Category :**Sepsis/septic shock: management**

A122 - ***Aseptimab® a humanized monoclonal antibody candidate immunotherapeutic to effectively treat sepsis***

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Introduction:

Circulating inducible Nitric Oxide Synthase (iNOS) was discovered by us, and it is an accurate and predictive biomarker for the onset of sepsis [1]. Our further discoveries include (a) circulating extracellular microvesicle-associated iNOS (MV-A iNOS) and (b) MV-A iNOS's putative role of causing the cellular damage, vascular leak, and organ dysfunction that are the hallmarks of sepsis by its production of toxic quantities of nitric oxide (NO). We developed a humanized anti-MV-A iNOS monoclonal antibody candidate immunotherapeutic, AseptiMab®, to specifically target circulating MV-A iNOS and to neutralize its harmful effects.

Methods:

The ability of AseptiMab to inhibit the sepsis cascade and rescue challenged animals from sepsis was tested in 3 different animal models of sepsis. One model used an LD_{80} dose of endotoxin (LPS); another model used an LD_{80} dose of TNFα, and the third model used an LD_{80} dose of MV-A iNOS. At 0, 2, or 6 hours after the animals were challenged, they were administered either saline (as placebo controls), a low dose of AseptiMab, or a high dose of AseptiMab.

Results:

In all 3 animal models of sepsis tested, AseptiMab was effective at rescuing challenged animals from sepsis compared to the saline control groups. The Kaplan-Meyer curves conclusively demonstrate that treating the challenged animals with AseptiMab was effective. Up to 80% of the challenged animals can be rescued from sepsis by AseptiMab. Its effectiveness was both time and dose dependent: earlier and higher doses result in improved survival. If a high dose was administered early after the challenge, all the animals could be rescued.

Conclusion:

In 3 different animal models of sepsis, AseptiMab effectively treated the sepsis pathology as compared to placebo.

References:

1. Webber RJ, et al. J Appl Lab Med 3(4): 698–711, 2019. doi:10.1373/jalm.2018.026377