ΑΝΑΒΟΛΙΚΗ ΑΓΩΓΗ

Χ. Κ. ΚΟΣΜΙΔΗΣ
Ορθοπεδικός

18-3-2023

Bone
Volume 168, March 2023, 116647

Cardiac adverse events in bisphosphonate and teriparatide users: An international pharmacovigilance study

Alexander J.Rodríguez, NiteshNerlekar, Peter R.Ebeling

465 episodes of angina, (στηθάγχη)
287 ACA, (στένωση στεφανιαίων)
13,385 arrhythmias, (αρρυθμίες)
792 CAD, (στεφανιαία νόσος)
6743 TE, (θρομβοεμβολικά επεισόδια)
3264 IHD, (ισχαιμική νόσος μυοκαρδίου)
1037 myocardial infarcts, (εμφράγματα μυοκαρδίου)and
3714 TDP events (ΗΚΓ επιμήκυνση QT διαστήματος)

were recorded across

50,365 alendronate,
52,436 zoledronic acid and
137,629 teriparatide users.

Bone
Volume 168, March 2023, 116647

Cardiac adverse events in bisphosphonate and teriparatide users: An international pharmacovigilance study

Alexander J.Rodríguez, NiteshNerlekar, Peter R.Ebeling

There was a significant association between alendronate and zoledronate with all outcomes except MI (εμφράγματα).

Teriparatide use was associated with AF (κολπική μαρμαρυγή), arrythmias (αρρυθμίες) and angina (στηθάγχη) only.

In head-to-head comparisons, teriparatide use was associated with fewer ACA (στένωση στεφανιαίων) and CAD (στεφανιαία νόσο) events than alendronate and fewer ACA (στένωση στεφανιαίων) than zoledronic acid.

<u>Συνολικά:</u> Υπεροχή της τεριπαρατίδης έναντι αλενδρονάτης και ζολενδρονικού στην εμφάνιση καρδειαγγειακών συμβαμάτων.

Osteoporosis International (2023) 34:189–199

Sequential therapy with once-weekly teriparatide injection followed by alendronate versus monotherapy with alendronate alone in patients at high risk of osteoporotic fracture: final results of the Japanese Osteoporosis Intervention Trial-05

Satoshi Mori · Hiroshi Hagino · Toshitsugu Sugimoto · Shiro Tanaka · Yuji Mitomo · Kaito Takahashi · Teruki Sone · Toshitaka Nakamura · Satoshi Soen

Methods Japanese women aged at least 75 years were eligible for the study, if they had primary osteoporosis and if they were at high risk of fracture. Patients were randomly assigned (1:1) to receive **the sequential therapy (once-weekly subcutaneous injection of teriparatide 56.5 μg for 72 weeks, followed by alendronate for 48 weeks)** or **monotherapy with alendronate for 120 weeks**. The primary endpoint in the final analysis was **the incidence of morphometric vertebral fracture during the 120-week follow-up period**.

Results Between October 2014 and June 2020, 505 patients in the sequential therapy group and 506 in the monotherapy group were enrolled. Of these, 489 and 496, respectively, were included in the main analysis. **The incidence of morphometric vertebral fracture during the 120-week follow-up period in the sequential therapy group (64 per 627.5 person-years, annual incidence rate 0.1020) was significantly lower than that in the monotherapy group (126 per 844.2 person-years, annual incidence rate 0.1492), with a rate ratio of 0.69 (95% confidence interval 0.54 to 0.88, P < 0.01).** After 72 weeks, no patient had a severe adverse event that was considered related to the study drug.

31% λιγότερα σπονδυλικά κατάγματα τις 120 εβδομάδες μετά από διαδοχική αγωγή (εβδομαδιαία τεριπαρατίδη 56,5μg για 72 εβδομάδες ακολουθούμενη από αλενδρονάτη για 48 εβδομάδες) σε σχέση με συνεχή αγωγή με μόνη αλενδρονάτη για 120 εβδομάδες.

