ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992

ORIGINAL PAPER
ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

ARCHIVES OF HELLENIC MEDICINE 2012, 29(4):454–460
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2012, 29(4):454–460

# The European Forsteo Observational Study (EFOS)

## 18-month follow-up of Greek women completing teriparatide treatment for osteoporosis

**K. Aloumanis,[1]**
**V. Drossinos,[1]**
**D. Trikka,[1]**
**D. Karras[2]**
**for the Hellenic EFOS study group**

*[1]Department of Medical Research, Pharmaserve-Lilly SACI, Kifissia*
*[2]Rheumatology Department, Veterans Administration Hospital, Athens, Greece*

OBJECTIVE **The European Forsteo Observational Study (EFOS) examined the long-term fractures, back pain (BP), health-related quality of life (HRQoL) and compliance with treatment in post-menopausal women with osteoporosis (OP) treated with teriparatide (TPTD) for the maximum approved period (18 months), with follow-up for a further 18 months. This paper describes the 18 month follow-up outcomes of Greek patients completing TPTD treatment.** METHOD **EFOS, a 3-year, multinational, observational study recorded the incidence of clinical vertebral and non-vertebral fractures, BP [using a 100 mm Visual Analogue Scale (VAS)], and HRQoL [using the EuroQol Standardized Questionnaire (EQ-5D)]. Changes from baseline in BP and EQ parameters were analyzed using a repeated measures model. Improvement over the baseline in frequency and severity of BP and limitations in activity due to BP were assessed using the sign test.** RESULTS **Of the 301 Greek women aged 69.5±8.5 years enrolled in the study, 83.7% reported previous OP treatment. A sustained decrease in BP and concurrent limitation of movement, a reduction of days in bed, improvement of mobility and increase in the scale on self-reported QoL were observed 18 months after completion of treatment with TPTD. These findings should be interpreted in the context of a non-controlled observational study.** CONCLUSIONS **An 18-month course of TPTD appears to have a beneficial effect on BP, mobility and QoL that is sustained up to 18 months after completion of treatment.**

Η ευρωπαϊκή μελέτη παρατήρησης για την τεριπαρατίδη (EFOS): Δεκαοκτάμηνη παρακολούθηση Ελληνίδων που ολοκλήρωσαν τη θεραπεία

*Περίληψη στο τέλος του άρθρου*

**Key words**

Back pain
Compliance
Osteoporosis
Quality of life
Teriparatide

*Submitted 14.11.2011*
*Accepted 25.11.2011*

Osteoporosis (OP) is a ubiquitous disease that currently affects an estimated 75 million people in Europe, the USA and Japan; one in 3 women over 50 years of age experiences fractures as a consequence of this disease. It produces major socioeconomic costs for health and hospital care; the annual combined medical costs of treating 2.3 million osteoporotic fractures in Europe and the US was $ 27 billion in 2002. OP has a profound impact on the quality of daily living and activities of individuals, due to back pain (BP), loss of height, deformity, immobility, increased numbers of bed days and even reduced pulmonary function.[1]

Teriparatide (TPTD) –recombinant human parathyroid hormone [rhPTH (1-34)]– is an established anti-osteoporotic anabolic agent that increases predominantly trabecular bone in the lumbar spine and femoral neck, with a resultant decrease in fractures.[2,3] Meta-analyses have provided evidence of favorable effects of TPTD on BP in comparison to placebo, hormone replacement therapy or alendronate.[4]

In Greece, TPTD has been approved for the treatment of established OP, but in everyday practice, for various reasons such as cost and administration route, it is considered to be a second line treatment, following failure of other anti-osteoporotic agents. The multiple benefits of its use, although documented in clinical trials,[3,5–7] have only been addressed in clinical practice in a routine care setting. In order to provide further evidence of the impact of TPTD on OP related health outcomes in real-time conditions, the European Forsteo Observational Study (EFOS) was

*The EFOS study was funded by Eli Lilly & Co.*

conducted in Greece and 7 other European countries for an overall 3-year period. Women were enrolled in the EFOS study who suffered from severe OP accompanied by serious limitations in mobility and daily activities and who experienced intense BP, anxiety, depression and diminished health related quality of life (HRQoL).[8–11] In the overall study population, changes in the incidence of clinical vertebral and non-vertebral fractures, BP and HRQoL were recorded and there was evidence of a decrease in fracture risk during treatment.[10] No further change in the fracture rate was reported after discontinuation of TPTD, but the improvement in BP observed during treatment was maintained for at least 18 months after discontinuation.[11] Results from the analysis of the Greek subpopulation during TPTD treatment have already been published.[12] This paper presents the results from the Greek subpopulation examined 18 months after completion of TPTD treatment.

