

Implementation of an anabolic therapy program and follow-up of patients prescribed abaloparatide: real-world results of a pharmacist-led osteoporosis clinic

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ABSTRACT

Utilizing anabolic osteoporosis therapies presents with challenges, including patient acceptance of injections, addressing medication safety concerns, and achieving medication access. We developed a pharmacist-run clinic to ensure the safe and effective use of these therapies. Primary endpoints were comparison of dual energy X-ray absorptiometry (DXA) T-scores and bone mineral density (BMD) values of the total hip, femoral neck, spine, and wrist at baseline, after abaloparatide therapy, and following 1 year of follow-on antiresorptive therapy. The secondary endpoint was the number of documented fractures during the evaluation period. 146 patients were referred for abaloparatide treatment. Ninety-one patients initiated treatment: average age was 66.7 (\pm 7.7) years, 56% had a history of osteoporotic fracture, baseline T-Scores of the femoral neck and spine were -2.5 (\pm 0.7), and -2.4 (\pm 1.3), respectfully. Mean length of therapy was 12 \pm 2 months (range 9-18 months). T-scores and BMD significantly improved at all sites except for a significant decrease in T-score at the 1/3 radius. After 1 year of follow-on anti-resorptive treatment, T-scores and BMD significantly increased at the total hip and at the lumbar spine compared to post-abaloparatide, with nonsignificant changes in the

femoral neck and 1/3 radius. There was one reported fracture. Eighteen patients (19.8%) discontinued therapy due to adverse drug reactions and there was a 72.5% medication persistence rate. Abaloparatide is effective in increasing BMD and T-scores and in preventing osteoporosis-related fractures. While significant barriers to anabolic osteoporosis treatment remain, involvement of a pharmacist-led clinic may increase medication persistence.

KEYWORDS: anabolic, abaloparatide, BMD, osteoporosis, fracture, adherence.

INTRODUCTION

Osteoporosis is a major public health problem, representing the most common bone disorder worldwide [1] and is associated with increased morbidity and mortality [2]. Less than 25% of women over 65 years of age with an osteoporosis-related fracture undergo bone density measurements or initiate treatment for osteoporosis [3]. Available osteoporosis treatments include antiresorptive agents (bisphosphonates, denosumab, hormonal therapies, calcitonin) and anabolic therapies (teriparatide, abaloparatide, romosozumab). Anabolic therapy is indicated in patients at high risk of osteoporotic fracture [4], including patients with a history of fragility fracture, multiple risk factors for fracture, or failure to respond to antiresorptive drug therapy [5].

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Abaloparatide is a synthetic analogue of human parathyroid hormone-related peptide and was approved by the Food and Drug Administration on April 28, 2017 [6]. It acts as an agonist at the parathyroid hormone 1 (PTH1) receptor resulting in stimulation of osteoblast function which results in increased bone mass. Abaloparatide therapy reduced new vertebral fractures by 86% and nonvertebral fractures by 43% compared to placebo in the Abaloparatide Comparator Trial In Vertebral Endpoints (ACTIVE) trial [7].

Patient utilization of anabolic osteoporosis therapies presents with challenges, however. Many patients are reluctant to initiate a medication which requires a daily subcutaneous injection and typically requires administration training. Concerns about medication safety must be addressed, and contraindications to therapy must be ruled out prior to drug initiation. Finally, completion of medication prior authorization is standard as the use of anabolic therapy is expensive. While labor intensive, these actions are vital for medication access. We developed a pharmacist-run anabolic osteoporosis clinic [8] in this ambulatory-care endocrinology practice to ensure the safe and effective use of anabolic osteoporosis therapy. The purpose of this report is to describe the 4-year, real-world results of this clinic.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board of Albany College of Pharmacy and Health Sciences prior to its initiation. This pharmacist-led clinic is embedded into an ambulatory care endocrinology specialty practice. Endocrinologists, nurse practitioners and physician assistants at the practice identified patients who were potential candidates for anabolic osteoporosis therapy during regularly scheduled patient visits. Potential candidates were determined to be at a high risk of an osteoporotic fracture, including patients with a history of fragility fracture, very low bone mineral density (e.g., T-score of ≤ -3), or failure to respond to antiresorptive drug therapy. Patients were referred to this clinic for treatment with teriparatide, abaloparatide or romosozumab. This study discusses a cohort of patients referred to this clinic that received treatment with abaloparatide.