Osteoporosis International (2023) 34:179–188

Comparison of pharmacokinetics, pharmacodynamics, safety, and immunogenicity of teriparatide biosimilar with EUand US-approved teriparatide reference products in healthy men and postmenopausal women

Steven Fenwick · Vishal Vekariya · Ronak Patel · Pallavi Hajela · Ketul Modi · Prashant Kale · Akshaya Nath

Methods One hundred and five subjects randomly (1:1:1) received single subcutaneous 20 µg injection of teriparatide biosimilar, EU- and US-teriparatide on 3 consecutive days in this assessor-blind, three-period, single-dose, crossover study.

Results Baseline demographics were similar across the three-treatment sequence groups. **The 90% confidence intervals (CI) for the geometric mean ratios (test:reference) of Cmax, AUC 0-t, and AUC 0-∞ were within the predefined bioequivalence criterion of 80.00% to 125.00%, which demonstrated PK equivalence of teriparatide biosimilar to EU- and US-teriparatide for all primary endpoints**. The PD comparability was demonstrated by similar serum calcium levels. Study treatments were generally well tolerated and showed no meaningful differences in safety or immunogenicity profiles. There were no deaths, or serious AEs were reported during this study.

Conclusion The study demonstrated PK bioequivalence of teriparatide biosimilar to the EU- and US-teriparatide reference products with comparable PD, safety, and immunogenicity profiles.

PLOS ONE
May 31, 2022

The efficiency and safety of alendronate versus teriparatide for treatment glucocorticoid-induced osteoporosis: A metaanalysis and systematic review of randomized controlled trials

Zhi-Ming Liu, Min Zhang, Yuan Zong, Ding Zhang, Zhu-Bin Shen, Xiao-Qing Guan, Fei Yin

Results

A total of 4102 patients were enrolled in all 5 studies that met the admission criteria.

We found that compared with ALE, TPTD could reduce the rate of new vertebral fracture (RR = 0.13, 95% CI: 0.05–0.34, P<0.00001).

TPTD increased LS bone mineral density (BMD) (0.53, 95% CI 0.42–0.64, <0.00001), TH BMD (0.17, 95% CI 0.05–0.28, P = 0.004) and FN BMD (0.17, 95% CI 0.05–0.29, P = 0.006) compared to ALE.

However, there was no significant difference in the incidence of non-vertebral fracture and adverse events between the two groups.

Conclusions

Compared with ALE, TPTD is an effective drug to reduce vertebral fracture risk in patients with GIOP. Furthermore, long-term use of TPTD can increase the bone mineral density of LS, FN, and TH.

BMC Musculoskeletal Disorders (2022) 23:1011

Teriparatide treatment in severe osteoporosis – a controlled 10-year follow-up study

Georgios Kontogeorgos, Emily Krantz, Penelope Trimpou, Christine M. Laine and Kerstin Landin-Wilhelmsen

Methods: A **10-year follow-up** was performed after a prospective, open-labelled study with teriparatide 20 μg given subcutaneously daily for a mean of 18 months (range 14–24 months) in 40 women, **mean age 69 years**, with osteoporosis and vertebral compression. Placebo treated women, n = 25, mean age 60 years, from a randomized, doubleblind, placebo-controlled growth hormone trial with daily subcutaneous injections for 18 months, with osteoporosis were used as controls. Dual energy x-ray absorptiometry and questionnaires were performed at start, after 18 months, after 36 months and after 10 years. Women, n = 233, of similar age from a random population sample, also served as controls and were followed in parallel. All fractures were X-ray verified.

Results: Fractures decreased from 100 to 35% in the teriparatide treated patients ($p < 0.0001$) to similar levels as in the population sample, 25 to 28% at start and after 10 years, respectively. Bone mineral density increased on teriparatide but returned to levels at treatment start after 10 years. Health Related Quality of Life was lower in the teriparatide group than in the population ($p < 0.001$) before and, after treatment and at 10 years.

Conclusions: Anabolic hormonal treatment with teriparatide reduced fracture prevalence to similar levels as in the general population at 10 years' follow-up. Health Related Quality of Life was low in osteoporosis and unaffected by bone specific treatment.

