Contemporary Clinical Trials 31 (2010) 336–344

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

The primary care osteoporosis risk of fracture screening (POROS) study: Design and baseline characteristics

Diane L. Schneider [a], Karen Worley [b,*], Mary K. Beard [c], Mark Iannini [d], Marcia Ko [e], James McCallum [f], Riya Pulicharam [g], Michael Steinbuch [b,1]

[a] University of California San Diego, 9500 Gilman Drive, La Jolla, CA 92093
[b] Warner Chilcott Pharmaceuticals, formerly Procter & Gamble Pharmaceuticals, 8700 Mason-Montgomery Road, Mason, OH 45040, USA
[c] Utah Osteoporosis and Menopause Center, 455 East South Temple, Suite 202, Salt Lake City, UT 84111, USA
[d] Southern Arizona Rheumatology Associates, 630 North Alvernon, Suite 371, Tucson, AZ 85711, USA
[e] Mayo Clinic Arizona, 13737 North 92nd Street, Scottsdale, AZ 85260, USA
[f] Scripps Clinic, 10666 North Torrey Pines Road, Maildrop MS212A, La Jolla, CA 92037, USA
[g] Healthcare Partners Medical Group, 1025 West Olympic Boulevard, Los Angeles, CA 90015, USA

ARTICLE INFO

Article history:
Received 23 October 2009
Accepted 30 March 2010

Keywords:
Osteoporosis
Fracture
Risk factors
N-telopeptides
Screening

ABSTRACT

Objective: POROS evaluates a 3-step fracture risk screening program in women 50–64 not previously diagnosed with osteoporosis. This report details the research design and baseline characteristics.
Methods: Recruiting from 6 primary care sites, baseline characteristics, including fracture risk factors, were assessed via self-administered questionnaires (SAQs). Subjects with ≥1 risk factor were randomized to Intervention or Non-Intervention. Those without any risk factors were placed in the No Risk Factors group. Bone turnover was measured in the Intervention group via urine N-telopeptide (NTx) testing. Subjects with NTx>50 had central hip and spine Dual-energy X-ray Absorptiometry (dxa). All groups were followed for 24 months, completing SAQs on osteoporosis management and fractures. At baseline, comparisons were made on demographics, health status, and prevalence of fracture risk factors.
Results: 2839 women were enrolled and included in baseline analyses (1464 Intervention, 372 Non-Intervention, and 1003 No Risk Factors). The mean age was 56.1 and 81.1% were postmenopausal. As expected by randomization, the Intervention and Non-Intervention groups had similar baseline characteristics. The most commonly reported fracture risk factors were body mass index <24 kg/m^2 and needing to use arms to stand from a chair. Subjects in the No Risk Factors group were more likely to be younger, heavier, Hispanic, in good health, a non-smoker, and to drink less alcohol.

Abbreviations: BCE, Bone collagen equivalents; BMD, Bone mineral density; BMI, Body mass index; BTM, Bone turnover marker; CFR, Code of federal regulations; CRA, Clinical research associate; CRO, Contract research organization; CRF, Case report form; dL, Deciliter; dxa, Dual-energy X-ray absorptiometry; ET, Estrogen therapy; FDA, Food and Drug Administration; FRAX, WHO fracture risk assessment tool; HT, Hormone therapy; ICF, Informed consent form; ICH, International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use; IRB, Institutional review board; kg, Kilogram; L, Lumbar; LMP, Last menstrual period; m^2, Meter squared; mM, Millimole; mg, Milligram; Naturalistic study, A type of study in which the researcher very carefully observes and records some behavior or phenomenon, sometimes over a prolonged period, in its natural setting while interfering as little as possible with the subjects or phenomena; nM, Nanomole; NTx, N-telopeptides (urine test for bone turnover markers); OTC, Over-the-counter; PBI, Pacific Biometrics, Inc.; PCP, Primary care physician; RB, Regulatory binder; RCT, Randomized clinical trial; SAQ, Self-administered questionnaire; SERMs, Selective estrogen receptor modulators; *T*-score, The number of standard deviations the bone mineral density is above or below the average for a young adult at peak bone density; WHO, World Health Organization.

* Corresponding author. Tel.: +1 513 622 4635; fax: +1 513 622 4321.
E-mail addresses: drdi@san.rr.com (D.L. Schneider), karen.worley@wcrx.com (K. Worley), drmarykbeard@msn.com (M.K. Beard), iannini@sarahealth.net (M. Iannini), ko.marcia@mayo.edu (M. Ko), jmccallum@scrippsclinic.com (J. McCallum), rpulicharam@healthcarepartners.com (R. Pulicharam), mstein32@its.jnj.com (M. Steinbuch).
[1] Present address: Johnson & Johnson, 4545 Creek Road, Cincinnati, OH 45242, USA.

