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Baseline characteristics of postmenopausal women with osteoporosis treated with teriparatide in a real-world setting in Latin America: a subregional analysis from the Asia and Latin America Fracture Observational Study (ALAFOS)

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Abstract

Background: Osteoporosis is a major healthcare concern in Latin America. Factors such as changing demographics, fragmented healthcare systems, and financial considerations may result in a huge increase in the burden of osteoporosis in this region. The aim of this article is to describe the baseline clinical characteristics and fracture history of patients who are prescribed teriparatide in normal clinical practice in Latin America.

Methods: We conducted a prospective, multinational, observational study (the Asia and Latin America Fracture Observational Study [ALAFOS]) in 20 countries worldwide to assess the incidence of fractures in postmenopausal women with osteoporosis receiving teriparatide as a part of routine clinical practice in a real-world setting. In this subregional analysis of the ALAFOS study, we report the clinical characteristics, fracture history, risk factors for osteoporosis, comorbidities, previous osteoporosis therapies and health-related quality of life measures at baseline for patients from the four participant Latin American countries: Argentina, Brazil, Colombia, and Mexico.

Results: The Latin America subregional cohort included 546 postmenopausal women (mean [SD] age: 71.0 [10.1] years; range: 40–94 years), constituting 18% of the ALAFOS total population. The baseline mean (SD) bone mineral density T-scores were – 3.02 (1.23) at the lumbar spine and – 2.31 (0.96) at the femoral neck; 62.8% of patients had a history of low trauma fracture after the age of 40 years and 39.7% of patients had experienced ≥ 1 fall in the past year. Osteoporosis medications were used by 70.9% of patients before initiating teriparatide. The median (Q1, Q3) EQ-5D-5 L Visual Analog Scale (VAS) scores for perceived health status at baseline was 70 (50, 80). The mean (SD) worst back pain numeric rating scale score for the overall Latin American cohort was 4.3 (3.4) at baseline.

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Conclusions: This baseline analysis of the Latin America subregion of the ALAFOS study indicates that patients who are prescribed teriparatide in the four participant countries had severe osteoporosis and high prevalence of fractures. They also had back pain and poor health-related quality of life. The proportions of patients with severe or extreme problems on the EQ-5D-5 L individual domains were lower than those in the overall ALAFOS study population.

Keywords: Osteoporosis, Teriparatide, Latin America, Observational study, ALAFOS

Background

Osteoporosis is a systemic bone disease characterized by loss of bone mass and deterioration of bone microarchitecture and bone quality, leading to an increased risk of fragility fractures [1]. Since there are no obvious symptoms of osteoporosis, this condition is often diagnosed after the occurrence of a fragility fracture [2]. Osteoporotic fractures can lead to pain, loss of functionality, limitation of daily activities, and extensive morbidity [1]. Osteoporotic hip and vertebral fractures have a significant adverse impact on the quality of life [3]. There is also increasing awareness about the importance of osteoporotic fractures at sites other than the hip and spine, which also contribute substantially to disability and impaired quality of life [4]. Consequently, osteoporotic fractures highly burden the healthcare system in terms of increased hospitalizations, surgeries, and prolonged home care and rehabilitation requirements [1]. For example, a large study conducted in the United States over a 12-year period (2000–2011) in postmenopausal women ≥ 55 years of age found that the hospitalization costs for osteoporotic fractures were greater than those for other serious conditions such as stroke, myocardial infarction, and breast cancer [5]. The direct and indirect annual costs of hip fracture were estimated to be USD 34.8 billion worldwide in the year 1990; worldwide costs of osteoporosis are expected to reach approximately USD 132 billion by the year 2050 [1, 3].

In the Latin America (LA) region, osteoporosis and osteoporotic fractures continue to be a major healthcare concern [1]. The Latin American Vertebral Osteoporosis Study (LAVOS) conducted in five countries across LA in women ≥ 50 years old found that the standardized prevalence of radiographic vertebral fractures was 11.18 (95% confidence interval [CI] 9.23–13.4) [6]. Another population-based study found that LA accounted for $\sim 7\%$ of all hip fractures in the world in the year 1990, and this percentage is predicted to increase to 12.5% by the year 2050 [7]. This increase may be attributable to demographic changes such as increasing life expectancy accompanied by a corresponding increase in the elderly population in LA; the proportion of people over 50 years of age in LA is expected to increase from $\sim 13\text{--}20\%$ of the population in 2018 to $\sim 28\text{--}40\%$ in 2050 [1]. A recent consensus position

paper reports that the increase in the elderly population in LA, along with other factors such as fragmented healthcare systems, limited resources, and financial considerations, may lead to an enormous increase in the burden of osteoporosis in this region [1].

Teriparatide is a bone-forming drug approved worldwide for the treatment of men and postmenopausal women at a high risk for fracture [8, 9]. The Asia and Latin America Fracture Observational Study (ALAFOS) is a large, multinational, prospective, observational study being conducted in 20 countries across the world to evaluate the incidence of fractures in postmenopausal women with osteoporosis receiving teriparatide as a part of normal clinical practice and to assess factors related to treatment persistence and adherence [10]. This analysis focuses on the LA subregion of the ALAFOS study, which includes the following four countries: Argentina, Brazil, Colombia, and Mexico. We describe the baseline clinical characteristics and fracture history of patients who are prescribed teriparatide in routine clinical practice in LA. We believe that the results of the ALAFOS study will be useful to healthcare providers, payers, and health agencies to help them better understand the profile of patients who are prescribed teriparatide in the participant countries, how they compare with other countries around the globe, and provide real-world insights into factors influencing treatment persistence and response to treatment.