JBMR® Plus (WOA), Vol. 6, No. 7, July 2022

The Real-World Effect of 12 Months of Romosozumab Treatment on Patients With Osteoporosis With a High Risk of Fracture and Factors Predicting the Rate of Bone Mass Increase: A Multicenter Retrospective Study

Hiroyuki Inose, Akane Ariga, Takayuki Motoyoshi, Kazuyuki Fukushima, Shoji Tomizawa, Tsuyoshi Kato, Kunihiko Takahashi, Toshitaka Yoshii, and Atsushi Okawa

We retrospectively investigated 106 patients who completed a 12-month romosozumab treatment for osteoporosis with a high risk of fractures at four hospitals from March 2020 to March 2022.

After 1 year of treatment, the lumbar spine BMD increased by 14.6%, and femoral neck BMD increased by 5.1%.

Univariate regression analysis found that :

- **male sex,**
- **high tartrate-resistant acid phosphatase 5b (TRACP-5b) value before romosozumab administration,**
- **absence of osteoporosis medications before romosozumab administration, and**
- **low baseline lumbar spine BMD**

were associated with the extent of lumbar spine BMD increase.

From a clinical perspective, because teriparatide promotes both bone formation and resorption, patients with low levels of TRACP-5b and P1NP before romosozumab administration may have a greater BMD increase if they receive teriparatide first and then romosozumab than if they receive romosozumab only.

Osteoporosis International (2022) 33:2527–2536

Romosozumab efficacy and safety in European patients enrolled in the FRAME trial

Bente Langdahl · Lorenz C. Hofbauer · Serge Ferrari · Zhenxun Wang · Astrid Fahrleitner-Pammer · Evelien Gielen · Péter Lakatos · Edward Czerwinski · Esteban Jódar Gimeno · Jen Timoshanko · Mary Oates · Cesar Libanati

Results In FRAME, 3013/7180 (41.96%) patients were European; 1494 received romosozumab and 1519 received placebo.

Through 12 months, romosozumab reduced fracture risk versus placebo for

- **non-vertebral fracture (1.4% versus 3.0%; p = 0.004),**
- **clinical fracture (1.4% versus 3.6%; p < 0.001),**
- **new vertebral fracture (0.4% versus 2.1%; p < 0.001) and**
- **major osteoporotic fracture (0.9% versus 2.8%; p < 0.001),**

with results sustained through 36 months following transition to denosumab.

Hip fractures were numerically reduced with romosozumab at month 12 (0.2% versus 0.6%; p = 0.092).

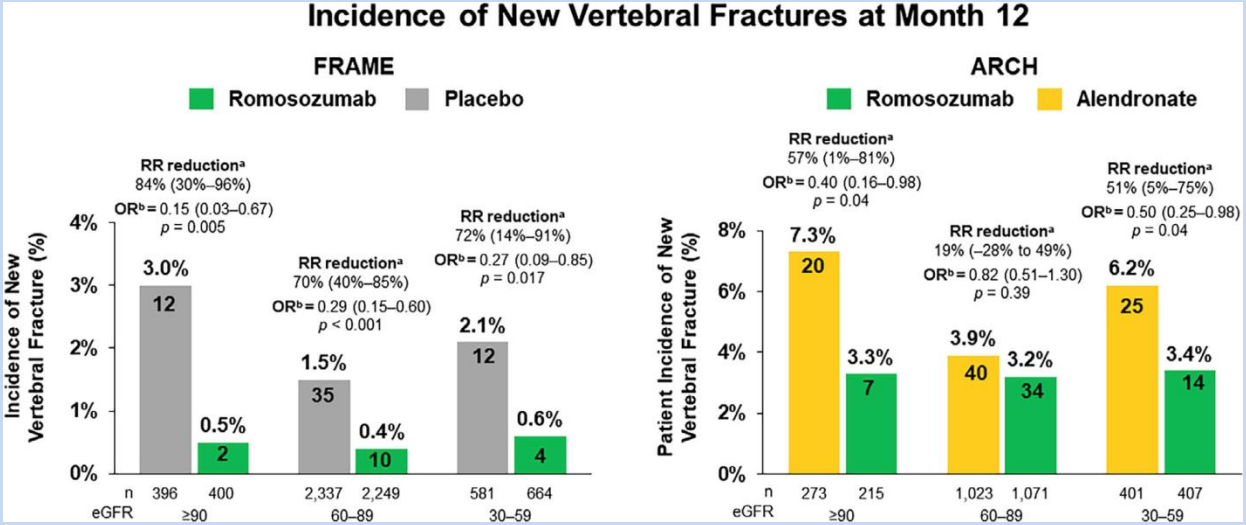
Romosozumab increased BMD versus placebo at month 12; all patients in the romosozumab and placebo groups experienced further increases by month 36 after transition to denosumab. **Adverse events were balanced between groups.**

