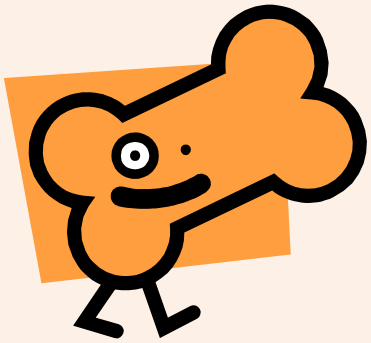
BONE TURNOVER MARKERS, A LEGITIMATE PERSONALIZED MEDICINE TOOL OR A WISHFUL THINKING?

Liana Tripto-Shkolnik
Mineral and Bone Diseases Service,
Division of Endocrinology, Diabetes and Metabolism
Sheba Medical Center
Tel Hashomer

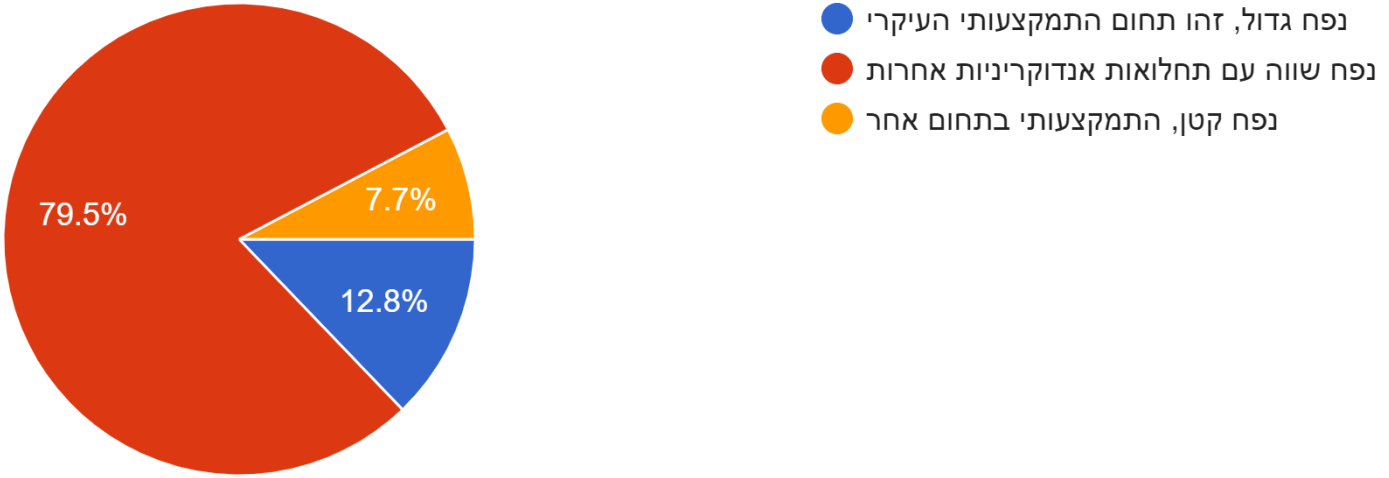


11.2022

THE BTM POLL

מהו נפח העיסוק שלך באוסטאופורוזיס?

78 responses

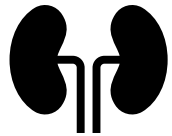


OUTLINE

- Preferred markers, assays, reference values, least significant change
- Guidelines and position statements
- Baseline assessment, treatment follow-up, drug holiday, post DMAB
- CKD-MBD
- Regulatory issues

BONE TURNOVER MARKERS-FULL LIST, SOME NOT USED TODAY

Serum or urine	Measurand
Serum	Procollagen type I *N*-propeptide (PINP)
	C-terminal telopeptide type I collagen (β-CTX)
	Osteocalcin
	Alkaline phosphatase, bone (B-ALP)
	Acid phosphatase tartrate-resistant (TRACP)
Urine	Deoxypyridinoline/creatinine, first morning
	Hydroxyproline/minute—excretion rate, first morning
	N-telopeptide type I collagen concentration

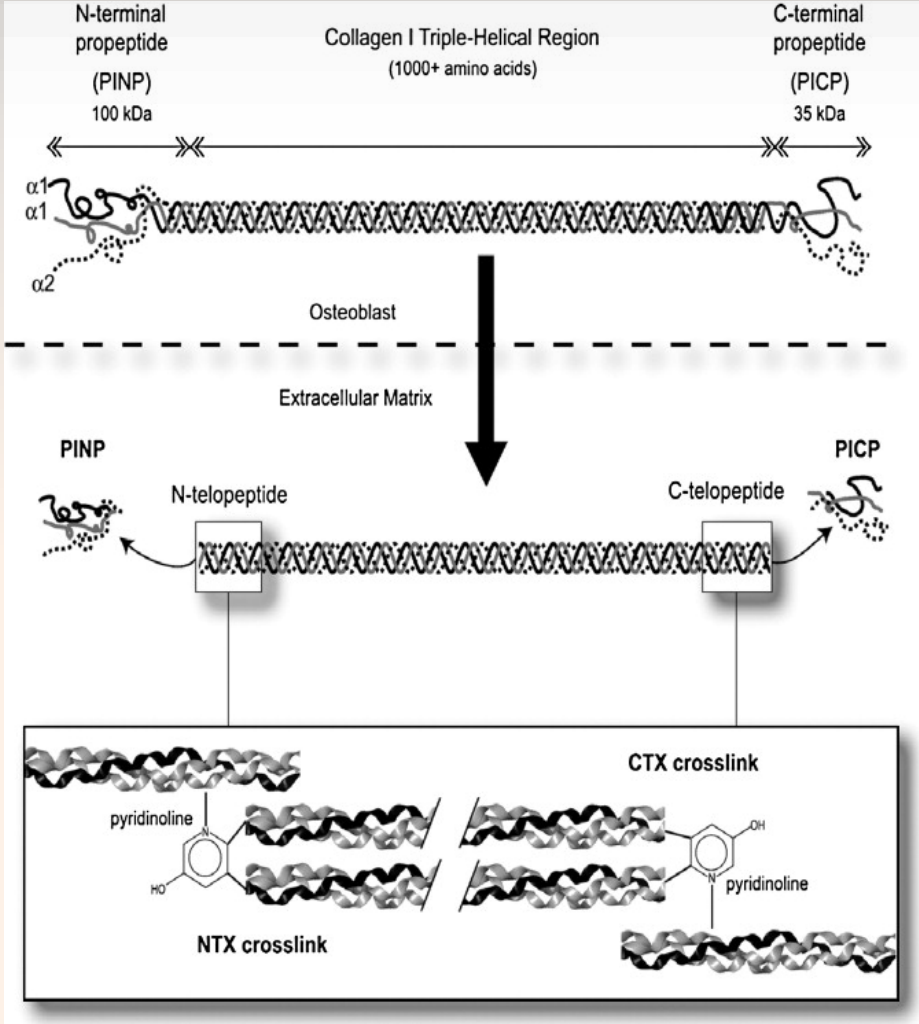


Vasikaran, Samuel D et al. "Practical Considerations for the Clinical Application of Bone Turnover Markers in Osteoporosis." Calcified tissue international, 10.1007/s00223-021-00930-4. 30 Nov. 2021, doi:10.1007/s00223-021-00930-4

PROPEPTIDE AND TELOPEPTIDE

Procollagen type 1 N-propeptide:

P_1NP



C-terminal telopeptide type 1 collagen crosslinking:

CTX

Herrmann, Markus, and Markus J Seibel. "The amino- and carboxyterminal cross-linked telopeptides of collagen type I, NTX-I and CTX-I: a comparative review." Clinica chimica acta; international journal of clinical chemistry vol. 393,2 (2008): 57-75. doi:10.1016/j.cca.2008.03.020

COMMERCIAL AUTOMATED BTM ASSAYS

- **P_1NP**

Table 5 Commonly used commercial immunoassays available for serum PINP measurement (based on Bhattoa et al. [27])

Vendor	Methodology	Measurand	Analytics
Cobas, Roche Diagnostics, Germany	Electrochemiluminescence immunoassay	Total PINP	Automated
iSYS, Immunodiagnostics Systems (IDS), UK	Chemiluminescence immunoassay	Intact PINP	Automated

Table 7 Commonly used commercial assays for β-CTX in blood (based on Bhattoa et al. [27])