Methods

Study design and participants

The ALAFOS study population included teriparatide-naïve, postmenopausal women with osteoporosis at a high risk of fracture who were prescribed teriparatide (Forteo[®], 20 $\mu\text{g}/\text{day}$) as per the clinical judgment of their treating physician and local medical care practices. The manufacturer of Forteo[®], Eli Lilly and Company, did not provide teriparatide for this study. Patients were excluded from the study if they had any contraindications described in the teriparatide label. The treating physicians were responsible for all decisions regarding diagnosis and treatment of patients.

The detailed study design and the baseline patient characteristics of the overall ALAFOS study cohort have

been previously published [10]. The study consists of an active treatment phase where patients receive teriparatide up to 24 months and a post-treatment, follow-up phase up to 12 months. Routine patient visits are scheduled at baseline, and at approximately 3 months, 6 months, and every 6 months thereafter (Fig. 1). Data collection is planned at the time of these routine visits. Information collected at baseline includes demographic characteristics, risk factors for osteoporosis/fractures, concomitant illnesses/medications, use of specific back pain/osteoporosis medications, past history of fragility fractures after 40 years of age, and health-related quality of life (HRQoL) scores.

The first patient visit was in September 2015 and the planned last patient visit for the study will be approximately November 2019. The study is being conducted as per the principles of Good Clinical Practice and in compliance with applicable local laws and regulations. The study has been approved by the appropriate local bodies and all eligible participants need to sign a Consent to Release Information form.

Outcome measures

The primary effectiveness variable is the occurrence of new clinical fractures (a composite of clinical vertebral and nonvertebral fragility fractures) in postmenopausal women receiving teriparatide for up to 24 months, in relation to the duration of treatment with teriparatide. The effectiveness analysis population includes all patients for whom teriparatide therapy start and end dates are available.

Secondary endpoints include evaluation of HRQoL, back pain, physical function, and factors related to medication adherence. Details regarding the scoring systems used for evaluation of these measures have been previously published [10]. Data regarding protocol-defined adverse events will also be collected (including all fractures, fracture-related hospitalizations/surgeries, any fatal outcomes, and any adverse events that result in teriparatide treatment discontinuation).

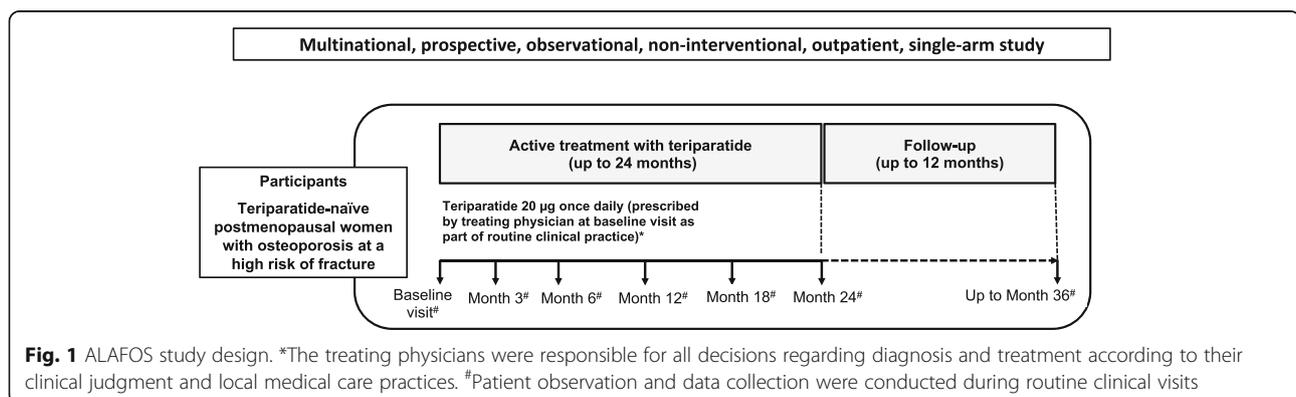
Statistical analyses

In this article, we present the baseline data for the LA subregion (a pre-specified subregion defined based on similar ethnic/racial origins, comparable health care systems, and guidelines for teriparatide use; $N=546$ patients), along with the baseline data for the four countries from this subregion (Colombia [$N=277$; 50.7%], Brazil [$N=130$; 23.8%], Mexico [$N=83$; 15.2%], and Argentina [$N=56$; 10.3%]). We have used descriptive statistics to analyze the study population over time (means and standard deviations [SDs] or medians and first and third quartiles [Q1, Q3] for continuous variables; counts and percentages for categorical variables). Data analysis was performed using SAS v9.4 or higher (SAS Institute Inc., Cary, NC, USA). No statistical comparisons were performed among the four countries and the overall LA subregional group.

Results

The final baseline analysis of the overall population enrolled in the ALAFOS study across 20 countries included 3031 patients [10]. The LA subregion included 556 patients, of which 10 patients were excluded due to some key missing demographic data at the datalock time point. Thus, the final baseline analysis for the LA subregion included 546 patients, constituting 18% of the ALAFOS total population.

