

Traitement de l'ostéoporose : est-ce finalement mieux de combinaison ?

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JOURNÉE SCIENTIFIQUE DU GRIO

Options thérapeutiques en 2014

1 - Anti-ostéoclastiques

- Estrogènes
- SERMs: Raloxifène
- Bisphosphonates : Alendronate, Risédronate, *Ibandronate*, Acide zolédronique
- Ac anti-RANK ligand : Dénosumab

2 - Ostéoformateurs

- Tériparatide

3 - Autres (pas d'effet sur le remodelage osseux)

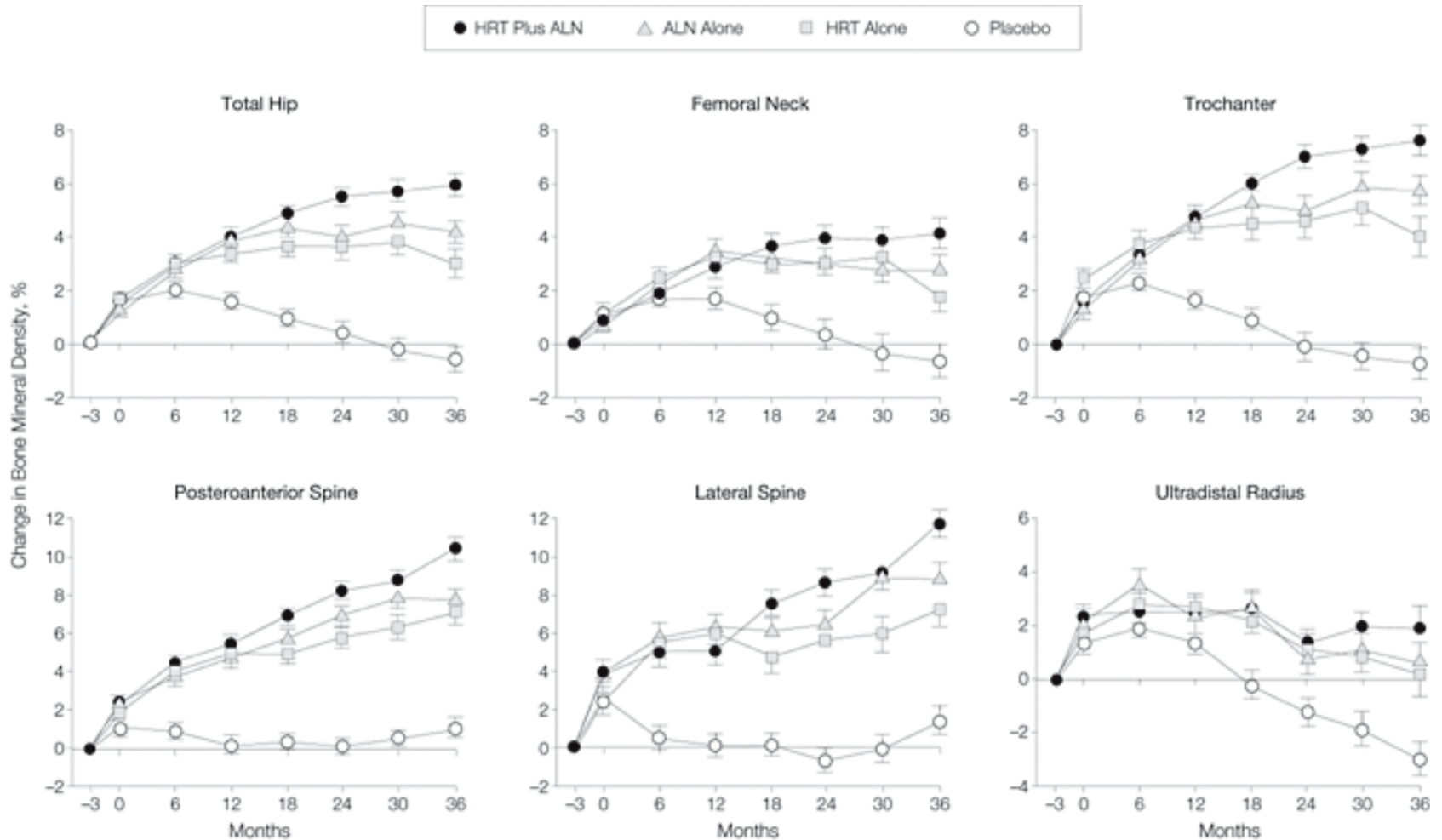
- Ranélate de strontium

Impact osseux des traitements

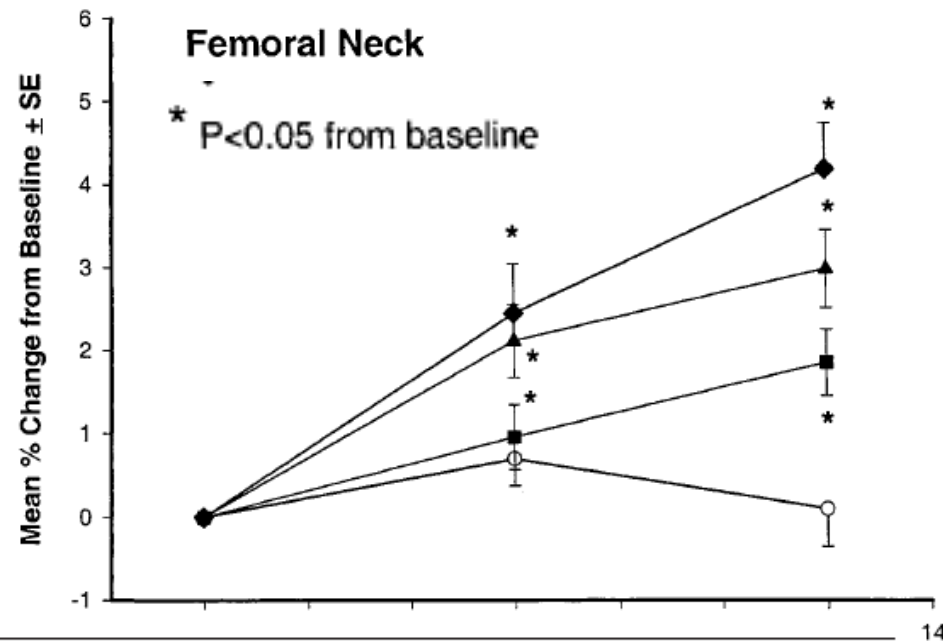
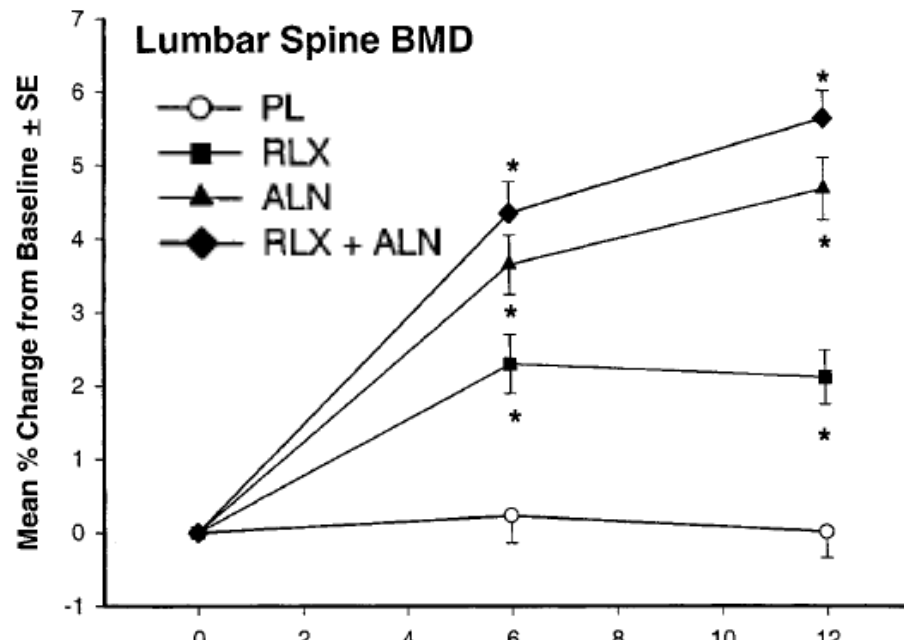
	Variation DMO vertébrale ⁽¹⁾	Efficacité FV	Efficacité FNV
Estrogènes	+ 4-5 %	+	+
Raloxifène	+ 2-3 %	+	-
BPs	+ 3-6 %	+	+
Ac antiRankL	+ 6-7 %	+	+
Tériparatide	+ 8-10 %	+	-
Ran. Strontium	+ 8-9 %	+	+/-

