Romosozumab as an Adjunct to Physiologic Estrogen Replacement in Functional Hypothalamic Amenorrhea

Status: RECRUITING

Eligibility Criteria

Age: 14 years to 30 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

For FHA and controls: * Female, age 14-30 years, skeletally mature with bone age ≥ 14 years (only 2% of growth left) * For women of reproductive age, agree to use an effective non-hormonal contraceptive method or a progestin releasing intrauterine device (no evidence of systemic skeletal effects) for the study duration * Biochemical criteria: * Negative βHCG (pregnancy test) * TSH within twice the upper limit of normal; potassium, magnesium within the normal range; prolactin \<10 ng/mL above the upper limit of normal; FSH not elevated. * Serum ALT ≤ 3 times upper limit of normal, LDL ≤ 190 mg/dl * eGFR ≥ 30ml/minute * If the diagnosis of FHA is unclear, we may check additional labs (e.g., testosterone and sex hormone binding globulin if there is a suspicion of PCOS based on clinical hyperandrogenism). Additional inclusion criteria for FHA: * Less than 3 menses in the preceding 6 months * BMD Z-score ≤ -1.0 at ≥ 1 skeletal site (for subjects \<18 years old, we will use the height Z-score-adjusted BMD Z-score using the pediatric bone density calculator developed by the National Institutes of Health and currently maintained by the Children's Hospital of Philadelphia) * Dental check-up within the past year * If the menstrual status of the subject is unclear due to the presence of a progestin-releasing IUD, serum estradiol levels will be checked twice, at least one week apart. Both estradiol levels must be \< 50 pg/mL.

Exclusion Criteria:

For FHA and controls * Disease other than FHA known to affect bone, including untreated thyroid dysfunction, Cushing's disease, renal failure, diabetes mellitus * Use of bisphosphonates * Use of other medications known to affect bone metabolism within 3 months of the study (other than calcium and vitamin D supplementation). * Current use of systemic corticosteroids * Migraine with aura. * Personal history of or first-degree relative with unprovoked thromboembolism (unless the subject has been tested and ruled out for a hypercoagulable state). * Active substance use disorder; current smoker * History of malignancy or Paget disease of bone * Pregnant, planning to become pregnant within 12 months after the end of treatment and/or breastfeeding Additional exclusion criteria for FHA * Cardiovascular: History of myocardial infarction or stroke; history of hypertension or use of anti-hypertensive medications * Immunodeficiency or taking immunosuppressive therapy * Other conditions that can cause oligo-amenorrhea such as PCOS, primary ovarian insufficiency * Dental: Osteonecrosis of the jaw (ONJ) or risk factor for ONJ, such as invasive dental procedures (tooth extraction, dental implants, oral surgery in the past 3 months), poor oral hygiene, periodontal and/or pre-existing dental disease * Planned invasive dental procedure or other planned major surgery for 18 months after the baseline visit * Known sensitivity or absolute contraindication to any of the products or components of the medications to be administered (romosozumab, zoledronic acid, transdermal estradiol, micronized progesterone, calcium or vitamin D supplements) * Concerning EKG findings for ischemia Additional exclusion criteria for normal-weight healthy controls • BMD Z-score \<-2.5 (who we will refer for evaluation)

Conditions & Interventions

Interventions:
DRUG: Romosozumab, DRUG: Placebo, DRUG: Zoledronic acid
Conditions:
FHA (Functional Hypothalamic Amenorrhea)

More Information

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