



A LA UNE

La vitamine D contre le cancer du sein



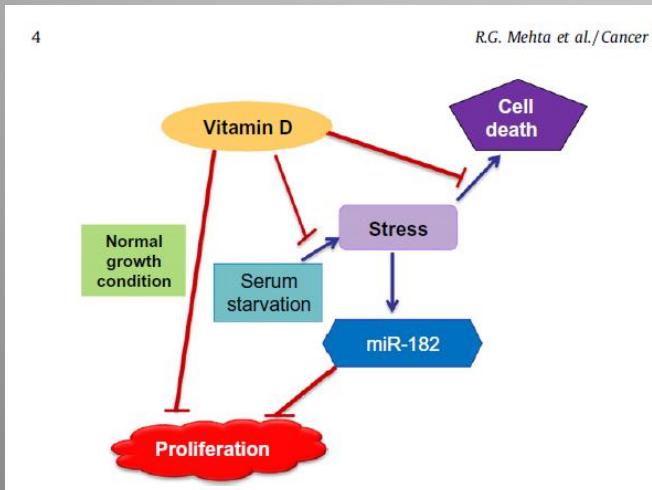
# Discussion *Faut il doser la Vitamine D ?*

*Dr A.Lesur, Parcours sein*

# Question posée : dosage ?

## ■ Question supplémentaire ...

- S' intéresser à la Vitamine D oui non ...?
- Supplémenter à quel niveau ?
- Intérêt potentiel si la femme ménopausée **et** malade?
  - . Si elle a un *cancer du sein* par exemple ....
  - . Si elle est sous hormonothérapie par AI
  - . Et plus si affinité !!!! ( BRCA, NEOADJUVANT...)



Cancer Letters xxx (2012) xxx-xxx  
Contents lists available at SciVerse ScienceDirect  
 ELSEVIER  
Cancer Letters  
journal homepage: [www.elsevier.com/locate/canlet](http://www.elsevier.com/locate/canlet)

Mini-review  
Vitamin D and breast cancer: Emerging concepts  
Rajendra G. Mehta\*, Xinjian Peng, Fatouma Alimirah, Genoveva Murillo, Rajeshwari Mehta  
IIT Research Institute, 10 West 35th Street, Chicago, IL 60616, United States



Research

Original Investigation

# Treatment of Vitamin D Insufficiency in Postmenopausal Women A Randomized Clinical Trial

Karen E. Hansen, MD, MS; R. Erin Johnson, BS; Kaitlin R. Chambers, BS; Michael G. Johnson, MS;  
Christina C. Lemon, MS, RD, CD; Tien Nguyen Thuy Vo, MS; Sheeva Marvdashti, BS

Jama 2015

Medscape France

MEDPULSE

21 OCTOBRE 2015

ACTUALITES

» Toutes les actualités



Rhumatologie

## Ménopause : la supplémentation en vitamine D n'apporte rien

Selon un nouvel essai randomisé, supplémenter les femmes ménopausées non-ostéoporotiques carencées en vitamine D pendant un an n'apporte pas de bénéfice clinique.

News....

*Q J Med* 2005; 98:667–676  
doi:10.1093/qjmed/hci096

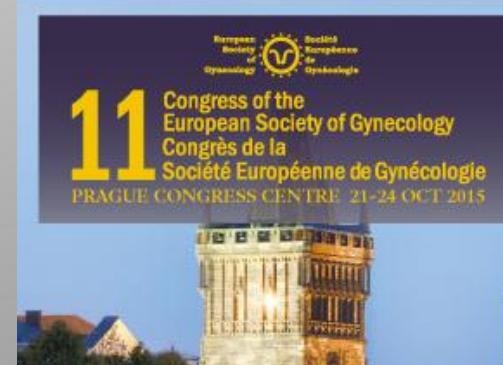
Advance Access publication 8 July 2005

## Vitamin D inadequacy among post-menopausal women: a systematic review 2005

S. GAUGRIS<sup>1</sup>, R.P. HEANEY<sup>2</sup>, S. BOONEN<sup>3</sup>, H. KURTH<sup>4</sup>,  
J.D. BENTKOVER<sup>4</sup> and S.S. SEN<sup>5</sup>

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Received 3 December 2004 and in revised form 2 June 2005



[www.icl-lorraine.fr](http://www.icl-lorraine.fr)