After referral, pharmacists completed chart review on referred patients, identifying any contraindications from the patient's medical history and ensuring appropriate laboratory work up for secondary causes of osteoporosis and contraindications for therapy were completed. Laboratory values of interest included serum Ca, albumin, 24-hr urine Ca, vitamin D, alkaline phosphatase (ALP), free T4, TSH, intact PTH, serum phosphate, serum protein electrophoresis and/or urine protein electrophoresis. A clinic pharmacist contacted the patient to discuss potential therapies. During this discussion, the pharmacist inquired about the patient's pertinent medical history, including potential contraindications, prior osteoporosis therapy, and insurance coverage. The pharmacist addressed the required method of drug administration, its mechanism of action, common side effects, patient preferences regarding treatment options, and patient concerns and questions regarding therapy.

If a patient was not an appropriate candidate for anabolic osteoporosis therapy, the pharmacist contacted the clinician and explained the rationale for not pursuing anabolic therapy as well as providing recommendations for alternative therapies. If the patient was an appropriate candidate, clinicians and pharmacists would collaborate to determine the most ideal treatment option for the patient's osteoporosis and to pursue insurance coverage for that option. Insurance coverage generally required the completion of prior authorizations or use of patient assistance programs.

Once a patient obtained teriparatide or abaloparatide, a 1-hour counseling visit was scheduled with the pharmacist for the patient to learn to perform daily injections. This was not necessary for romosozumab, which is given monthly in-office by a nurse. After counseling on administration technique, the patient demonstrated injection technique with a demonstration pen using the teach back method. The patient then self-administered the first dose of teriparatide or abaloparatide in the office under the pharmacist's direct supervision. A note would be entered into the patient's chart regarding the education. As part of documentation, the pharmacist would ensure the patient had a follow-up appointment and DXA scheduled with the referring clinician.

The pharmacist contacted the patient after 1 week of therapy to assess adherence and potential challenges. The patient was counseled to reach out at any point in the treatment course if treatment was discontinued for any reason, due to the need for follow-on antiresorptive therapy. The pharmacist served as a contact person for patient concerns and questions during the entire therapeutic course of anabolic therapy.

Data were retrospectively collected *via* a computerized text search of the patient electronic medical records (EMR) at this practice. Search terms included Tymlos, abaloparatide and osteoporosis. Start and end dates for the data ranged from May 1, 2017 until October 1, 2021. The records of patients with abaloparatide or Tymlos appearing in the medication field were reviewed manually to identify referred patients.

Patient information from abaloparatide referrals were compiled as follows: baseline demographic information (sex, race, age, height, weight), contraindications to anabolic therapy (if applicable), osteoporosis information including bone mineral density (BMD) and T-scores from dual energy X-ray absorptiometry (DXA) tests, history of osteoporosis-related fracture, and other osteoporosis medications used prior to (if applicable) and immediately after abaloparatide use. Information regarding the duration of anabolic therapy, identification of reasons why patients did not receive anabolic therapy, as well as documentation of discontinuation of therapy were also collected.

The primary study endpoint was the comparison of DXA T-scores and BMD values of the total hip, femoral neck, spine, and one-third radius (wrist) at baseline, after abaloparatide therapy, and following 1 year of follow-on antiresorptive therapy. The secondary end point was the number of documented fractures occurring during this time. Each patient served as his/her own control. Paired T-tests were performed to compare mean differences in pre- and post- T-scores and BMD values obtained at baseline, after completion of abaloparatide therapy, and after a minimum of 1 year of follow-up antiresorptive therapy. P values of less than 0.05 were considered statistically significant.

RESULTS

A total of 205 patients were identified *via* text search of the EMR, with records of 159 patients including the term abaloparatide or Tymlos in the medication field. Of these, 146 patients were referred for abaloparatide therapy and are the focus of this review.

