

Abstract Text:

Skin scars can arise from most types of dermal injuries and represent an unmet medical need for which no approved targeted therapy exists. Associated cosmetic disfigurement can also lead patients to suffer from psychosocial problems, which in turn may result in a decreased quality of life. A novel approach to reduce the severity of post-surgical skin scarring has been developed, which utilizes an antisense oligonucleotide (ASO) designed to inhibit the expression of connective tissue growth factor (CTGF) (EXC 001). CTGF is a matricellular growth factor known to play a fundamental role in the process of tissue fibrosis and scar formation, and therefore inhibiting its expression should lead to a reduction in the severity of skin scarring. EXC 001 has been evaluated in two Phase 1 studies and three Phase 2 studies of skin scarring. One of the Phase 2 studies (study 202) was a randomized, double-blind study in 32 subjects in which EXC 001 or placebo was administered intradermally in patients who were undergoing elective abdominoplasty surgery. In this study, analysis of the resultant fine line scars was performed at 12 and 24 weeks post surgery. Data from 12 weeks post surgery showed that treatment with EXC 001 significantly reduced the severity of fine line scars and accelerated resolution of scarring compared to placebo ($p=0.003$). At 24 weeks post-surgery, patients treated with EXC 001 maintained improved reduction in scar severity as seen at 12 weeks, and, as expected, a similar resolution of fine line scarring was also observed in placebo treated patients. A second Phase 2 study (201) was a randomized, double-blind, within-subject, placebo controlled dose-ranging study in 28 subjects to evaluate the safety and activity of EXC 001. Different doses of EXC 001 were administered intradermally on a subject's abdomen prior to scheduled elective abdominoplasty. Analysis of biomarkers of scarring demonstrated a dose dependent reduction in CTGF, as well as inhibition of CTGF-stimulated collagen and other pro-fibrotic genes. These results clearly demonstrate an antisense mechanism of action for EXC 001 and support further investigation of EXC 001 as a novel therapeutic agent to reduce the severity of post surgical scars.