The baseline demographic characteristics and reproductive history of patients included in the LA subregion and the four constituent countries are described in Table 1. At baseline, the mean (SD) age in the LA subregional cohort was 71.0 (10.1) years. The mean (SD) body mass index (BMI) was 25.2 (3.9) kg/m² and was consistent across all four participant countries (Table 1). The mean (SD) age at onset of menopause was 47.5 (5.6) years and early menopause was reported in 7.3% of patients. Surgical menopause was reported in 20.3% of patients in the LA subregional cohort with Mexico reporting the highest rate (42.2%; Table 1).



for Mexico, and 53.6% for Argentina; Fig. 2). A previous history of vertebral fractures was reported by 30.4% of patients, while non-vertebral fractures were reported by 32.2% of patients (Table 1).

Risk factors for osteoporosis and fractures

Some of the common risk factors for osteoporosis and fractures are summarized in Table 2. Approximately 30% of patients in the overall LA cohort had a maternal history of osteoporosis or hip fracture; this number was higher for Brazil and Mexico (40.2 and 39.7%, respectively). Around 50% of patients had problems with vision, and 39.7% of patients reported having experienced ≥ 1 fall in the past year. In the overall LA cohort, 57.2% of

patients reported using the support of arms while standing up from a chair (Table 2).

Current comorbidities and concomitant medications

Table 2 also summarizes the most commonly reported comorbidities and concomitant medications. Hypertension was the most common comorbidity in the overall LA subregion (46.2%) as well as in Colombia (44.8%), Brazil (51.2%), Mexico (44.6%) and Argentina (44.6%). Rheumatoid arthritis or other rheumatologic conditions were reported by 22.8% of patients and type 2 diabetes mellitus was reported by 8.3% of patients. Glucocorticoids were used by 6.2% of patients in the overall LA cohort (prednisone daily equivalent dose ≥ 7.5 mg for ≥ 3

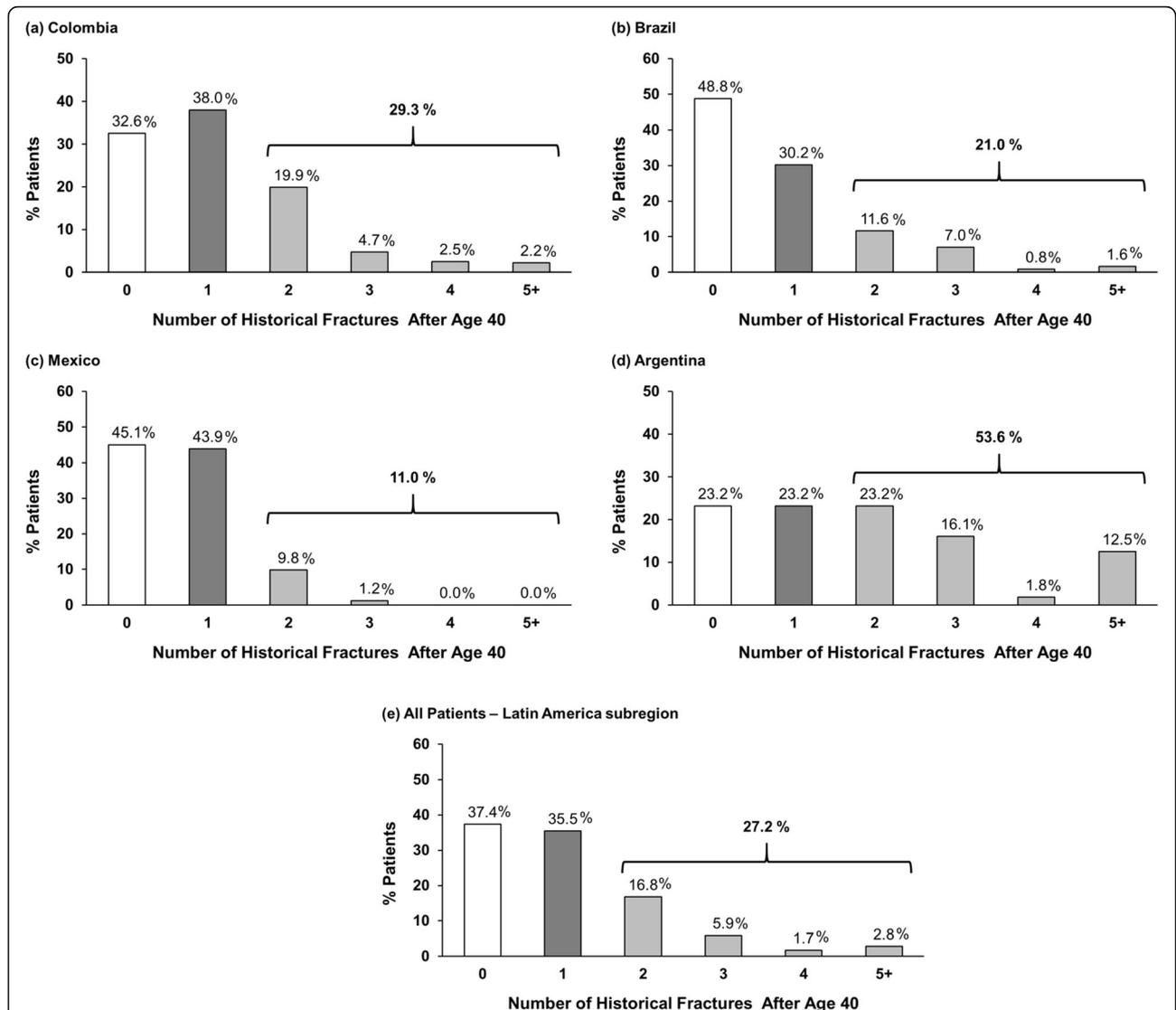


Fig. 2 Percent of patients with osteoporotic fractures after 40 years of age. **a** Colombia (N = 277); **b** Brazil (N = 130); **c** Mexico (N = 83); **d** Argentina (N = 56); **e** All Patients - Latin America subregion (N = 546). Note: Percentages are calculated using n, the number of valid (not missing or unknown) responses for each item