Overall, 91 (62.3%) referred patients initiated treatment with abaloparatide (Figure 1). Ten patients were found to have a contraindication to therapy and/or a secondary cause of osteoporosis during the secondary workup (seven with elevated parathyroid hormone levels, two with an elevated serum protein electrophoresis, and one patient with an unexplained increased serum alkaline phosphatase level) and did not begin treatment. Eighteen of the referred patients refused to initiate abaloparatide because of concerns of adverse drug reactions, lack of interest in treating their osteoporosis, or because of the required route of drug administration. Fifteen additional patients declined treatment after subsequent identification of high medication co-pay costs. Patient insurance dictated teriparatide be used in 11 other cases, and insurance refused coverage for any anabolic therapy in one case. Table 1 presents the baseline characteristics of the 91 patients who initiated abaloparatide therapy. These patients were predominately older, white women, with a majority having a history of osteoporotic fracture and half having received previous osteoporosis therapy. Interestingly, 45% (23/51) of patients with a previous fracture were osteoporosis-drug naïve, including twelve patients with a history of multiple fractures. Conversely, 45% (18/40) of patients with no history of fracture received previous osteoporosis treatment. Table 2 presents the baseline T-scores and bone mineral density (BMD) data of this 91-patient cohort.

The changes in DXA T-scores and BMD at the total hip, femoral neck, lumbar spine, and one-third radius (wrist) from baseline to post-abaloparatide are presented in Table 3. There were significant increases at all sites except for a significant decrease in T-score at the wrist after a mean of 12 ± 2 months (range 9-18 months) of therapy. Duration of abaloparatide treatment in the 45 patients who have completed a course of

