RESPIRATIO

A phase 2, multinational, randomized, double-blind trial (NCT05496868) is ongoing to evaluate the efficacy and safety of reparixin as an add-on therapy to standard of care in adults hospitalized with moderate-to-severe acute respiratory distress syndrome (ARDS)

Inclusion criteria

- Signed informed consent
- Adults ≥18 years old
- Mechanically ventilated (invasive) patients with PaO_2/FiO_2 ratio ≤200 mmHg in the presence of PEEP ≥5 cm H_2O
- Respiratory failure not fully explained by cardiac failure or fluid overload
- Bilateral radiologic opacities consistent with pulmonary edema on the frontal chest x-ray or bilateral ground-glass opacities on a chest CT scan
- ≤48 hours from fulfilling above ARDS criteria (plus 12 hours if the patient is transferred from another institution)
- Women of childbearing potential who are sexually active must be willing not to get pregnant within 30 days after their last dose and must agree to ≥1 reliable method of contraception. For all women of childbearing potential, a pregnancy test result must be negative before first drug intake

Primary endpoints

- Change in oxygenation index (percentage of mean airway pressure × FiO_2/PaO_2) from baseline to Day 7 of treatment
- Ventilator-free days at Day 28

Treatment regimen

- Patients will be randomized (1:1) to receive reparixin 1200 mg or placebo, in addition to standard of care, through a gastric tube three times daily for 14 days, with the option of extension up to 21 days if the patient is still intubated on Day 14

Reparixin is an investigational drug that is not approved for use in any country and is currently being investigated in clinical trials.
Contact usmedinfo@dompe.com for any questions.
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RESPIRATIO Phase 2 Clinical Trial

Medications to be used with caution

Reparixin is catalyzed by CYP2C9 and, to a lesser extent, by CYP2C19. In vitro, reparixin has potential for noncompetitive inhibition of the human hepatic enzyme CYP3A4. However, clinically significant interactions have not been identified to date. Patients should remain under close observation during administration of drugs with similar metabolic pathways if given concomitantly with reparixin.

The following medications can be used with caution if the clinical benefit outweighs the perceived risk according to the PI's discretion:

- CYP2C9 inducers (rifampin, phenytoin, carbamazepine, aprepitant, bosentan, phenobarbital)
- CYP2C9 inhibitors (amiodarone, fluconazole, miconazole, oxandrolone, capecitabine, cotrimoxazole, etravirine, fluvastatin, fluvoxamine, metronidazole, sulfinpyrazone, tigecycline, voriconazole, zafirlukast)

Exclusion criteria

- Chronic hepatic dysfunction defined as a Child-Pugh Score ≥7, OR ALT/AST ≥3× ULN + total bilirubin >2× ULN, OR ALT/AST ≥5× ULN
- Chronic renal dysfunction: eGFR (2021 CKD-EPI) <30 mL/min/1.73m^2 or in need of acute renal replacement therapy
- Participation in another interventional clinical trial
- Patients who are clinically determined to have a high likelihood of death within the next 24 hours (per PI's judgment)
- Currently receiving ECMO or high-frequency oscillatory ventilation
- Anticipated extubation within 24 hours of enrollment
- Evidence of gastrointestinal dysmotility as demonstrated by all three: persistent gastric distention, enteral feeding intolerability, and persistent gastric residuals >500 mL
- History of lactase deficiency, galactosemia, or glucose-galactose malabsorption
- Anticipated discharge from the hospital or transfer to another hospital within 72 hours of screening
- Decision to withhold or withdraw life-sustaining treatment (patients with a DNR order may still be eligible if there is a commitment to full support except for cardiopulmonary resuscitation in the case of cardiac arrest)
- Documented allergy/hypersensitivity to sulfonamides, ibuprofen, and other COX-1 and -2 inhibitors and to the study product and/or its excipients
- Active bleeding (excluding menses) or bleeding diathesis (including patients on chronically high doses of NSAIDs)
- Pregnant or lactating women or women of childbearing potential and fertile men who do not agree to use ≥1 primary form of contraception during the study and up to 30 days after the last dose
- History of peptic ulcer, GI bleeding, or perforation due to previous NSAID therapy

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; COX, cyclooxygenase; CT, computerized tomography; CYP, cytochrome P450; DNR, do not resuscitate; ECMO, extracorporeal membrane oxygenation; eGFR, estimated glomerular filtration rate; FiO_2, fraction of inspired oxygen; NSAID, nonsteroidal anti-inflammatory drug; PaO_2, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure; PI, principal investigator; ULN, upper limit of normal.

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