NOVEDADES DE ASBMR 2023

Dr. Pablo Florenzano V.
Profesor Asistente UC
Vice-Presidente SCHOMM

Conflictos de Interés

Declaro que en los últimos 5 años he recibido de laboratorios, industrias o instituciones con fines comerciales:

- Fondos para investigacion:
    - Unrestricted research grant Ultragenyx pharmaceuticals:
        - Clinical And Molecular Characterization Of Patients With XLH And Other Forms Of FGF23-Mediated Hypophosphatemia In Chile.
        - Enthesopathy, osteoarthritis and muscular involvement and its correlation with biochemical abnormalities and quality of life in patients with X-Linked Hypophosphatemia (XLH)
- Consultorías: International Hypophosphataemia Network (IHN) Steering Committee (SC). Kyowa Kirin
- Invitación o apoyo para asistencia a cursos o congresos: No

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Journal of Bone and Mineral Research

February 2024
Volume 39
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March 2024
Volume 8
Issue 3

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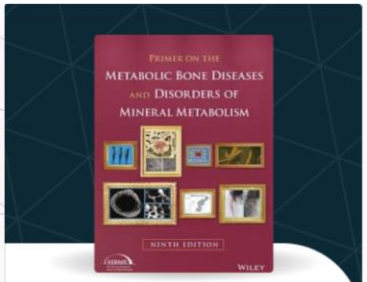

Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 9th Edition

October 2018

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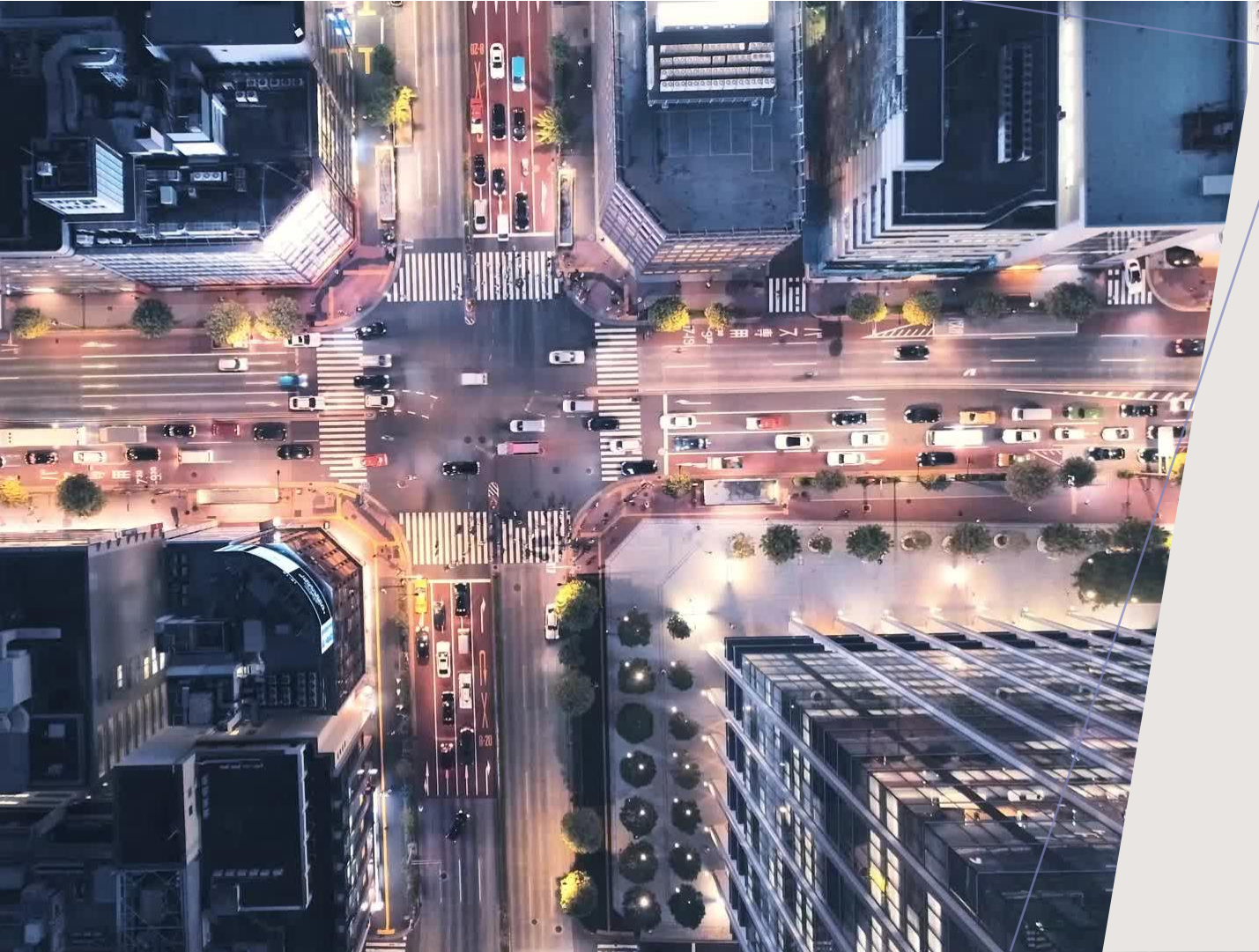


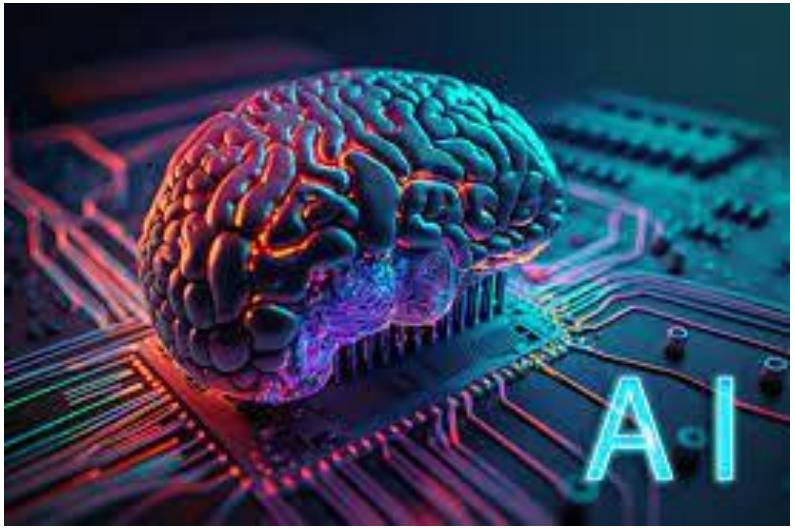
ASBMR 2023 ANNUAL MEETING, VANCOUVER CANADA

CLINICAL HIGHLIGHTS

SERGE FERRARI

GENEVA, SWITZERLAND

DOS TEMAS PREDOMINANTES



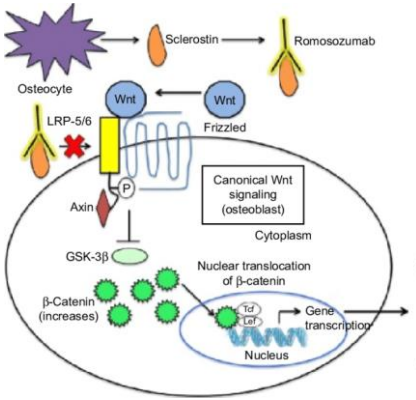
DRUG DEVELOPMENT...FOR OI ?