Journal of Bone and Mineral Research, Vol. 37, No. 8, August 2022, pp 1437–1445

Efficacy and Safety of Romosozumab Among Postmenopausal Women With Osteoporosis and Mild-to-Moderate Chronic Kidney Disease

Paul D Miller, Jonathan D Adachi, Ben-Hur Albergaria, Angela M Cheung, Arkadi A Chines, Evelien Gielen, Bente L Langdahl, Akimitsu Miyauchi, Mary Oates, Ian R Reid, Norma Ruiz Santiago, Mark Vanderkelen, Zhenxun Wang, and Zhigang Yu

The analysis included data from 7147 patients from FRAME and 4077 from ARCH. Eighty-one percent of patients from FRAME and 85% from ARCH had mild or moderate reduction in estimated glomerular filtration rate (eGFR) at baseline, and part of this reduction is likely age related.



Incidences of adverse events, asymptomatic decreases in serum calcium, and evolution of kidney function during the studies were similar across all baseline kidney function groups.

Romosozumab is an effective treatment option for postmenopausal women with osteoporosis and mild-to moderate reduction in kidney function, with a similar safety profile across different levels of kidney function.

AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

MEETING ABSTRACTS

ABSTRACT NUMBER: L11

Romosozumab versus Denosumab in High-risk Patients with Glucocorticoid-induced Osteoporosis: A Pilot Randomized Controlled Trial

Wai Han Ma[1], **Chi Chiu Mok**[2], Ling Yin Ho[2], Kar Li Chan[3], Sau Mei Tse[4] and Sammy Chen[5], [1]Department of Nuclear Medicine, Hong Kong, Hong Kong, [2]Tuen Mun Hospital, Hong Kong, Hong Kong, [3]Tuen Mun Hospital, Tsing Yi, Hong Kong, [4]Department of Medicine, Tuen Mun Hospital, Hong Kong, Hong Kong, [5]Department of Pathology, Hong Kong, Hong Kong

Meeting: ACR Convergence 2022

Date of first publication: October 18, 2022

Conclusion: Romosozumab was superior to denosumab in raising the spine BMD at month 12 in chronic GC users with high fracture risk. Both drugs were well-tolerated. Romosozumab may offer a new treatment option for GIOP in high-risk patients.

AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

Empowering rheumatology professionals to excel in their specialty

2200 Lake Boulevard NE, Atlanta, GA 30319
Phone: (404) 633-3777 • Fax (404) 633-1870 • www.rheumatology.org

2022 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis

Treatments	*Recommended pharmacological treatment strategy*	
Calcium and Vitamin D	In addition to lifestyle modifications, optimized intake of dietary and supplemental calcium and vitamin D based on age-appropriate U.S. Recommended Dietary Allowances.	
Bisphosphonates (BP) Alendronate (oral) Risedronate (oral) Ibandronate (oral/ IV) Zoledronic acid (IV) **PTH & PTHrP Agonists** Teriparatide (TER) Abaloparatide (ABL) **Anti-RANKL** Denosumab (DEN) **SERM** Raloxifene (RAL) Bazedoxifene (BAZ) **Anti-sclerostin** Romosozumab (ROM)	*First line:* *Strong recommendation based on fracture data in GIOP:* Oral BP *Conditional recommendation due to lack of fracture data in GIOP:* IV BP[$], DEN, PTH/PTHrP Conditionally *recommended against due to CVD and thrombosis risk unless first-line therapies are contraindicated or not tolerated:* *ROM, SERM*	*First line:* *Conditional recommendation* Oral or IV BP[$], PTH/PTHrP or DEN Conditionally *recommended against due to CVD and thrombosis risk unless first-line therapies are contraindicated or not tolerated:* SERM and ROM

Osteoporosis International https://doi.org/10.1007/s00198-022-06626-1
REVIEW

A systematic review of cost-effectiveness analyses of sequential treatment for osteoporosis