(1) Variation de la DMO vertébrale à 2 ans

Les 1ères associations : THM + ALN



Les 1ères associations : RLX + ALN



Variable	RLX ^a	ALN ^a	RLX + ALN Interaction ^a	Additive? ^b
Lumbar spine BMD	<0.001	<0.001	0.153	Yes
Femoral neck BMD	0.008	<0.001	0.654	Yes
OC	<0.001	<0.001	0.150	Yes
BSAP	0.009	<0.001	0.078	No
CTx/Cr	<0.001	<0.001	0.499	Yes
NTx/Cr	<0.001	<0.001	0.053	No

^a P values were obtained from a two-way ANOVA analysis model on rank transformed data.

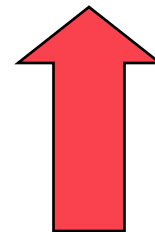
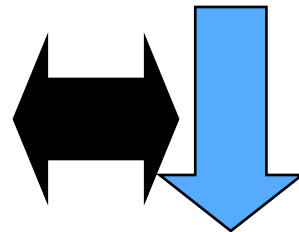
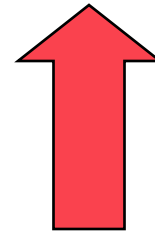
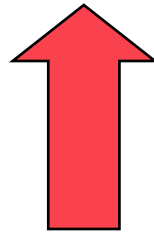
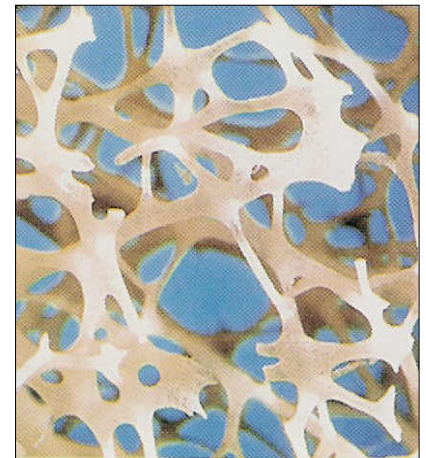
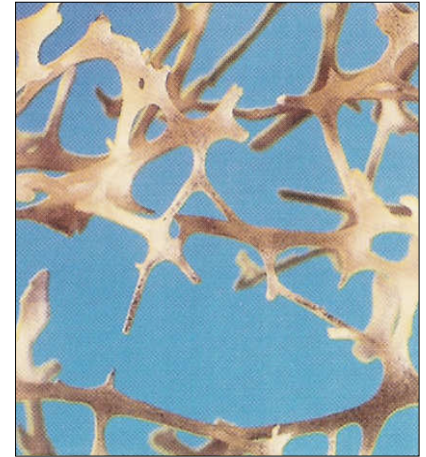
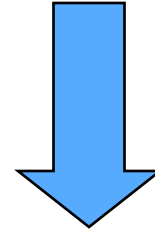
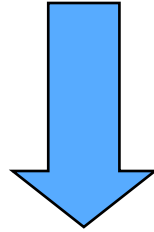
^b The effects of RLX and ALN were considered to be additive and independent of each other if the interaction effect was not statistically significant ($P > 0.10$).

Catégories

Résorption Formation

↓ Remodelage
osseux

E, SERMs, BP, AcRankL



↑ Remodelage
osseux

*Tériparatide
PTH*

Combinaison

Les associations avec PTH et PTH(1-34)

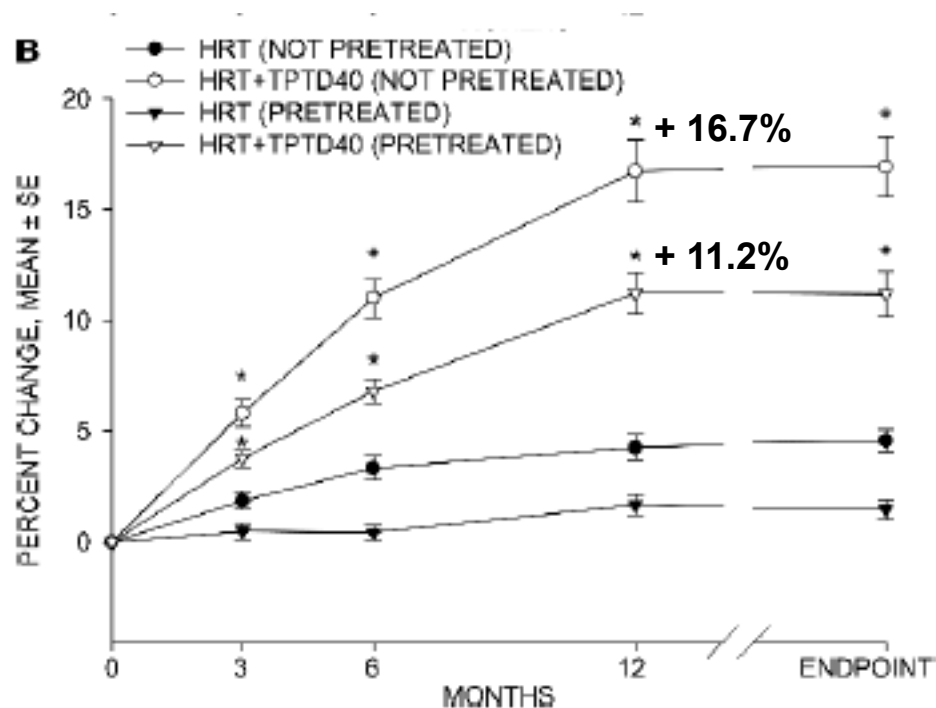
- En association avec les antiostéoclastiques d'emblée ou en complément d'un tt préalable :

THM	+ PTH/PTH(1-34)
Raloxifène	+ PTH(1-34)
Alendronate	+ PTH/PTH(1-34)
Acide zolédronique	+ PTH(1-34)