## MATERIAL AND METHOD

EFOS, a 36-month, non-interventional, multi-national, prospective, observational study, included post-menopausal women initiating TPTD for treatment of osteoporosis in specific everyday care settings. Patients who were being treated with any investigational drug or procedure at study entry, or who presented one of the known contraindications for the use of TPTD, as listed in the Summary of Product Characteristics (SmPC) were excluded. Each patient signed an informed consent form prior to enrollment, to permit medical data collection, and could withdraw from the study at any time. The study was conducted according to good clinical practice (GCP) standards and ethical review board permission was given at all participating investigational sites. The study design, the demographic characteristics of the patients and the disease related data at baseline have been presented elsewhere.[8–12]

New clinical vertebral and non-vertebral fractures were diagnosed and verified by X-ray and or from the patients' history of orthopedic interventions. Suspected new or exacerbations of older fractures were ascertained by the clinical symptoms and findings, such as acute BP or lumbago, and confirmed with a new comparative X-ray.

A specific questionnaire for BP evaluation was completed at each visit, covering the frequency and severity of BP, limitation of activities, and days spent in bed due to BP in the previous month. The perceived severity of BP was estimated using a 100 mm Visual Analogue Scale (VAS), with 0 representing the absence of pain and 100 the worst possible pain.[13]

HRQoL was evaluated using the EuroQol (EQ-5D) questionnaire,[14] which consists of 5 parameters (mobility, self-care, daily activities, pain/discomfort and anxiety/depression), each of which has three possible levels (no problem – some problems – extreme problems). In addition, patients expressed their overall perception of their QoL using a VAS (ranging from 0: the worst possible QoL to 100: the best possible QoL).

During the follow-up period the patients visited the physician at 6 and 18 months after completion of TPTD treatment. Spontaneously reported adverse events were collected throughout the study.

Descriptive statistics, including frequencies, percentages, means, standard deviations (SD) and ranges, were used to describe the study population over time.

The number of fractures occurring in patients in the overall study population was summarized in 6-month intervals. The regression models used to analyze fracture rating for the total cohort have been described elsewhere.[9] In the Greek sub-population such analysis was not carried out due to the small sample and thus will not be presented here.

The BP and QoL results were analyzed over the treatment period. The number and percentage of patients with improvement, no change or worsening in each domain of the EQ-5D questionnaire was summarized at each visit and the sign test was used to determine whether significantly more patients showed improvement as opposed to worsening. BP changes from baseline as estimated by VAS were analyzed using a mixed model for repeated measures (MMRM), adjusting for multiple factors as has been already described.[9] As the EQ-5D health state valuation (HSV) had a continuous, non-parametric, bimodal distribution the Wilcoxon sign-rank test was used to assess changes from baseline in this parameter.

The number of patients reporting improvement or worsening in the severity and frequency of BP, limitation of activities and number of days in bed (≤2 days: no change) was analyzed using the sign test.

## RESULTS

A total of 1,648 patients were enrolled in the pan-European study including 301 post-menopausal women from Greece. For the Greek sample, the mean age was 69.5±8.5 years and their mean body mass index (BMI) was 26.3±4.0. Baseline characteristics of the total cohort including the Greek sub-population of the EFOS study have been already presented.[6,9] A history of fracture after 40 years of age was reported by 92.5% of the Greek patients, vertebral fractures being the most prevalent (89.7%), and approximately 40% percent of the women had experienced at least 2 fractures. Data from the 18-month follow-up period after completion of TPTD treatment was available for 350 Greek patients (83% of those initially enrolled). Questionnaires were also returned by some patients who prematurely stopped TPTD treatment (total maximum number of patients responding: 257) (tab. 3).