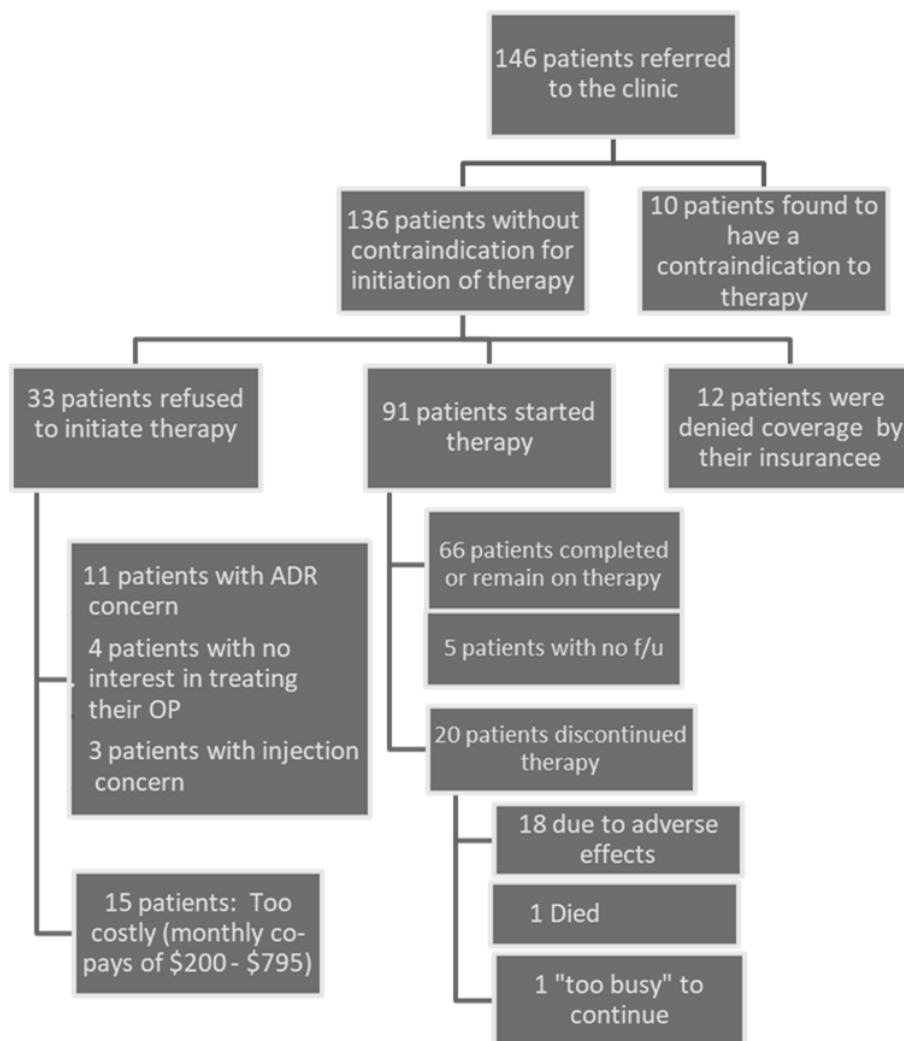


Figure 1. Flow diagram of patients referred to the pharmacist-run clinic.

therapy to date was 15 ± 4 months with a range of 12-24 months. Of note, 17 patients completed 18 months of therapy while 19 patients completed 12 months of therapy prior to initiation of antiresorptive treatment.

A comparison between baseline and post-antiresorptive therapy scores lacked statistical power as there were only six cases where all three DXA's were performed at the same practice, on the same machine, and by the same technician. However, Table 4 shows the changes between post-abaloparatide and post-antiresorptive T-scores and BMD in the 21 patients where DXA's were performed as described above. Significant increases in T-scores and BMD were seen at the

total hip and at the lumbar spine, with nonsignificant increases in the femoral neck and wrist.

There was one reported fracture at last follow-up; a wrist fracture which occurred one month after beginning treatment with abaloparatide.

Sixty-six of 91 (72.5%) patients who initiated abaloparatide therapy have completed their course of therapy or are currently completing their therapy. Eighteen patients (19.8%) discontinued therapy due to an adverse drug event, with an average duration of use of 67 days (range, one day to nine months) before medication discontinuation. Discontinuation due to adverse drug events included headache (4), fatigue (4), dizziness (2),

Table 1. Patient baseline characteristics.

Characteristic (N = 91)	Value
Female	89 (97.8%)
White	90 (98.9%)
Age, mean \pm SD (years)	66.7 \pm 7.7
BMI, mean \pm SD (kg/m ²)	25.2 \pm 6.0
History of previous osteoporosis-related fracture	
Total number of fractures	106*
Type of osteoporotic fracture	
Hip	16 (15.1%)
Vertebral	54 (50.9%)
Wrist	8 (7.5%)
Other	28 (26.4%)
Previous osteoporosis drug use	46 (50.5%)
Previous osteoporosis drug therapy**	
Bisphosphonates	41
Denosumab	25
Raloxifene	1
HRT	2
Calcitonin	1
Teriparatide	1

*28 patients had a history of multiple fractures.

**15 patients received more than 1 previous osteoporosis therapy.

BMI: body mass index; HRT: hormone replacement therapy.

palpitations (2), muscle aches/pains (2), and hypercalcemia, nausea, weight gain, and temporal artery inflammation (1 each). One patient discontinued treatment because she was “too busy” to continue therapy. One other patient died three months into therapy due to a presumed myocardial infarction, and the use of abaloparatide was not thought to be associated with his death. Five additional patients were lost to follow-up.

Each patient who completed her/his course of abaloparatide has received follow-on treatment, with 84.1% prescribed denosumab and the remaining patients receiving an intravenous (9.1%) or oral bisphosphonates (4.5%), or raloxifene (2.3%).

DISCUSSION

Anabolic therapy is indicated for individuals at high fracture risk and for patients unable to tolerate or do not respond to antiresorptive therapy [9]. In the ACTIVE trial, Miller *et al.* evaluated the efficacy and safety of abaloparatide for the prevention of new vertebral fracture in postmenopausal women with osteoporosis. Abaloparatide 80 μ g significantly reduced the risk of new vertebral fracture by 86% and nonvertebral fractures by 43% over 18 months versus placebo and was associated with one-third less new vertebral and nonvertebral fractures compared to teriparatide 20 μ g [7]. Consistent with clinical trial data, patients in our real-world cohort demonstrated an increase in BMD and T-scores in

Table 2. Baseline DXA results.