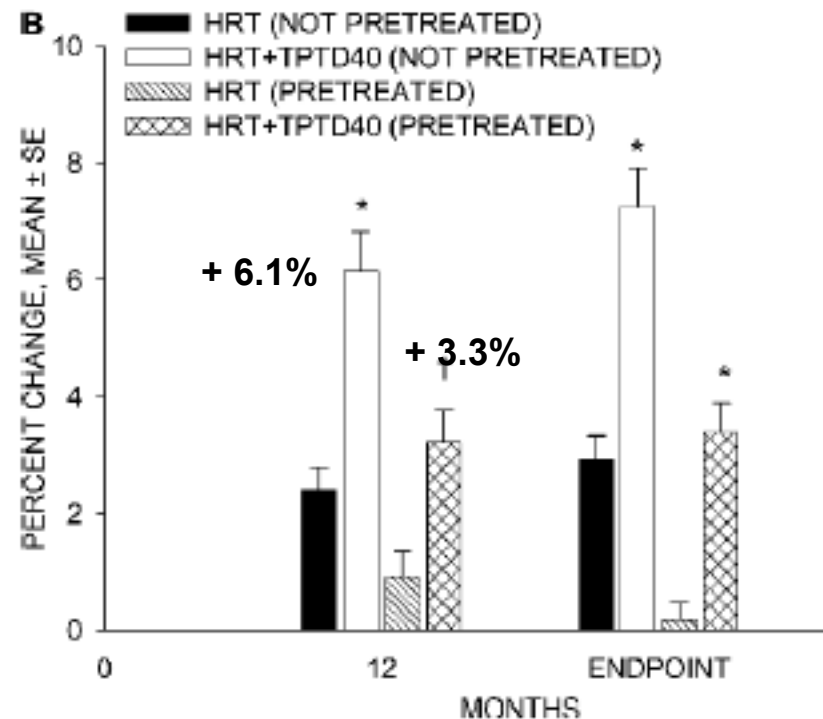
- Traitement par PTH(1-34) préalable :
 - + Alendronate
 - + Raloxifène
- Association PTH(1-34) et dénosumab

Addition de PTH(1-34) au THM

	<i>HRT (N = 125)</i>	<i>TPTD40 + HRT (N = 122)</i>
Age (years)	61.1 ± 7.4	62.0 ± 7.6
Number of years since menopause	14.5 ± 7.9	15.0 ± 8.1
BMI	25.8 ± 4.7	25.9 ± 4.8
BMD, vertebral (g/cm ²)	0.91 ± 0.15	0.90 ± 0.15



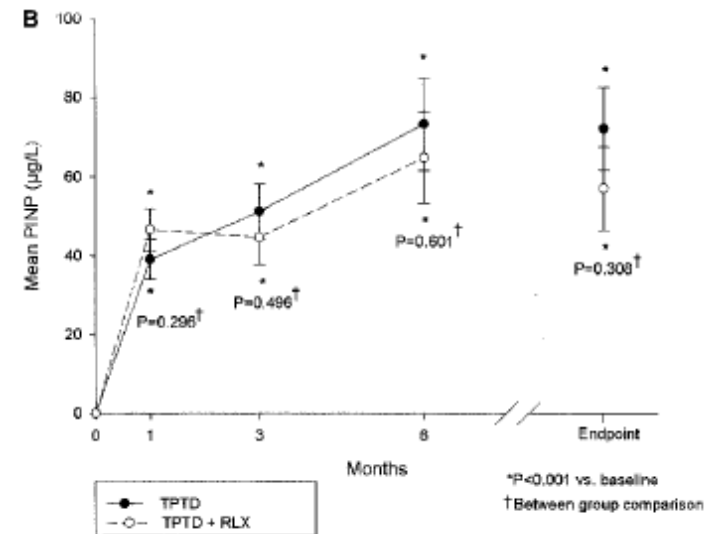
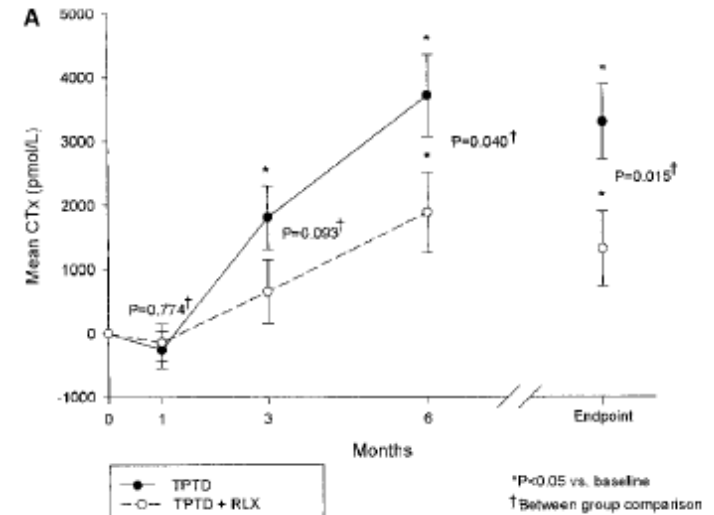
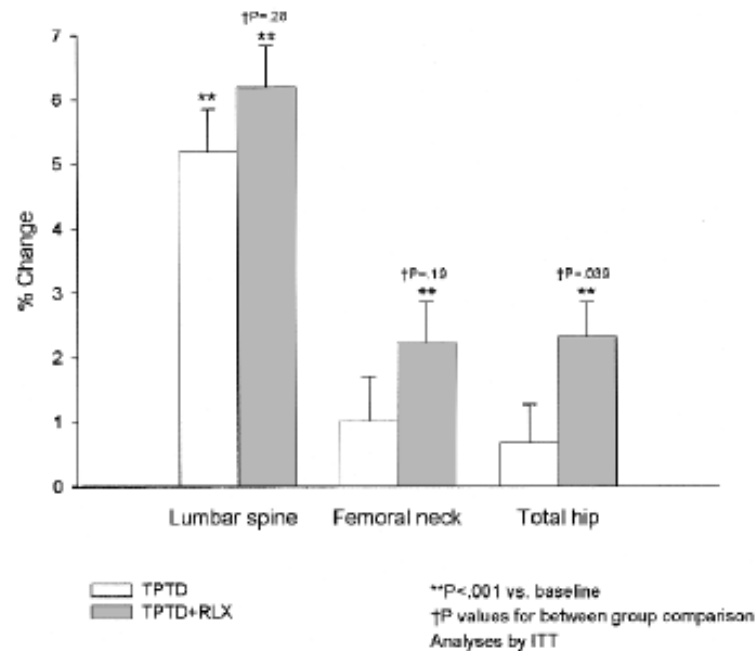
Rachis lombaire



