Novel Approach to Fat Reduction: A Phase I Study Evaluating Safety and Tolerability of STP705 in Abdominoplasty

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Background

There is a clinical need for minimally invasive treatment of unwanted fat and while current injectables like sodium deoxycholic acid (DCA) are effective, they often cause inflammation and pain, which may last for days or weeks following injections, highlighting the need for alternatives with fewer side effects. RNA interference, using small interfering RNA (siRNA) molecules, offers targeted fat reduction by silencing genes involved in fat maintenance including TGF-β1 and COX-2, offering a promising, non-invasive approach to address unwanted fat.. STP705, has shown promising preclinical results both in vitro and in animal models and those studies suggest that STP705 is at least as effective as DCA at reducing subcutaneous fat thickness (Figure 1). This randomized, double-blind trial evaluates the safety and tolerability of STP705 (a TGF-β1/COX-2 siRNA complex) and evaluates its effect on adipocyte apoptosis for fat reduction.

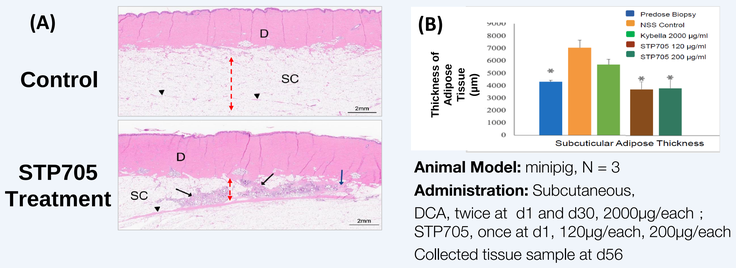

Figure 1. (A) Histological comparison of subcutaneous thickness in control versus STP705-treated patients. **(B)** Animal model comparing the efficacy of DCA and STP705 in reduction of adipose tissue thickness.

METHODS

This Phase I dose-ranging, randomized, vehicle-controlled trial consisted of 3 rounds of 7 subcutaneous injections of STP705 or placebo at varying concentrations and volumes in designated abdominal zones. Treatments were administered 28 days apart, with follow-ups occurring at 2 and 7 days post-procedure. Tissue samples from each injection sites were harvested from total abdominoplasty excisional specimens obtained 28 days after the final round of injections. Safety assessments were conducted, including physical examination, clinical lab tests, ECGs, local skin reactions (LSRs), and adverse events (AEs). Tissue samples from each injection sites were harvested from total abdominoplasty excisional specimens obtained 28 days after the final round of injections. Lipolytic and inflammatory effects of STP705 were assessed by blinded histologic analysis of harvested tissue samples.

Results

Regarding safety, STP705 demonstrated a favorable safety profile with no clinically significant changes in lab values, vital signs, or ECGs. Across 168 total injections, only 3 moderate AEs deemed likely to be related to STP705 were observed; none required intervention, and all resolved without dose modification. The incidence, intensity, and duration of LSRs were low throughout the study **(Figure 2)**.

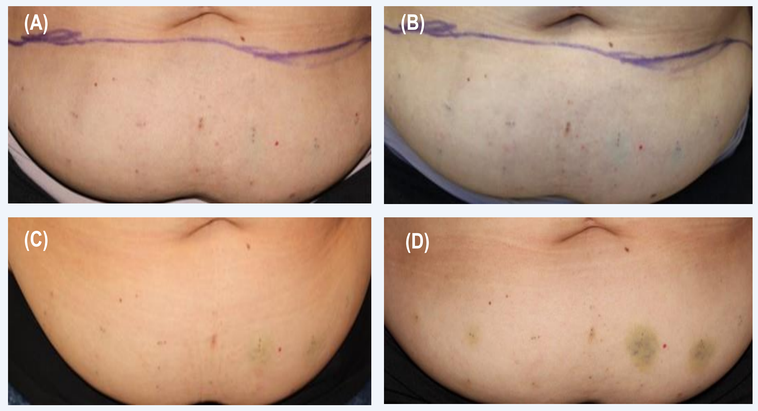

Figure 2. Photographic example of injection sites **(A)** pre-treatment **(B)** post-treatment **(C)** post-treatment day 3 **(D)** post-treatment day 8.