- LB Sat-650, Evaluación de setrusumab para el tratamiento de osteogénesis imperfecta: datos de fase 2 del estudio ORBIT de fase 2/3 (pediátricos y adultos jóvenes).

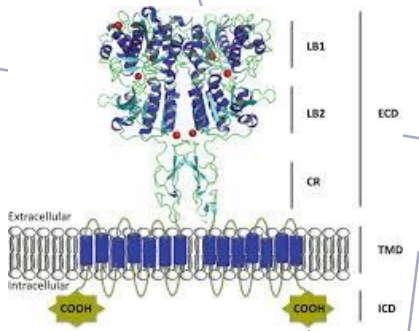
  - ORBIT fase 2> OI I-II-IV , edad 5-26 años, N 26, 1 año de tratamiento ,dosis 20 vs 40 mg /kg
  - RRR fracturas 67%, ganancia DMO 15 % en 6 meses, aumento marcadores formación ósea ++

Proximos pasos:

- Nuevo diseño de RCT que compara Setrusumab con BP en OI infantil
- Fase 3> 195 pacientes , 20mg/kg



RBD



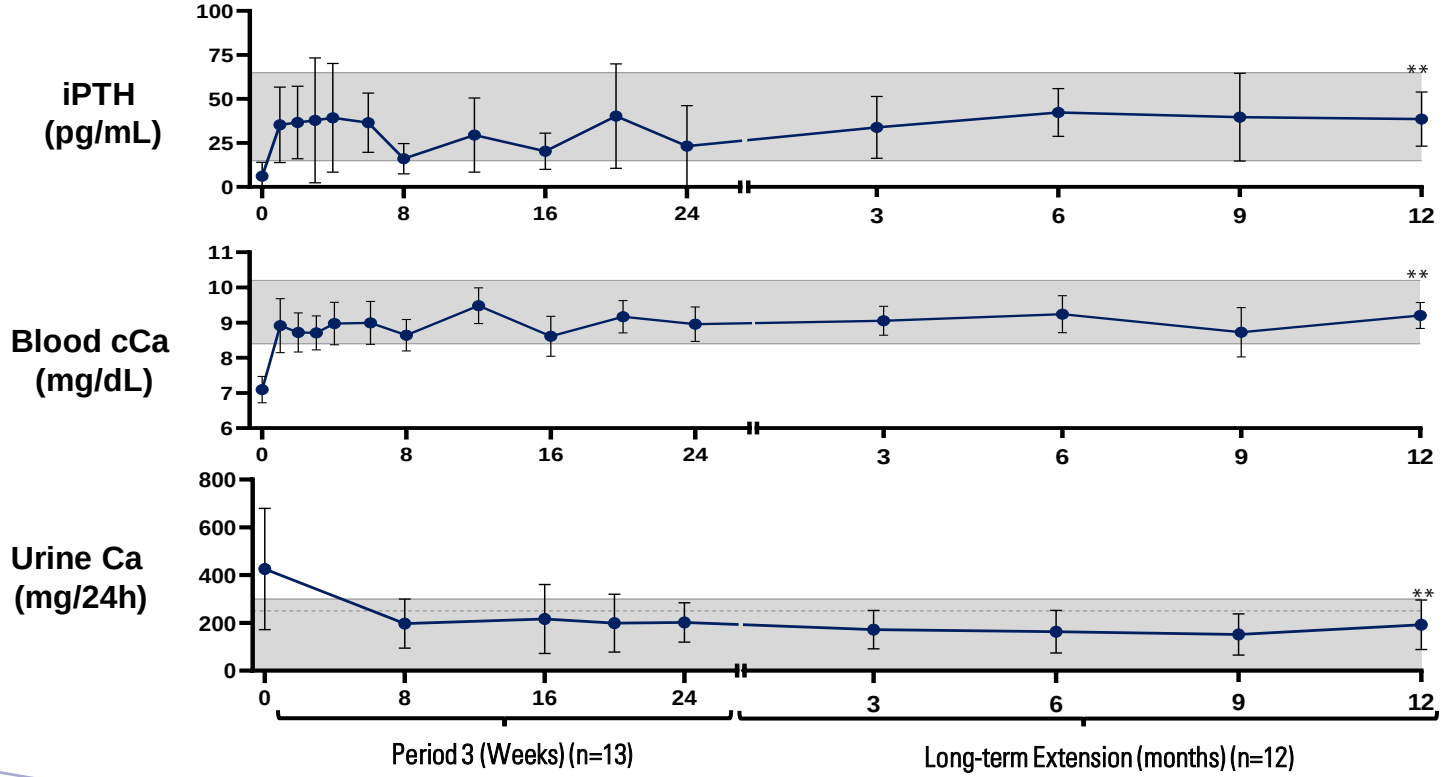
- 1023, Sat, Clinical Updates in Rare Bone Disease - Session 1

R Gafni,…,M Collins (NIH)

Encaleret (CLTX-305) Normalizes Mineral Homeostasis Parameters in Patients with Autosomal Dominant Hypocalcemia Type 1 over 18 months in a Phase 2 Study

Estudio abierto de fase 2b del calcilítico oral (modulador negativo de CaSR) en 13 adultos con ADH1, extendido a 24 semanas (seguridad/eficacia), con una extensión a largo plazo (12m).

THE CALCILYTIC ENCALERET NORMALIZED MEAN IPTH AND BLOOD AND URINE CALCIUM IN 12 ADULTS WITH AUTOSOMAL DOMINANT HYPOCALCEMIA TYPE 1 OVER 18 MONTHS



Data reported as mean+SD. Values below limit of assay quantitation recorded as "0". Gray shading reflects normal range. Solid line for urine calcium reflects the upper limit for men and dashed line reflects upper limit for women. ** p-value < 0.01 Month 18 compared to Baseline.