Guangyi Yu · Suiju Tong · Jinyu Liu · Yuansheng Wan · Min Wan · Sujuan Li · Ruxu You

Published online: 17 December 2022

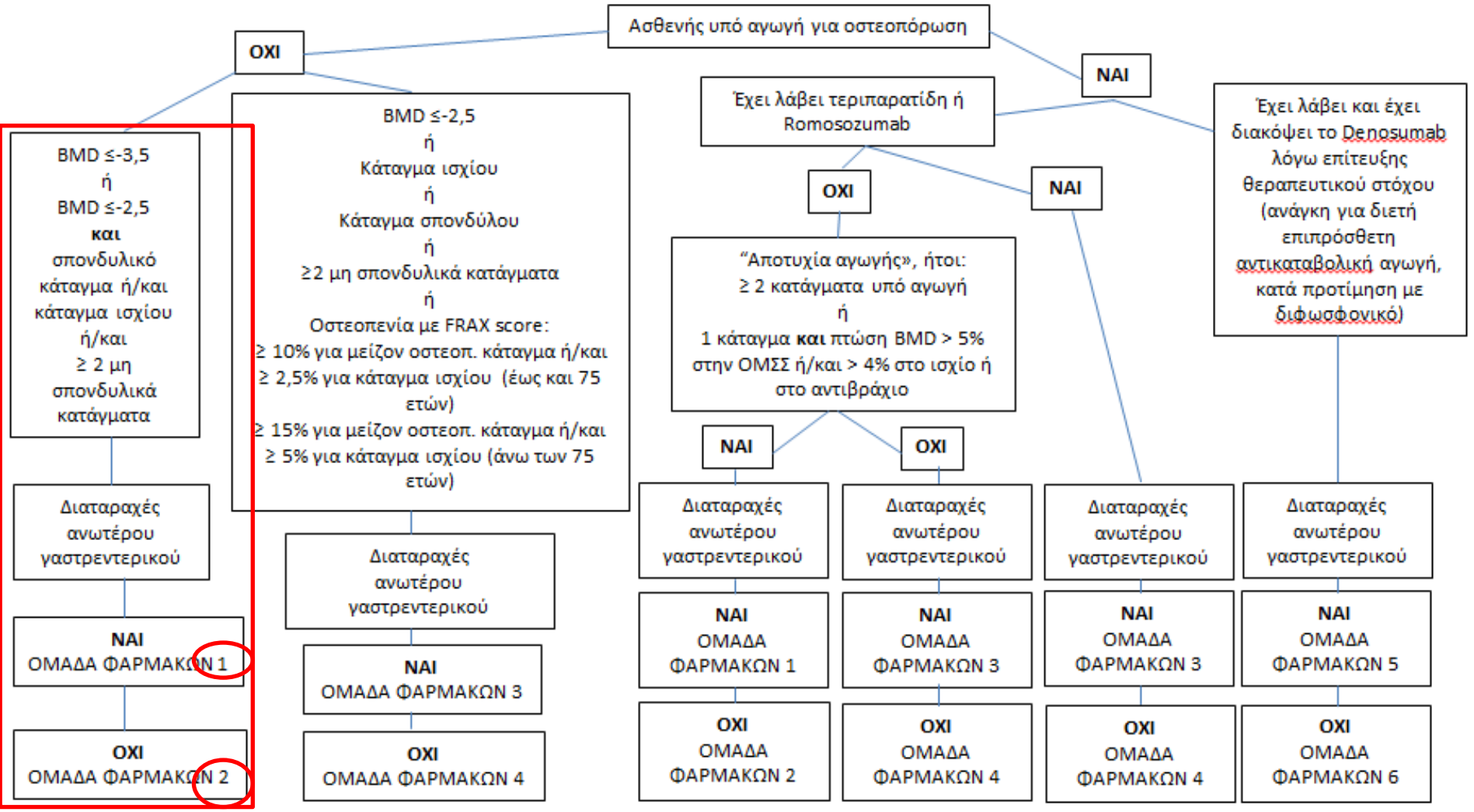
... ten articles were included in this review.

The most of studies were identified as high quality in CHEERS (2022) and ESCEO-IOF.