Table 2 Risk factors for osteoporosis and fractures, current comorbidities, and concomitant medications

| Characteristic | Colombia (N = 277) | Brazil (N = 130) | Mexico (N = 83) | Argentina (N = 56) | All Patients Latin America Subregion (N = 546) |
|--|-----------------------|---------------------|--------------------|-----------------------|--|
| Maternal history of osteoporosis or hip fracture, n (%) | 57 (23.4%) | 37 (40.2%) | 23 (39.7%) | 14 (30.4%) | 131 (29.8%) |
| Sight problems, n (%) | 133 (50.6%) | 84 (68.9%) | 22 (26.5%) | 24 (42.9%) | 263 (50.2%) |
| Patients experiencing falls in the past year, n (%) | 103 (38.6%) | 39 (31.5%) | 44 (62.9%) | 18 (34.0%) | 204 (39.7%) |
| Number of falls in the past year, n (%) | | | | | |
| No falls | 164 (61.4%) | 85 (68.5%) | 26 (37.1%) | 35 (66.0%) | 310 (60.3%) |
| 1 fall | 62 (23.2%) | 24 (19.4%) | 14 (20.0%) | 10 (18.9%) | 110 (21.4%) |
| 2 falls | 21 (7.9%) | 7 (5.6%) | 9 (12.9%) | 3 (5.7%) | 40 (7.8%) |
| 3 or more falls | 20 (7.5%) | 8 (6.5%) | 21 (30.0%) | 5 (9.4%) | 54 (10.5%) |
| Hours of exercise per week, mean (SD) | 2.6 (8.3) | 1.2 (1.8) | 2.1 (2.6) | 2.0 (2.4) | 2.1 (6.2) |
| Use of arms when standing up from a chair, n (%) | 159 (58.2%) | 74 (59.2%) | 57 (68.7%) | 17 (30.4%) | 307 (57.2%) |
| Immobilized for > 12 months, n (%) | 3 (1.1%) | 6 (4.8%) | 1 (1.2%) | 1 (1.8%) | 11 (2.1%) |
| Currently smoking, n (%) | 16 (5.9%) | 9 (7.0%) | 10 (12.0%) | 4 (7.1%) | 39 (7.2%) |
| Alcoholic drinks per week, mean (SD) | 0.2 (1.2) | 0.3 (1.1) | 0.2 (0.8) | 0.4 (1.9) | 0.2 (1.2) |
| Caffeinated drinks per week, mean (SD) | 8.1 (9.6) | 11.0 (13.6) | 7.2 (6.0) | 3.4 (5.0) | 8.2 (10.2) |
| Patients with current comorbidities ^a , n (%) | | | | | |
| Hypertension | 124 (44.8%) | 66 (51.2%) | 37 (44.6%) | 25 (44.6%) | 252 (46.2%) |
| Rheumatoid arthritis or other rheumatologic conditions | 81 (29.5%) | 17 (13.4%) | 19 (22.9%) | 6 (10.9%) | 123 (22.8%) |
| Type 2 diabetes mellitus | 18 (6.5%) | 18 (14.3%) | 8 (9.6%) | 1 (1.8%) | 45 (8.3%) |
| Concomitant medications ^b , n (%) | | | | | |
| Antihypertensives | 83 (30.0%) | 61 (46.9%) | 30 (36.1%) | 17 (30.4%) | 191 (35.0%) |
| Thyroid hormones | 63 (22.7%) | 18 (13.8%) | 18 (21.7%) | 17 (30.4%) | 116 (21.2%) |
| Antidepressants | 15 (5.4%) | 24 (18.5%) | 1 (1.2%) | 3 (5.4%) | 43 (7.9%) |
| Insulins/oral hypoglycemics | 20 (7.2%) | 14 (10.8%) | 5 (6.0%) | 1 (1.8%) | 40 (7.3%) |
| Glucocorticoids ^c | 12 (7.5%) | 7 (8.0%) | 0 (0.0%) | 1 (2.9%) | 20 (6.2%) |

N = total number of patients available; n = number of patients with valid (non-missing or unknown) values; SD = standard deviation

^aThe three most frequently reported comorbidities in the overall ALAFOS study cohort [10] are listed here

^bConcomitant medications related to risk of osteoporosis and falls taken by > 5% of all patients in the overall Latin American subregional cohort at baseline. Other medications included oral anticoagulants/heparin (1.3% of all patients), benzodiazepines (3.8%), antiarrhythmics (4.8%), and anticonvulsants (3.3%)

^cDuration of therapy ≥3 months or a prednisone daily equivalent dose ≥7.5 mg

Note: Percentages are calculated using n, the number of valid (not missing or unknown) responses for each item

months); the use of glucocorticoids was lower in Argentina (2.9%) and Mexico (0.0%; Table 2).