Fémur total

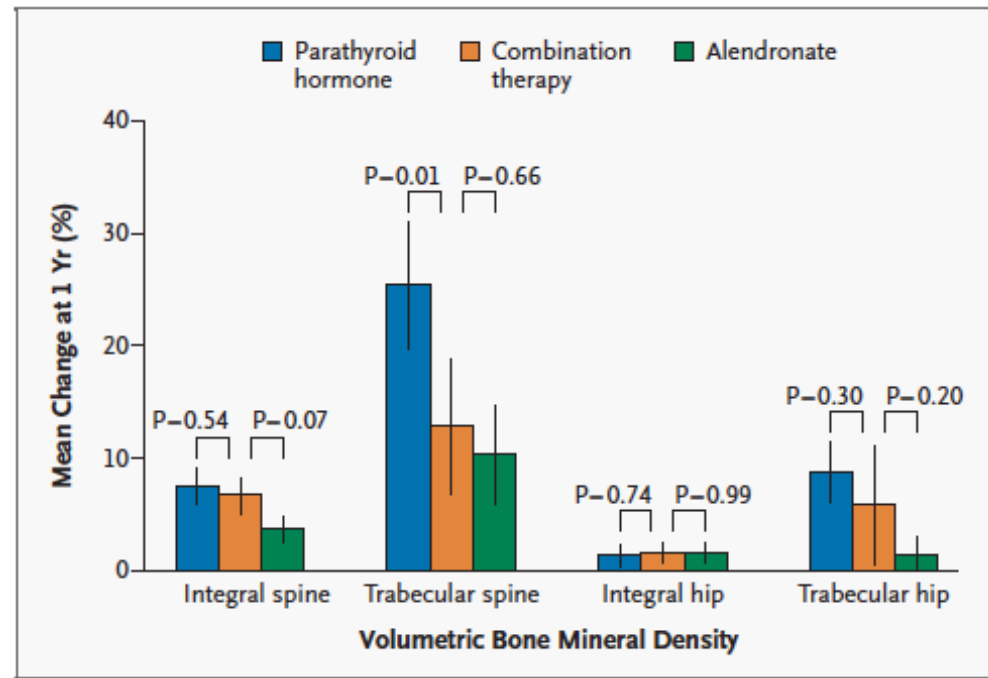
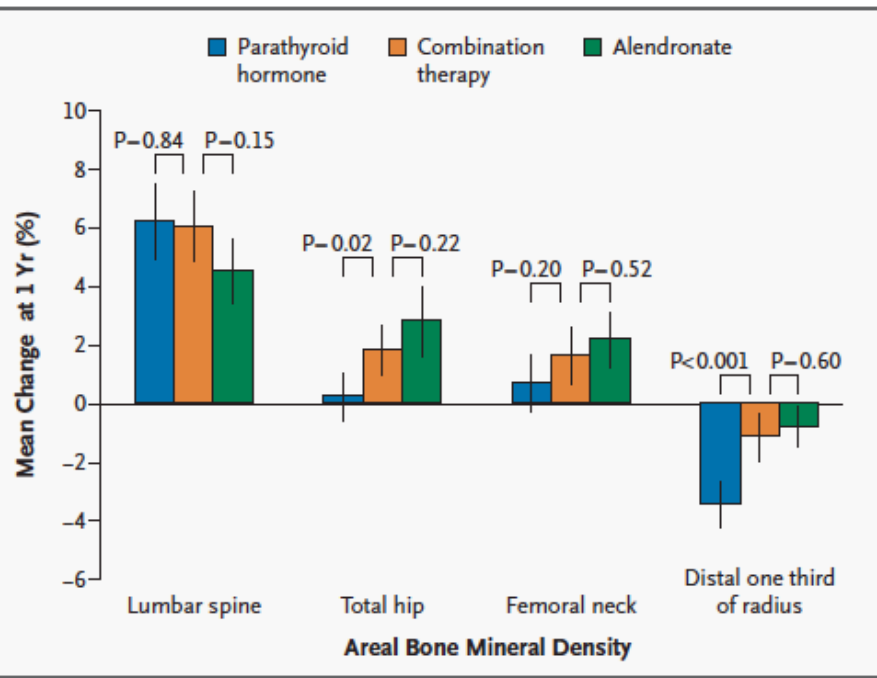
Association de PTH(1-34) au RLX

Characteristic	TPTD20 (N = 68)	TPTD + RLX (N = 69)	p*
Age (years)	66.1 ± 7.8	66.6 ± 7.5	.73
BMI (kg/m ²)	25.7 ± 5.9	25.3 ± 4.2	.79
LS BMD T score	-2.92 ± 0.84	-2.67 ± 1.14	.18
FN BMD T score	-2.42 ± 0.81	-2.47 ± 0.82	.68
Total hip BMD T score	-2.12 ± 0.90	-2.04 ± 0.95	.62

