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# BAXTER SUPPORTS NEW STUDY SHOWING BLOOD PURIFICATION WITH OXIRIS FILTER SET CAN PLAY A ROLE IN THE MANAGEMENT OF SEVERELY ILL COVID-19 PATIENTS

- *Marks largest study of its kind on COVID-19 patients treated with extracorporeal blood purification (EBP) using* **Oxiris**
- *Study investigators assessed serum IL-6 levels, indicators of organ dysfunction and intensive care unit (ICU) mortality rate in patients undergoing EBP with* **Oxiris**
- *Findings provide clinicians with new insights on EBP initiation in COVID-19 patients*

**DEERFIELD, Ill., OCTOBER 27, 2020** – Baxter International Inc. (NYSE:BAX), a global leader in acute care, recognizes the findings of a prospective, multicenter, observational study on data from the **Oxiris**Net Registry evaluating severely ill patients with COVID-19 in Italy treated with extracorporeal (outside the body) blood purification (EBP) using the company's **Oxiris** filter set. From the study, recently published in *Critical Care*, the investigators reported that patients experienced a significant reduction in serum IL-6 (a pro-inflammatory cytokine) levels, improvement in indicators of organ dysfunction and reduction in expected intensive care unit (ICU) mortality rate as compared to a historical control. Due to the study design, the results do not provide evidence of a causal relationship between EBP treatment with **Oxiris** and these outcomes. The results do, however, support the feasibility of the use of **Oxiris** with severely ill COVID-19 patients and provide new insights for clinicians treating this vulnerable patient population.

Systemic inflammation in COVID-19 can lead to multiple organ failure, including acute kidney injury (AKI). COVID-19 patients may also develop a cytokine storm, which occurs when high levels of inflammatory mediators circulate in the blood as an intense immune reaction to the virus. Up to 67% of severely ill patients with pneumonia-caused COVID-19 may present with additional organ dysfunction syndromes that could be induced by a high level of circulating cytokines.[1] A cytokine

storm can be life-threatening and requires intervention. EBP techniques have been shown to remove cytokines, damage-associated molecular patterns and pathogen-associated molecular patterns, including endotoxins and circulating viral particles, in critically ill patients with COVID-19.[2]

"In our study population, all patients showed significant IL-6 reduction and associated improvement in multiorgan dysfunction, particularly for short-term outcomes such as hemodynamic stability and oxygenation index," said Gianluca Villa, M.D., assistant professor of anesthesiology, intensive care and pain medicine at the University of Florence, Italy and primary investigator of the study. "These findings provide a strong foundation for further research on EBP in COVID-19 patients and may have a long-term impact on best practices in caring for these patients."

The study, which was supported by Baxter through an investigator-initiated research grant, evaluated 37 patients at four hospitals based on data from the OxirisNet Registry. The patients had a confirmed diagnosis of COVID-19, were admitted to the ICU between February and April 2020 and received treatment with **Oxiris** on Baxter's **Prismaflex** system for immunomodulation and/or support of renal function during AKI. Clinical parameters were reported at baseline and at 12, 24, 48, and 72 hours post-treatment initiation. Patients received antimicrobials, blood purification, mechanical ventilation and other supportive treatments in accordance with the clinical judgment of the treating center.

Levels of IL-6 decreased over time from a baseline of 1230 pg/ml (IQR 895) during the first 72 hours of treatment ($p < 0.001$ Kruskal-Wallis test), with a significant decrease in the first 24 hours ($p = 0.001$). The reduction in serum IL-6 concentrations correlated with the improvement in organ function, as measured in the decrease of the Sequential Organ Failure Assessment (SOFA) score (rho = 0.48, $p = 0.0003$). Median baseline SOFA was 13 (IQR 6) and decreased significantly over time ($p < 0.001$ at Kruskal-Wallis test) during the first 72 hours of the treatment, with a significant decrease at 48 hours (median 8 IQR 5, $p = 0.001$). Compared to the expected mortality rate, as calculated by the Acute Physiologic Assessment and Chronic Health Evaluation (APACHE IV) score, the mean observed rate was 8.3% lower after treatment. The greatest improvement in mortality rate appeared to be in patients receiving EBP early on during the ICU stay. Because the study design does not allow for conclusions to be drawn on causality, the investigators note that further controlled studies would be necessary in order to establish the efficacy of EBP in improving patient outcomes such as organ dysfunction and ICU mortality, or the optimal time for initiating EBP.

"Baxter supported the development of the **Oxiris**Net Registry with the goal of continuously advancing research that will contribute to scientific understanding of the role of EBP in treating critically ill patients," said Kai Harenski, global medical lead for Baxter's Acute Therapies business. "We remain focused on gathering high-quality data throughout the COVID-19 pandemic, while also expanding access to **Oxiris** and other products to help address patient needs around the world."