Osteoporosis and back pain therapies

A large proportion of patients in the overall LA cohort (70.9%) had used osteoporosis medications prior to initiating teriparatide (Table 3). Patients from Argentina reported the highest use of osteoporosis medications in the past (92.9%). The most commonly used class of antiresorptive osteoporosis medications was bisphosphonates (34.8% of patients in the overall LA cohort had taken at least one bisphosphonate); bisphosphonate use was higher in Mexico (55.4%) than in the other countries in LA (Colombia [26.4%], Brazil [37.7%], and Argentina [39.3%]). More patients in Argentina (69.6%) reported using calcium than other participant countries from the LA subregion (Brazil [50.0%], Colombia [43.0%], and Mexico

[41.0%]). A similar trend was noted for vitamin D use (Argentina [80.4%], Brazil [46.9%], Mexico [37.3%], and Colombia [29.6%]). About 31% of patients in the overall LA cohort reported using ≥1 medication for back pain in the past 24 h (Table 3); this figure was highest for patients from Argentina (46.4%) and lowest for Brazil (17.7%). The most commonly used medication for back pain in the overall LA cohort was paracetamol (16.3%) followed by nonsteroidal anti-inflammatory drugs (9.2%; Table 3).

Health-related quality of life and back pain

The baseline HRQoL scores for the overall LA subregion and the four participant countries are shown in Table 4. The median (Q1, Q3) EQ-5D-5 L Visual Analog Scale (VAS) score for perceived health status was 70 (50, 80) in the overall LA cohort; this was generally consistent across the four participant countries (Table 4). The median (Q1,

Table 3 Previous use of osteoporosis and analgesic medications

| Characteristic | Colombia (N = 277) | Brazil (N = 130) | Mexico (N = 83) | Argentina (N = 56) | All Patients Latin America Subregion (N = 546) |
|--|-----------------------|---------------------|--------------------|-----------------------|--|
| Past use of osteoporosis medication ^a , n (%) | 181 (65.3%) | 96 (73.8%) | 58 (69.9%) | 52 (92.9%) | 387 (70.9%) |
| Number of previous osteoporosis medications, n (%) | | | | | |
| 0 | 96 (34.7%) | 34 (26.2%) | 25 (30.1%) | 4 (7.1%) | 159 (29.1%) |
| 1 | 95 (34.3%) | 29 (22.3%) | 12 (14.5%) | 10 (17.9%) | 146 (26.7%) |
| 2 | 60 (21.7%) | 39 (30.0%) | 14 (16.9%) | 23 (41.1%) | 136 (24.9%) |
| 3 | 20 (7.2%) | 24 (18.5%) | 11 (13.3%) | 17 (30.4%) | 72 (13.2%) |
| 4 | 5 (1.8%) | 4 (3.1%) | 17 (20.5%) | 1 (1.8%) | 27 (4.9%) |
| 5 or more | 1 (0.4%) | 0 (0.0%) | 4 (4.8%) | 1 (1.8%) | 6 (1.1%) |
| Previous pharmacotherapy for osteoporosis ^b , n (%) | | | | | |
| <i>Alendronate</i> | 31 (11.2%) | 37 (28.5%) | 20 (24.1%) | 6 (10.7%) | 94 (17.2%) |
| <i>Ibandronate</i> | 23 (8.3%) | 3 (2.3%) | 9 (10.8%) | 11 (19.6%) | 46 (8.4%) |
| <i>Risedronate</i> | 4 (1.4%) | 10 (7.7%) | 4 (4.8%) | 6 (10.7%) | 24 (4.4%) |
| <i>Zoledronate</i> | 21 (7.6%) | 6 (4.6%) | 23 (27.7%) | 1 (1.8%) | 51 (9.3%) |
| <i>Other bisphosphonates</i> | 1 (0.4%) | 1 (0.8%) | 1 (1.2%) | 2 (3.6%) | 5 (0.9%) |
| <i>Any one or more bisphosphonates</i> | 73 (26.4%) | 49 (37.7%) | 46 (55.4%) | 22 (39.3%) | 190 (34.8%) |
| <i>Calcitonin</i> | 3 (1.1%) | 3 (2.3%) | 1 (1.2%) | 0 (0.0%) | 7 (1.3%) |
| <i>Calcium only</i> | 119 (43.0%) | 65 (50.0%) | 34 (41.0%) | 39 (69.6%) | 257 (47.1%) |
| <i>Denosumab</i> | 13 (4.7%) | 0 (0.0%) | 8 (9.6%) | 5 (8.9%) | 26 (4.8%) |
| <i>Raloxifene</i> | 0 (0.0%) | 1 (0.8%) | 3 (3.6%) | 0 (0.0%) | 4 (0.7%) |
| <i>Strontium ranelate</i> | 2 (0.7%) | 4 (3.1%) | 1 (1.2%) | 2 (3.6%) | 9 (1.6%) |
| <i>Vitamin D only</i> | 82 (29.6%) | 61 (46.9%) | 31 (37.3%) | 45 (80.4%) | 219 (40.1%) |
| Use of ≥1 back pain medication over the past 24 h, n (%) | 94 (33.9%) | 23 (17.7%) | 24 (28.9%) | 26 (46.4%) | 167 (30.6%) |
| Specific back pain medications, n (%) | | | | | |
| <i>NSAIDs</i> | 11 (4.0%) | 6 (4.6%) | 19 (22.9%) | 14 (25.0%) | 50 (9.2%) |
| <i>Paracetamol</i> | 66 (23.8%) | 5 (3.8%) | 10 (12.0%) | 8 (14.3%) | 89 (16.3%) |
| <i>Opioids</i> | 22 (7.9%) | 2 (1.5%) | 0 (0.0%) | 4 (7.1%) | 28 (5.1%) |
| <i>Paracetamol and opioid combination</i> | 2 (0.7%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (0.4%) |

N = total number of patients available; n = number of patients with valid (non-missing or unknown) values; NSAIDs = nonsteroidal anti-inflammatory drugs

^aThis includes ongoing medications as well as those stopped before baseline

^bPrior osteoporosis medications taken by > 0.5% of all patients in the overall Latin American subregional cohort

Note: Percentages are calculated using n, the number of valid (not missing or unknown) responses for each item

Q3) EQ-5D-5L utility total score was 0.65 (0.53, 0.77) for the overall LA cohort. A substantial number of patients reported experiencing severe/extreme problems on the individual domain scores of the EQ-5D-5L questionnaire (mobility, self-care, usual activities, pain/discomfort and anxiety/depression; Table 4). The mean (SD) back pain numeric rating scale scores for the overall LA cohort were 4.3 (3.4) for worst pain in the last 24 h and 3.7 (3.1) for average pain in the last 24 h (Table 4).