- Generally, the sequential treatments involving abaloparatide, romosozumab, denosumab, and bisphosphonates may be considered as the preferred option for osteoporosis with high fracture risk.

ΕΕΜΜΟ - ΟΔΗΓΙΕΣ ΔΙΑΓΝΩΣΗΣ ΚΑΙ ΘΕΡΑΠΕΙΑΣ ΤΗΣ ΟΣΤΕΟΠΟΡΩΣΗΣ – 2022

ΑΛΓΟΡΙΘΜΟΣ ΘΕΡΑΠΕΙΑΣ ΓΙΑ ΤΗΝ ΟΣΤΕΟΠΟΡΩΣΗ 2022



ΟΜΑΔΕΣ ΦΑΡΜΑΚΩΝ

1. Διφωσφονικά (I.V.), Τεριπαρατίδη, Romosozumab, Denosumab, Ραλοξιφαίνη, Βαζεδοξιφαίνη.
2. Διφωσφονικά (Peros & I.V.), Τεριπαρατίδη, Romosozumab, Denosumab, Ραλοξιφαίνη, Βαζεδοξιφαίνη.
3. Διφωσφονικά (I.V.), Denosumab, Ραλοξιφαίνη, Βαζεδοξιφαίνη.
4. Διφωσφονικά (Peros & I.V.), Denosumab, Ραλοξιφαίνη, Βαζεδοξιφαίνη.
5 Διφωσφονικά (I.V.), Ραλοξιφαίνη, Βαζεδοξιφαίνη.
6. Διφωσφονικά (Peros & I.V.), Ραλοξιφαίνη, Βαζεδοξιφαίνη.

ΕΕΜΜΟ - ΟΔΗΓΙΕΣ ΔΙΑΓΝΩΣΗΣ ΚΑΙ ΘΕΡΑΠΕΙΑΣ ΤΗΣ ΟΣΤΕΟΠΟΡΩΣΗΣ – 2022

-Σε ασθενείς με ιδιαίτερα υψηλό κίνδυνο κατάγματος χαμηλής βίας, που δεν έχουν ακόμη λάβει αγωγή (T-score ≤ -3,5 ή T-score ≤ -2,5 με ταυτόχρονο ιστορικό κατάγματος ισχίου ή σπονδύλου(ων) ή δύο καταγμάτων), θεωρείται ιδιαίτερα ωφέλιμη ως εναρκτήρια η αναβολική αγωγή (τεριπαρατίδη ή romosozumab).