Gafni , Collins at al,, NEJM Sept 28, 2023

NEW DATA AND OBSERVATIONAL STUDIES: RBD

- 1114, Mon, Clinical Updates in Rare Bone Disease - Session 2

A Khan,…,L Renjmark (McMaster Univ)

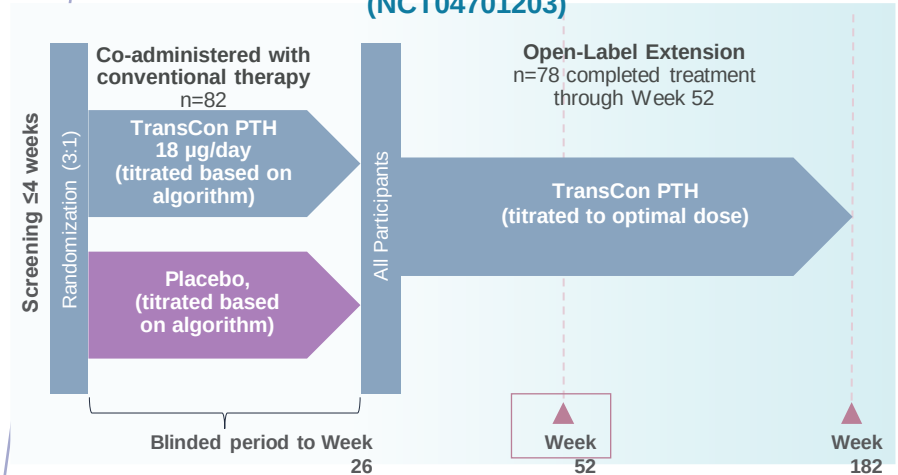
Improved Skeletal Dynamics in Adults Treated With Palopegteriparatide for Hypoparathyroidism: 52-Week Analysis of Phase 3 PaTHway Trial

59 participantes, que mostraron un aumento transitorio de BTM y una regresión de la DMO hacia "valores normales emparejadas por edad y/o sexo", de forma menos marcada después de la semana 26

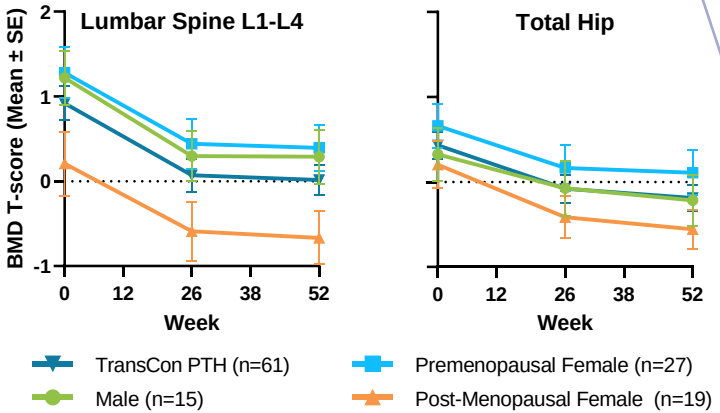
1. Khan,…, Shu, *PaTH Forward: A Randomized, Double-Blind, Placebo-Controlled Phase 2 Trial of TransCon PTH in Adult Hypoparathyroidism*, JCEM 2022, 37: 372-
2. Khan,…,Renjmark, *Efficacy and Safety of Parathyroid Hormone Replacement With TransCon PTH in Hypoparathyroidism: 26-Week Results From the Phase 3 PaTHway Trial, JBMR 2023, 38:14-*

IMPROVED SKELETAL DYNAMICS IN ADULTS TREATED WITH PALOPEGTERIPARATIDE FOR HYPOPARATHYROIDISM: 52-WEEK ANALYSIS OF PHASE 3 PATHWAY TRIAL

TransCon PTH Phase 3 PaTHway Trial Design (NCT04701203)



BMD T-Scores in Participants Treated With TransCon PTH Through Week 52 Overall and by Sex and Menopausal Status



81% of participants treated with TransCon PTH met the multi-component efficacy endpoint[a] and 95% achieved independence from conventional therapy[b] at Week 52 of the PaTHway trial.

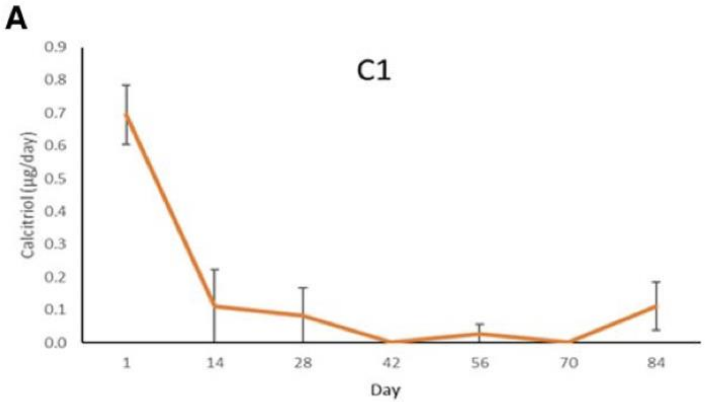
T-scores remained within the normal range[c] with TransCon PTH treatment over 52 weeks and largely stabilized after 26 weeks of treatment with TransCon PTH, regardless of sex and menopausal status.

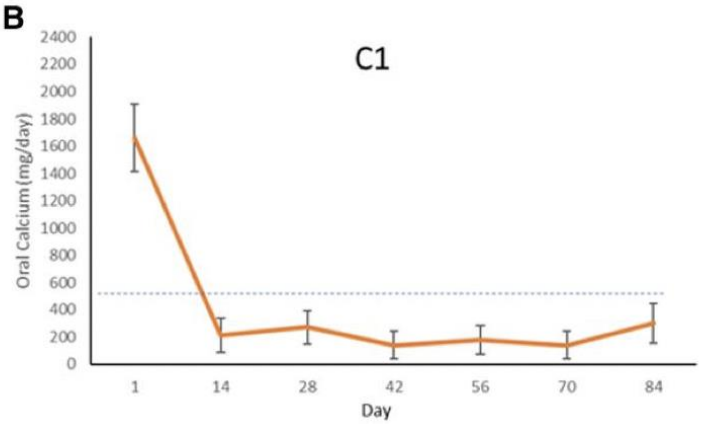
[a]Proportion of participants with serum calcium in the normal range (8.3–10.6 mg/dL), independence from therapeutic doses of calcium (defined as a standing dose of elemental calcium ≤600 mg on the day prior to the week 52 visit), and independence from active vitamin D (defined as a standing dose of active vitamin D equal to zero on the day prior to the week 52 visit). [b]Defined as a standing dose of active vitamin D equal to zero and elemental calcium ≤600 mg on the day prior to the week 52 visit. [c]T-score reference point: young (30-year-old) Caucasian adult.
BMD, bone mineral density; PTH, parathyroid hormone.

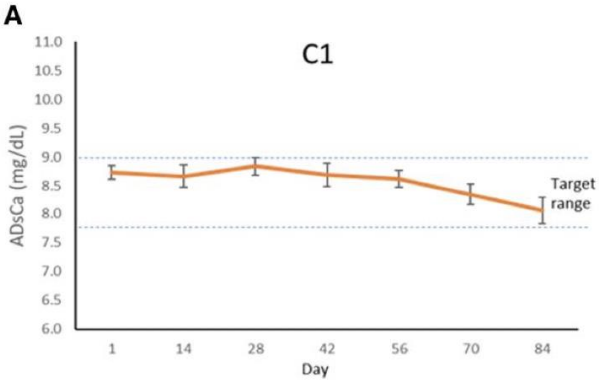
TransCon PTH is investigational. Intended for education and scientific exchange only. Not for use in promotion or product commercialization.