Variable	Value
Total hip	
T-score (n = 84)	-2.1 ± 0.9
BMD (g/cm ²) (n = 73)	0.697 ± 0.112
Femoral neck	
T-score (n = 79)	-2.5 ± 0.7
BMD (g/cm ²) (n = 75)	0.574 ± 0.084
Lumbar spine	
T-score (n = 88)	-2.4 ± 1.3
BMD (g/cm ²) (n = 75)	0.786 ± 0.137
Wrist	
T-score (n = 50)	-2.0 ± 1.5
BMD (g/cm ²) (n = 44)	0.569 ± 0.100

BMD: bone mineral density; DXA: dual energy X-ray absorptiometry.

Table 3. Comparative BMD and T-score changes from baseline to post-abaloparatide therapy.

	N	Mean difference	95% CI lower	95% CI upper	p-value
T-score Hip	15	0.207	0.086	0.328	0.0026
BMD Hip	15	0.026	0.012	0.039	0.0012
T-score FN	15	0.267	0.092	0.441	0.0055
BMD FN	15	0.031	0.015	0.05	0.0028
T-score Spine	16	0.7	0.475	0.925	<0.0001
BMD Spine	16	0.08	0.054	0.105	<0.0001
T-score Wrist	16	-0.188	-0.345	-0.03	0.0231
BMD Wrist	16	-0.0048	-0.017	0.0079	0.44

BMD: bone mineral density (g/cm²); FN: femoral neck.

the total hip and lumbar spine and experienced a very low rate of fracture.

A significant decrease in T-score at the distal radius following abaloparatide treatment was seen in this study. While positive changes in BMD and T-scores are seen within the first year of treatment, areas of predominantly cortical bone, such as the distal radius, may show an apparent decrease per DXA. This is thought to be due to enhanced endocortical remodeling associated with

anabolic drug therapy, causing a relatively greater increase in bone diameter than in cortical thickness. The result is an apparent decrease in bone density, although to date no studies have assessed the impact of this apparent decrease with respect to wrist fractures. One wrist fracture did occur one month into therapy in a patient with a previous history of humerus fracture who was osteoporosis drug naïve prior to initiating abaloparatide. In an exploratory analysis of the

Table 4. Differences in T-scores and BMD between abaloparatide finish and 1 year of antiresorptive therapies.

	N	Mean difference	95% CI lower	95% CI upper	p-value
T-score Hip	20	0.165	0.051	0.279	0.0069
BMD Hip	20	0.02	0.0066	0.034	0.0059
T-score FN	20	0.145	-0.02	0.31	0.082
BMD FN	20	0.015	-0.0028	0.033	0.094
T-score Spine	20	0.335	0.024	0.646	0.0363
BMD Spine	20	0.026	0.0056	0.046	0.015
T-score Wrist	21	0.0095	-0.128	0.147	0.89
BMD Wrist	21	0.00071	-0.007	0.0085	0.85

BMD: bone mineral density (g/cm^2); FN: femoral neck.

ACTIVE trial, BMD decreases at the 1/3 radius were comparable between the placebo and abaloparatide groups [10].

Fewer than one-quarter of women over 65 years of age with an osteoporosis-related fracture undergo bone density measurements or initiate treatment for osteoporosis [3] despite guideline recommendations [9]. Recurrent fractures are a major public health burden, as 15-25% of patients experience a second fracture within 10 years [11]. Almost half of the patients in our real-world population were osteoporosis drug naïve at the time of referral, including 45% (23/51) of patients who had sustained a previous osteoporosis-related fracture, twelve of whom had histories of multiple fractures. Many patients fail to receive appropriate treatment for osteoporosis after a sentinel fragility fracture, which increases the risks of refracture. This discrepancy between guideline-recommended practice and real-world practice has been termed the osteoporosis care gap, with some studies showing fewer than 20% of patients who sustain a fragility fracture receive osteoporosis treatment [12].