Vendor	Methodology	Measurand	Analytics
IDS, UK	Chemiluminescence immunoassay	β-CTX	Automated
Roche Diagnostics, Germany	Electrochemiluminescence immunoassay	β-CTX	Automated

- **CTX**

- **IDS-iSYS (immunodiagnostic systems)- Sheba**
- **Roche –COBAS, Ichilov**

Lorentzon, Mattias et al. "Algorithm for the Use of Biochemical Markers of Bone Turnover in the Diagnosis, Assessment and Follow-Up of Treatment for Osteoporosis." Advances in therapy vol. 36,10 (2019): 2811-2824. doi:10.1007/s12325-019-01063-9

PRE-ANALITICAL VARIABILITY

	Effect	Recommendation	Importance
Controllable sources			
Circadian rhythm	High BTM concentrations at night and early morning, lowest in the afternoon	Collect serum samples in the morning (7.30–10.00 h)	High
Food intake	Decrease in BTMs, especially bone resorption markers (about 20–40%) after food intake	Collect samples of bone resorption markers after overnight fast	High
Fracture	BTMs increase after fracture, with maximum effect 2–12 weeks, but remains elevated up to 52 weeks	Limits evaluation in patients with recent fracture	High
Bed rest/ immobility	Bone resorption markers increase and formation markers decrease	Consider different expected baseline level when evaluating BTMs	High

Lorentzon, Mattias et al. "Algorithm for the Use of Biochemical Markers of Bone Turnover in the Diagnosis, Assessment and Follow-Up of Treatment for Osteoporosis." Advances in therapy vol. 36,10 (2019): 2811-2824. doi:10.1007/s12325-019-01063-9

CTX: COMMERCIAL REFERENCE VALUES

- **IDS-iSYS (immunodiagnostic systems)- Sheba**

Populations	Number of subjects	Mean values (ng/mL)	95% Confidence Interval (ng/mL)
Males	245	0.212	0.038 - 0.724
Pre-menopausal women	94	0.136	0.034 - 0.635
Post-menopausal women	134	0.257	0.034 – 1.037

- **Roche –COBAS, Ichilov (ref)**

GM: geometric mean

Age range (years)	Men			Women		
	N	GM (pg/mL)	95 % RI (pg/mL)	N	GM (pg/mL)	95 % RI (pg/mL)
< 29.9	39	492	238-1019	58	378	148-967
30-39.9	80	459	225-936	111	308	150-635
40-49.9	234	382	182-801	257	296	131-670
50-59.9	248	345	161-737	281	440	183-1060
60-69.9	303	316	132-752	234	408	171-970
>70	135	302	118-776	88	362	152-858
Pre-menopause	-	-	-	449	306	136-689
Post-menopause	-	-	-	578	424	177-1015

Jørgensen, N R et al. "Comparison of two automated assays of BTM (CTX and P1NP) and reference intervals in a Danish population." Osteoporosis international : vol. 28,7 (2017): 2103-2113. doi:10.1007/s00198-017-4026-z

P1NP: COMMERCIAL REFERENCE VALUES

- **IDS-iSYS (immunodiagnostic systems)- Sheba**

Normal Adults 27.7 – 127.6 ng/mL (n = 150)

- **Roche – Ichilov (OFELY study reference)**

	Post-menopausal			Pre-menopausal
	All	HRT[b)] yes	HRT no	All
N	444	154	290	129
5th percentile	16.27	14.28	20.25	15.13
Median	37.09	28.48	42.94	27.80
Mean	40.43	31.74	45.05	30.10
95th percentile	73.87	58.92	76.31	58.59

Garnero, P et al. "Markers of bone turnover predict postmenopausal forearm bone loss over 4 years: the OFELY study." Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research vol. 14,9 (1999): 1614-21. doi:10.1359/jbmr.1999.14.9.1614

Garnero, P et al. "Biochemical markers of bone turnover, endogenous hormones and the risk of fractures in postmenopausal women: the OFELY study." Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research vol. 15,8 (2000): 1526-36. doi:10.1359/jbmr.2000.15.8.1526

REFERENCE VALUES FROM THE DANISH STUDY

Fasting samples from 2308 individuals (1250 males and 1058 females, age range 24–76 years) participating in the Health2006 study were analyzed for CTX and P1NP using IDS-iSYS analyzer and the Cobas-Roche, people with osteoporotic treatment were excluded

Gender	Age group (years)	iSYS IDS		Cobas Roche	
		P1NP (µg/L)	CTX (ng/L)	P1NP (µg/L)	CTX (ng/L)
Men	25–29.9	30–126	202–1436	32–123	238–1019
	30–30.9	30–104	180–1340	32–106	225–936
	40–80	19–82	90–1086	19–90	146–778
Women	25–29.9	16–142	91–1318	18–170	148–967
	≥30. pre-menopausal	18–87	70–920	19–92	137–643
	≥30, post-menopausal	22–114	125–1477	23–125	177–1015

Jørgensen, N R et al. "Comparison of two automated assays of BTM (CTX and P1NP) and reference intervals in a Danish population." Osteoporosis international : vol. 28,7 (2017): 2103-2113. doi:10.1007/s00198-017-4026-z

VARIABILITY, LEAST SIGNIFICANT CHANGE (REFERENCE CHANGE VALUES)

- **"The statement that BTMs are bedevilled by large intra-individual variation has become accepted as fact, but we argue that this is not the whole picture and the effect of biological variation on BTMs should be treated in a nuanced way"**
- **European biological variation study (2020), 91 subjects from 6 labs, fasting blood samples were obtained weekly for 10 weeks and CV and LSC were calculated**

Table 4 Intra individual variation [within-subject (CV_I) biological variation (BV)] estimates for the reference BTMs for osteoporosis, PINP and β-CTX, with 95% confidence interval (CI), based on Cavalier et al. [25]

Measurand	Mean value (95% CI)	CV_A % (95% CI)[a]	CV_I % (95% CI)
PINP, µg/L	63.7 (62.3–65.0)	3.7 (3.6–3.9)	8.8 (8.4–9.3)
β-CTX, ng/L	514.3 (499.5–529.1)	5.0 (4.8–5.3)	15.1 (14.4–16.0)

[a]Analytical variation (CV_A) estimates were based on CV-ANOVA of duplicate analysis of all study samples

LSC

Measurand	RCV (%)
PINP	– 19.9
β-CTX	– 30.8

Vasikaran, Samuel D et al. "Practical Considerations for the Clinical Application of Bone Turnover Markers in Osteoporosis." Calcified tissue international, 10.1007/s00223-021-00930-4. 30 Nov. 2021, doi:10.1007/s00223-021-00930-4

Cavalier, E et al. "European Biological Variation Study (EuBIVAS): within- and between-subject biological variation estimates of β-isomerized C-terminal telopeptide of type I collagen (β-CTX), N-terminal propeptide of type I collagen (PINP), osteocalcin, intact fibroblast growth factor 23 and uncarboxylated-unphosphorylated matrix-Gla protein-a cooperation between the EFLM Working Group on Biological Variation and the International Osteoporosis Foundation-International Federation of Clinical Chemistry Committee on Bone Metabolism." Osteoporosis international vol. 31,8 (2020): 1461-1470. doi:10.1007/s00198-020-05362-8

OUTLINE

- Preferred markers, assays, reference values, least significant change
- **Guidelines and position statements**
- **Baseline assessment, treatment follow-up, drug holiday, post DMAB**
- **CKD-MBD**
- **Regulatory issues**

TIMELINE OF GUIDELINES/POSITION STATEMENTS – SPECIFIC TO BONE TURNOVER MARKERS

- **2000: IOF[1]**

"Their clinical use in the management of the individual patient is not clearly defined and is a matter of debate"

- **2011: IOF-NOF-IFCC[2] (CTX and P1NP preferred)**

"BTM hold promise in fracture risk prediction and for monitoring treatment. Uncertainties over their clinical use can be in part resolved by adopting international reference standards"

- **2017: IOF-ESCEO (BP adherence)[3]**

"the working group recommends measuring PINP and CTX at baseline and 3 months after starting oral BP therapy to check for a decrease above the least significant change"

- **2019: ESCEO[4]**

"In conclusion, the currently available evidence indicates that the principal clinical utility of BTMs is for monitoring oral bisphosphonate therapy".

