ALTASCIENCES

CASE STUDY

GLP-1 RA: Rapid Phase I Study Execution

STUDY OVERVIEW

Altasciences was contracted to conduct a clinical study to investigate the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of subcutaneous doses of a novel GLP-1 receptor agonist in overweight but otherwise healthy adults. The sponsor presented Altasciences with an aggressive timeline to determine safety and validate the half-life of the study drug with the goal of progressing to a Phase II program within six months. To meet this goal, Altasciences created an adaptive design study with an optimized and streamlined timeline, which included tightly scheduled Safety Review Committee meetings, rapid dose escalation, overlapping cohorts, and rapid turnaround of PK results.

STUDY DETAILS

- **Drug Development Phase:** Phase I First-in-Human
- **Class of Drug:** Small molecule
- **Indication:** Weight loss
- **# of Participants:** 116
- **Dose Route:** Subcutaneous (SC)
- **Dose Regimen:** SAD/MAD – weekly for 5 weeks

STUDY PURPOSE

- **Primary:** To assess the safety and tolerability of single ascending or multiple ascending SC doses (administered weekly for 5 weeks) of study drug
- **Secondary:** To assess the PK profile of single or weekly SC doses of study drug
- **Exploratory:** To assess weight loss (PD measure) following single ascending or weekly ascending SC doses of study drug

STUDY DESIGN

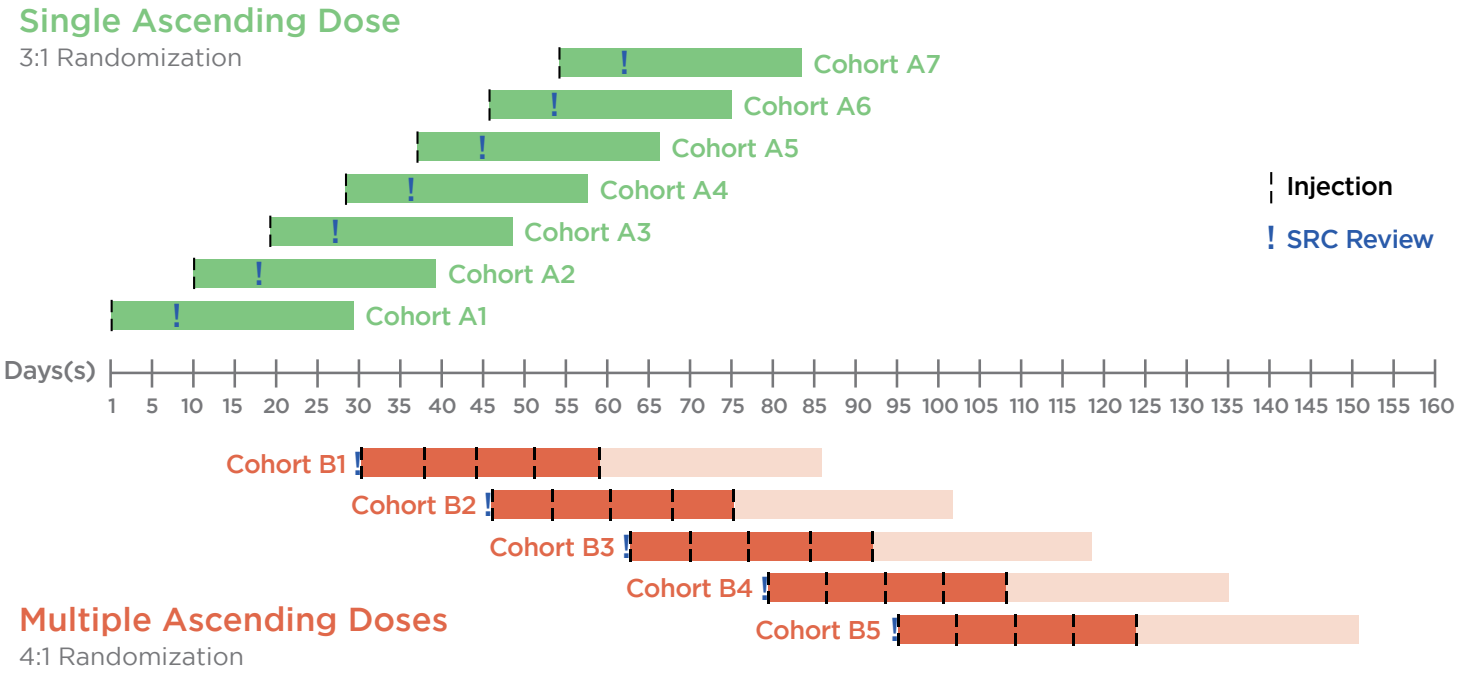
Randomized, placebo-controlled, double-blind study in healthy adult participants with a body mass index (BMI) of 27 to 38 kg/m^2.