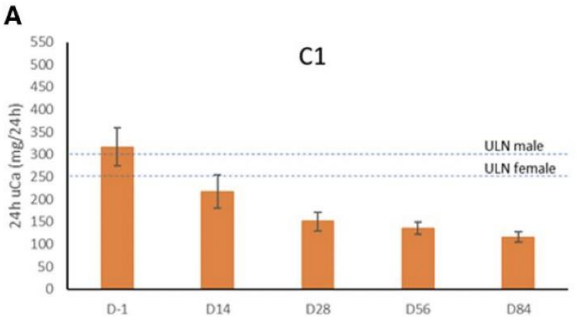
An Open-label Phase 2 Study of Eneboparatide, a Novel PTH Receptor 1 Agonist, in Hypoparathyroidism

Istvan Takacs,[1] Emese Mezosi,[2] Alfonso Soto,[3] Peter Kamenický,[4] Lucile Figueres,[5] Maria Angeles Galvez Moreno,[6] Sandrine Lemoine,[7] Francoise Borson-Chazot,[8] Ismael Capel,[9] Taha Ouldrouis,[10] Nadège Lucas,[10] Soraya Allas,[10] Mark Sumeray,[10] Michel Ovize,[10] and Michael Mannstadt[11]









OP: ESTUDIOS OBSERVACIONALES

- 1006, Fri, John H. Carstens Memorial Session on Osteoporosis Treatment

J Curtis,…,M Kim (Univ. of Alabama at Birmingham)

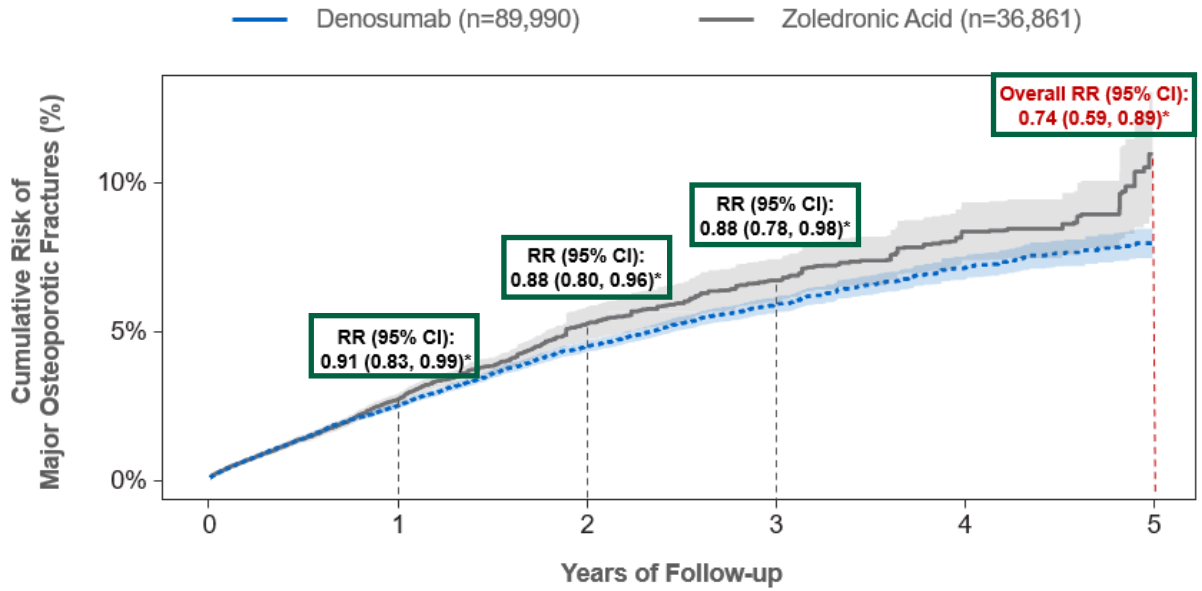
Comparative Effectiveness of Denosumab versus Zoledronic Acid among Postmenopausal Women with Osteoporosis in the U.S. Medicare Program

Estudio de cohorte retrospectivo entre mujeres con osteoporosis posmenopáusica (PMO) en los EE. UU. Beneficiarios de Medicare >= 66 años de edad que iniciaron recientemente Dmab (n = 89,990) o ZA (n = 36,861).

Métodos estadísticos "doblemente robustos" (Propensity Score), seguimiento máximo 5 años.

Dmab es más eficaz que Zol...

DENOSUMAB REDUCED THE RISK OF MAJOR OSTEOPOROTIC FRACTURE BY 12% (3Y) AND 26% (5Y) COMPARED WITH ZOLEDRONIC ACID



Persons at risk						
Denosumab	89,990	53,979	22,946	10,184	4,458	1,725
Zoledronic Acid	36,861	31,167	7,693	2,880	1,018	354

*P< 0.05. Shaded area represents CI. Major osteoporotic fracture is defined as nonvertebral fractures or hospitalized vertebral fractures. 'Overall' covers the entirety of follow-up.
CI, confidence interval; MOP, major osteoporotic; RR, risk ratio.

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OP CLINICAL TRIAL

- Sat-439, Osteoporosis Treatment Poster Session 1

J Ha,…,KH Baek (Catholic Univ Korea)

Effects of denosumab or zoledronic acid on bone density and muscle mass in drug-naive patients with postmenopausal osteoporosis : multicenter 3-year observational study

120 pts recibiendo Zol o Dmab para OP durante 3 años.

Los aumentos de la DMO son comparables, pero solo el grupo de denosumab mostró un aumento significativo de la masa muscular esquelética a 1 año, según lo evaluado por impedancia bioeléctrica

1. Bonnet et al. ***RANKL inhibition improves muscle strength and insulin sensitivity and restores bone mass,*** *J Clin Invest 2019, 129: 3214-*

2. Chotiyarnwong et al. ***A Pooled Analysis of Fall Incidence From Placebo-Controlled Trials of Denosumab****, JBMR 2020, 35:1014-*

3. Rupp et al. ***Beneficial effects of denosumab on muscle performance in patients with low BMD: a retrospective, propensity score-matched study****, Osteop Int 2022, 33: 2177-*

OP CLINICAL TRIAL

- SUN-448, Osteoporosis Treatment Poster Session 2 and Wellcome

G Pfeiler,…,M Gnant (Med. Univ. Vienna, AUS)

A Single Dose of Zoledronic Acid after Stopping Denosumab in Early Hormone-receptor-positive Breast Cancer Patients: a Randomized Controlled Trial