1. Delmas, P D et al. "The use of biochemical markers of bone turnover in osteoporosis. Committee of Scientific Advisors of the International Osteoporosis Foundation." OI vol. 11 Suppl 6 (2000): S2-17. doi:10.1007/s001980070002

2. Vasikaran, S et al. "Markers of bone turnover for the prediction of fracture risk and monitoring of osteoporosis treatment: a need for international reference standards." Osteoporosis international vol. 22,2 (2011): 391-420. doi:10.1007/s00198-010-1501-1

3. Diez-Perez, A et al. "International Osteoporosis Foundation and European Calcified Tissue Society Working Group. Recommendations for the screening of adherence to oral bisphosphonates." Osteoporosis international vol. 28,3 (2017): 767-774. doi:10.1007/s00198-017-3906-6

4. Lorentzon, Mattias et al. "Algorithm for the Use of Biochemical Markers of Bone Turnover in the Diagnosis, Assessment and Follow-Up of Treatment for Osteoporosis." Advances in therapy vol. 36,10 (2019): 2811-2824. doi:10.1007/s12325-019-01063-9

RECENT GUIDELINES

European guidance for the diagnosis and management of osteoporosis in postmenopausal women

J.A. Kanis [1,2] • C. Cooper [3,4] • R. Rizzoli [5] • J.-Y. Reginster [6,7] • on behalf of the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF)

- **European 2018[1]**

"BTM have some prognostic significance for fracture in situations where BMD is unavailable"

"Patients may be encouraged to adhere when presented with measurements of biochemical markers of bone turnover together with an explanation of how these measures relate to risk reduction."

"Despite limited evidence, failure of treatment may be inferred when /// serial measurements of bone turnover markers are not suppressed by anti-resorptive therapy"

Table 10 Routine procedures proposed in the investigation of osteoporosis. From [2], with kind permission from Springer Science and Business Media

Routine
History including the FRAX clinical risk factors
Examination including height and weight
Blood cell count, sedimentation rate, serum calcium, albumin, creatinine, phosphate, alkaline phosphatase and liver transaminases
Lateral radiograph of lumbar and thoracic spine
Bone densitometry (dual energy X-ray absorptiometry at hip and spine)
Other procedures
Lateral imaging DXA for vertebral fracture assessment (VFA)
Markers of bone turnover, when available

Kanis, J A et al. "European guidance for the diagnosis and management of osteoporosis in postmenopausal women." Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA vol. 30,1 (2019): 3-44. doi:10.1007/s00198-018-4704-5

RECENT GUIDELINES

Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society* Clinical Practice Guideline

Richard Eastell,[1] Clifford J. Rosen,[2] Dennis M. Black,[3] Angela M. Cheung,[4] M. Hassan Murad,[5] and Dolores Shoback[6,7]

- **Endocrine society 2019[1]**

"Monitoring bone turnover markers is an alternative way of identifying poor response or nonadherence to therapy"

"Monitoring treatment with BTMs requires attention to detail. Changes can be compared only if the laboratory continues to use the same assay"

"Some experts recommend measuring BTMs before and 3 to 6 months after starting treatment. If the change in markers exceeds the least significant change (40%), then one goal has been met. In women, a low risk of fractures while on treatment is associated with BTMs that are below the median of the reference interval for young women."

Eastell, Richard et al. "Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society* Clinical Practice Guideline." The Journal of clinical endocrinology and metabolism vol. 104,5 (2019): 1595-1622. doi:10.1210/jc.2019-00221

RECENT GUIDELINES

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/ AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS— 2020 UPDATE

Pauline M. Camacho, MD, FACE[1]; Steven M. Petak, MD, JD, FACP, FCLM, MACE, CCD[2]; Neil Binkley, MD[3]; Dima L. Diab, MD, FACE, FACP, CCD[4]; Leslie S. Eldeiry, MD[5]; Azeez Farooki, MD[6]; Steven T. Harris, MD, FACP, FASBMR[7]; Daniel L. Hurley, MD, FACE[8]; Jennifer Kelly, DO, FACE[9]; E. Michael Lewiecki, MD, FACE, FACP, CCD[10]; Rachel Pessah-Pollack, MD, FACE[11]; Michael McClung, MD, FACP, FACE[12]; Sunil J. Wimalawansa, MD, PhD, MBA, FCCP, FACP, FRCP, DSc, FACE[13]; Nelson B. Watts, MD, FACP, CCD, FASBMR, MACE[14]

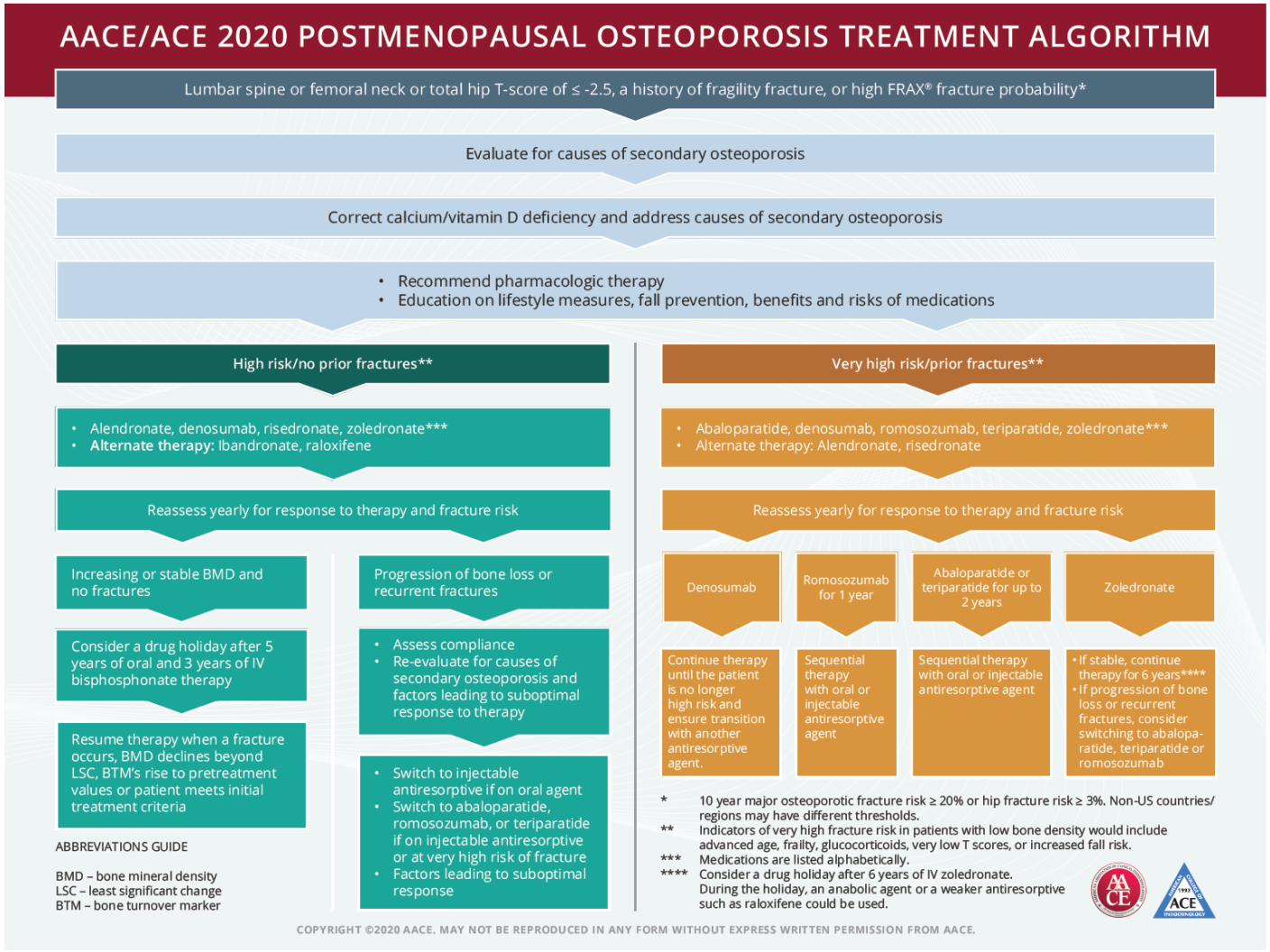
- **AACE/ACE 2020**

"An additional potential use of BTMs is in the setting of a bisphosphonate drug holiday, where highly suppressed bone turnover (as compared with a baseline value) indicates continued antiresorptive effect and, theoretically, continued antifracture benefit. However, presently, there are no peer-reviewed trials supporting or refuting this approach"

