or <36°C (before or during admission) or leukocytosis (>local ULN)
  - New/Increased pulmonary infiltrate(s) by chest imaging
- Need for noninvasive supplemental oxygen
- Not pregnant or planning to become pregnant
- No known hypersensitivity to ibuprofen or medications belonging to the sulfonamide class
- No complex CAP-associated conditions such as fungal infection, empyema, or pulmonary embolism
- Lack of renal or hepatic dysfunction
  - Renal dysfunction: <50 mL/min/1.73 m^2 eGFR
  - Hepatic dysfunction: ALT or AST >5× ULN; Child-Pugh class B or C

INVESTIGATIONAL AGENT: REPARIXIN

- Reparixin is an investigational, potent, noncompetitive allosteric inhibitor of the interleukin-8 receptors CXCR1 and CXCR2[2]
- Reducing interleukin-8 signaling may attenuate inflammatory responses by reducing neutrophil recruitment and neutrophil extracellular trap formation in severe CAP and associated complications (**Figure**)[3,4]
- Patients with severe COVID-19 who received reparixin in a phase 2 trial exhibited a significant reduction in the rate of clinical events[a] and demonstrated less progression to more invasive treatment in a phase 3 clinical trial[5,6]

Proposed Mechanism of Action[2-4,7-11]



Reparixin is an investigational agent and may affect outcomes as proposed in the figure through inhibition of IL-8.

To learn more about the clinical trial, enrollment, and principal investigator at your site, visit **repavid-22.researchstudytrial.com** or contact **usmedinfo@dompe.com** for additional information on how you can get involved in clinical research at your site!

Recruitment is ongoing and anticipated to be completed by the end of 2024

ALT, alanine transaminase; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; CXCR, chemokine receptor; eGFR, estimated glomerular filtration rate; FDA, Food and Drug Administration; IL, interleukin; NET, neutrophil extracellular trap; ULN, upper limit of normal.

[a]Clinical events included use of supplemental oxygen, need for mechanical ventilation, intensive care unit admission, or use of rescue medication.

1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05254990. Accessed September 7, 2023. **2.** Bertini et al. *Proc Natl Acad Sci U S A.* 2004;101:11791-11796. **3.** Zarbock et al. *Br J Pharmacol*. 2008;155:357-364. **4.** Alsabani et al. *Br J Anaesth*. 2022;128:283-293. **5.** Landoni et al. *Infect Dis Ther*. 2022;11:1559-1574. **6.** Landoni et al. Efficacy and safety of reparixin in patients with severe COVID-19 pneumonia: a phase 3, randomized, double-blind placebo-controlled study. *Infect Dis Ther.* In press. **7.** Hosoki et al. *Clin Exp Allergy*. 2019;49:130-132. **8.** Russo et al. *Am J Respir Cell Mol Biol*. 2009;40:410-421. **9.** Schraufstatter et al. *Am J Physiol Lung Cell Mol Physiol.* 2001;280:L1094-L1103. **10.** Song et al. *Respir Res.* 2022;23:155. **11.** Boro et al. *J Immunol.* 2017;199:1660-1671.

Reparixin is an investigational drug that is not approved for use in any country and is currently being investigated in clinical trials.

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