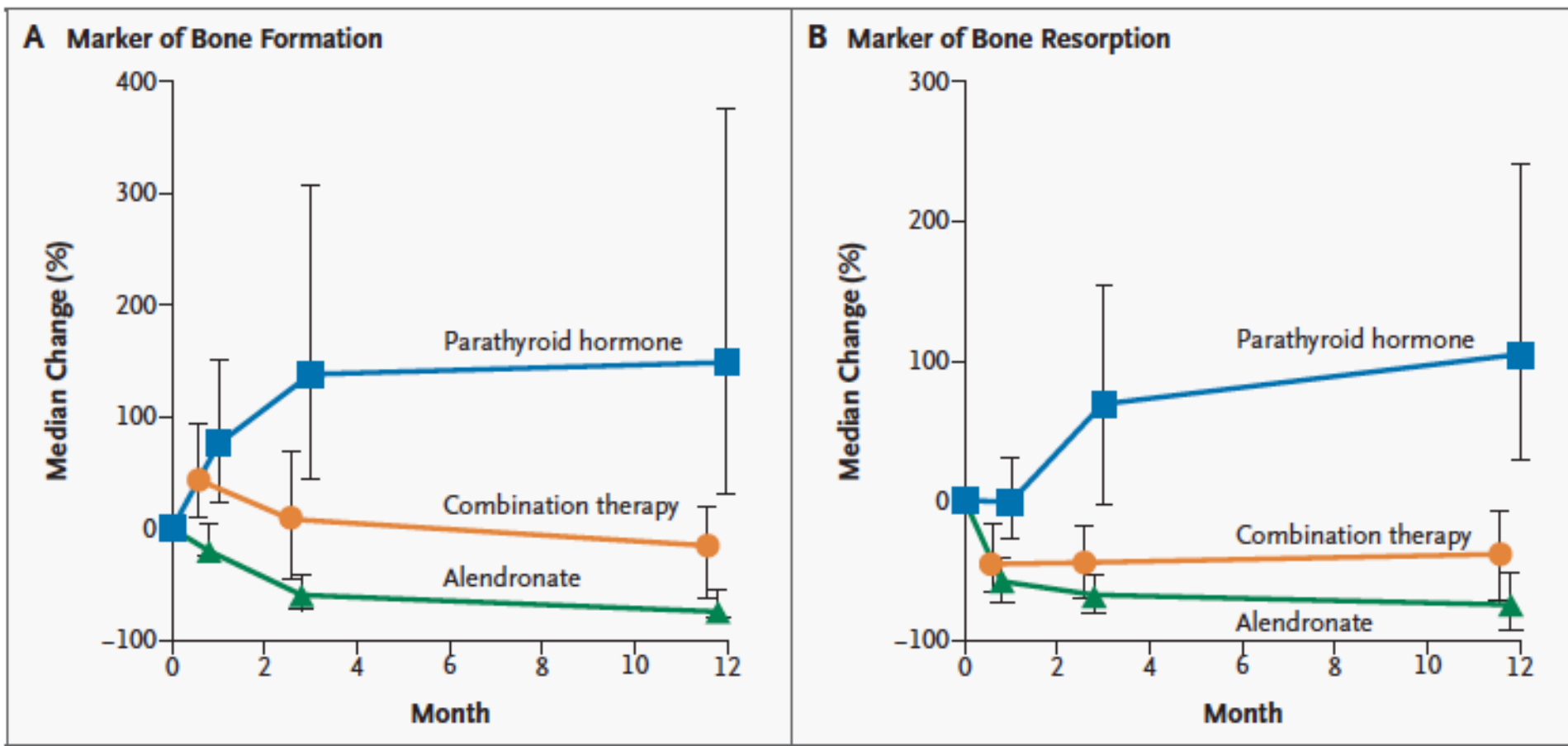


Impact osseux de l'association PTH + ALN

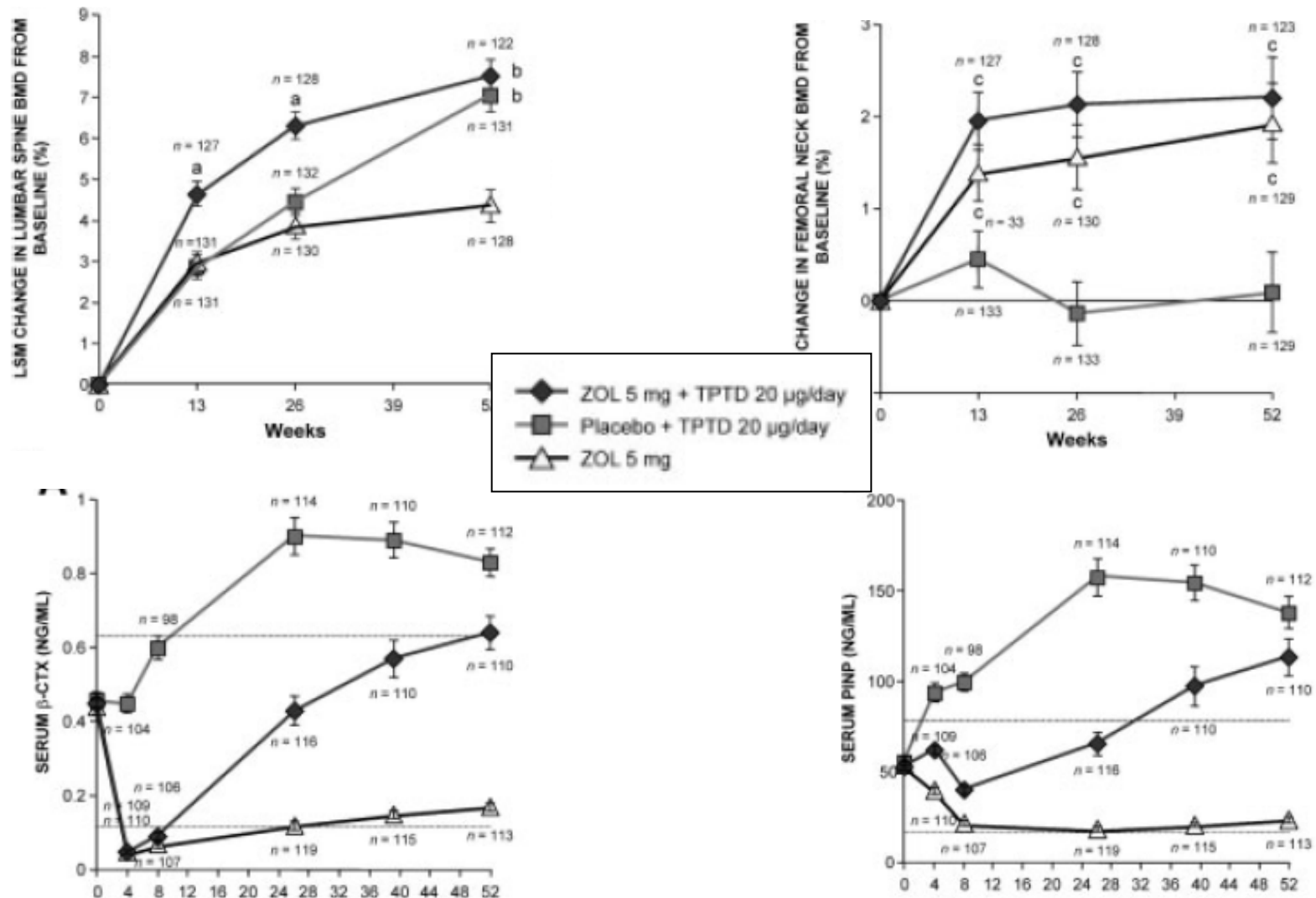
Characteristic	Parathyroid Hormone Group (N=119)	Combination-Therapy Group (N=59)	Alendronate Group (N=60)	P Value
Age — yr	69.4±7.3	70.2±6.8	70.7±6.8	0.47
Clinical fracture since 45 yr of age — no. (%)	57 (47.9)	30 (50.8)	25 (41.7)	0.64
Any previous alendronate use — no. (%)	13 (10.9)	4 (6.8)	10 (16.7)	0.23



Impact osseux de l'association PTH + ALN



Impact osseux de l'association PTH(1-34)+ZLN



Les associations avec PTH et PTH(1-34)

- En association avec les antiostéoclastiques d'emblée ou en complément d'un Tt préalable :

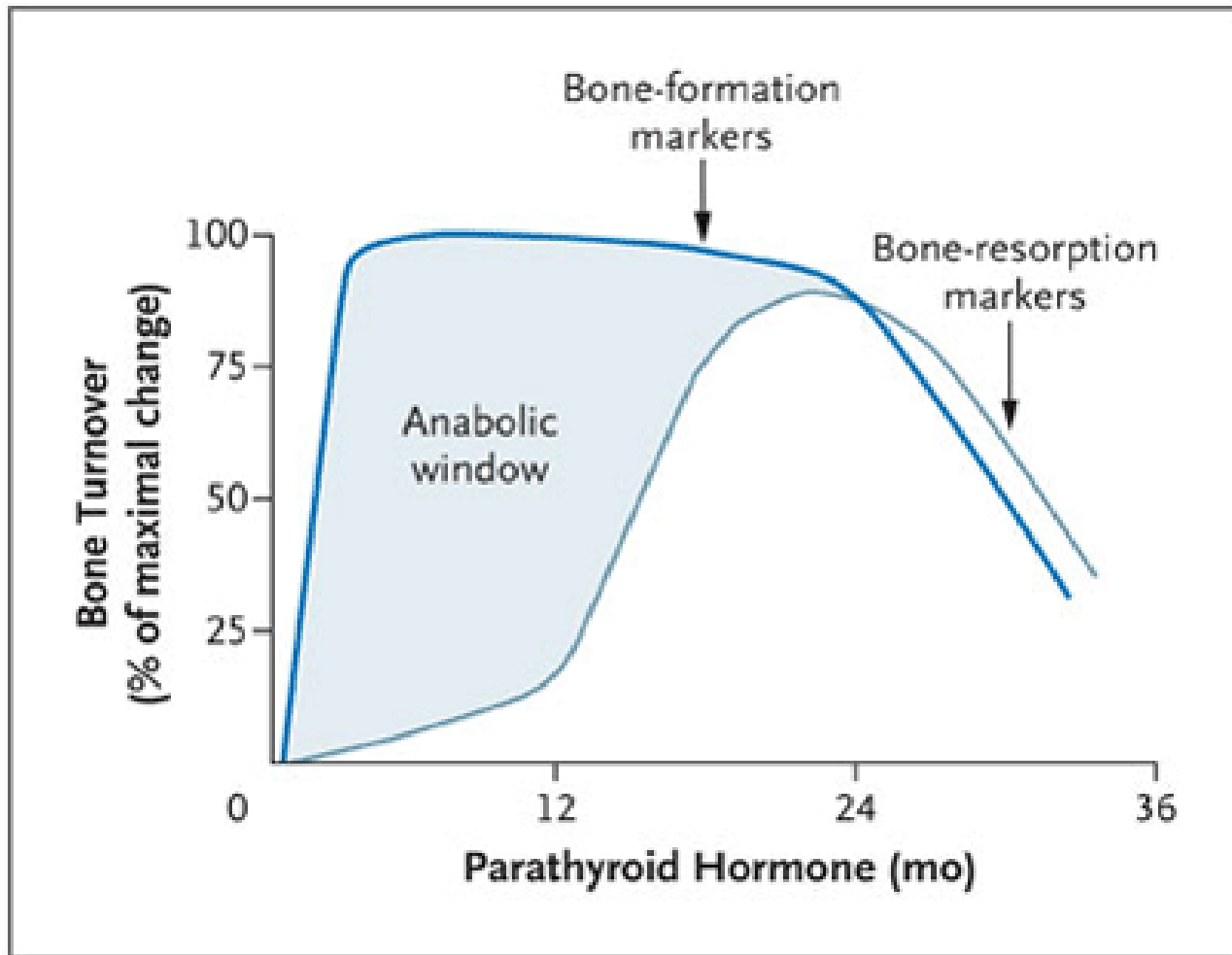
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Alendronate	+ PTH/PTH(1-34)
Acide zolédronique	+ PTH(1-34)

- PTH(1-34) préalable :