## Treatment following teriparatide

In the Greek cohort the number of patients complying with TPTD treatment was high. Off label use regarding TPTD therapy beyond 18 months was seen in a minority of patients (fig. 1). After completion of TPTD treatment, 86.4% of patients received alternative OP therapy; 68% received an anti-resorptive (AR), 54.8% a bisphosphonate, alendronate (26.4%), risedronate (20.4%), etidronate (0.4%) or other bisphosphonate (14.0%). Other post-TPTD medications included raloxifene and calcitonin taken by 8% and 8.8% of patients, respectively. The percentage of patients taking calcium and vitamin D supplementation ranged between 72% and 82% throughout the study (tab. 1). Based on supplementary data, 2 patients (0.7%) reported taking strontium ranelate and 2 patients PTH 1–84 use after discontinuation of TPTD, but the TPTD treatment duration was not available.

**Table 1.** Anti-osteoporotic medication used before and after completion of teriparatide (TPTD) treatment by post-menopausal women in Greece.

| Medication | Prior use [n (%)] (n=301) | Post-treatment [n (%)] (n=250) |
|---|---|---|
| Any OP medication | 251 (83.7%) | 216 (86.4%) |
| Any AR medication | 245 (81.7%) | 170 (68.0%) |
| Any BP medication | 114 (38.0%) | 137 (54.8%) |
| None reported | 49 (16.3%) | 34 (13.6%) |
| Alendronate | 72 (24.0%) | 66 (26.4%) |
| Risedronate | 45 (15.0%) | 51 (20.4%) |
| Etidronate | 9 (3.0%) | 1 (0.4%) |
| Other bisphosphonates | 2 (0.7%) | 35 (14.0%) |
| Raloxifene | 21 (7.0%) | 20 (8.0%) |
| Calcitonin | 195 (65.0%) | 22 (8.8%) |
| Calcium | 204 (68.0%) | 203 (81.2%) |
| Vitamin D | 161 (53.7%) | 200 (80.0%) |

OP: Osteoporosis; AR: Anti-resorptive; BP: Back pain

## Incidence of new osteoporotic fractures

The incidence of fractures is presented in table 2. There was a numerical decrease of total fractures per 10,000 patient-years, but no statistical significance was demonstrated due to small Greek sample size. Bone mineral density (BMD) was not systematically evaluated as part of the EFOS study, but in the Greek patients the BMD T-score in the lumbar spine and the femoral neck were collected and are also shown in table 2.

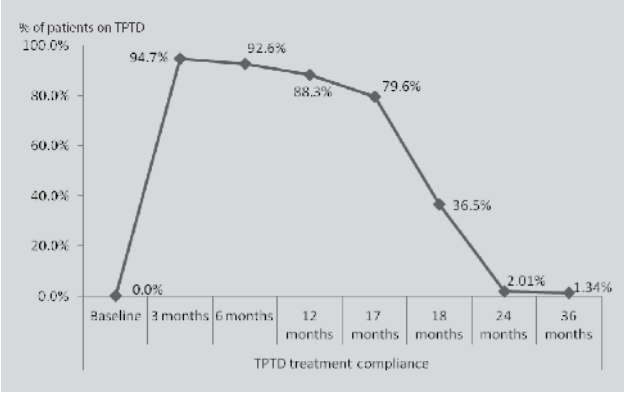


**Figure 1.** Compliance with teriparatide (TPTD) treatment among Greek post-menopausal women (n=301) (% of patients receiving TPTD at any given time).
Note: Approved duration of treatment at the time of the study was 18 months.

## Back pain and health-related quality of life

All self-reported parameters affecting QoL, which were estimated via the EQ-5D questionnaire and VAS, showed marked improvement from baseline to treatment completion. Throughout the 18-month follow-up period, after completion of TPTD treatment this improvement continued; specific observations included a sustained decrease in BP and concurrent movement limitations, reduction of reported days in bed, improvement of overall mobility, amelioration of depression and anxiety and increase in self-reported QoL. All the relevant values were numerically comparable to those shown at the end of TPTD treatment and the

**Table 2.** Fractures and bone density in Greek post-menopausal women followed for 36 months after initiation of teriparatide (TPTD) treatment (n=301).