Camacho, Pauline M et al. "AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS- 2020 UPDATE EXECUTIVE SUMMARY." Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists vol. 26,5 (2020): 564-570. doi:10.4158/GL-2020-0524

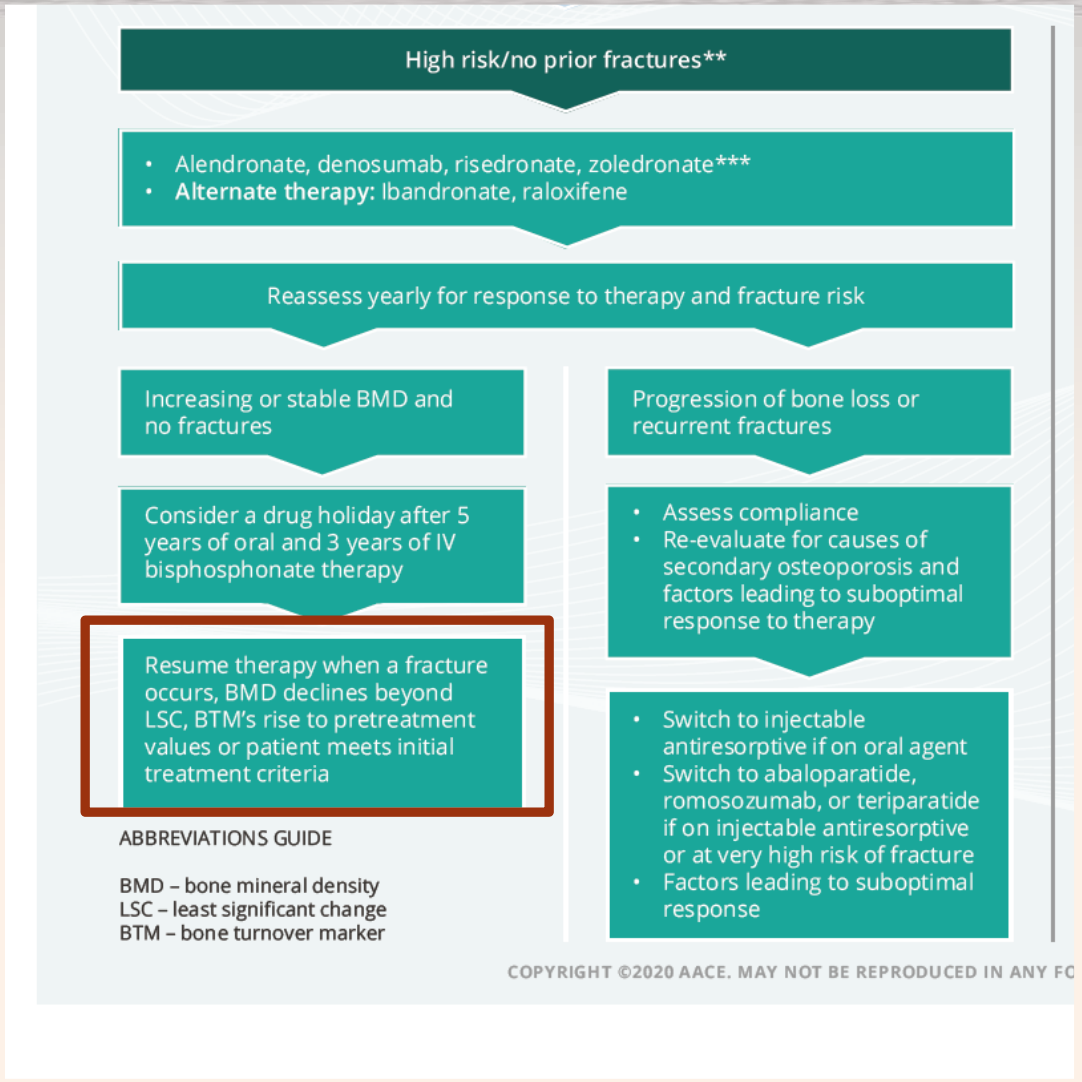
BEL: best evidence level

RECENT GUIDELINES



Camacho, Pauline M et al. "AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS- 2020 UPDATE EXECUTIVE SUMMARY." Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists vol. 26,5 (2020): 564-570. doi:10.4158/GL-2020-0524

RECENT GUIDELINES

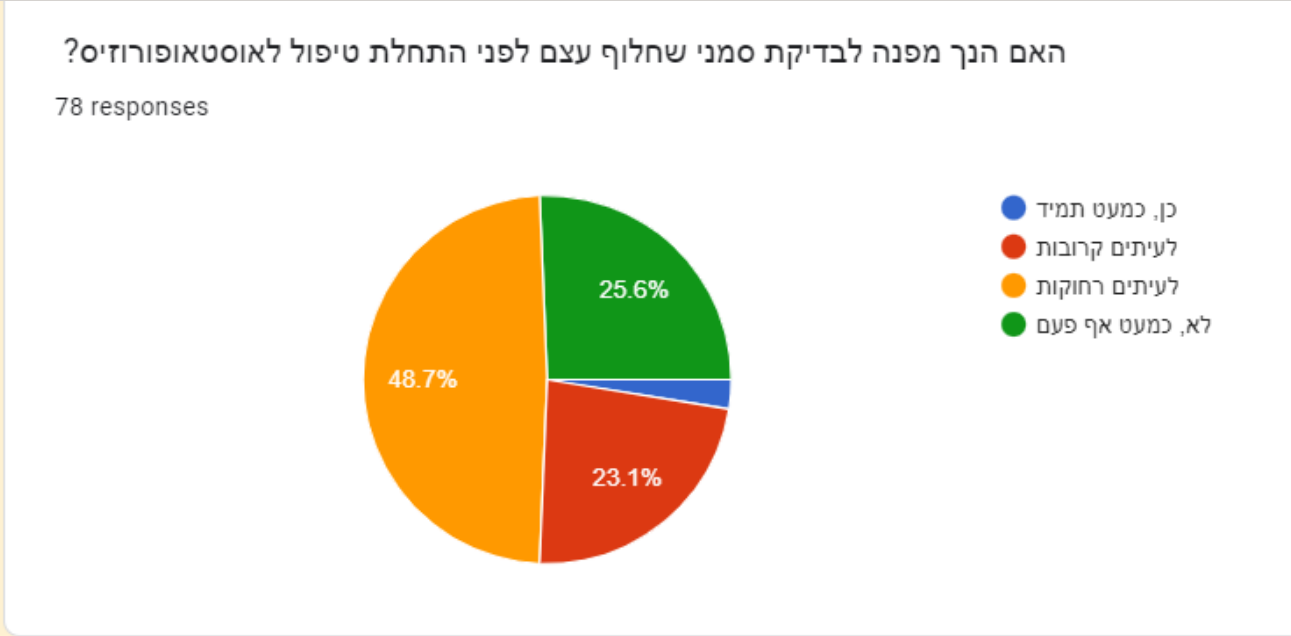


Camacho, Pauline M et al. "AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS- 2020 UPDATE EXECUTIVE SUMMARY." Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists vol. 26,5 (2020): 564-570. doi:10.4158/GL-2020-0524

OUTLINE

- Preferred markers, assays, reference values, least significant change
- Guidelines and position statements
- **Baseline assessment, treatment follow-up, drug holiday, post DMAB**
- **CKD-MBD**
- **Regulatory issues**