Histology showed adipocyte destruction and fat remodeling across all dose parameters **(Figures 3 & 4)**.

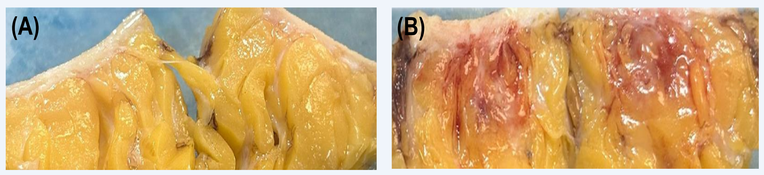

Figure 3. Excisional adipose tissue samples. **(A)** Site with placebo injection demonstrating normal tissue appearance. **(B)** Site with 240 µg STP705 in a 1.0 ml injection volume. The sample displays gross evidence of adipocyte necrosis at the injection sites.

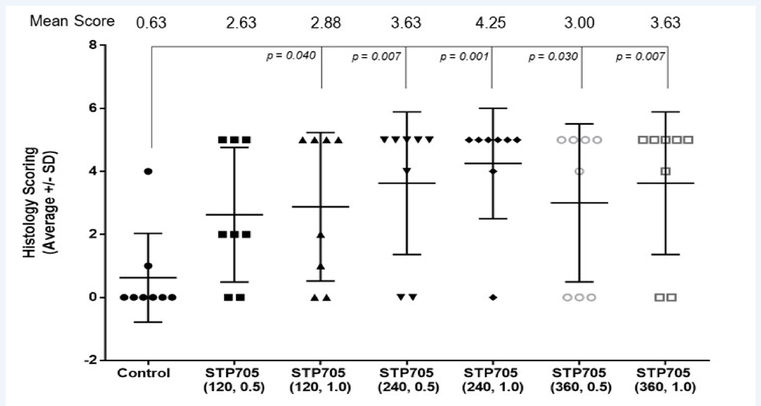

Figure 4. Chart of accumulated severity score of histologic change following injection of the study drug or placebo, stratified by the drug dosage (µg) and volume (ml). Injection of placebo was associated with the lowest score, while injection with 240 µg STP705 in a 1.0 ml injection was associated with the greatest severity score.

Discussion

The demand for focal fat reduction is increasing, and while many current procedures are efficacious, injection techniques such as DCA are routinely associated with inflammation, pain, and LSRs, which are meaningful caveats to their use. Such injection procedures are popular because of their simplicity and therefore, it is important to explore viable alternatives with more favorable safety profiles and fewer LSRs. STP705 injection has been shown to be effective at reducing subcutaneous adipose tissue thickness in vitro and in animal models, and its efficacy was at least equivalent to that of the current market comparator, DCA. This phase I study has now shown STP705 to be safe and very well-tolerated in human subjects. The occurrence of LSRs was low, with erythema being the most common, and overall were mild and resolved without intervention suggesting that STP705 may have a more favorable safety profile than DCA. Additionally, histologic analysis performed on excised tissue samples showed preliminary efficacy in inducing adipocyte apoptosis and tissue remodeling and provided further evidence of STP705's activity in adipocyte destruction, which occurred in a marginally dose-dependent manner. These findings support further trials to establish the safety and efficacy of STP705 for targeted fat reduction and body contouring.

References & Disclosures

1. Nestor MS, Hetzel J, Awad N, Bhupalam V, Lu P, Molyneaux M. Novel injectable polypeptide nanoparticle encapsulated siRNA targeting TGF-β1 and COX-2 for localized fat reduction I: Preclinical in vitro and animal models. J Cosmet Dermatol. 2024 Aug 21. doi: 10.1111/jocd.16535. Epub ahead of print. PMID: 39166716.

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