| Observational period (months) | 0–<6 | 6–<12 | 12–<18 | 18–<24 | 24–<30 | 30–36 |
|---|---|---|---|---|---|---|
| Total fractures per 10,000 pt-yrs (Gr) | 402 | 342 | 346 | 352 | 147 | 78 |
| | | Baseline | | 18 months – end of TPTD treatment | | 36 months – end of study |
| Lumbar spine BMD T score (mean±SD) | | -3.45±0.72 (n=208) | | -2.57±0.77 (n=125) | | -2.25±0.80 (n=111) |
| Femoral neck BMD T score (mean±SD) | | -3.07±0.84 (n=47) | | -2.37±0.69 (n=12) | | -2.39±0.61 (n=15) |

Pts: Patients; BMD: Bone mineral density; SD: Standard deviation; Gr: Greece; pt-yrs: Patient-years

improvement over the baseline values was statistically significant (tab. 3). In addition, compared to the baseline, more patients reported engaging in some form of exercise at the end of treatment and remained active throughout the 18-month follow-up period (baseline: 26.9%, treatment completion: 40.4%, 18-month follow-up: 40.5%).

**Table 3.** Changes from baseline in back pain (BP) and self-reported quality of life (EQ-5D) in Greek post-menopausal women patients (n=301) followed for 36 months after teriparatide (TPTD) treatment initiation (18 months treatment and 18 months follow-up).

| Parameters | 18 months (treatment) | 36 months |
|---|---|---|
| BP improvement | 213/269 (79.2%[a])* | 198/257 (77.0%[a])* |
| Improvement of limitation due to BP | 195/269 (72.5%[a])* | 183/258 (70.9%[a])* |
| Reduction of days in bed due to BP | 0 (-5.0)[a,#] | 0 (-5.0)[a,#] |
| VAS–BP decrease | -38.6±1.7[a,§] | -42.0±1.7[a,§] |
| EQ-5D–pain/discomfort improvement | 176/271 (64.9%[a])* | 152/256 (59.4%[a])* |
| EQ-5D–mobility improvement | 130/271 (48.0%[a])* | 120/256 (46.9%[a])* |
| EQ-5D–self-care improvement | 108/271 (39.9%[a])* | 100/256 (39.1%[a])* |
| EQ-5D–usual activities improvement | 148/271 (54.6%[a])* | 124/256 (48.4%[a])* |
| EQ-5D–anxiety/depression improvement | 124/271 (45.8%[a])* | 109/256 (42.6%[a])* |
| EQ-5D–health state value increased | 0.309 (0.117, 0.801)[a,#] | 0.275 (0.036, 0.766)[a,#] |
| EQ-5D–dimension VAS | 22.7±1.5[a,§] | 24.9±1.5[a,§] |

VAS: Visual analogue scale;
*$N/N_{total}$, percentage; [#]Median (Q1, Q3); [§]LSmean±standard error; [a]p <0.001

## DISCUSSION

Post-menopausal OP is characterized by bone remodeling with an imbalance between excessive bone resorption and inadequate bone formation. Disability and BP complicating osteoporotic fractures can affect HRQoL.[15–18] The introduction of anabolic agents such as TPTD that stimulate bone formation has expanded the range of treatment options.[19] The reported evidence of fracture decrease[3] and favorable effects of TPTD on BP[4,20] needs to be established in the context of health care provision. Observational studies bridge that gap between research and clinical practice, offering supplementary information and answers to a wide variety of clinical questions emerging in every day clinical practice.