Discussion

The ALAFOS is a large observational study evaluating teriparatide use in postmenopausal women with osteoporosis during routine clinical practice in 20 countries across the world [10]. The LA subregional analysis of the ALAFOS

study is the first analysis evaluating teriparatide in a community setting in the Latin American population.

A recent consensus paper discussing treatment and prevention of osteoporosis in LA [1] states that osteoporosis treatment should be initiated in patients with low BMD (T-score ≤ -2.5 at the lumbar spine, total hip, or femoral neck), or a history of fragility fracture, or in osteopenic patients with a FRAX[®] score above the designated interventional level [1, 11, 12]. Country-specific validated FRAX[®] tools are available for several Latin American countries [1, 2, 11]. Currently, several antiresorptive therapies such as bisphosphonates, denosumab, selective estrogen receptor modulators, and hormone replacement therapy are available for the treatment of osteoporosis in LA. However, teriparatide is the only bone-forming therapy that is currently available

Table 4 Health-related quality of life scores at baseline

| Characteristic | Colombia (N = 277) | Brazil (N = 130) | Mexico (N = 83) | Argentina (N = 56) | All Patients Latin America Subregion (N = 546) |
|--|-----------------------|---------------------|--------------------|-----------------------|--|
| EQ-5D-5 L-VAS score ^a | | | | | |
| Median (Q1, Q3) | 70.0 (50.0, 80.0) | 65.0 (50.0, 80.0) | 60.0 (45.0, 75.0) | 70.0 (60.0, 80.0) | 70.0 (50.0, 80.0) |
| Mean (SD) | 67.0 (20.5) | 62.6 (22.2) | 59.2 (21.4) | 70.5 (16.7) | 65.2 (20.9) |
| EQ-5D-5 L severe/extreme problems ^b , n (%) | | | | | |
| Mobility | 24 (8.7%) | 13 (10.0%) | 3 (3.6%) | 3 (5.4%) | 43 (7.9%) |
| Self-care | 17 (6.2%) | 4 (3.1%) | 3 (3.6%) | 0 (0.0%) | 24 (4.4%) |
| Usual activities | 35 (12.7%) | 10 (7.7%) | 4 (4.8%) | 3 (5.4%) | 52 (9.5%) |
| Pain/discomfort | 47 (17.1%) | 22 (16.9%) | 13 (15.7%) | 6 (10.7%) | 88 (16.2%) |
| Anxiety/depression | 34 (12.3%) | 15 (11.5%) | 3 (3.6%) | 2 (3.6%) | 54 (9.9%) |
| EQ-5D-5 L – Utility Total Score, median (Q1, Q3) | 0.65 (0.50, 0.78) | 0.64 (0.52, 0.74) | 0.65 (0.60, 0.77) | 0.71 (0.59, 0.80) | 0.65 (0.53, 0.77) |
| Back Pain Numeric Rating Scale ^c | | | | | |
| Worst pain in the last 24 h | | | | | |
| Median (Q1, Q3) | 3.0 (0.0, 7.0) | 5.0 (3.0, 8.0) | 7.0 (3.0, 8.0) | 5.0 (0.0, 7.0) | 5.0 (0.0, 8.0) |
| Mean (SD) | 3.6 (3.4) | 5.1 (3.3) | 5.5 (3.3) | 4.2 (3.4) | 4.3 (3.4) |
| Average pain in the last 24 h | | | | | |
| Median (Q1, Q3) | 3.0 (0.0, 6.0) | 5.0 (2.0, 7.0) | 3.0 (2.0, 5.0) | 3.0 (0.0, 7.0) | 4.0 (0.0, 6.0) |
| Mean (SD) | 3.4 (3.3) | 4.7 (3.0) | 3.4 (2.5) | 3.6 (3.0) | 3.7 (3.1) |

N = total number of patients; n = number of patients with valid (non-missing or unknown) values; Q1 = first quartile; Q3 = third quartile; VAS=Visual Analog Scale
^aA 100-mm visual analog scale was used to indicate perceived overall health status (0 = the worst health you can imagine; 100 = the best health you can imagine)

^bFor the “mobility,” “self-care,” and “usual activities” domains, extreme problems refers to inability to move, inability to take care of self and inability to perform usual activities, respectively

^cBack pain was self-assessed by patients on a rating scale of 0 to 10 (0 = no back pain; 10 = worst possible back pain)

Note: Percentages are calculated using n, the number of valid (not missing or unknown) responses for each item