+ Alendronate
+ Raloxifène

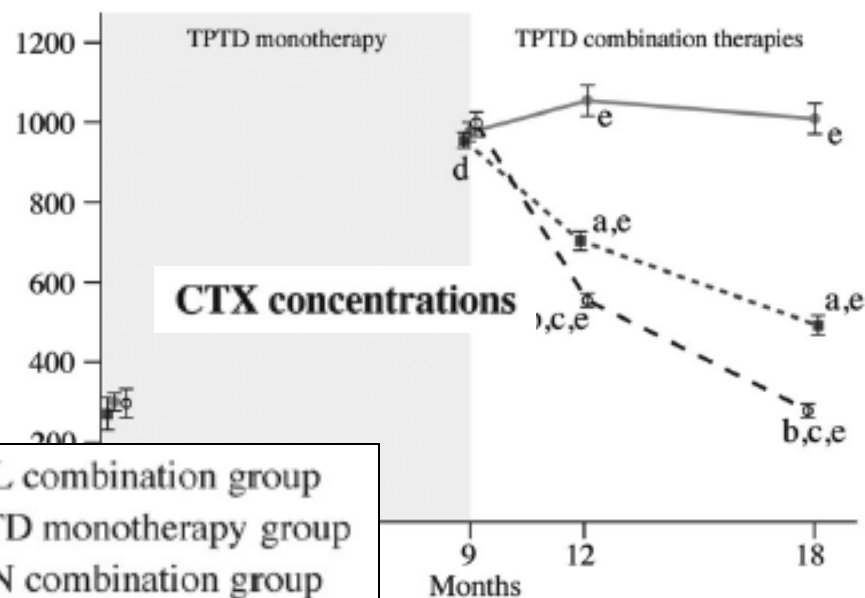
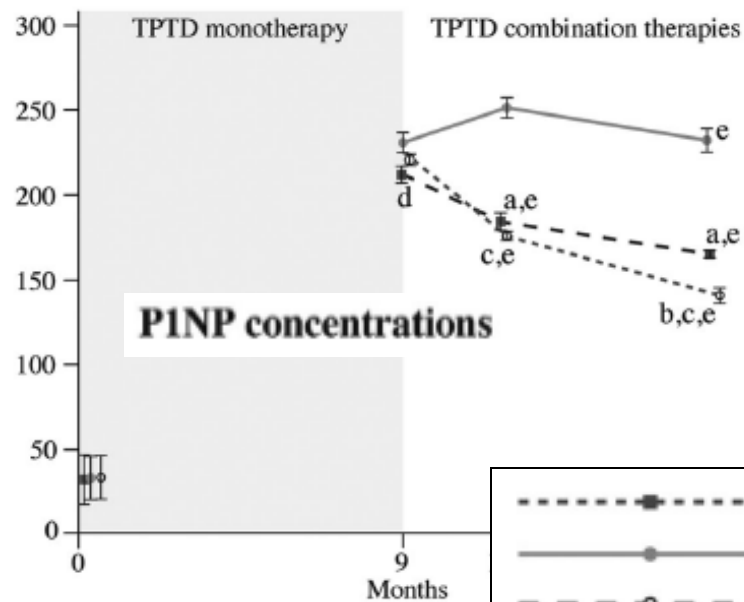
- Association PTH(1-34) et dénosumab

Effet anabolique de la PTH

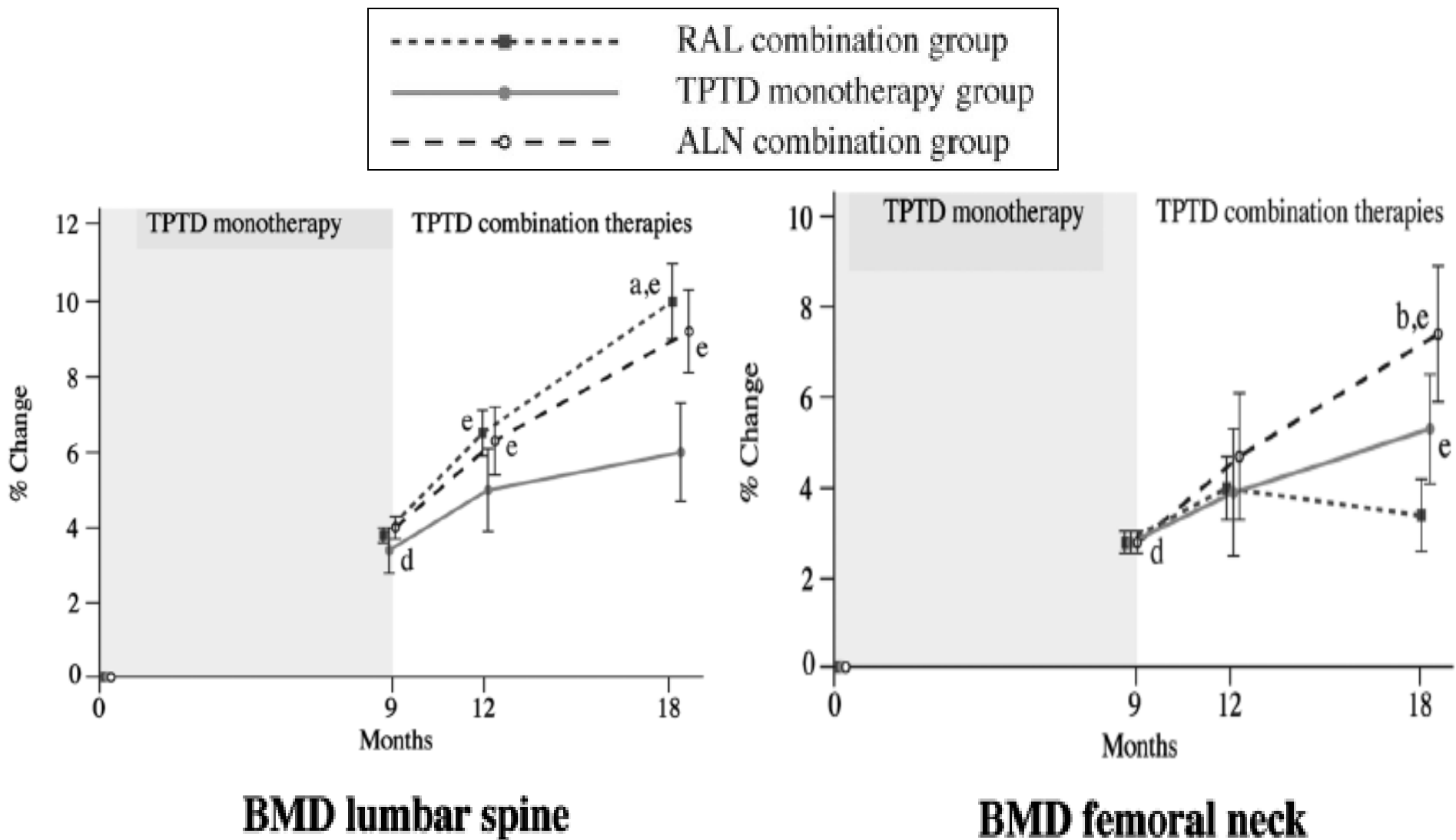


Addition d' 1 anti-ostéoclastique à la PTH(1-34)

Variable	TPTD monotherapy group (n = 47)	ALN combination group (n = 41)	RAL combination group (n = 37)
Age (years)	71.7 ± 9.3	71.6 ± 8.5	69.7 ± 7.5
BMI (kg/m ²)	25.7 ± 5.3	25.2 ± 3.7	24.9 ± 4.5
Years since menopause	23.3 ± 10.4	23.2 ± 9.9	21.4 ± 9.3
Prevalent fractures, n (%)			
Vertebral fractures	32 (68)	36 (88)	29 (78)
Nonvertebral fractures	21 (45)	23 (56)	22 (59)
Hip fractures	7 (5)	5 (12)	5 (14)