EFOS, a 36-month, multi-national, observational study, provides information on the effects of 18-month TPTD treatment on bone strength (expressed by fracture rates) and other health aspects affected by OP, including BP and movement limitation, for the period of treatment, but also for an extra period of 18 months after treatment completion.[9–11] The Greek post-menopausal women who were enrolled in this study had severe OP; 92.5% of them reported a history of fractures after 40 years of age. Bisphosphonates were the drugs most often prescribed, and their use, in terms of percentages, was higher after the TPTD treatment. This is in accordance with the recommendation of using an anti-resorptive therapy after TPTD to maintain BMD.[21] Calcitonin treatment has been effective in the management of acute pain associated with acute osteoporotic vertebral compression fractures, and is reported to shorten time to mobilization,[22,23] although its effectiveness in the relief of chronic pain is not clearly proven.[23] In the present study, even though the vast majority of the patients had received calcitonin treatment in the past, a greater improvement in self-estimated BP was observed during and after TPTD treatment. The use of calcitonin following TPDT treatment was notably lower (in absolute percentages) compared to before the study. Calcium plus vitamin D (CaD) supplementation has a modest but significant effect on slowing down the loss of femoral bone mass and reducing the risk of hip fractures in post-menopausal women through a mechanism that may be independent of bone density or geometric changes in the bone.[24,25] EFOS documented widespread use of CaD supplementation after TPTD treatment in the Greek sub-population, confirming high levels of adherence to anti-osteoporotic therapy. Physicians' prescription of PTH 1–84 after an uncompleted period of TPTD use (supplemental data – 2 patients), unique in Greece among the EFOS study centers,[12] may be attributed to factors affecting treatment decisions other than drug efficacy. Supplementary data have also shown that strontium use at the time of the study was less frequent in the Greek sub-population than in the overall European cohort (0.7% vs 5%),[12] perhaps due to its very recent launch in the local market.

The Greek data are not sufficiently large to produce statistical evidence of fracture decrease following TPTD treatment, although there is a clear trend towards reduction in fractures sustained throughout the follow-up period.

The statistically significant improvement shown by the various questionnaires in BP, movement limitations, days in bed, depression and anxiety levels, self-care ability and overall QoL, at the end of TPTD treatment, and reported elsewhere,[9] continued roughly unchanged throughout

the 18-month follow-up period after the completion of TPTD treatment. This observation confirms, in real life, the data of clinical trials regarding the effects of TPTD on OP induced disability/functional impairment, and shows that this effect remains constant long after treatment discontinuation.[4,8,26] Bisphosphonates, with the possible exception of iv bisphosphonates,[26,27] do not exhibit major analgesic effects, but alendronate therapy has been associated with reduction of the number of days in bed and of limited activity caused by BP in post-menopausal women with pre-existing vertebral fracture.[28] The further improvement in BP, however, recorded during and for as long as 18 months after TPTD treatment could not be attributed to these other forms of OP treatment, since these treatments were the most widely used even before TPTD.

The major factors that reduce adherence to treatment, leading to sub-optimal compliance with all forms of OP therapy, include concerns about drug-related side effects, the cost of medications, lack of understanding or motivation on the part of the patient, difficulty in treating an asymptomatic disease, inconvenience[29] and fear of injections.[30] Adherence to anti-OP treatment is quite high in clinical trials; in routine care, however, rates as low as 25% have been reported.[28,31] The Greek patients in the EFOS study showed high compliance with TPTD treatment in "real-time" conditions. As high adherence and persistence are needed to ensure an optimal therapeutic outcome in OP treatment, the long duration of favorable effects observed here may be attributed to high compliance. Other researchers have previously described similar levels of compliance with TPTD treatment (as high as 80%) after 12 months with TPTD compared to 49% and 39% for bisphophonates and raloxifene, respectively.[32] This may be partly explained by the sustained severe OP and fragility fractures that the majority of the patients taking TPTD have already suffered, which increases their perseverance.

In conclusion, Greek women with severe OP enrolled in the EFOS multi-national observational study for the use of TPTD provided evidence of a potentially beneficial effect of TPTD on BP, mobility and QoL, which appeared to be maintained for 18 months after treatment completion. Significantly reduced fracture risk sustained throughout the follow-up period was documented on analysis of the total EFOS cohort. All the findings should be interpreted in the context of a non-controlled observational study and taking into consideration the small number of patients in the Greek subgroup.

ACKNOWLEDGEMENTS

*The Hellenic EFOS study group: Alexiou P, Boukis M, Dimopoulos N, Dreatakis K, Farchat J, Giota A, Theodorakopoulos P, Kakavouli G, Karambatsas D, Karras D, Kaskani E, Kefallinou M, Kosmidis C, Lagoudakis A, Lasithiotakis I, Lazaridis G, Maidanoglou P, Makiev G, Maltas N, Mantzilas T, Matsouka A, Notaras I, Papakitsou E, Rambidis I, Repousis P, Saddik G, Sideridis A, Stamatiadou A, Trovas G, Xirogiannis G.*

