



US DEPARTMENT OF DEFENSE

BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

Anti-infective Studies

A Novel, Broad Spectrum Anti-infective that Provides Novel Regenerative Properties in Skin

Interleukin-12 (IL-12) is a key modulator of the immune system and extensive literature documents that induction, or application of exogenous IL-12, elicits broad spectrum activity against an extensive number of bacterial, viral, fungal, and parasitic organisms implicated in local and disseminated infections (*Bashyam 2007, Gluzman-Poltorak et al. 2014; Nguyen et al. 2015; Romani, Puccetti, and Bistoni 1997; Trinchieri 2003*). Novel wound healing properties for IL-12 have also been demonstrated by Neumedicines, Inc., (Pasadena, California) in several mouse models of skin damage and repair, resulting in significant acceleration of wound healing and closure (*Li et al. 2015; Neumedicines Internal Report 2014*). Three Phase I safety trials of recombinant human IL-12 (rHuIL-12), a naturally occurring protein, have been completed by Neumedicines, Inc., in 217 healthy human volunteers, with a safe and well-tolerated dose of 12 micrograms established for further testing in other populations (*Gokhale et al. 2014*).

Neumedicines, Inc. has conducted a Phase 2a open-label, randomized study, the primary objective of which was to compare safety and tolerability of rHuIL-12 to standard of care (SOC) in patients with large, open surgical wounds following colostomy takedown allowed to heal by secondary intention, and to establish a safe dose and dosing schedule for subsequent Phase 2b efficacy studies in patients. Secondary objectives include determining pharmacokinetic (PK) profile, pharmacodynamic (PD) response and immunogenicity, and evaluating accelerated wound healing properties via determination of time to 50 percent wound closure and wound closure rate at 14, 28, and 42 days after starting the study.

Study subjects were consented, screened, and enrolled at the Surgical and Wound Care Clinic Barnes-Jewish (Saint Louis, Missouri), a center that specializes in treatment of wounds and treats some 500 patients a year. Twelve (12) per protocol patients have now completed the study (eight subjects randomized to receive rHuIL-12 treatment + SOC and four subjects randomized to the SOC alone arm). There were no rHuIL-12-related adverse events reported. Three of the eight rHuIL-12-treated patients had complete (100 percent) wound closure after 28 days, where end of the study was at 42 days, compared with one of the four SOC-treated patients. rHuIL-12-induced accelerated healing with wounds that were 18 percent larger than those in the SOC-treated patients, and in patients that were on average approximately 18 years older. In addition to determination of wound dimensions and extent of closure, wound photographs were assessed in a blinded and independent medical review and showed accelerated healing in three of eight rHuIL-12-treated patients as early as 14 days, but in only one of the four SOC-treated patients. PK/PD and immunogenicity data is currently being processed (Figure 1).

Neumedicines envisions rHuIL-12, with an excellent safety profile, as a novel treatment for management of contaminated combat-related or trauma-induced wounds, which will accelerate the closure, healing, and repair of the wound and prevent development of secondary infections.





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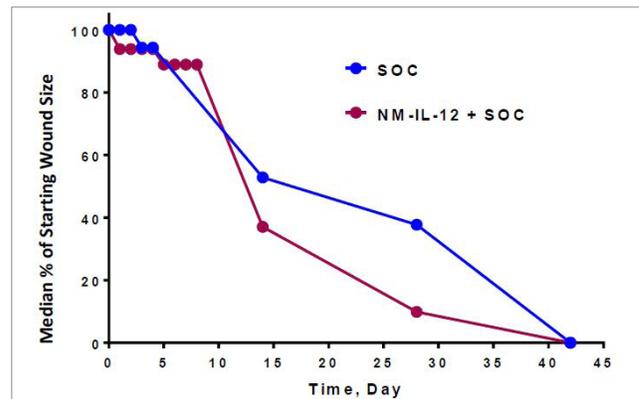


FIGURE 1: Figure demonstrates the accelerated wound closure induced by rHuIL-12 (NM-IL-12) versus SOC. (Figure used with permission from the authors)

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