[1]. The Iberoamerican Consensus on Osteoporosis recommends that teriparatide can be used in postmenopausal women ≥ 65 years with confirmed osteoporosis and prevalent vertebral fracture [13]. Several country-specific guidelines for diagnosis and treatment of osteoporosis are available and the recommendations regarding teriparatide use are generally similar [1]. The 2017 Colombian Consensus on Osteoporosis recommends teriparatide in patients with vertebral fragility fractures (1 severe or ≥ 2 with any grade of severity), or in patients with lumbar spine T-score ≤ -3.5 [14]. The Argentine Guidelines for Osteoporosis recommend teriparatide as first-line therapy in men or women with a high risk for osteoporotic fractures (including those with a history of clinical or radiological, vertebral fractures), in patients with other fragility fractures associated with low BMD values, or in patients with very low BMD (T-score < -3) without history of fractures [15]. Teriparatide is also recommended in patients who have had a suboptimal response to antiresorptive therapy [15]. The Brazilian Society of Rheumatology and the Brazilian Medical Association recommend that teriparatide can be used for the treatment of osteoporosis in postmenopausal women at high risk of fractures, those with previous fractures, or those who did not have adequate response to other forms of osteoporosis treatment [16]. It is also

important to note that access to teriparatide may vary across countries. For example, although guidelines recommend teriparatide in Brazil [16], it has not been included in the National Clinical Protocol and Osteoporosis Therapeutic Guidelines published by the Ministry of Health to be reimbursed by the Brazilian government program. The use of teriparatide in Brazil in the general population occurs from states where local policy reimburses teriparatide after careful revision, private medical insurance that covers teriparatide treatment and in patients who demand justice for access to the treatment [17]. In Mexico, teriparatide is not included in the guidelines for the National Healthcare System [18]. In this case, use of teriparatide in the general population may be restricted to those who have private insurance policies, which cover teriparatide treatment. This LA subregional analysis of the ALAFOS study provides useful insights into the patient population that is currently being prescribed teriparatide in the four participant countries in a real-world setting.

In this subregional analysis of the ALAFOS baseline data, we found that patients who are prescribed teriparatide in LA are usually elderly women (average age: 71 years) with severe osteoporosis who are at a high risk of fracture. This is in line with the approved labels for

teriparatide in major geographies such as Europe and the United States, which state that teriparatide is indicated for the treatment of osteoporosis in postmenopausal women at an increased risk for fracture [8, 9]. The patients who were prescribed teriparatide in our LA cohort typically had a high BMI with low BMD values, especially at the lumbar spine. Many patients (~ 30%) had a maternal history of osteoporosis/hip fracture and > 60% of patients had experienced a fragility fracture themselves after the age of 40 years. In general, these findings are similar to those observed in the overall ALAFOS study population [10], as well as other observational studies conducted in Europe and the United States [19–23].

Across the LA subregion, there was wide variation among the participant countries with respect to the fracture history at baseline. The proportion of patients who had experienced at least one fragility fracture after 40 years of age at baseline ranged from 51.5% in Brazil to 76.8% in Argentina. The percentage of patients with two or more fragility fractures after 40 years of age ranged from 11.0% in Mexico to 53.6% in Argentina. With respect to the previous fracture sites, vertebral fractures were more common than non-vertebral fractures in Argentina (vertebral fractures: 62.5% of patients; non-vertebral fractures: 35.7%), while the opposite was observed in Mexico (vertebral fractures: 8.4% of patients; non-vertebral fractures: 45.8%). However, it is important to note that patients were not uniformly distributed across countries. Moreover, these differences in the previous fracture status may reflect a patient selection bias based on the medical specialties of the participant sites.

The Brazilian Osteoporosis Study (BRAZOS) identified advanced age, early menopause, sedentary lifestyle, family history of hip fracture, and recurrent falls as important risk factors for osteoporosis [24]. Many patients in this ALAFOS LA subregional analysis presented a high prevalence of these risk factors at baseline such as early menopause (7.3%), surgical menopause (20.3%), immobilization for > 12 months (2.1%), maternal history of osteoporosis/hip fracture (29.8%), and falls in the past year (39.7%).

Back pain was frequent among patients in the LA subregion at baseline, and around 30% of patients were taking ≥ 1 medication for relief of back pain before enrollment. This observation was similar to the overall ALAFOS study cohort [10]. Previous observational studies have also reported severe and disabling back pain at baseline in patients with osteoporosis who were treated with teriparatide in Europe [20, 22]. The LA subregional analysis of the ALAFOS found that use of back pain medications was highest in Argentina, probably reflecting the higher prevalence of previous fractures in the patients enrolled from this country. The use of osteoporosis medications, calcium, and vitamin D at baseline was also highest

in Argentina, while bisphosphonate use at baseline was highest in Mexico.

A recent study conducted by Cano-Gutiérrez, et al. using data from the SABE Bogotá Study, found a correlation between the presence of osteoporosis and impairment in functionality in 2000 people aged 60 years or older [25]. Many patients in the overall LA subregion as well as in all participant countries reported a low HRQoL at baseline as indicated by the low EQ-5D-5L VAS and utility total scores. Several patients in the LA subregional cohort reported experiencing severe to extreme problems with respect to mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. However, the proportions of patients reporting severe/extreme problems in the LA subregion were lower than those in the overall ALAFOS study cohort [10]. Similarly, within the LA subregion, more patients from Colombia and Brazil reported severe/extreme problems compared to patients from Argentina. These findings provide a baseline evaluation of the HRQoL and back pain parameters in patients with osteoporosis. The ALAFOS study will further evaluate HRQoL over time on teriparatide treatment. We believe this information is important since to our knowledge, there are no other studies reporting HRQoL in patients with osteoporosis in Latin America.