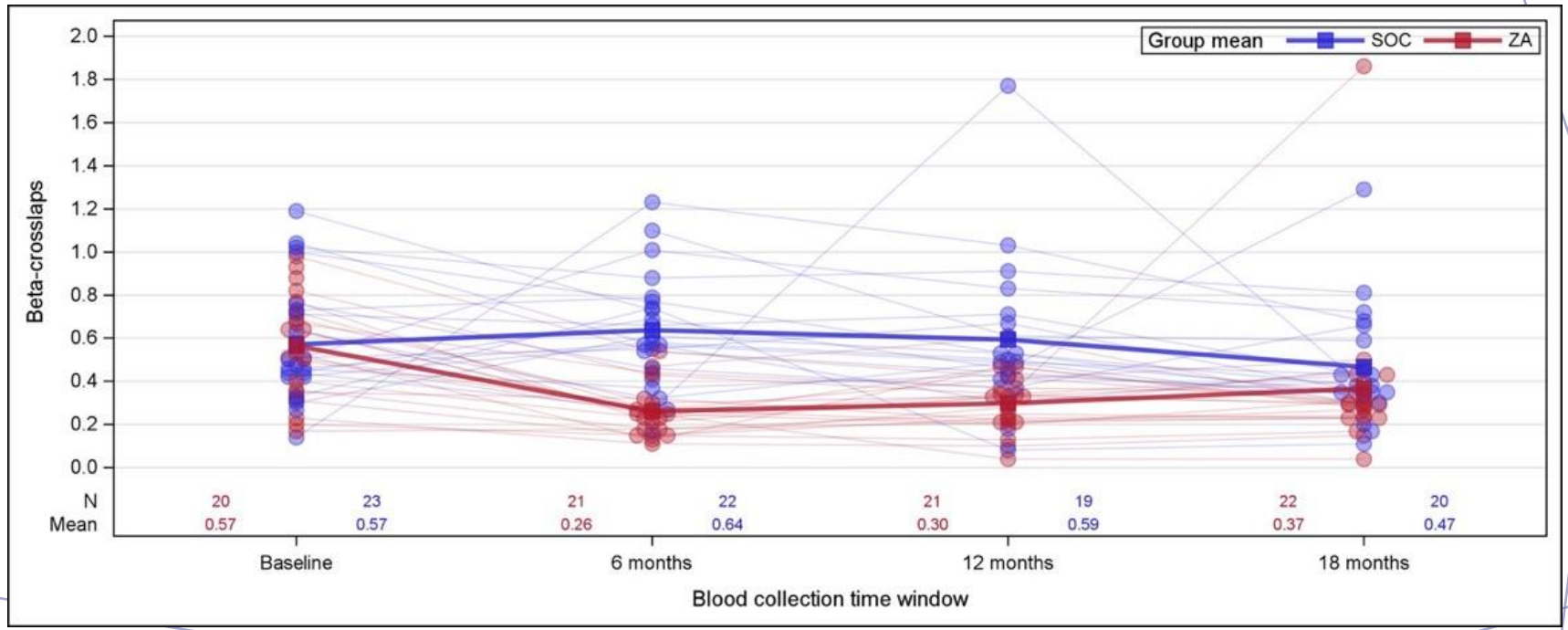
Estudio de seguimiento del ensayo ABCSG-18 de Dmab vs PBO en mujeres con Ca de mama que reciben inhibidores de la aromatasa*.

50 mujeres que recibieron 7 dosis de Dmab y luego se aleatorizaron a una dosis única de 5 mg de Zol administrada 8 ± 1 m. después de Dmab, en comparación con ningún tratamiento.

La CTX basal ya aumentó (570 ng/ml). Luego CTX disminuyó 50% en Zol a los 6 y 12 m., vs 7% en ctrls (fig.).

**Gnant et al., Lancet 2015*
Also see: Mastrantoni et al., Adjuvant denosumab in early breast cancer: a systematic review and meta-analysis of randomized controlled clinical trials. Ther Adv Med Oncol 2023

ABCSG
AUSTRIAN BREAST & COLORECTAL CANCER STUDY GROUP

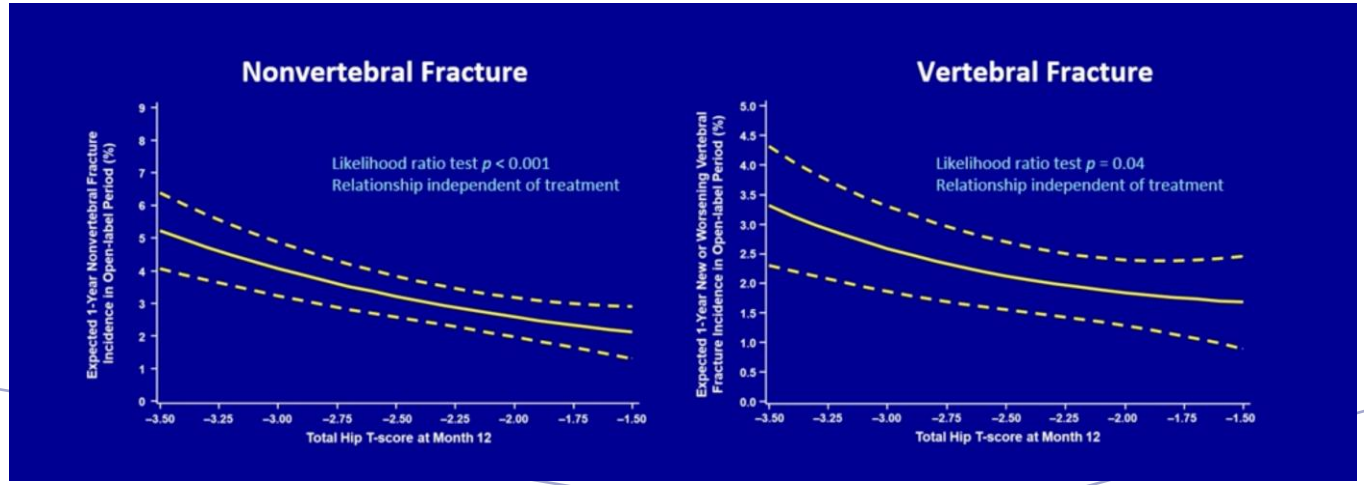


Pfeiler et al.

Goal Directed Osteoporosis Treatment: Update from the ASBMR/BHOF Task Force

Felicia Cosman
Professor of Medicine

- Individualizar meta terapéutica en cada paciente previo al inicio del tratamiento.
- Metas :
  - Ausencia de fracturas
  - T score > -2,5 para en CL, CF y CT para pacientes riesgo promedio
  - T score >-2 para pacientes alto riesgo (Fx previa, alto riesgo caídas, bajo performance status). Sitio?



Goal Directed Osteoporosis Treatment: Update from the ASBMR/BHOF Task Force

Felicia Cosman
Professor of Medicine

- Una vez seleccionada la meta, iniciar tratamiento con fármaco que permita que > 50% de las pacientes tratadas logren meta planteada en 3 años o menos.