# Mais encore ....

Research

Original Investigation

## Treatment of Vitamin D Insufficiency in Postmenopausal Women A Randomized Clinical Trial

Karen E. Hansen, MD, MS; R. Erin Johnson, BS; Kaitlin R. Chambers, BS; Michael G. Johnson, MS; Christina C. Lemon, MS, RD, CD; Tien Nguyen Thuy Vo, MS; Sheeva Marvasti, BS

Les femmes ont été randomisées dans l'un des trois bras suivants :

- Faible dose en vitamine D : 800 UI de vitamine D3 par jour (pilule blanche) et pilules jaunes de placebo deux fois par mois (n=75) ;
- Forte dose de vitamine D : pilule blanche de placebo une fois par jour et pilules jaunes de vitamine D3 à 50 000 UI deux fois par mois (n=75) ;
- Placebo : pilule blanche de placebo tous les jours et pilules jaunes de placebo deux fois par mois (n=76).

En outre, les participantes ont reçu de la crème solaire pour minimiser les apports en vitamine D dus à l'exposition solaire. Et, celles qui ne consommaient pas assez de produits laitiers ont bénéficié de conseils spécifiques.

### Aucun bénéfice clinique quelle que soit la dose de vitamine D

L'absorption fractionnelle du calcium a été mesurée par méthode isotopique et les taux de 25(OH)D par chromatographie liquide haute performance.

Editor's Note

## How Much Vitamin D Is Enough?

Deborah Grady, MD, MPH

There is ongoing controversy regarding the definition of vitamin D insufficiency and the optimal treatment goal: should treatment aim to maintain a serum vitamin D level above 20 ng/mL or above 30 ng/mL? We found

Related article page 1612  
 Hansen et al<sup>1</sup> informative because it enrolled women with

low vitamin D levels and tested both a lower-dose treatment to maintain vitamin D levels greater than 20 ng/mL, and a higher-dose treatment to maintain levels greater than 30 ng/mL. After

1 year of treatment, randomization to a higher dose of cholecalciferol resulted in slightly better fractional excretion of calcium compared with low-dose cholecalciferol or placebo, but these differences are not clinically meaningful. Of more clinical importance, neither dose of cholecalciferol improved bone density, strength, muscle mass, functional status, or fall rate. It is possible that treatment beyond 1 year would result in better outcomes, but these data provide no support for use of higher-dose cholecalciferol replacement therapy or indeed any dose of cholecalciferol compared with placebo.

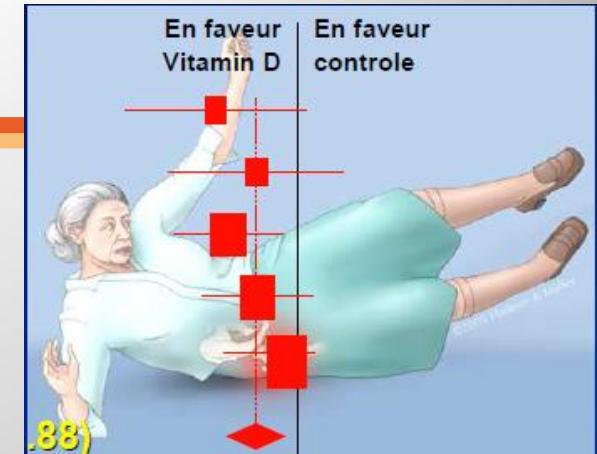
Conflict of Interest Disclosures: None reported.

