Dr. Elizabeth Shane

Idiopathic osteoporosis (IOP) in premenopausal women is defined as osteoporosis that occurs in young, otherwise healthy women with intact gonadal function and no secondary cause of bone loss. IOP in premenopausal women is an uncommon disorder. The estimated prevalence in the United States, based on women with documented low trauma fractures or low femoral neck bone mineral density (BMD), is approximately 113,000. There is no FDA--approved therapy for premenopausal women with IOP, many of whom have sustained multiple fractures or have extremely low BMD. This proposal seeks support for a Phase 2 clinical trial to investigate the efficacy and safety of teriparatide, human recombinant PTH(1--34), for IOP in premenopausal women. It is based upon our previous work in which we have defined microarchitectural abnormalities in this disorder: thin cortices, trabecular loss, fewer trabecular plates, fewer and longer trabecular rods, decreased connectivity between rods and plates, and reduced stiffness or strength. We will test the central hypothesis that anabolic therapy with teriparatide, a drug that increases osteoblast--mediated bone formation, will safely increase areal and volumetric BMD in premenopausal women with IOP. We will also test the hypothesis that teriparatide will restore abnormal microstructure towards normal, and improve other aspects of bone quality in premenopausal IOP. In this phase 2 clinical trial, which is randomized and placebo--controlled, we will characterize effects of teriparatide on areal and volumetric BMD, microarchitecture, remodeling, stiffness, mineralization and collagen properties in women with IOP. We will use both state--of--the--art and novel approaches to skeletal macro-- and micro--imaging that have never been applied to the therapy of IOP. These new approaches will provide a rational basis for a much--needed therapeutic approach to IOP in premenopausal women and will have high impact upon clinical practice. By investigating the therapy of IOP and improving the health of young women with unexplained osteoporosis, this proposal addresses a key goal of the FDA's Office of Orphan Product Development OPD grant program, namely to support the clinical development of products for use in rare diseases or conditions where no current therapy exists.