## ΠΕΡΙΛΗΨΗ

**Η ευρωπαϊκή μελέτη παρατήρησης για την τεριπαρατίδη (EFOS): Δεκαοκτάμηνη παρακολούθηση Ελληνίδων που ολοκλήρωσαν τη θεραπεία**

Κ. ΑΛΟΥΜΑΝΗΣ,[1] Ε. ΔΡΟΣΙΝΟΣ,[1] Δ. ΤΡΙΚΚΑ,[1] Δ. ΚΑΡΡΑΣ[2] ΓΙΑ ΤΗΝ ΕΛΛΗΝΙΚΗ ΟΜΑΔΑ ΜΕΛΕΤΗΣ EFOS

*[1]Τμήμα Κλινικής Έρευνας, Pharmaserve-Lilly, Κηφισιά, [2]Ρευματολογική Κλινική, Νοσοκομείο «ΝΙΜΙΤΣ», Αθήνα*

*Αρχεία Ελληνικής Ιατρικής 2012, 29(4):454–460*

**ΣΚΟΠΟΣ** Η ευρωπαϊκή μελέτη παρατήρησης για την τεριπαρατίδη (European Forsteo Observational Study, EFOS) εξέτασε τα μακροπρόθεσμα αποτελέσματα σε κατάγματα, ραχιαλγία, συμμόρφωση στην αγωγή και σχετική με την υγεία ποιότητα ζωής σε μετεμμηνοπαυσιακές γυναίκες με οστεοπόρωση που έλαβαν τεριπαρατίδη για τη μέγιστη εγκεκριμένη περίοδο (περίοδος 18 μηνών, όταν εκπονήθηκε η μελέτη) και παρακολουθήθηκαν για επί πλέον 18 μήνες. Περιγράφονται τα αποτελέσματα της περιόδου παρακολούθησης των Ελληνίδων ασθενών που ολοκλήρωσαν τη θεραπεία με τεριπαρατίδη. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Στην τριετή, πολυεθνική μελέτη παρατήρησης EFOS καταγράφηκαν τα κλινικά κατάγματα (σπονδυλικά και μη σπονδυλικά), η ραχιαλγία [με χρήση οπτικής αναλογικής κλίμακας 100 mm (VAS)] και η σχετική με την υγεία ποιότητα ζωής (HRQoL) [με χρήση τυποποιημένου ερωτηματολογίου EuroQuol (EQ-5D)]. Μεταβολές από την έναρξη της μελέτης στις ανωτέρω παραμέτρους αναλύθηκαν, χρησιμοποιώντας ένα μοντέλο επανειλημμένων μετρήσεων. Βελτίωση στη συχνότητα, στη σοβαρότητα και στους περιορισμούς αναφορικά με την κινητικότητα που προκαλεί η ραχιαλγία υπολογίστηκαν, χρησιμοποιώντας τη δοκιμασία προσήμου. Πα-

ρουσιάζονται δεδομένα από τον ελληνικό υποπληθυσμό της μελέτης. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Από 301 Ελληνίδες (ηλικίας [±SD] 69,5±8,5 ετών) που εντάχθηκαν στη μελέτη, ποσοστό 83,7% ανέφερε προηγούμενη λήψη αντιοστεοπορωτικής θεραπείας. Τόσο κατά τη διάρκεια της αγωγής όσο και καθ' όλο το διάστημα παρακολούθησης παρατηρήθηκε σημαντική βελτίωση στη ραχιαλγία, τους συνακόλουθους περιορισμούς της κινητικότητας, τις ημέρες σε κατάκλιση και στην ποιότητα ζωής, όπως καταγράφονταν με βάση τις προσωπικές αναφορές των ασθενών. **ΣΥΜΠΕΡΑΣΜΑΤΑ** Η τεριπαρατίδη φαίνεται να έχει ευεργετικά αποτελέσματα για την κινητικότητα και την ποιότητα ζωής, αποτελέσματα που φαίνεται να είναι διατηρήσιμα μέχρι και 18 μήνες μετά από τη θεραπεία. Τα συμπεράσματα πρέπει να ερμηνεύονται στο πλαίσιο μελετών παρατήρησης.