1. Hansen KE, Johnson RE, Chambers KR, et al. Treatment of vitamin D insufficiency in

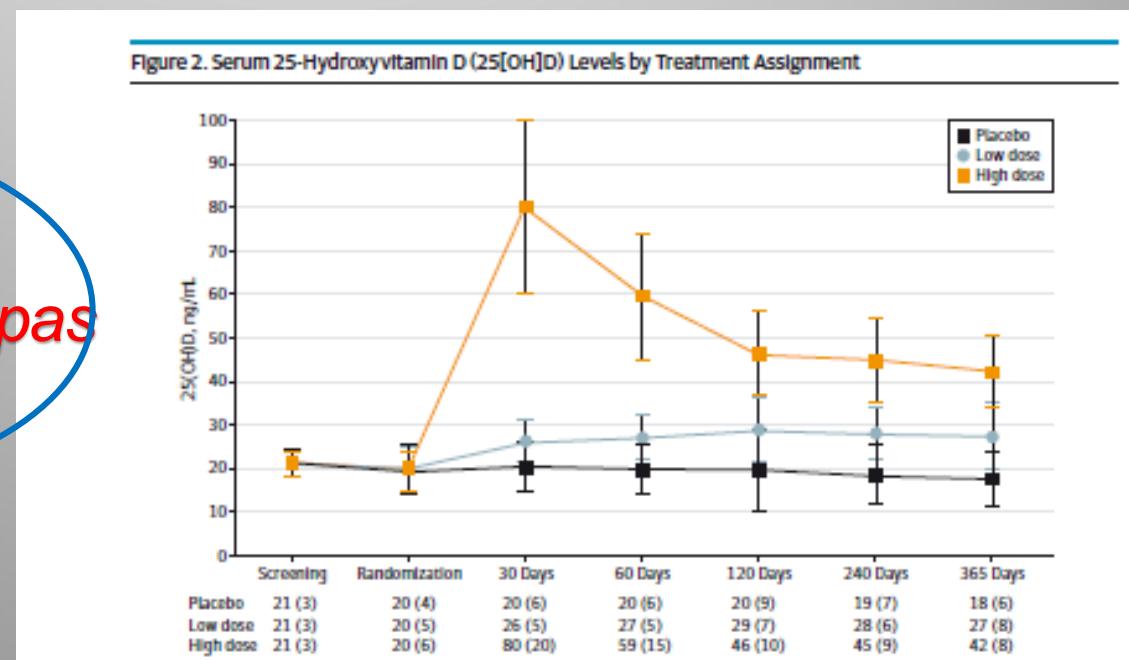
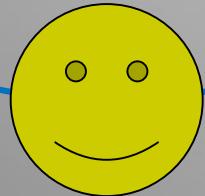
postmenopausal women: a randomized clinical trial [published online August 3, 2015]. JAMA Intern Med. doi:10.1001/jamainternmed.2015.3874.

# Etude biologique....

- 2531 femmes pressenties
- 230 randomisées
  - 73 sur 76 pour placebo
  - 74 sur 75 pour dose faible cholecalciferol
  - 74 sur 79 pour dose élevée.



*Au bout d'un an,  
Cela ne marche pas*





# En Pologne ....mais en 2015 ....

DOI: 10.5114/pm.2015.52149

Prz Menopausalny 2015; 14(2): 75-81

FEATURED PAPER

## Clinical implications of vitamin D deficiency

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### Abstract

Vitamin D deficiency is a common medical problem worldwide and its prevalence rises along with latitude, obesity, sedentary lifestyle, limited sunlight exposure and aging. A great body of evidence has shown that patients with vitamin D deficiency have increased cardiovascular risks and total mortality. Conversely, the presence of comorbidities progressive with age such as abdominal obesity, insulin resistance, type 2 diabetes and hypertension places the patients at an increased risk of vitamin D deficiency. The multidirectional effect of vitamin D deficiency is present in different phases of the aging process. Based on the literature review, the risk factors for vitamin D insufficiency most often found in post-menopausal women include limited sun exposure and time spent outdoors, inadequate dietary vitamin D intake, winter season and increased age. Vitamin D supplementation in this group might offer prevention of falls and fractures and may be beneficial for cardiovascular health, what may be especially important in osteoporotic and elderly populations. Prevention and treatment processes involve education regarding sunlight exposure and pharmacological cholecalciferol supplementation according to the recommendations for Central Europe. This manuscript reviews the role of vitamin D and its deficiency and considers their clinical implications, with particular regard to peri- and postmenopausal women.

**Key words:** vitamin D, deficiency, perimenopause, menopause.



# A part cette bonne nouvelle...

## Skeletal adverse effects with aromatase inhibitors in early breast cancer: evidence to date and clinical guidance

Sonia Servitja, Tamara Martos, Maria Rodriguez Sanz, Natalia Garcia-Giralt,  
Daniel Prieto-Alhambra, Laia Garrigos, Xavier Nogues and Ignasi Tusquets

