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Title: A Pooled Analysis of the Safety and Efficacy Results of the Multicenter, Double-Blind, Randomized, Placebo-Controlled Phase 3 REFINE-1 and REFINE-2 Trials of ATX-101, a Submental Contouring Injectable Drug for the Reduction of Submental Fat

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ABSTRACT

Background

ATX-101, a proprietary, synthetic version of naturally-occurring deoxycholic acid, is an investigational injectable drug under development for the reduction of excess submental fat (SMF). ATX-101 causes focal adipocytolysis when injected into subcutaneous fat.

Study Design and Purpose

Two independent, identical, multicenter (US/Canada), randomized, double-blind, placebo-controlled phase 3 studies (REFINE-1 and REFINE-2) were conducted to evaluate the safety and efficacy of ATX-101. The pooled analysis from these two studies is presented here.

Methods

Patients (N=1022; 1019 treated with ATX-101 or placebo) with moderate-to-severe SMF, as rated by clinicians and patients, were randomized (1:1) to receive subcutaneous injections of ATX-101 (2 mg/cm^2) or placebo into the SMF for up to 6 treatment sessions, approximately 28 days apart. Primary endpoints were changed from pre-treatment to 12 weeks post-treatment in (1) percentage of patients with a ≥1-grade change in the Clinician-Reported (CR) and Patient-Reported (PR) Submental Fat Rating Scales (SMFRS) composite and (2) percentage of patients with a ≥2-grade change in the CR-SMFRS/PR-SMFRS composite. Secondary endpoints were (1) mean change from baseline in the PR Submental Fat Impact Scale (PR-SMFIS) and (2) reduction in SMF volume by magnetic resonance imaging (MRI) in a subset of 449 patients. Adverse events (AEs) were monitored throughout.

Results

ATX-101 resulted in statistically significant reductions in SMF. The percentage of patients with a ≥1-grade change in the CR-SMFRS/PR-SMFRS composite was 68.2% for ATX-101 vs. 20.5% for placebo (p<.001). The percentage of patients with a ≥2-grade change in the CR-SMFRS/PR-SMFRS composite was 16.0% for ATX-101 vs. 1.5% for placebo (p<.001). ATX-101 treatment decreased the PR-SMFIS total score from baseline (7.3) compared with placebo (7.3; 3.7 vs. 1.3;

p<.001) and increased the percentage of patients attaining a pre-specified reduction in SM volume by MRI (ATX-101 vs. placebo: 43.3% vs. 5.3%; *p*<.001). Most AEs were transient, mild or moderate in severity, and associated with the treatment area. The most common AEs were pain, swelling/edema, hematoma (bruising), anesthesia (numbness), all of which were expected as a result of the pharmacologic action of the drug. Only 1.4% of patients discontinued the studies due to AEs.

Conclusion

The pooled analysis of the REFINE-1 and REFINE-2 phase 3 trials supports the efficacy and acceptable safety profile of ATX-101, a potential first-in-class injectable drug for contouring the submental region.

Table to include in submission: Pooled analysis from REFINE-1 and REFINE-2 pivotal phase 3 trials of ATX-101 vs. placebo.

Analysis	Placebo (N=508)	ATX-101 (N=514)	*p*-value
≥1-grade change CR-SMFRS/PR-SMFS composite (% patients)	20.5%	68.2%	< 0.001
≥2-grade change CR-SMFRS/PR-SMFS composite (% patients)	1.5%	16.0%	< 0.001
Mean change from baseline in PR-SMFIS total score	1.3	3.7	< 0.001
MRI responder rate (% of patients)	5.3%	43.3%	< 0.001

CR-SMFRS, Clinician-Reported Submental Fat Rating Scale; PR-SMFS, Patient Reported Submental Fat Rating Scales; PR-SMFIS, Patient-Reported Submental Fat Impact Scale; SMF, submental fat; MRI, magnetic resonance imaging