BASELINE

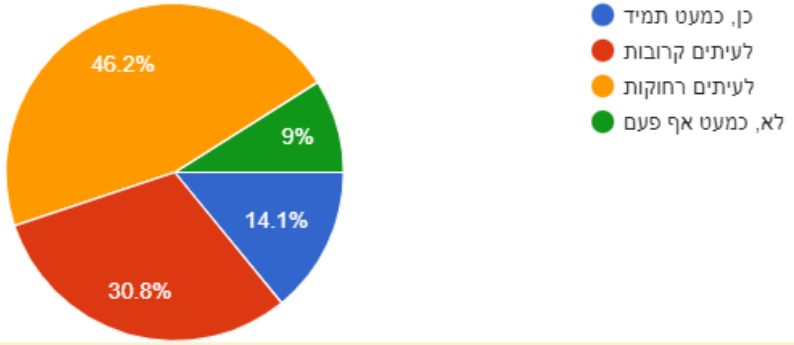


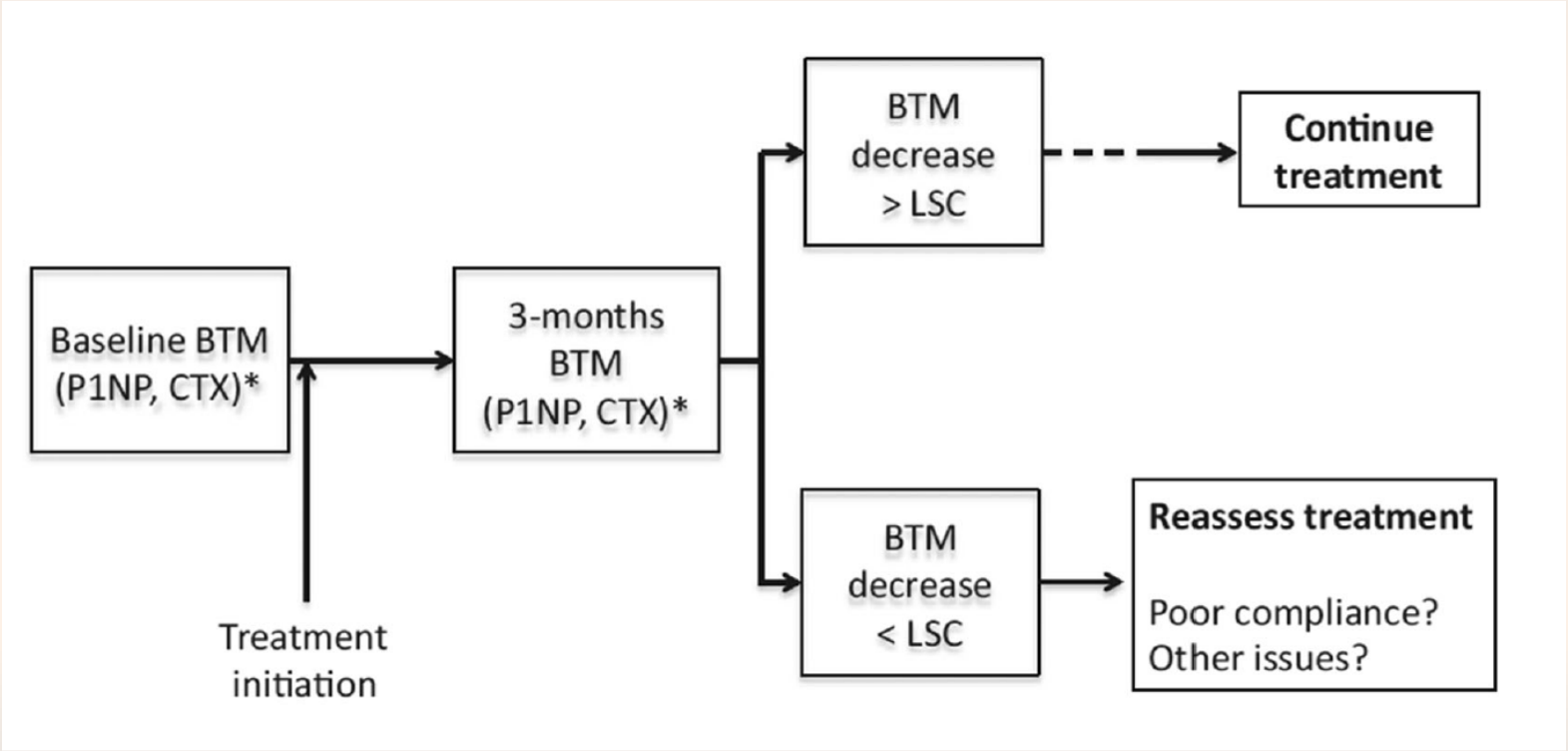
- **To create baseline for follow-up**
- **To detect high turnover that will raise a suspicion of a secondary cause**
- **To improve fracture prediction (although not clinically mandatory)**

ORAL BP FOLLOW-UP

האם הנך מפנה לבדיקת סמני שחלוף עצם לבחינת היענות ויעילות הטיפול בביספוספונטים פומיים?

78 responses



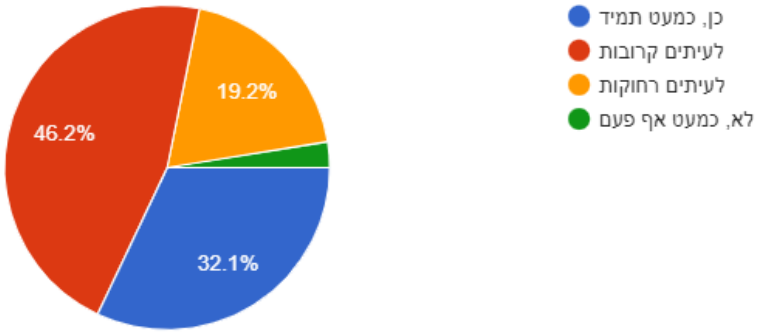


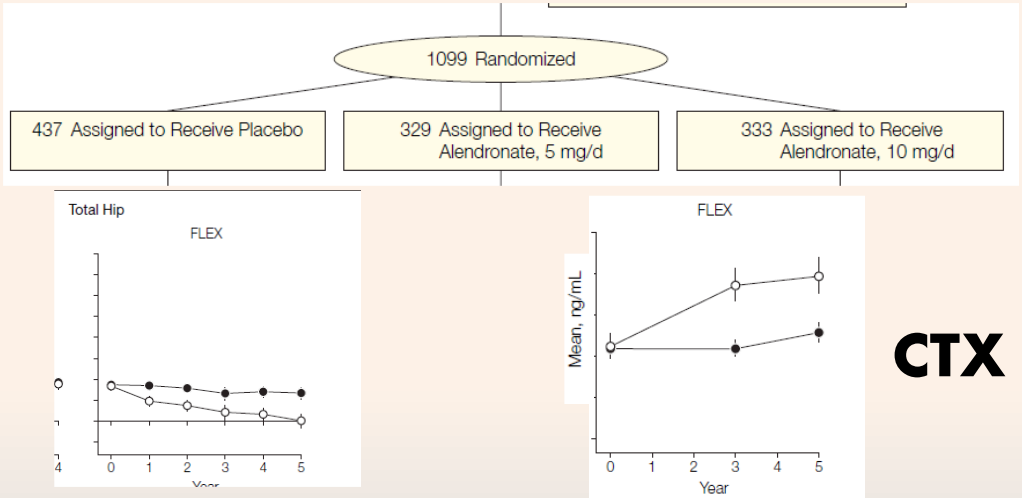
Lorentzon, Mattias et al. "Algorithm for the Use of Biochemical Markers of Bone Turnover in the Diagnosis, Assessment and Follow-Up of Treatment for Osteoporosis." Advances in therapy vol. 36,10 (2019): 2811-2824. doi:10.1007/s12325-019-01063-9

DRUG HOLIDAY

האם הנך מפנה לבדיקת סמני שחלוף עצם להחלטה על "חופשה טיפולית" מביספוספונטים פומיים ועל חידוש הטיפול?

78 responses



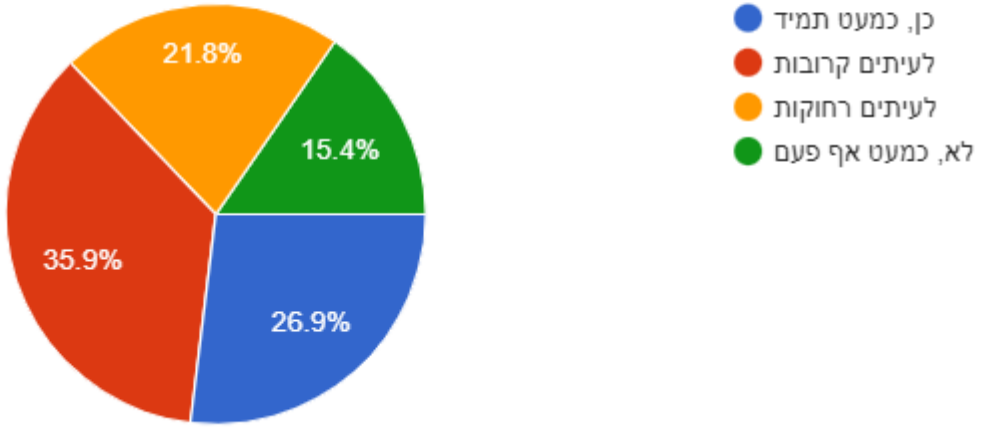


Black, Dennis M et al. "Effects of continuing or stopping alendronate after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (FLEX): a randomized trial." JAMA vol. 296,24 (2006): 2927-38. doi:10.1001/jama.296.24.2927

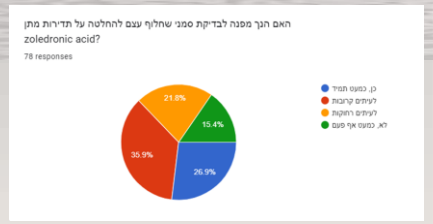
ZOLEDRONIC ACID FREQUENCY

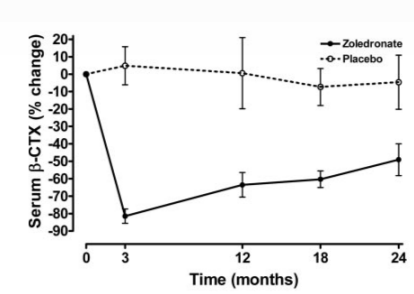
האם הנך מפנה לבדיקת סמני שחלוף עצם להחלטה על תדירות מתן zoledronic acid?