During blood purification therapy, the patient's blood passes through the **Oxiris** filter set, where it then removes cytokines, endotoxin, fluid and uremic toxins simultaneously, before returning the patient's blood to the body. **Oxiris** is currently registered in more than 50 countries worldwide and has been used for more than 10 years to treat thousands of patients. Baxter received emergency use authorization (EUA) from the U.S. Food and Drug Administration (FDA) for **Oxiris** in April 2020. The FDA has not cleared or approved the **Oxiris** filter set; rather, the EUA authorizes the use of **Oxiris** during the COVID-19 pandemic. **Oxiris** is the only filter set currently available in the U.S. to reduce pro-inflammatory cytokine levels in the blood, including for use in continuous renal replacement therapy (CRRT), for confirmed COVID-19 cases admitted to the ICU with confirmed or imminent respiratory failure who require blood purification.

**Oxiris** has been validated for use with Baxter's leading **PrisMax** and **Prismaflex** systems. **PrisMax**, which was launched in Europe in 2018 and the U.S. in 2019, is the company's next-generation blood purification platform that helps simplify therapy delivery, while providing hospitals the flexibility to meet the unique demands of the ICU.

**About Baxter**

Every day, millions of patients and caregivers rely on Baxter's leading portfolio of critical care, nutrition, renal, hospital and surgical products. For more than 85 years, we've been operating at the critical intersection where innovations that save and sustain lives meet the healthcare providers that make it happen. With products, technologies and therapies available in more than 100 countries, Baxter's employees worldwide are now building upon the company's rich heritage of medical breakthroughs to advance the next generation of transformative healthcare innovations. To learn more, visit www.baxter.com and follow us on Twitter, LinkedIn and Facebook.

**Rx Only.** For safe and proper use of this device, including contraindications, refer to the full Instructions for Use.

**Important Safety Information for Oxiris (oXiris)**

The **Oxiris** Set is indicated for use only with the **Prismaflex** or **PrisMax** control unit.

The **Oxiris** Set is authorized by FDA under an Emergency Use Authorization (EUA) to treat patients with COVID-19 infection. The **Oxiris** Set is authorized for use for no longer than the duration of the COVID-19 public health emergency and has neither been cleared or approved by the FDA to treat patients with COVID-19 infection. Under the terms of the EUA, it is intended to treat patients 18 years of age or older with confirmed COVID-19 admitted to the ICU with confirmed or imminent respiratory failure in need of blood purification, including use in continuous renal replacement therapy, to reduce pro-inflammatory cytokine levels, who have any one of the following conditions:

- Early acute lung injury (ALI)/ early acute respiratory distress syndrome (ARDS);
- Severe disease, such as:
    - o dyspnea,
    - o respiratory frequency ≥ 30/min,
    - o blood oxygen saturation ≤ 93%,
    - o partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300,and/or
    - o lung infiltrates >50% within 24 to 48 hours; or
- Life-threatening disease, defined as:
    - o respiratory failure,
    - o septic shock, and/or
    - o multiple organ dysfunction or failure

This set is intended for use in the following veno-venous therapies: SCUF; CVVH; CVVHD; CVVHDF.

**Important Safety Information for PrisMax and Prismaflex**

The **PrisMax** and **Prismaflex** systems are intended for:

CRRT for patients weighing 20 kg or more with acute renal failure and/or fluid overload.

TPE therapy for patients weighing 20 kg or more with diseases where removal of plasma components is indicated.

All treatments administered via the **PrisMax** and **Prismaflex** control units must be prescribed by a physician.

*This release includes forward-looking statements concerning **Oxiris**, **PrisMax** and **Prismaflex**, including potential benefits associated with their use. The statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those in the forward-looking statements: satisfaction of regulatory and other requirements; actions of regulatory bodies and other governmental authorities; product quality,*

*manufacturing or supply, or patient safety issues; changes in law and regulations; and other risks identified in Baxter's most recent filing on Form 10-K and other SEC filings, all of which are available on Baxter's website. Baxter does not undertake to update its forward-looking statements.*



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[1] Ronco C, Reis T, De Rosa S. Coronavirus epidemic and extracorporeal therapies in intensive care: si vis pacem para bellum [published online ahead of print, 2020 Mar 13]. Blood Purif. 2020;1–4. doi:10.1159/000507039

[2] Nadim, M.K., Forni, L.G., Mehta, R.L. et al. COVID-19-associated acute kidney injury: consensus report of the 25th Acute Disease Quality Initiative (ADQI) Workgroup. Nat Rev Nephrol (2020). https://doi.org/10.1038/s41581-020-00356-5