Part A—SAD

- 56 participants were randomized into 7 sequential dosing cohorts randomly assigned to the study drug or placebo (6:2).
- Participants were admitted to the clinical research unit (CRU) on Day 1 for baseline evaluations prior to dosing.
- Study drug dosing (SC) occurred on Day 1. Participants remained in the CRU under medical supervision for 7 days.
- Participants returned for 4 weekly outpatient follow-up assessments.
- A SRC convened after each dosed cohort to review all blinded clinical safety data and available PK data. The SRC assessed the safety of proceeding to the next cohort and determined the dose level for the next cohort.
- The study design allowed for the number of cohorts (maximum of 9) and dose level to be adapted based on cumulative data obtained from preceding cohorts.

Part B—MAD

- 60 participants were randomized into 6 sequential dose cohorts (10 participants per cohort) randomly assigned to the study drug or placebo (8:2).
- Participants were admitted to the CRU on Day 1 for baseline evaluations prior to dosing.
- Study drug dosing (SC) occurred weekly for 5 weeks. Participants remained in the CRU under medical supervision for 3 days after the 1st and 5th doses and remained for at least 4 hours after the 2nd, 3rd, and 4th doses.
- Participants returned for an additional 8 weekly outpatient study visits and a final visit 12 weeks post first dose.
- A SRC convened after each dosed cohort to review all blinded clinical safety data and available PK data. The SRC assessed the safety of proceeding to the next cohort and determined the dose level for the next cohort.
- The study design allowed the number of cohorts (maximum of 7) and dose level to be adapted based on cumulative data obtained from preceding cohorts.



Assessments

- Safety was assessed via evaluation of adverse events (AEs), vital signs (including temperature, heart rate, and blood pressure), 12-lead electrocardiogram (ECG), corrected QT (QTc) analysis, laboratory evaluations, physical examination, glucose monitoring, and injection site reactions.
- Tolerability was assessed via an assessment of treatment-emergent adverse events (TEAEs).
- Drug blood concentrations were analyzed via a liquid chromatography-mass spectrometry (LC-MS) bioanalytical method for PK analysis.
- Absolute and percent weight loss at pre-specified timepoints was assessed.

RESULTS

The study drug was well tolerated by healthy participants at the doses evaluated. There were no study drug-related severe AEs or serious adverse events (SAEs) and no discontinuation or participant withdrawal due to study drug-related AEs. The most common AEs were consistent with the known safety profile of GLP-1 RAs, and consisted of nausea, decreased appetite, headache, vomiting, and dyspepsia. Most of these AEs were assessed as mild and possibly or probably related to the study treatment by the Investigator. No clinically significant changes were reported in vital signs, physical examinations, or ECGs. The half-life of the study drug was successfully calculated with concentration data from the validated LC-MS method.

ABOUT ALTASCIENCES

Altasciences is an integrated drug development solution company offering pharmaceutical and biotechnology companies a proven, flexible approach to preclinical and clinical pharmacology studies, including formulation, manufacturing, and analytical services. For over 25 years, Altasciences has been partnering with sponsors to help support educated, faster, and more complete early drug development decisions. Altasciences' integrated, full-service solutions include preclinical safety testing, clinical pharmacology and proof of concept, bioanalysis, program management, medical writing, biostatistics, clinical monitoring, and data management, all customizable to specific sponsor requirements. Altasciences helps sponsors get better drugs to the people who need them, faster.