	Total Hip	Lumbar Spine
Alendronate[1]	-2.7	-3.0
Denosumab[2]	-2.8	-3.1
Romosozumab/Alendronate[1]	-2.9	-3.5
Abaloparatide/Alendronate[3]	-2.9	-3.5
Romosozumab/Denosumab[1]	-3.1	-3.7

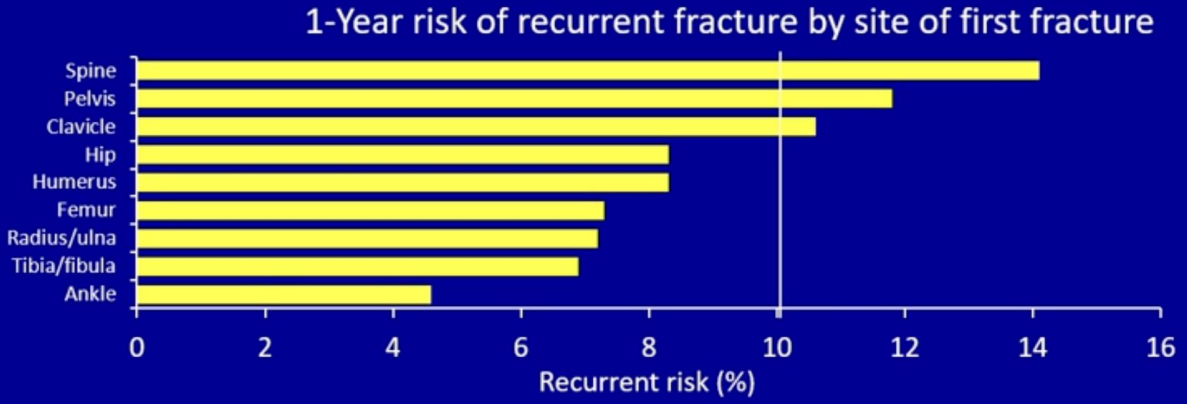
Data not available for all agents- e.g. teriparatide, zoledronic acid

Goal Directed Osteoporosis Treatment: Update from the ASBMR/BHOF Task Force

Felicia Cosman
Professor of Medicine

- Riesgo inminente : > 10% nueva fractura en los próximos 2 años

- Recent clinical fracture[1]



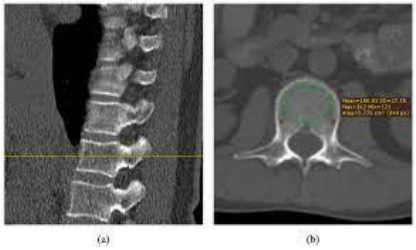
Goal Directed Osteoporosis Treatment: Update from the ASBMR/BHOF Task Force

Felicia Cosman
Professor of Medicine

- En resumen, recomendación de inicio de tratamiento según meta basal:
  - Riesgo inminente:
    - Fx vertebral o pelvis> anabólicos
    - Fx extremidades> BF, Denosumab o Anabólicos
  - T score CT basal:
    - ≧ -2,8 : Denosumab, BF
    - < -2,8 : Anabólicos
  - T score CL basal:
    - ≧ -3,1 : Denosumab, BF
    - < -3,1 : Anabólicos

¿IA MEJORA EN LA PREDICCIÓN DE FRACTURAS?

AI FOR FRACTURE DETECTION AND PREDICTION



- SUN-395, Osteoporosis Assessment, Poster Session 2 and Welcome

EB Yilmaz,…,C Meyer (Christian-Albrechts-Universität Kiel)

Automated Deep Learning-based CT-Scout View Assessment of Prevalent Vertebral Fractures

Detección precisa de FV basada CT Scouts de torax –abdomen

Refs: *Automated Deep Learning-Based Detection of Osteoporotic Fractures in CT Images, MLMI 2021, p. 376-385*

Towards fracture risk assessment by deep-learning-based classification of prevalent vertebral fractures, SPIE proceed. 2023, Vol 12465

- SAT-391, Osteoporosis Assessment, Poster Session 1

N Krekiehn,…,K Gluer (Univ. Kiel, GER)

Automated Deep Learning-based Bone Mineral Density Assessment of Vertebral Bodies in CT Scans

vBMD del cuerpo trabecular vertebral evaluado a partir de CT tan adecuado como QCT (AUC 0.76)

FRACTURE PREDICTION

- 1129, Mon, Late-breaking oral presentations: Clinical Science 1

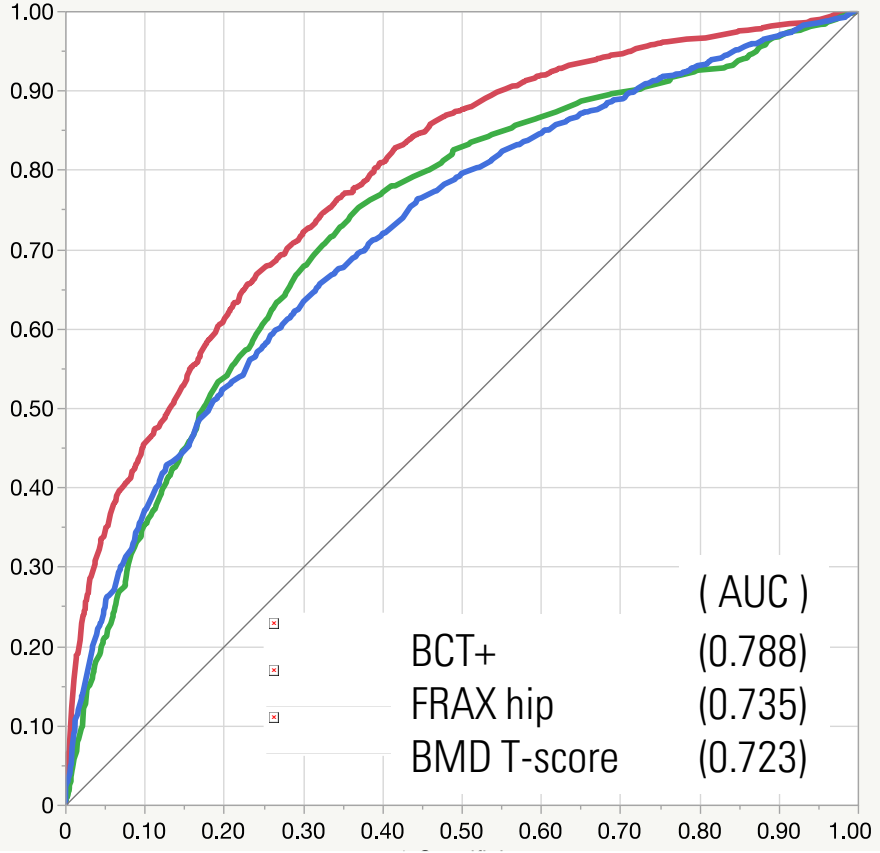
Keaveny et al. (Berkeley)

Improved Real-World Prediction of Hip Fracture Using CT-Based Measurements of Bone, Muscle, and Soft Tissue in Women and Men

- Muestra de 11.000 pacientes de 65+ años con CT de cadera, 1/2 con fracturas de cadera a los 5 años
- Evaluación de la resistencia de la cadera (FEA),…; morfología muscular, composición corporal; Espesor de los tejidos blandos
- AUC mejor que BMD y FRAX

No se puede mostrar la imagen.