78 responses



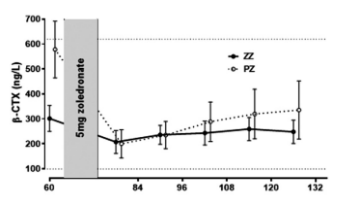
(VERY) PROLONGED ANTIRESORPTIVE EFFECT OF ZA





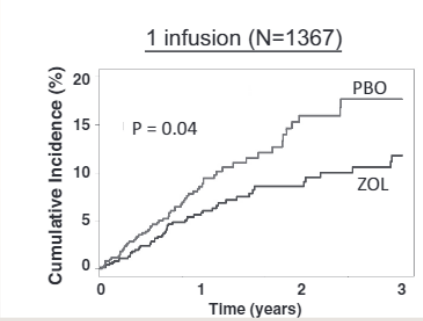
- **25 postmenopausal women, follow-up following single ZOL, CTX remained low**

Grey, Andrew et al. "The antiresorptive effects of a single dose of zoledronate persist for two years: a randomized, placebo-controlled trial in osteopenic postmenopausal women." The Journal of clinical endocrinology and metabolism vol. 94,2 (2009): 538-44. doi:10.1210/jc.2008-2241



- **33 women, 5 years of follow-up following a single ZOL**

Grey, Andrew et al. "Ten Years of Very Infrequent Zoledronate Therapy in Older Women: An Open-Label Extension of a Randomized Trial." *The Journal of clinical endocrinology and metabolism* vol. 105,4 (2020): dgaa062. doi:10.1210/clinem/dgaa062



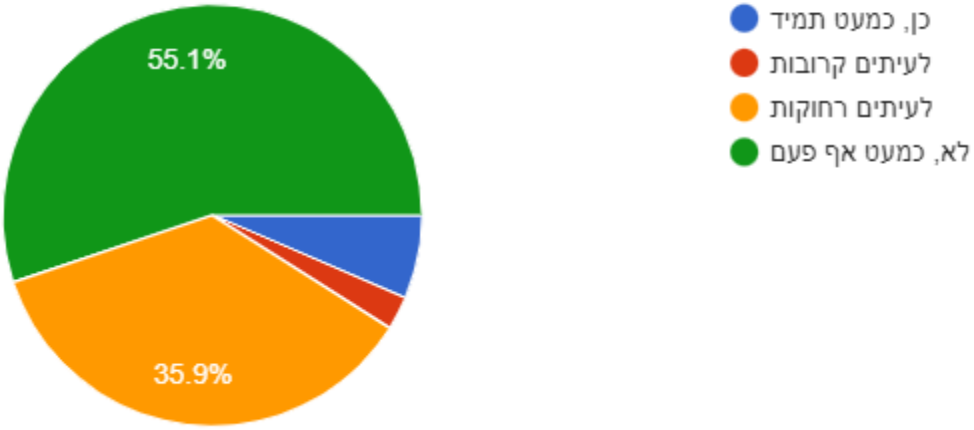
- **Post-hoc, 1367 subjects from HORIZON and HORIZON-HIP, receiving single ZOL of the three planned, all clinical fractures 30 % less**

Reid, I R et al. "Reduction in the risk of clinical fractures after a single dose of zoledronic Acid 5 milligrams." *The Journal of clinical endocrinology and metabolism* vol. 98,2 (2013): 557-63. doi:10.1210/jc.2012-2868

BTM ON TERIPARATIDE

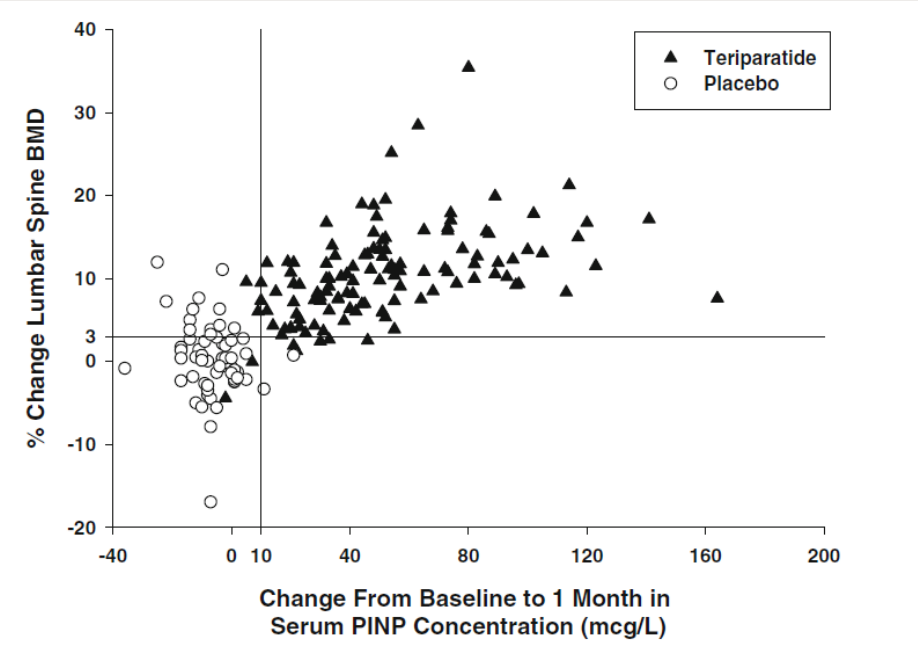
האם הנך מפנה לבדיקת סמני שחלוף עצם למעקב אחרי השפעת teriparatide?

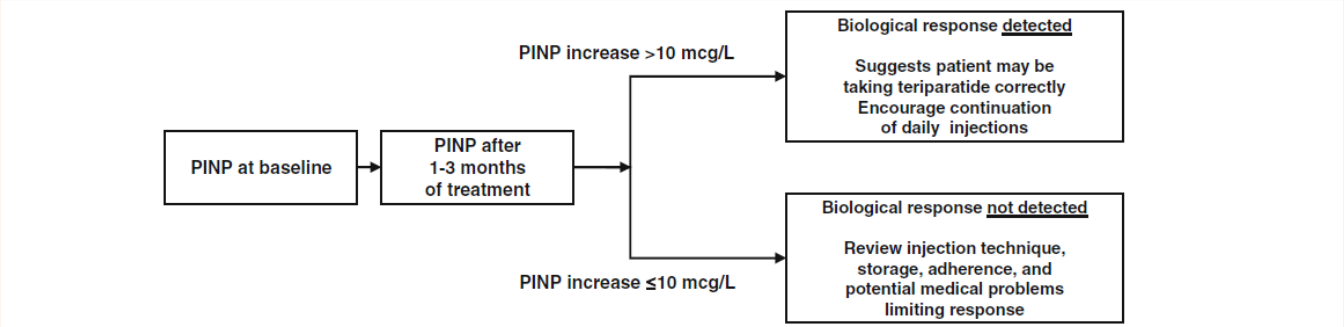
78 responses



BTM ON TERIPARATIDE

- **Japanese study, 207 patients randomized to TPTD or placebo for 12 month**





Krege, J H et al. "PINP as a biological response marker during teriparatide treatment for osteoporosis." Osteoporosis international vol. 25,9 (2014): 2159-71. doi:10.1007/s00198-014-2646-0