**Λέξεις ευρετηρίου:** Οστεοπόρωση, Ποιότητα ζωής, Ραχιαλγία, Συμμόρφωση στην αγωγή, Τεριπαρατίδη

## References

1. INTERNATIONAL OSTEOPOROSIS FOUNDATION. About osteoporosis. Available at: http://www.iofbonehealth.org/health-professionals/about-osteoporosis
2. BLICK SK, DHILLON S, KEAM SJ. Teriparatide: A review of its use in osteoporosis. *Drugs* 2008, 68:2709–2737
3. NEER RM, ARNAUD CD, ZANCHETTA JR, PRINCE R, GAICH GA, REGINSTER JY ET AL. Effect of parathyroid hormone (1–34) on fractures and bone mineral density in postmenopausal women with osteoporosis. *N Engl J Med* 2001, 344:1434–1441
4. NEVITT MC, CHEN P, DORE RK, REGINSTER JY, KIEL DP, ZANCHETTA JR ET AL. Reduced risk of back pain following teriparatide treatment: A meta-analysis. *Osteoporos Int* 2006, 17:273–280
5. OGLESBY AK, MINSHALL ME, SHEN W, XIE S, SILVERMAN SL. The impact of incident vertebral and non-vertebral fragility fractures on health-related quality of life in established postmenopausal osteoporosis: Results from teriparatide randomized, placebo-controlled trial in postmenopausal women. *J Rheumatol* 2003, 30:1579–1583
6. SAAG KG, SHANE E, BOONEN S, MARÍN F, DONLEY DW, TAYLOR KA ET AL. Teriparatide or alendronate in glucocorticoid-induced osteoporosis. *N Engl J Med* 2007, 357:2028–2039
7. SAAG KG, ZANCHETTA JR, DEVOGELAER JP, ADLER RA, EASTELL R, SEE K ET AL. Effects of teriparatide versus alendronate for treating glucocorticoid-induced osteoporosis: Thirty-six-month results of a randomized, double-blind, controlled trial. *Arthritis Rheum* 2009, 60:3346–3355
8. KARRAS D, DROSSINOS V, BARKER C, KORELIS E. Baseline characteristics and quality of life evaluation in Greek women with osteoporosis enrolled in the European Teriparatide Observational Study (EFOS). *Bone J Hellen Society for the Study of Bone Metabolism* 2009, 20:156
9. RAJZBAUM G, JAKOB F, KARRAS D, LJUNGGREN O, LEMS WF, LANGDAHL BL ET AL. Characterization of patients in the European Forsteo Observational Study (EFOS): Postmenopausal women entering teriparatide treatment in a community setting. *Curr Med Res Opin* 2008, 24:377–384
10. LANGDAHL BL, RAJZBAUM G, JAKOB F, KARRAS D, LJUNGGREN O, LEMS WF ET AL. Reduction in fracture rate and back pain and increased quality of life in postmenopausal women treated with teriparatide: 18-month data from the European Forsteo Observational Study (EFOS). *Calcif Tissue Int* 2009, 85:484–493
11. FAHRLEITNER-PAMMER A, LANGDAHL BL, MARIN F, JAKOB F, KARRAS D, BARRETT A ET AL. Fracture rate and back pain during and after discontinuation of teriparatide: 36-month data from the European Forsteo Observational Study (EFOS). *Osteoporos Int* 2011, 22:2709–2719
12. ALOUMANIS K, KARRAS D, DROSSINOS V, KORELIS E, POLYDORAKIS A. Fracture incidence, quality of life and back pain during 18-months' treatment with teriparatide in Greek post-menopausal women with osteoporosis: Results from the European Forsteo Observational Study (EFOS). *J Osteoporos* 2011:510398
13. WEWERS ME, LOWE NK. A critical review of visual analogue scales in the measurement of clinical phenomena. *Res Nurs Health* 1990, 13:227–236
14. ANONYMOUS. EuroQol – a new facility for the measurement of health-related quality of life. The EuroQol Group. *Health Policy* 1990, 16:199–208
15. GOLD DT. The clinical impact of vertebral fractures: Quality of life in women with osteoporosis. *Bone* 1996, 18(Suppl 3):S185–S189
16. NEVITT MC, ETTINGER B, BLACK DM, STONE K, JAMAL SA, ENSRUD K ET AL. The association of radiographically detected vertebral fractures with back pain and function: A prospective study. *Ann Intern Med* 1998, 128:793–800
17. EDMOND SL, KIEL DP, SAMELSON EJ, KELLY-HAYES M, FELSON DT. Vertebral deformity, back symptoms, and functional limitations among older women: The Framingham Study. *Osteoporos Int* 2005, 16:1086–1095
18. ETTINGER B, BLACK DM, NEVITT MC, RUNDLE AC, CAULEY JA, CUMMINGS SR ET AL. Contribution of vertebral deformities to chronic back pain and disability. The Study of Osteoporotic Fractures Research Group. *J Bone Miner Res* 1992, 7:449–456
19. ROUX S. New treatment targets in osteoporosis. *Joint Bone Spine* 2010, 77:222–228
20. GENANT HK, HALSE J, BRINEY WG, XIE L, GLASS EV, KREGE JH. The effects of teriparatide on the incidence of back pain in postmenopausal women with osteoporosis. *Curr Med Res Opin* 2005, 21:1027–1034
21. STROUP J, KANE MP, ABU-BAKER AM. Teriparatide in the treatment of osteoporosis. *Am J Health Syst Pharm* 2008, 65:532–539
22. KNOPP JA, DINER BM, BLITZ M, LYRITIS GP, ROWE BH. Calcitonin for treating acute pain of osteoporotic vertebral compression