FIGURE: Sensitivity vs. (1-Specificity)



Keaveny et al.

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Eighteenth Fellows Forum

On Osteoporosis and Metabolic Bone Diseases

ASBMR
The American Society for Bone and Mineral Research

Metro Toronto Convention Centre, Toronto, Ontario, Canada
September 25-26, 2024

Accepting Applications through Wednesday, May 22.

Application Portal

The Endocrine Fellows Foundation (EFF) and the American Society for Bone and Mineral Research (ASBMR) are pleased to offer fellows training in osteoporosis and other metabolic bone diseases a unique opportunity to participate in a Fellows Forum on Osteoporosis and Metabolic Bone Diseases held prior to the ASBMR Annual Meeting.

NOVEDADES DE ASBMR 2023

Dr. Pablo Florenzano V.
Profesor Asistente UC
Vice-Presidente SCHOMM

pflorenz@uc.cl

NEW DATA AND OBSERVATIONAL STUDIES

- SAT-455, Friday Early Career Plenary Poster Spotlight

M Schini,…, R Eastell (Univ. Sheffield, UK)

*Influence of age on the efficacy of pharmacologic treatments on fracture risk reduction and increases in BMD: Results from the FNIH-ASBMR SABRE Project **

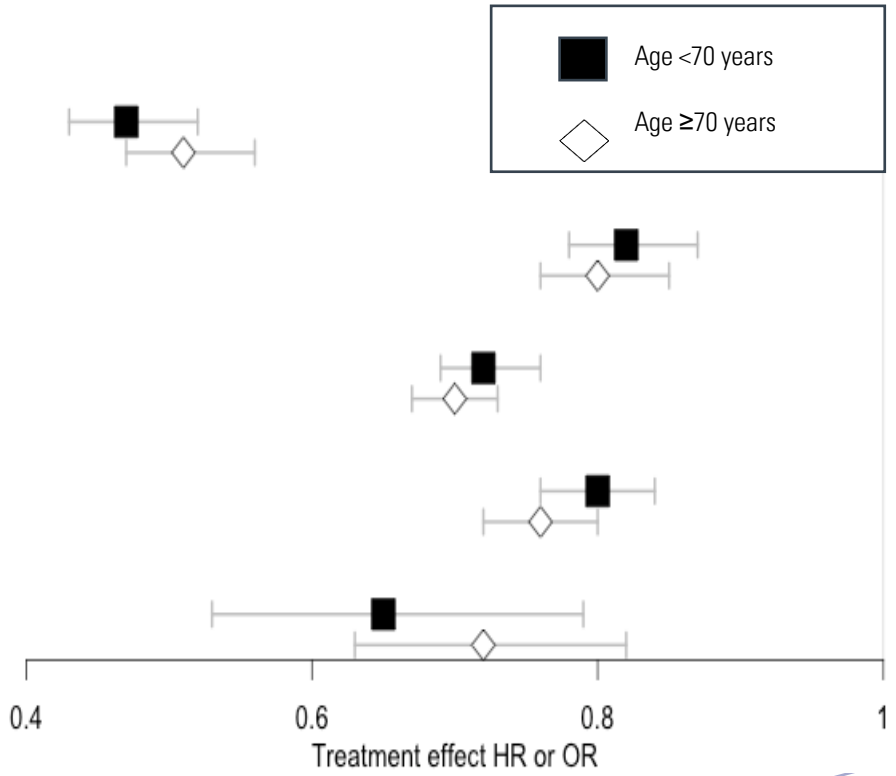
Data were stratified by age (<70 and >=70 years old), and the treatment-related fracture risk reduction was estimated in each subgroup . Similar reductions in fracture risk but greater % increase in BMD in older group.

** Eastell et al., Validation of the Surrogate Threshold Effect for Change in Bone Mineral Density as a Surrogate Endpoint for Fracture Outcomes: The FNIH-ASBMR SABRE Project. JBMR 2022*

Age does not have an effect on fracture risk reduction

Sat-455

Type of fracture	HR or OR (95% CI)	p for interaction
Vertebral	0.47 (0.43, 0.52) 0.51 (0.47, 0.56)	0.19
Non-vertebral	0.82 (0.78, 0.87) 0.80 (0.76, 0.85)	0.41
All	0.72 (0.69, 0.76) 0.70 (0.67, 0.73)	0.20
All clinical	0.80 (0.76, 0.84) 0.76 (0.72, 0.80)	0.10
Hip	0.65 (0.53, 0.79) 0.72 (0.63, 0.82)	0.50



DRUG DEVELOPMENT…FOR OI ?

- Oral 1112, Mon, Clinical Updates in Rare Bone Disease - Session 1

I-Wen Song,…, B Lee (Baylor Coll. med)

Development of bone targeted anti-TGFß antibody for the treatment of osteogenesis imperfecta

Reports pharmacokinetics and -dynamics of fresolimumab in a Phase 1 study on various types of OI…and the preliminary results of a bone-targeted anti-TGFß antibody in Wt and OI mice

- *TGFß elevada como driver de fenotipo oseo en OI*
- *Fresolimumab (anti-TGFß antibody) en dosis 1mg /kg vs 4 mg/kg dosis unica*
- *N= 8*
- *Ganancia DMO en fenotipo leve, no en severo*

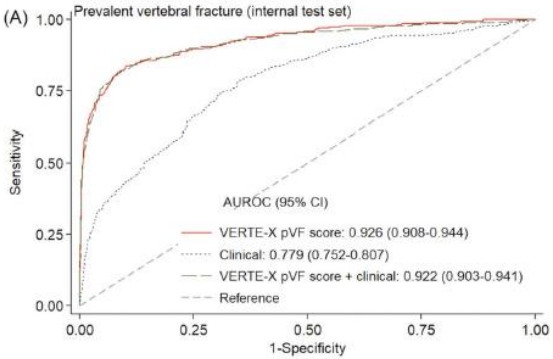
AI FOR FRACTURE DETECTION AND PREDICTION

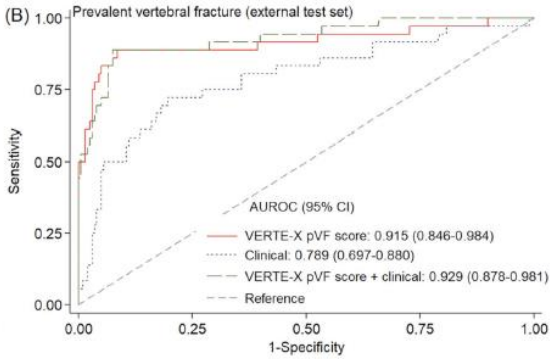
RESEARCH ARTICLE

JBMR®

Deep-Learning-Based Detection of Vertebral Fracture and Osteoporosis Using Lateral Spine X-Ray Radiography