ΠΕΡΙΛΗΨΗ - ΣΥΜΠΕΡΑΣΜΑΤΑ

ΤΕΡΙΠΑΡΑΤΙΔΗ

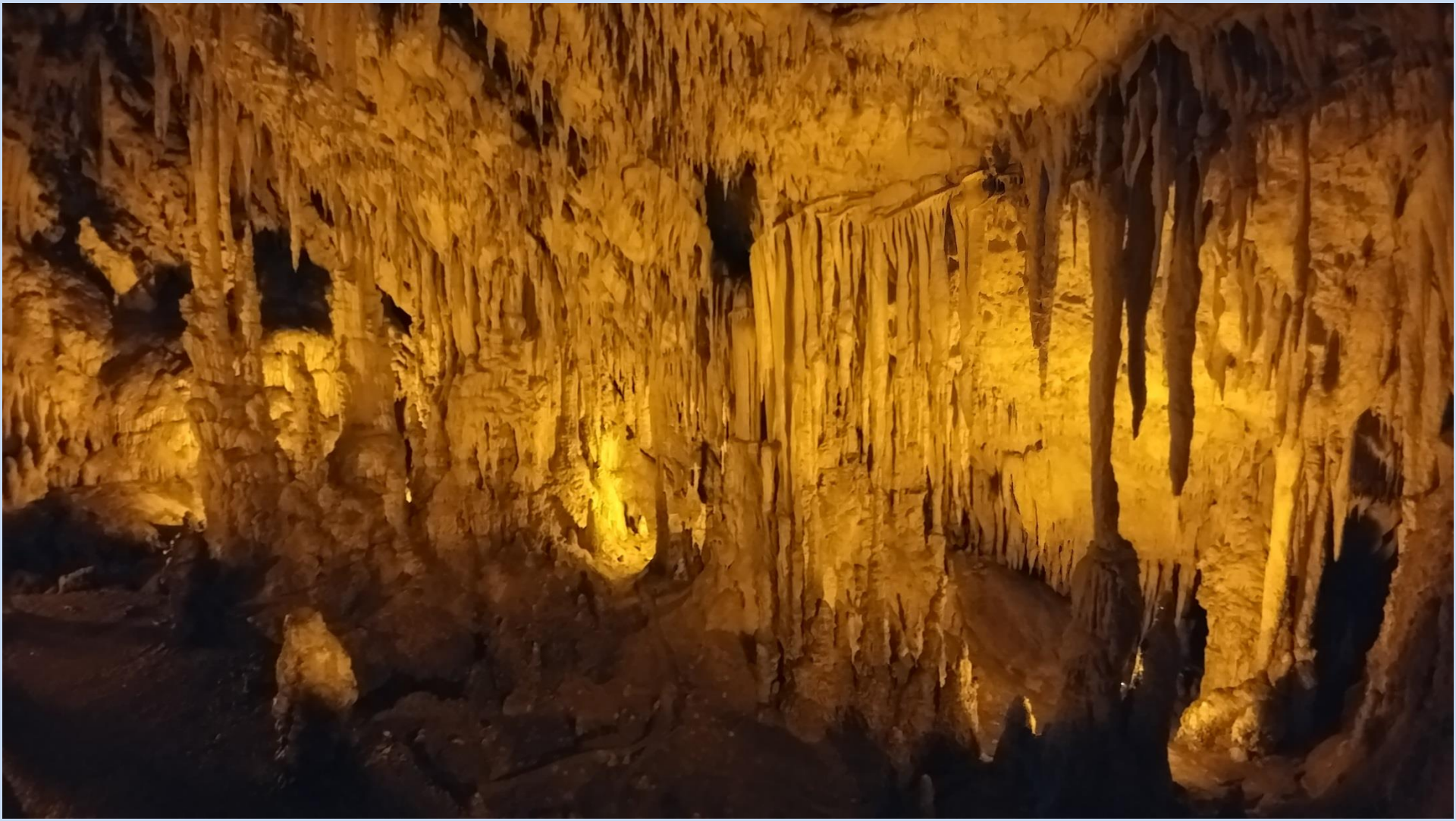
- Λιγότερα περιστατικά στεφανιαίας νόσου από ALE, ZOL.
- 31% λιγότερα κατάγματα ΣΣ μετά από αγωγή 120 εβδομάδων σε σχέση με ALE.
- Τα βιοϊσοδύναμα της τεριπαρατίδης έχουν την ίδια φαρμακοδυναμική, ανοσοσυμπεριφορά και ασφάλεια με την τεριπαρατίδη.
- Στην GIOP η τεριπαρατίδη αυξάνει την BMD και μειώνει τα κατάγματα ΣΣ περισσότερο από την ALE.
- 18 μήνες αγωγής με τεριπαρατίδη μείωσαν την επίπτωση όλων των καταγμάτων σε πληθυσμό υψηλού κινδύνου στα επίπεδα των υγιών μαρτύρων με παρακολούθηση 10 ετών.

ΡΟΜΟΣΟΖΟΥΜΑΜΠΗ

- Συγκεκριμένοι παράγοντες ευνοούν την αύξηση της BMD στην αγωγή με ROMO.
- Υψηλή αποτελεσματικότητα και ασφάλεια του ROMO στον ευρωπαϊκό πληθυσμό.
- Αποτελεσματικότητα και ασφάλεια του ROMO σε ασθενείς με χρόνια νεφρική νόσο.
- Υπεροχή του ROMO σε σχέση με το DENOSUMAB στην αύξηση της BMD σε ασθενείς με GIOP.

Προτιμότερη η έναρξη αγωγής με αναβολικό σε ασθενείς πολύ υψηλού κινδύνου για κάταγμα χαμηλής βίας

ΙΩΑΝΝΙΝΑ - ΣΠΗΛΑΙΟ ΠΕΡΑΜΑΤΟΣ



ΕΥΧΑΡΙΣΤΩ ΠΟΛΥ