Addition d' 1 anti-ostéoclastique à la PTH(1-34)



Les associations avec PTH et PTH(1-34)

- En association avec les antiostéoclastiques d'emblée ou en complément d'un Tt préalable :

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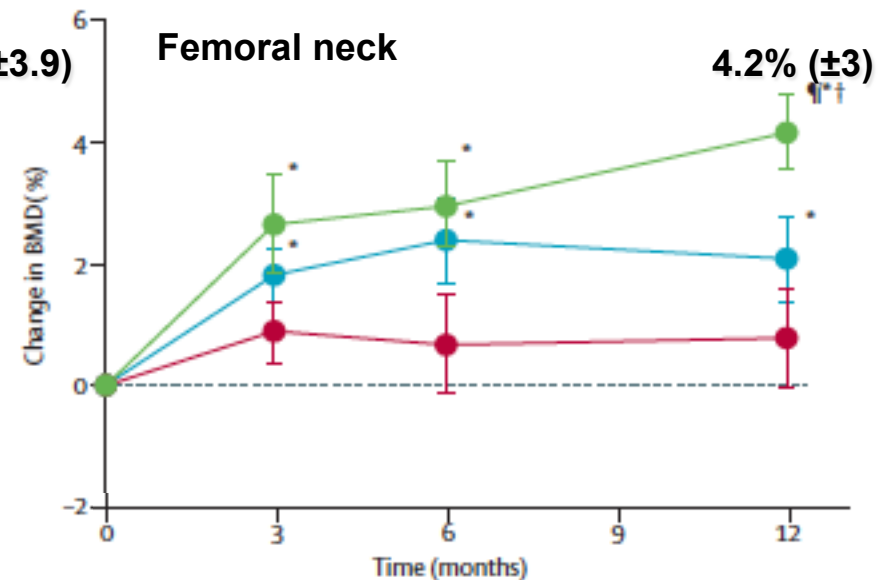
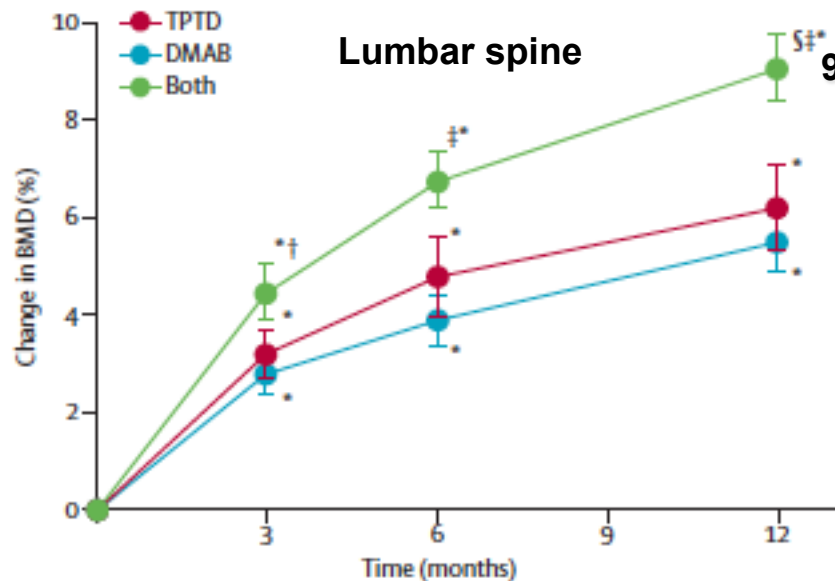
- PTH(1-34) préalable :

+ Alendronate
+ Raloxifène

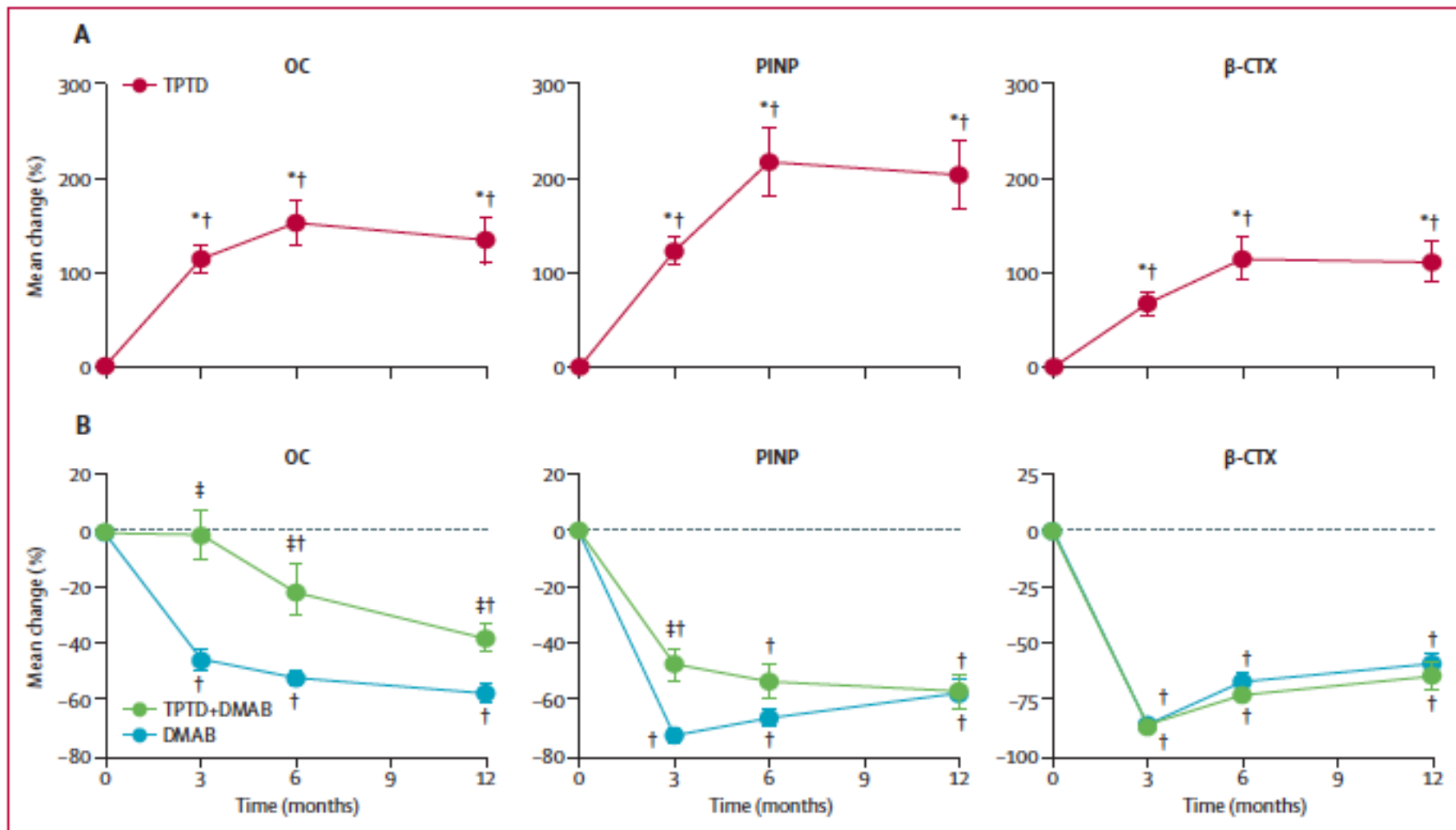
- Association PTH(1-34) et dénosumab

Association PTH (1-34) et denosumab

	Teriparatide group (n=31)	Denosumab group (n=33)	Combination therapy group (n=30)
Age (years)	65.5 (7.9)	66.3 (8.3)	65.9 (9.0)
Height (cm)	160.3 (7.2)	161.6 (6.8)	159.3 (5.8)
History of fragility fracture	16 (52%)	12 (36%)	10 (33%)
Previous oral bisphosphonate use	13 (42%)	12 (36%)	10 (33%)
Duration of use (months)	40 (25)	43 (27)	28 (21)
Time since discontinuation (months)	27 (20)	36 (23)	42 (17)
T score			
Posterior-anterior lumbar spine	-2.0 (1.0)	-1.6 (0.8)	-1.8 (1.4)
Femoral neck	-1.9 (0.5)	-1.9 (0.8)	-1.9 (0.6)