Namki Hong,[1] Sang Wouk Cho,[2] Sungjae Shin,[1] Seunghyun Lee,[1] Seol A Jang,[3] Seunghyun Roh,[1] Young Han Lee,[4] Yumie Rhee,[1] Steven R. Cummings,[5,6] Hwiyoung Kim,[7] and Kyoung Min Kim[3]



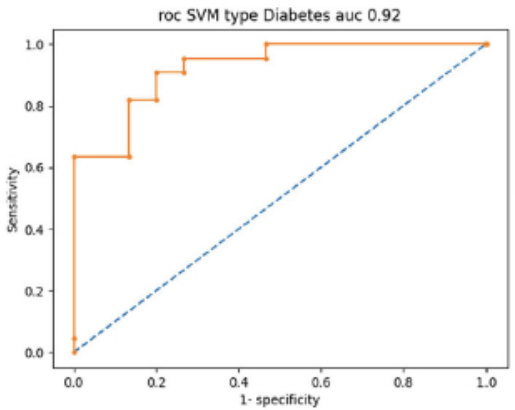


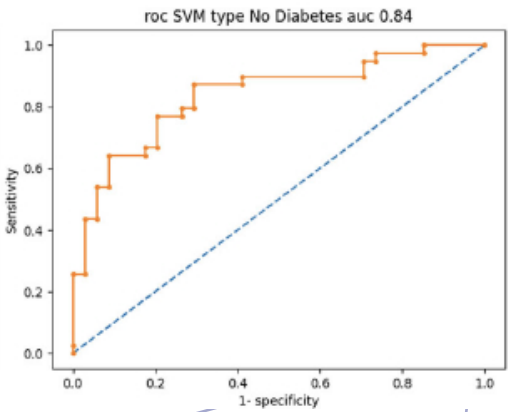
RESEARCH ARTICLE

JBMR®

Hip Fracture Risk Assessment in Elderly and Diabetic Patients: Combining Autonomous Finite Element Analysis and Machine Learning

Zohar Yosibash,[1,2] Nir Trabelsi,[2,3] Itay Buchnik,[4] Kent W Myers,[2] Moshe Salai,[5] Iris Eshed,[6,7] Yiftach Barash,[6,7] Eyal Klang,[6,7] and Liana Tripto-Shkolnik[7,8]





NUEVOS DATOS Y ESTUDIOS OBSERVACIONALES: RBD

- 1115, Mon, Clinical Updates in Rare Bone Disease - Session 2

V Zhukouskaya,…,A Linglart (Univ. Paris, Hop Cochin)

Newly Diagnosed Hyperparathyroidism After 3 Years Of Burosumab In Children Affected With X-Linked Hypophosphatemia

37 niños XLH (23 niñas / 14 niños; 8,8+/-3,2 años) fueron cambiados de la terapia convencional a burosumab y completaron al menos tres años de terapia con burosumab, excluyendo el HPT 2ry al inicio del estudio.

Los niveles de PTH aumentaron en general y 4 sujetos desarrollaron HPT secundario

1. *Imel, Glorieux et al., Burosumab versus continuation of conventional therapy in children with X-linked hypophosphatemia: a randomised, active- controlled, open-label, phase 3 trial. Lancet 2019, 393: 2416-*
2. *Linglart,…,Carpenter, Sustained Efficacy and Safety of Burosumab, a Monoclonal Antibody to FGF23, in Children With X-Linked Hypophosphatemia, JCEM 2022, 107: 813,*

Goal Directed Osteoporosis Treatment: Update from the ASBMR/BHOF Task Force

Felicia Cosman
Professor of Medicine

Selecting Treatment to Achieve BMD Targets

- Initial treatment selection should consider:
  - probability that T-score target can be reached within about 3 years
    - greater urgency in patients at imminent risk
  - ability to achieve BMD targets differs for spine and hip
  - if anabolic agents might be indicated, consider importance of anabolic/antiresorptive treatment sequence[1-4]
    - maximal BMD gains with anabolic agents first

1. Cosman F et al. J Bone Miner Res 2017;32:198-202
2. Langdahl BL et al. Lancet 2017;390:1585-94
3. Leder BZ, et al. *Lancet*. 2015;386:1147-1155.
4. Cosman F et al, Osteoporosis Int 2022;33:1243–1256

AI FOR FRACTURE DETECTION AND PREDICTION

- 1060, Sat, Osteoporosis – Epidemiology

W Leslie et al., (Univ. Manitoba)

Active Learning for the Efficient Annotation of Unlabeled Lateral Spine Images Acquired at Baseline from the Canadian Longitudinal Study on Aging

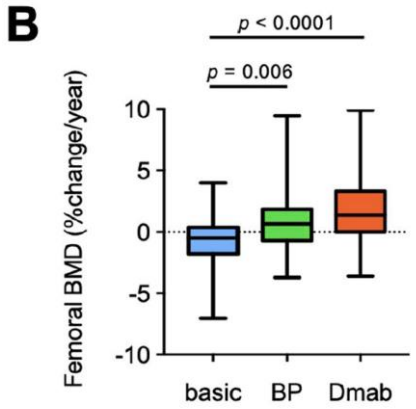
Detección precisa de FV basada en imágenes de VFA

Sensibilidad del conjunto medio después de seis iteraciones de aprendizaje activo, evaluada frente a VFA; estratificados por la gravedad de la FV

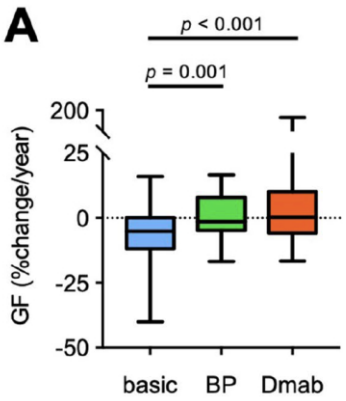
Overall Sensitivity	Sensitivity by VF severity		
	Grade 1	Grade 2	Grade 3
84.7%	80.2%	86.1%	88.6%

BENEFICIAL EFFECTS OF DENOSUMAB ON MUSCLE PERFORMANCE IN PATIENTS WITH LOW BMD: A RETROSPECTIVE, PROPENSITY SCORE-MATCHED STUDY

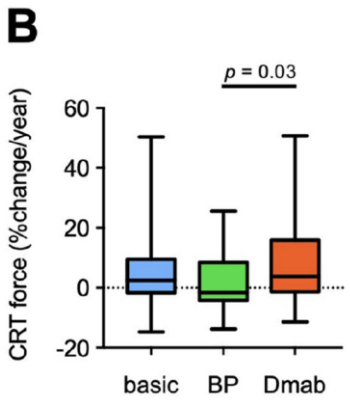
- 150 pacientes r/VitD solo (básico), Denosumab o BP entre 2010 y 2021, pareados (sexo, edad, IMC, seguimiento)



Hand grip



Chair rising



Rupp et al., Osteop Int 2022, 33: 2177-