As identified in this study, 55 patients referred for treatment did not initiate therapy (Figure 1). This modest initiation rate (62.3%) highlights current challenges in the treatment of osteoporosis. Approximately a third of patients who refused therapy (18 of 55) were not convinced of the need for treatment, cited side effect concerns, or declined use due to the requirement for daily

injections. Studies have identified similar challenges and recommend shared-decision making along with providing high quality information about osteoporosis, fracture risk and available treatment options [13]. We provided this approach as a pharmacist discussed potential medication side effects, reviewed boxed warnings, and answered patients' questions concerning therapy. The reality may be that patients with osteoporosis perceive fracture risk to be lower and risks of medications to be higher than what is actually experienced in practice.

High costs of medication copays or lack of insurance coverage were responsible for almost half (27 of 55 patients) of the patients in this study cohort not initiating therapy. Co-pay cards cover up to \$500 per month for patients with commercial insurance but are not allowed to use for patients with state (Medicaid) or federal (Medicare) insurances. Paradoxically, it is the elderly who typically have the greatest financial need, but who end up with the highest monthly co-pays (e.g., \$795 per month) because of the unavailability of a co-pay card. As biosimilars for PTH analogs become more widely available, the cost of therapy will likely decrease for patients (as well as for insurers). The current average wholesale price (AWP) of abaloparatide is \$2747.21 for 30 days of therapy, Forteo is \$4,759.93 for four weeks of therapy, and its biosimilar, teriparatide recombinant, is \$2,970 for four weeks of therapy [14].

Ten patients who were referred for abaloparatide were found to have a contraindication to therapy and/or a secondary cause of osteoporosis. In experimental studies, abaloparatide caused a dose-dependent increase in the incidence of osteosarcoma in rats after subcutaneous exposures 4-28 times human exposures. Product labeling includes warnings to avoid use in patients with increased risk of osteosarcoma including patients with open epiphyses, metabolic bone diseases including Paget's disease, bone metastases or history of skeletal malignancies, prior external beam or implant radiation therapy involving the skeleton, and hereditary disorders predisposing to osteosarcoma. The boxed warning of osteosarcoma was removed in December of 2021. Abaloparatide use should also be avoided in patients with pre-existing hypercalcemia and those known to have an underlying hypercalcemic disorder, such as primary hyperparathyroidism.

Following referral, a clinical pharmacist reviewed the patient's electronic medical record to rule out contraindications to anabolic therapy and to ensure work-up for secondary causes of osteoporosis (e.g., hyperparathyroidism, hyperthyroidism, Cushing's disease, vitamin D deficiency, multiple myeloma, drug-induced) had been completed. From our experience we conclude our pharmacist-run clinic has served as an effective safety net, which may have even greater utility in non-specialty practices.

The mean duration of treatment with abaloparatide among the 45 patients who completed therapy was 15 ± 4 months (range 12-24 months). Of note, while 17 patients completed a typical 18 month course of therapy (as per the ACTIVE trial), 19 patients completed 12 months of therapy. Anabolic effects on bone biochemistry are most marked during the first 12 months of therapy, and histomorphometric data confirm the substantial stimulation of bone formation observed early on with teriparatide [15], is no longer seen at 18 months [16]. Because the cumulative use of abaloparatide for more than 2 years is not recommended, some may interpret this as appropriate rationale for "banking" the balance of abaloparatide therapy for future use. As opposed to completing the traditional full course of therapy, the thought is to potentially divide

treatment into two courses of therapy (retreatment), with a course of an antiresorptive in between, in an attempt to maximize the full potential of abaloparatide. Given the lack of data, however, "banking" abaloparatide for a second course of treatment cannot be endorsed.