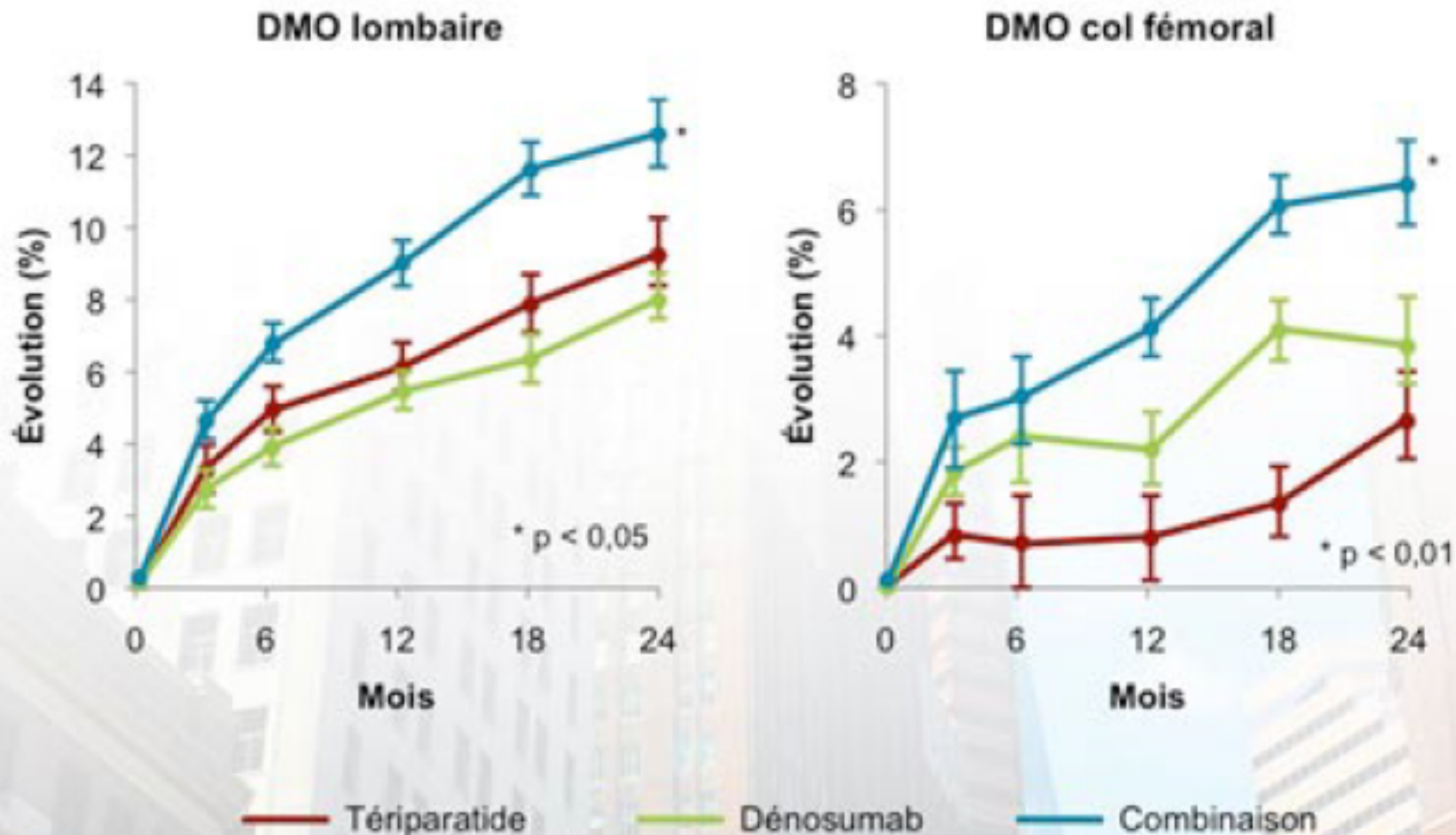


Association PTH(1-34) et denosumab



Association PTH(1-34) et dénosumab

Evolution densitométrique à 2 ans



Impact osseux des associations

Tt antérieur	Association PTH/TPD	Résorption	Formation	Gain DMO CL / FN	
	PTH/TPD⁽¹⁾	++	+++	++ / ±	
	ALN^(2,3)/ZLN⁽⁴⁾	-	±	+ / ±	
	THM⁽⁵⁾/RLX⁽⁶⁾	+ / ++	+++	+++ / +	
	DMB⁽⁷⁾	- - -	-	+++ / ++	
THM/RLX	THM^(5,8-10)/RLX^(11,12)	++	+++	+++ / ±	
ALN	ALN⁽¹²⁾	±	±	++ / ±	
TPD	RLX⁽¹³⁾	-	+	+++ / ±	
TPD	ALN⁽¹³⁾	- -	+	+++ / +	

(1) Neer NEJM 2001, (2) Black NEJM 2003, (3) Finkelstein JCEM 2010, (4) Cosman JBMR 2011, (5) Ste Marie JBMR 2006, (6) Deal JBMR 2005, (7) Tsai JBMR 2013, (8) Lindsay Lancet 1997, (9) Cosman JBMR 2001, (10) Fogelman CTI 2008, (11) Cosman OI 2008, (12) Cosman JCEM 2009, (13) Muschitz JBMR 2013,

Impact osseux des associations

Tt antérieur	Association PTH/TPD	Résorption	Formation	Gain DMO CL / FN	Efficacité FV
	PTH/TPD⁽¹⁾	++	+++	++ / ±	++
	ALN^(2,3)/ZLN⁽⁴⁾	-	±	+ / ±	?
	THM⁽⁵⁾/RLX⁽⁶⁾	+ / ++	+++	+++ / +	?
	DMB⁽⁷⁾	- - -	-	+++ / ++	?
THM/RLX	THM^(5,8-10)/RLX^(11,12)	++	+++	+++ / ±	?
ALN	ALN⁽¹²⁾	±	±	++ / ±	?
TPD	RLX⁽¹³⁾	-	+	+++ / ±	?
TPD	ALN⁽¹³⁾	- -	+	+++ / +	?

(1) Neer NEJM 2001, (2) Black NEJM 2003, (3) Finkelstein JCEM 2010, (4) Cosman JBMR 2011, (5) Ste Marie JBMR 2006, (6) Deal JBMR 2005, (7) Tsai JBMR 2013, (8) Lindsay Lancet 1997, (9) Cosman JBMR 2001, (10) Fogelman CTI 2008, (11) Cosman OI 2008, (12) Cosman JCEM 2009, (13) Muschitz JBMR 2013,

En synthèse

- La combinaison d'un anabolique avec un anti-ostéoclastique faible (E, SERMs) a un effet additif sur le gain densitométrique, ce qui n'est pas retrouvé avec les BPs les plus puissants
- Le découplage de la résorption et de la formation induite par certaines combinaison (PTH+DMB et ALN après 9 mois PTH) permet des gains densitométriques importants (FN)
- Le bénéfice anti-fracturaire n'est pas à ce jour documenté et ce type d'association doit rester réservé à des situations exceptionnelles de haut risque fracturaire
- La question des effets secondaires (additifs?) doit être posée