Osteoporosis continues to pose a major healthcare concern worldwide as well as in LA. The LAVOS study, a population-based study of vertebral fractures in LA, found that the prevalence (95% CI) of radiographic vertebral fractures in women between 50 and 79 years of age was 13.80 (10.03–17.56) in Argentina, 10.79 (7.34–14.23) in Brazil, 10.72 (6.94–14.50) in Colombia, and 13.26 (9.46–17.07) in Mexico [6]. The 2012 Latin American regional audit reported that 2,609,858 and 1,423,559 Colombian women ≥ 50 years of age were living with osteopenia and osteoporosis, respectively; by the year 2050, these numbers could increase to 3,852,200 and 2,101,000 for osteopenia and osteoporosis, respectively [26]. A survey conducted by the Mexican Institute of Social Security predicted that the number of hip fractures per year in Mexico is likely to increase from 29,732 in the year 2005 to 155,874 in 2050; this increase is possibly related to demographic changes, even if there is no increase in the age- and sex-specific incidence of hip fractures [27]. As a result of changing demographics, increasing elderly population, and changing lifestyles and disease patterns, the burden of osteoporosis in the LA region is expected to increase further over the years along with a corresponding increase in the associated costs [1, 28].

While discussing the epidemiology and patterns of treatment of osteoporosis in the LA region, it is important to note that LA region constitutes a very diverse mix of ethnicities including native Indians, Caucasians from

Europe, Africans as well as Asians [28]. There is wide variation between and within countries in socioeconomic conditions of the population and availability of good public healthcare systems. There are also differences with respect to access to private insurance systems, which are usually expensive. All these factors ultimately affect the availability of good quality healthcare in this region [1]. Observational studies have been valuable tools to gather information about real-world effectiveness of medicines, region/country-specific factors affecting the usage of medicines, local treatment practices, and patient perceptions. We believe that this subregional analysis of the ALAFOS study will provide physicians, payers, healthcare providers and governmental health agencies useful data about real-world use of teriparatide in LA including information about the profiles of patients who are prescribed teriparatide, their baseline risk factors, HRQoL measures, and the effectiveness of teriparatide over the course of treatment in the real world.

Strengths and limitations

The strength of this study is that it is the first observational, naturalistic study providing real-world data reflecting actual use of teriparatide in LA, but there are several limitations to this analysis. The ALAFOS is a single-arm, observational study. The sample size in each individual country is relatively small. Patients are not uniformly distributed across countries, and they may not truly represent the general population of that country. The study uses patient-reported data for information such as history of fractures/falls, comorbid conditions and concomitant medications, and thus there could be chances of recall bias. In case of the HRQoL outcomes, there could also be a possibility of perception bias.

Conclusions

This LA subregional analysis of the ALAFOS study is the first observational study evaluating use of teriparatide in a community setting in LA. This study will provide useful real-world insights into the similarities and differences in the patterns of prescription of teriparatide across four countries in LA. This is especially important in light of the increasing prevalence and burden of osteoporosis in this region. Our baseline analysis revealed that patients who are currently being prescribed teriparatide in LA are elderly women with osteoporosis at a high risk of fracture who are suffering from back pain and poor HRQoL. The proportions of patients reporting severe/extreme problems on the EQ-5D-5 L individual domains in this subregional analysis were lower than those observed in the overall ALAFOS study population. Subsequent results from the ALAFOS study would provide further insights on real-world effectiveness of teriparatide. This information would help

healthcare providers, physicians, health policy makers, and payers in the effective management of osteoporosis.

Abbreviations

ALAFOS: Asia and Latin America Fracture Observational Study; BMD: bone mineral density; BMI: body mass index; BRAZOS: Brazilian Osteoporosis Study; CI: confidence interval; HRQoL: health-related quality of life; LA: Latin America; LAVOS: Latin American Vertebral Osteoporosis Study; Q1: first quartile; Q3: third quartile; rhPTH(1–34): recombinant human parathyroid hormone analog; SD: standard deviation; VAS: Visual Analog Scale

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Authors' contributions

JLC, GMM, NC, AM, JFM, MLG and LGO were involved in recruitment of patients who participated in the study. All authors were involved in analysis and interpretation of the data, reviewing and revising the paper critically for intellectual content. All authors have approved the version to be published and agree to be accountable for all aspects of the work.

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Availability of data and materials

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

We declare that this study has been performed in accordance with Declaration of Helsinki and was approved by the appropriate local body. All participants have signed the informed consent form.

Consent for publication

Not applicable.

Competing interests

JLC-B reports having received lecture fees from Eli Lilly. GMM is an investigator of the ALAFOS study at Eli Lilly and Company. NC is an investigator of the ALAFOS study at Eli Lilly and Company. She is also a speaker for Eli Lilly and Company; she has participated as a principal investigator in phase III clinical studies and has served on the advisory board for Eli Lilly and Company. She has received fees for research from Lilly. She has also participated in clinical studies as principal investigator and speaker for Merck Sharp & Dohme, Novartis of Colombia, Pfizer, Amgen, and Biopas. She has no employment relationship with any of these organizations. AM is a speaker for Lilly, Amgen and FARMA de Colombia. JFM is a speaker for Lilly and has received fees for research from Lilly. MLG is an investigator of the ALAFOS study at Eli Lilly and Company. She is also a speaker for Eli Lilly and Company. LGO is an investigator of the ALAFOS study at Eli Lilly and Company; he is also a speaker for Eli Lilly and Company and an author on publications from Eli Lilly and Eurofarma; he also serves on the advisory board of UCB (Belgian Chemical Union) and the board of directors for Eurofarma. MSC, ACC, VI, and SF are employees of Eli Lilly and Company.

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