Conversion to antiresorptives after anabolic treatment is necessary to maintain (and subsequently augment) BMD increases, otherwise BMD is quickly lost over the ensuing 12 months [17-21]. There are few data establishing the ideal osteoporosis therapy after completion of a course of treatment with abaloparatide, though the results of the ACTIVE Extension Trial support the use of alendronate for at least 24 months after an initial 18 months of abaloparatide treatment. Treatment produced continued increases in BMD and reductions in the risk of vertebral, nonvertebral, clinical, and major osteoporotic fractures including a relative risk reduction for vertebral fractures of 87% with abaloparatide followed by alendronate compared to the placebo/alendronate group ($P = 0.001$) [22]. Based on experience with zoledronic acid and denosumab following teriparatide therapy, it is probable antiresorptive agents would also preserve the osteoanabolic benefits of abaloparatide [23, 24], though denosumab may be preferred due to greater improvements in BMD [25]. All participants in our cohort received follow-on antiresorptive therapy, with 84% receiving denosumab. Leder *et al.* reported a follow-on therapy rate of 56% [21]. Involvement of a pharmacist-led clinic and increased awareness by patients and providers of the need for antiresorptive treatment following anabolic therapy may have improved the rate of follow-on therapy in our cohort.

Ninety-one of the 146 (62.3%) patients referred to the clinic initiated treatment with abaloparatide (Figure 1). Of these, 18 patients (19.8%) discontinued treatment due to adverse effects, an additional patient discontinued treatment because she was "too busy", and one patient being evaluated for Cushing's disease died three months into therapy due to a reported myocardial infarction (not felt by the patient's physician to be related to therapy). Five additional patients were lost to follow-up, for an overall discontinuation rate of 27.5%. Patient compliance with osteoporosis therapy is

infamously poor. Approximately half of patients taking oral therapies for osteoporosis discontinue treatment within one year of initiation [26, 27]. A retrospective observational study utilizing administrative claims database among women prescribed injectable therapies demonstrated the majority of patients discontinue by the end of 12-months, with discontinuation rates of 69.1% with ibandronate, 67.1% with teriparatide, 59.2% with zoledronic acid and 48.8% with denosumab [28].

A retrospective cohort study utilizing a real-world population database to estimate the persistence of antiresorptive and anabolic medications for osteoporosis found an unadjusted 2-year persistence range of 10.3-45.4% [29]. Poor compliance with osteoporosis therapy is a significant problem, resulting in compromised therapeutic benefit and increased healthcare costs [30-33]. The 72.5% persistence rate in this real-world cohort is associated with the enhanced patient engagement afforded by our anabolic osteoporosis clinic. Patients have multiple opportunities to address the therapeutic rationale for initiating anabolic therapy, potential adverse effects and ways to mitigate them, and medication cost and administration concerns. In addition to the hour-long counseling session at therapy commencement, each patient received a follow-up phone call after one week of therapy, appointments for follow-up visits for DXA testing and with their prescriber were made, the rationale for the need of follow-on antiresorptive therapy was emphasized, and patients were instructed to contact the clinic in the event of subsequent questions or concerns.

To date, this is the first real-world analysis of abaloparatide use in a pharmacist-run anabolic osteoporosis clinic. This study, however, is not without limitations. While all but two patients had baseline DXA information available, most of the DXA's were completed at the institution of the referring provider. Consequently, comparative DXA data performed at the same site, on the same machine, by the same technician were available for 17 patients following abaloparatide therapy, and only 6 patients for comparison after a year of antiresorptive therapy after abaloparatide. In addition, several patients had baseline DXA scans at outside facilities that did not test all sites (e.g., wrist) or report both T-scores and bone

mineral density results. Bone turnover markers were not available for most patients. Fracture data were determined based on documentation available in the patient chart. Heights were not evaluated at baseline or at the end of therapy to determine if asymptomatic vertebral compression fractures occurred while on therapy. The effects of diet, calcium and vitamin D supplementation, weight bearing exercise, smoking cessation and medication compliance, for example, were not controlled for. Finally, the study population may not have external validity as 98% of our population were female and 99% were white.

CONCLUSION

The use of abaloparatide in a pharmacist-run clinic resulted in significant increases in BMD at the total hip and spine and was effective in preventing fractures in patients with osteoporosis. While significant barriers to anabolic osteoporosis treatment remain, involvement of a pharmacist-led clinic may increase medication persistence.

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CONFLICT OF INTEREST STATEMENT

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