Tsujimoto, Mika et al. "PINP as an aid for monitoring patients treated with teriparatide." Bone vol. 48,4 (2011): 798-803. doi:10.1016/j.bone.2010.12.006

PTH 1-34 ANALOGS

Bio-similar

PK/PD

efficacy+

טרוזה
TERROSA
מרכיב פעיל: TERIPARATIDE 250 MCG/ML
צורת מינון: תמיסה להזרקה
מספר רישום מלא: 00 163 82 35787
שם בעל הרישום: DEXCEL LTD, ISRAEL

לפרטים נוספים
בסל הבריאות
לתכשירים עם חומר פעיל זהה

Chemo-similar

PK/PD

טריפראטייד טבע ®
TERIPARATIDE TEVA ®
מרכיב פעיל: TERIPARATIDE AS ACETATE 250 MCG/ML
צורת מינון: תמיסה להזרקה
מספר רישום מלא: 00 163 24 35333
שם בעל הרישום: ABIC MARKETING LTD, ISRAEL

לפרטים נוספים
בסל הבריאות
לתכשירים עם חומר פעיל זהה

פורטאו זריקות
FORTEO INJECTION
מרכיב פעיל: TERIPARATIDE 250 MCG/ML
צורת מינון: תמיסה להזרקה
מספר רישום מלא: 00 129 28 30777
שם בעל הרישום: ELI LILLY ISRAEL LTD, ISRAEL

לפרטים נוספים
בסל הבריאות
לתכשירים עם חומר פעיל זהה

Different regulatory pathways

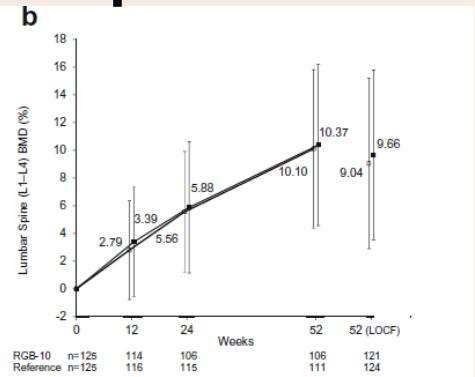
https://data.health.gov.il/Drugs/index.html#!/byDrug

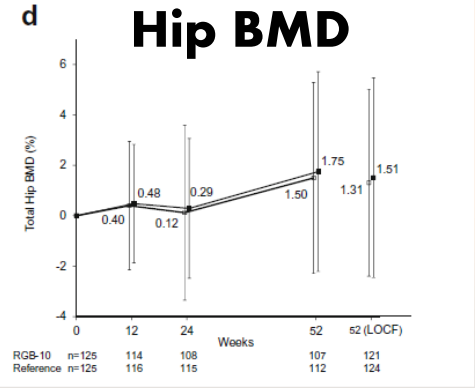
BIOSIMILAR

A multicenter, randomized, rater-blinded, parallel-group, phase 3 study to compare the efficacy, safety, and immunogenicity of biosimilar RGB-10 and reference once-daily teriparatide in patients with osteoporosis

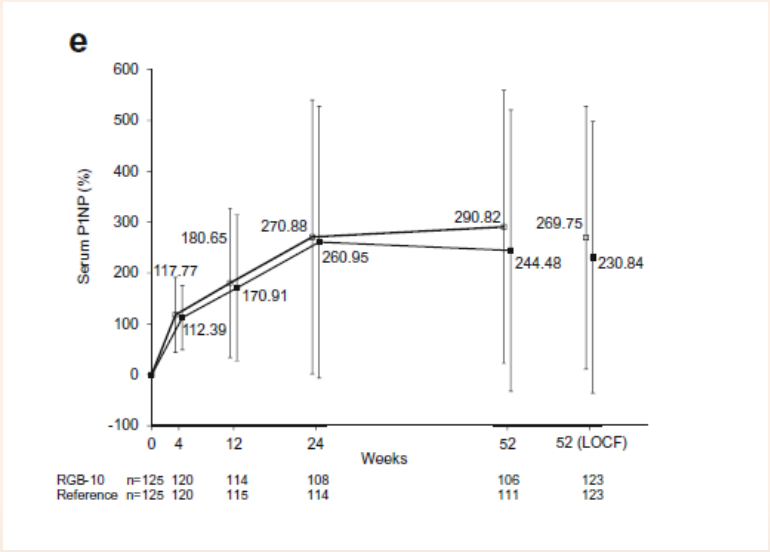
H. Hagino[1] · R. Narita[2] · Y. Yokoyama[2] · M. Watanabe[2] · M. Tomomitsu[2]

Spine BMD



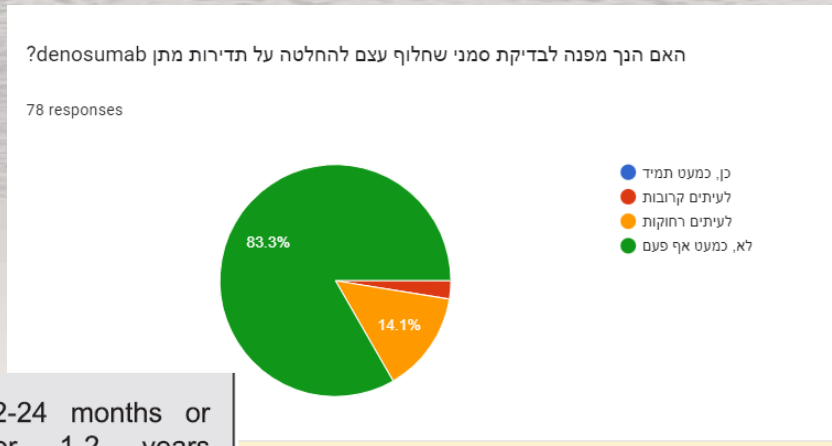


250 women and men, 52 weeks



Osteoporosis International (2019) 30:2027–2037
https://doi.org/10.1007/s00198-019-05038-y

DMAB



- **For DMAB discontinuation**

Denosumab treatment for short duration [i.e. up to 2.5 years] and low fracture risk → Switch to oral BPs for 12-24 months or administer zoledronate for 1-2 years depending on re-evaluation of BTMs and BMD

Denosumab treatment for long duration [i.e. more than 2.5 years] and/ or high fracture risk →

Continue denosumab for up to 10 years [Individualized decision after that timepoint]

Switch to zoledronate:

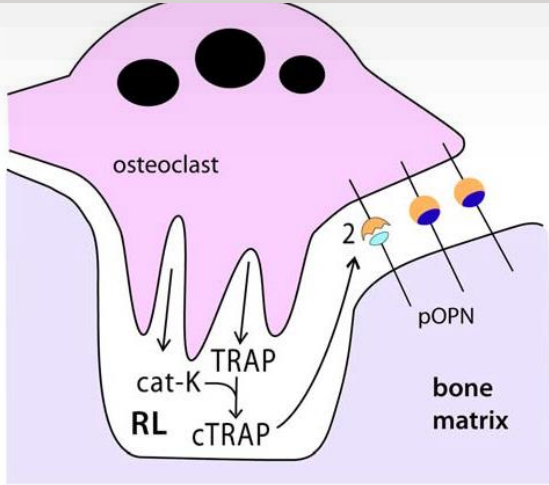
Begin 6 months after last denosumab injection and measure BTMs 3 and 6 months later. Consider repeated infusion of zoledronate in case of persistently increased BTMs

In case BTMs are not available administer zoledronate 6 and 12 months after last denosumab injection

If zoledronate is not an option due to availability, patient preference or intolerance: treat with oral BPs for 12-24 months depending on re-evaluation of BTMs and BMD

Tsourdi, Elena et al. "Fracture risk and management of discontinuation of denosumab therapy: a systematic review and position statement by ECTS." The Journal of clinical endocrinology and metabolism, dgaa756. 26 Oct. 2020, doi:10.1210/clinem/dgaa756