1551-7144/$ – see front matter
doi:10.1016/j.cct.2010.03.012

Conclusion: A stepwise screening program, utilizing data on fracture risk factors and high bone turnover prior to obtaining central bone density, can contribute significantly to fracture risk assessment in perimenopausal and younger postmenopausal women.

1. Introduction

Early identification of women at increased risk of osteoporotic fracture presents an opportunity for intervention to decrease fracture risk. Recent studies have shown women with osteopenia constitute the largest proportion of those who sustain fractures [1,2]. Low bone mass is the single best predictor of fracture risk in asymptomatic, postmenopausal women. However, assessment of bone density is not systematically performed as a screening tool in younger women (aged 50–64). In addition, low bone mineral density (BMD) alone does not provide adequate fracture risk stratification. Not all women with osteopenia (*T*-scores between −1.0 and −2.5) are at high risk for future fractures.

Risk factor identification tools may complement BMD testing in this younger, at-risk population. The World Health Organization's fracture risk assessment (FRAX) may be a useful tool to help risk stratify women with osteopenia [3–6]. Other strategies to assess the risk of bone loss and fractures in this early postmenopausal group may include measurement of bone turnover markers, such as urine N-telopeptide (NTx) [7–10]. A baseline BMD is a static assessment of the measured skeletal sites. In contrast, bone markers provide a dynamic indication of the current status of bone turnover and bone remodeling. The best screening methods for fracture risk in younger postmenopausal women should be both noninvasive and relatively low cost.

The Primary Care Osteoporosis Risk of Fracture Screening (POROS) study implements and evaluates a three-step fracture risk screening program in the primary care setting within a large, diverse patient population of women aged 50–64 who had not been diagnosed or treated for osteoporosis. It assesses fracture risk factors, high bone turnover, and low bone mass at baseline, with a 24-month follow-up period to observe osteoporosis disease management strategies and fractures. This report details the research design and summarizes the baseline characteristics of the study subjects.

1.1. Study objectives

The primary objective of the POROS Study is to determine the clinical utility of a three-step fracture risk screening program in a population of predominantly younger postmenopausal women. Clinical utility will be measured by comparing physician-recommended disease management strategies for subjects in the intervention group versus those without the intervention. It is hypothesized that physicians will be more likely to recommend preventive and treatment-oriented approaches to osteoporosis (e.g., exercise, calcium, medications) for patients with detailed information on fracture risk.

Secondary objectives of the study include assessing the differences in treatment initiation for subjects in the Intervention versus Non-Intervention group, evaluating the correlation between the three screening variables (risk factors, urine NTx, and dxa), comparing fracture rates (at 1- and 2-years post-baseline), exploring the association between number of fracture risk factors and fracture incidence, and determining the risk factors most predictive of fracture.

2. Methods

This 24-month, prospective screening and follow-up study enrolled patients from medical groups representing six primary care sites in the western United States. The study also includes an observational follow-up component using electronic pharmacy data and medical record review for validation. Each study site obtained Institutional Review Board approval. All subjects provided written informed consent prior to beginning the study.

2.1. Subjects

Women who were 50–64 years of age, under the care of the participating medical group, able to speak and read English or Spanish, ambulatory, and able to complete a self-administered questionnaires (SAQs), were eligible for the study. Subjects were excluded if they had previously used an osteoporosis medication; used an estrogen implant, hormone therapy (HT), or birth control pills within the past 6 months; had a terminal illness; lived in a long-term care facility; were enrolled in another clinical research study; or were a resident of the European Union.

2.2. Study design

The overall study design is summarized by flowchart in Fig. 1.

2.2.1. Recruitment

Site investigators invited women age 50 to 64 years who were patients under current care of their medical group. Subjects were recruited via mail invitations as well as during routine office visits or health fairs, with enrollment starting in August of 2006 and ending in February, 2008. The primary method of subject recruitment varied widely by site, with some sites recruiting about 99% of subjects from mailed invitations, and others using office visits, seminars, awareness sessions, and health fairs to recruit over 95% of their subjects.

2.2.2. Data collection

Enrolled and consented subjects were asked to complete baseline SAQs, which included questions about general health and fracture risk. The questions for fracture risk were a modification of the FRACTURE Index without bone BMD assessment developed by Black et al. [11]. Additional risk factors were a result of discussion in 2005 with John Kanis who was leading the development of the fracture risk assessment tool (FRAX) for the World Health Organization.