InnovoSep: A Non-Antibiotic Approach for Treating or Preventing Severe Bloodstream Infection

RCSI DEVELOPING HEALTHCARE LEADERS WHO MAKE A DIFFERENCE WORLDWIDE

Cilengitide, a potent inhibitor of αVβ3 integrin signalling, has been shown to inhibit bacterial binding to the vascular endothelium thereby inhibiting the main mechanism by which endothelial cell injury in sepsis leads to septic shock and organ failure. This technology represents a first-in class, non-antibiotic approach to targeting bacteraemia and severe bloodstream infections.

VALUE PROPOSITION

There are an estimated 30 million new cases of sepsis worldwide per year with a mortality rate of up to 50%. Currently there are no approved specific treatments for the underlying pathophysiology of sepsis and the clinical management is focused on reducing the infection through use of aggressive intravenous antibiotic therapy. Despite progress in our understanding of the pathophysiology of sepsis, targeted therapies to disrupt the aberrant host-pathogen interaction are lacking.

TECHNOLOGY

The Cardiovascular Infection Research Group in RCSI have discovered that antagonists of the major endothelial cell integrin, αVβ3, exemplified by drug candidate cilengitide, inhibits bacterial binding to the endothelium both *in vitro* and *in vivo*. By preventing bacteria from binding to the endothelium, downstream injurious effects such as thrombus formation, coagulation activation, inflammation and loss of barrier integrity are significantly reduced. These effects are the key events driving organ failure and mortality during severe infection.

FEATURES AND BENEFITS

Features	Benefits
Inhibition of bacterial binding to endothelial cells	Prevents endothelial injury thus preventing the infection from progressing to septic shock and multi-organ failure.
Non-antibiotic mechanism	Avoids selection for multi-drug resistance strains.
Prophylactic use	Allows early intervention to prevent serious infection progressing to sepsis.
Repositioned drug	Cilengitide previously taken into Phase III by Merck KGaA for Glioblastoma. Lower development risks as safety and toxicity profile are known.
Freedom to Operate	Cilengitide is off-patent for its original indication and a new patent has been filed by RCSI for its use in sepsis

Cilengitide inhibits *S. aureus* and *E. coli* binding to human endothelial cells – post-infection

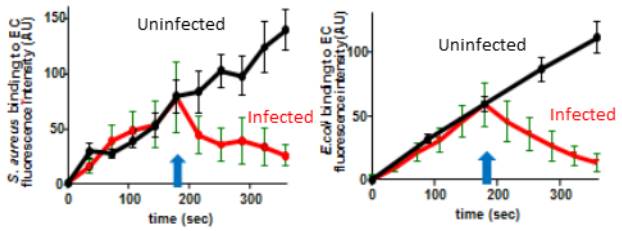

Figure 1. Cilengitide inhibits (A) S. aureus and (B) E. coli binding to human endothelial cells, blue arrow addition of cilengitide.

Cilengitide prevents rats with pneumonia from developing sepsis

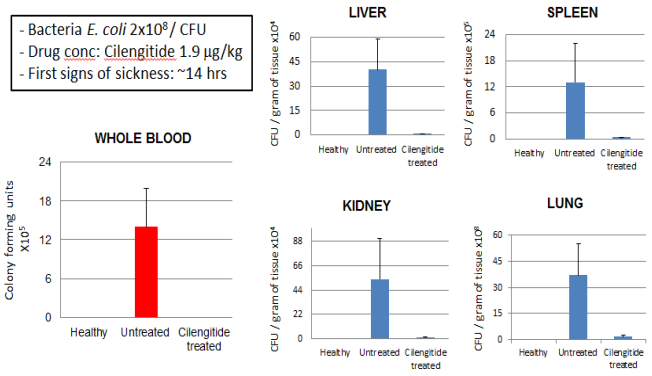

Figure 2. Cilengitide prevents bacterial spread from lungs to bloodstream/major organs in a rat pneumonia model of sepsis

Cilengitide increases survival in an in vivo model of sepsis in the absence of any other intervention.

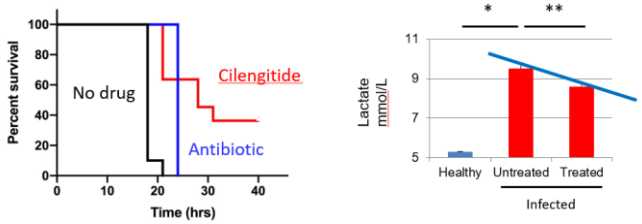

Figure 3. In the absence of any intervention cilengitide significantly prolongs survival of animals with sepsis.The biomarker lactate is also significantly reduced suggesting recovery.

APPLICATIONS

- Treatment of patients diagnosed with sepsis
- Pre-emptive use for patients with severe infection to prevent progression to sepsis.

TECHNOLOGY READINESS LEVEL

- *In Vivo* Proof of Concept achieved.
- Patent application filed.

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