CKD-MBD



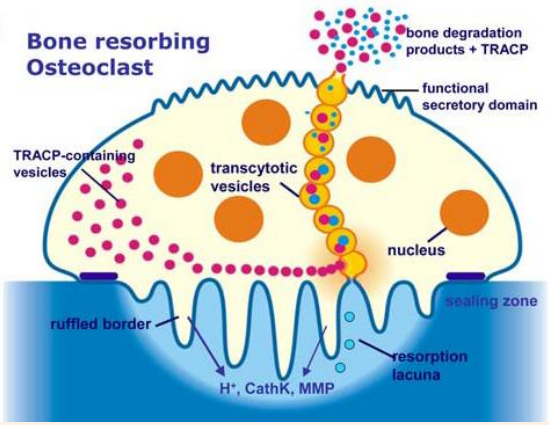


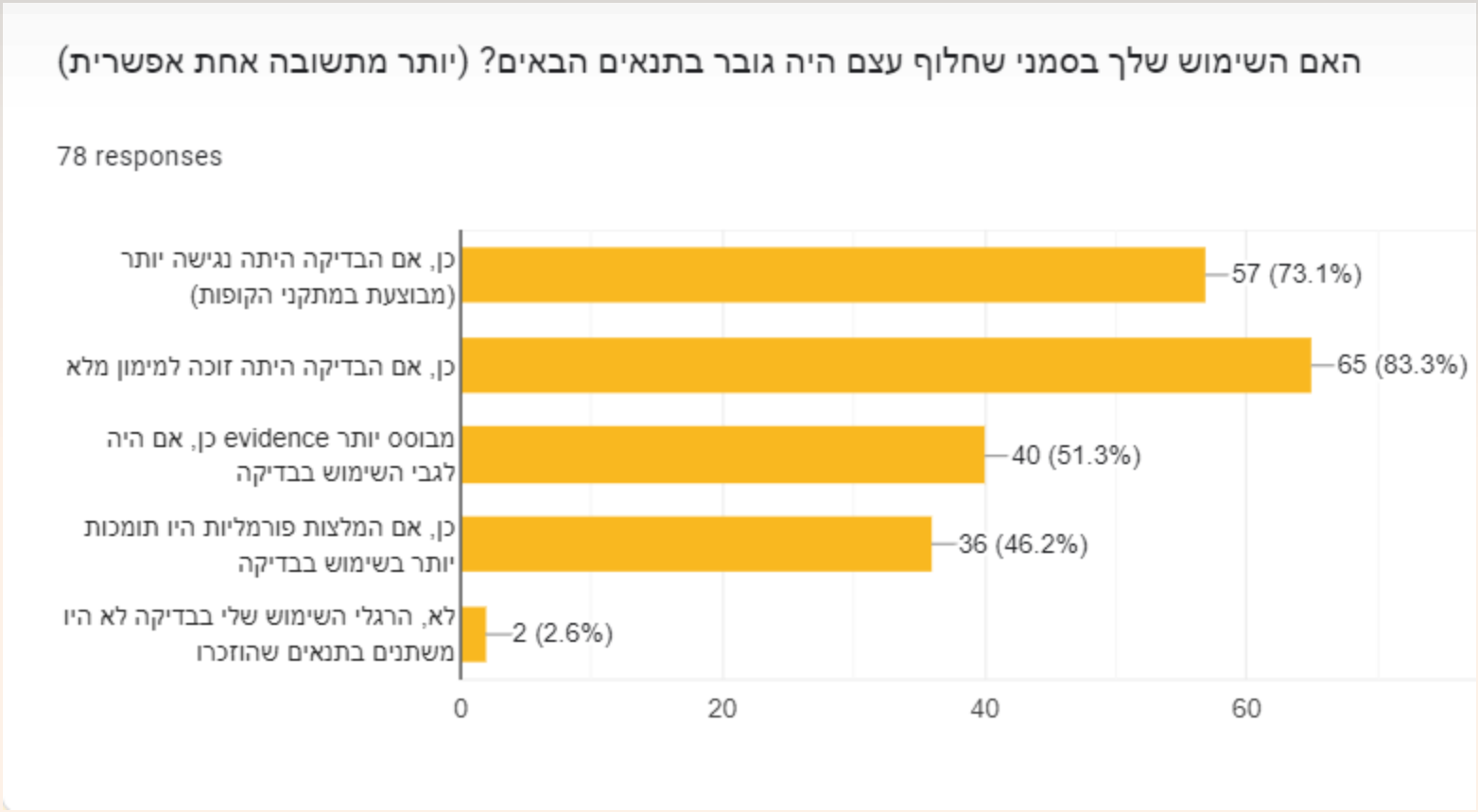
Table 1 Reference BTMs for osteoporosis, and BTMs least affected by renal failure

	Formation markers	Resorption markers
Reference BTMs in osteoporosis	PINP	β-CTX
BTMs least affected by renal failure	B-ALP	TRACP-5b

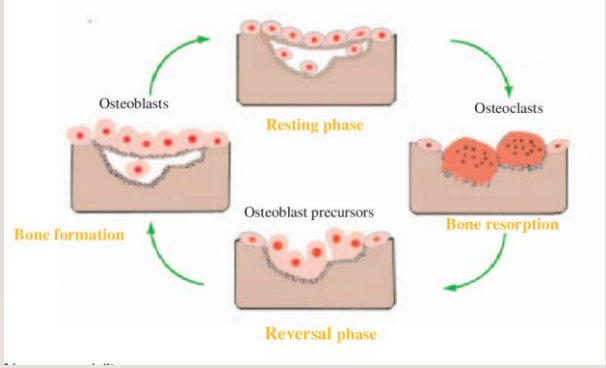
Janckila, Anthony J, and Lung T Yam. "Biology and clinical significance of tartrate-resistant acid phosphatases: new perspectives on an old enzyme." Calcified tissue international vol. 85,6 (2009): 465-83. doi:10.1007/s00223-009-9309-8

Vasikaran, Samuel D et al. "Practical Considerations for the Clinical Application of Bone Turnover Markers in Osteoporosis." Calcified tissue international, 10.1007/s00223-021-00930-4. 30 Nov. 2021, doi:10.1007/s00223-021-00930-4

REGULATORY


האם השימוש שלך בסמני שחלוף עצם היה גובר בתנאים הבאים? (יותר מתשובה אחת אפשרית)
78 responses
כן, אם הבדיקה היתה נגישה יותר (מבוצעת במתקני הקופות)
57 (73.1%)
כן, אם הבדיקה היתה זוכה למימון מלא
65 (83.3%)
כן, אם היה מבוסס יותר evidence לגבי השימוש בבדיקה
40 (51.3%)
כן, אם המלצות פורמליות היו תומכות יותר בשימוש בבדיקה
36 (46.2%)
לא, הרגלי השימוש שלי בבדיקה לא היו משתנים בתנאים שהוזכרו
2 (2.6%)
0
20
40
60

REGULATORY



הזכאות לבדיקת מדדים ביוכימיים של תחלופת העצם (CTX)

סוגיה נוספת בה עסקנו בשנת 2020 היא הזכאות לבדיקת מדדים ביוכימיים של תחלופת העצם (CTX). הסוגיה עלתה מתוך קבילה שהתבררה בנציבות. באותו מקרה הבדיקה נדרשה למטופלת הסובלת ממחלת ארתריטיס במסגרת קבלת טיפול תרופתי למעקב אחר התגובה הטיפולית והערכת הטיפול. **הכרעת נציבות הקבילות הייתה כי הבדיקה מקובלת בישראל ובעולם**, חיונית ויעילה באבחון מצבים רפואיים הקשורים בעליה בתחלופת עצם, ובמעקב והערכת יעילות טיפולים תרופתיים בחולי אוסטאופורוזיס. היא מומלצת על ידי האיגוד האנדוקרינולוגי ונמצאת בשימוש קליני. הבדיקה כלולה בסל השירותים הציבורי ועל קופת החולים לספק אותו במקרים המתאימים בהם היא נדרשת מבחינה רפואית.

SUMMARY

- The modern automated assays are more reliable, the CV and LSC are lower than previously postulated (pre-analitic conditions!)
- Well-validated reference range should be used, and serial measurements preferably performed by the same method
- Baseline measurement can be of value to allow further monitoring, identification of pathological high turnover states and maybe to improve fracture prediction
- Both LSC and lower half of the premenopausal range are acceptable approaches for monitoring oral BP treatment
- BTM can aid in drug holiday-related decisions
- Although not formally recommended, a less frequent ZOL can be considered, possibly guided by BTMs
- Some support TPTD anabolic effect monitoring
- Crucial in DMAB – BP transition monitoring to identify rebound
- Perhaps we need to balance the need for evidence with an understanding that this evidence is not going to emerge soon (or ever)?

תודה רבה