fractures: A systematic review of randomized, controlled trials. *Osteoporos Int* 2005, 16:1281–1290
23. KNOPP-SIHOTA JA, NEWBURN-COOK CV, HOMIK J, CUMMINGS GG, VOAKLANDER D. Calcitonin for treating acute and chronic pain of recent and remote osteoporotic vertebral compression fractures: A systematic review and meta-analysis. *Osteoporos Int* 2011 Jun 10 [Epub ahead of print]
24. JACKSON RD, WRIGHT NC, BECK TJ, SHERRILL D, CAULEY JA, LEWIS CE ET AL. Calcium plus vitamin D supplementation has limited effects on femoral geometric strength in older postmenopausal women: The Women's Health Initiative. *Calcif Tissue Int* 2011, 88:198–208
25. RABENDA V, BRUYÈRE O, REGINSTER JY. Relationship between bone mineral density changes and risk of fractures among patients receiving calcium with or without vitamin D supplementation: A meta-regression. *Osteoporos Int* 2011, 22:893–901
26. FRANCIS RM, ASPRAY TJ, HIDE G, SUTCLIFFE AM, WILKINSON P. Back pain in osteoporotic vertebral fractures. *Osteoporos Int* 2008, 19:895–903
27. GANGJI V, APPELBOOM T. Analgesic effect of intravenous pamidronate on chronic back pain due to osteoporotic vertebral fractures. *Clin Rheumatol* 1999, 18:266–267
28. NEVITT MC, THOMPSON DE, BLACK DM, RUBIN SR, ENSRUD K, YATES AJ ET AL. Effect of alendronate on limited-activity days and bed-disability days caused by back pain in postmenopausal women with existing vertebral fractures. Fracture Intervention Trial Research Group. *Arch Intern Med* 2000, 160:77–85
29. CASADEI K, BECKER C. Once-monthly risedronate for postmenopausal osteoporosis. *Int J Womens Health* 2010, 1:1–9
30. FU AZ, QIU Y, RADICAN L. Impact of fear of insulin or fear of injection on treatment outcomes of patients with diabetes. *Curr Med Res Opin* 2009, 25:1413–1420
31. McCOMBS JS, THIEBAUD P, McLAUGHLIN-MILEY C, SHI J. Compliance with drug therapies for the treatment and prevention of osteoporosis. *Maturitas* 2004, 48:271–287
32. ZILLER V, ZIMMERMANN SP, KALDER M, ZILLER M, SEKER-PEKTAS B, HELLMEYER L ET AL. Adherence and persistence in patients with severe osteoporosis treated with teriparatide. *Curr Med Res Opin* 2010, 26:675–681

*Corresponding author:*

K. Aloumanis, Department of Medical Research, Pharmaserve-Lilly, 15th km National Road Athens-Lamia, GR-145 64 Kifissia, Greece
e-mail: aloumanis_kyriakos@Lilly.com