*Ther Adv Med Oncol*  
2015, Vol. 7(5) 291–296  
DOI: 10.1177/  
1758834015598536  
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**Abstract:** Aromatase inhibitors (AIs) are routinely used in the adjuvant treatment of women with hormone receptor-positive early breast cancer. Patients who receive AIs have an increased risk of bone loss and arthralgia compared with those treated with tamoxifen. In addition to the effects of AIs, the population of women with early breast cancer has a high prevalence of 25-hydroxyvitamin D (25(OH)D) insufficiency. In our experience 88% of patients had concentrations lower than 30 ng/ml. Vitamin D supplementation should be adapted to the baseline concentration. Another relevant finding in our research program was the close relationship between 25(OH)D levels and intensity of AI-related arthralgia (AlrA). A target concentration of 40 ng/ml 25(OH)D may prevent development of AlrA. We also demonstrate that AlrA is genetically determined: single nucleotide polymorphisms located in genes encoding key factors for the metabolism of estrogens and vitamin D (*CYP17A1*, *VDR*, and *CYP27B1*) are associated with self-reported arthralgia during AI therapy. We recommend establishing an individualized protocol of bone-health surveillance based on baseline and evolutionary clinical variables.

**Keywords:** aromatase inhibitors, breast cancer, musculoskeletal toxicity

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*Plus compliqué qu'on ne croit*

RESEARCH ARTICLE

Open Access



CrossMark

# Arthralgia among women taking aromatase inhibitors: is there a shared inflammatory mechanism with co-morbid fatigue and insomnia?

Joshua Bauml<sup>1,2</sup>, Lu Chen<sup>3</sup>, Jinbo Chen<sup>3</sup>, Jean Boyer<sup>4</sup>, Michael Kalos<sup>5</sup>, Susan Q. Li<sup>3,6</sup>, Angela DeMichele<sup>1,2,3</sup> and Jun J. Mao<sup>1,3,6\*</sup>

## Abstract

**Introduction:** Arthralgia is a common toxicity among women taking aromatase inhibitors (AIs) and can lead to premature discontinuation of therapy. We evaluated the association between arthralgia, co-morbid fatigue and/or insomnia, and inflammatory biomarkers among women taking AIs.

**Methods:** Women taking AIs for early-stage breast cancer completed a modified version of the Brief Pain Inventory, the Brief Fatigue Inventory, and the Insomnia Severity Index and provided blood samples for simultaneous assessment of 34 inflammatory biomarkers with a Luminex kit. Two-sided *t* tests were used to compare inflammatory biomarker concentrations for patients with or without moderate to severe arthralgia. Multivariate linear regression analyses were performed to evaluate the relationship between comorbid arthralgia, fatigue, and insomnia with identified biomarker concentrations.

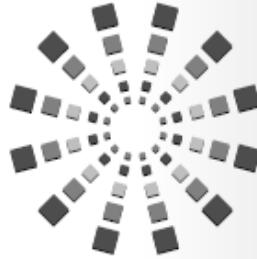
**Results:** Among 203 participants, the severity of arthralgia, fatigue, and insomnia were significantly correlated with each other ( $p < 0.001$  for all comparisons). After controlling for race, chemotherapy history, non-steroidal anti-inflammatory drug use, age, and body mass index, the coexistence of arthralgia, fatigue, and insomnia was associated with elevated C-reactive protein (CRP) ( $\beta = 93.1$ ; 95 % confidence interval (CI): 25.1–161.1;  $p = 0.008$ ), eotaxin ( $\beta = 79.9$ ; 95 % CI: 32.5–127.2;  $p = 0.001$ ), monocyte chemoattractant protein (MCP)-1 ( $\beta = 151.2$ ; 95 % CI: 32.7–269.8;  $p = 0.013$ ), and vitamin D-binding protein (VDBP) ( $\beta = 19,422$ ; 95 % CI: 5500.5–33,344;  $p = 0.006$ ).

**Conclusions:** Among women taking AIs, the coexistence of arthralgia, fatigue, and insomnia was associated with increased levels of inflammatory biomarkers (elevated CRP, eotaxin, MCP-1, and VDBP). These findings suggest a possible shared inflammatory mechanism underlying these common symptoms.



# Enfin, pour supporter les traitements ?

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## Vitamin D Insufficiency and Musculoskeletal Symptoms in Breast Cancer Survivors on Aromatase Inhibitor Therapy

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### KEY WORDS

25-Hydroxyvitamin D

Aromatase inhibitors therapy

Breast cancer

Musculoskeletal symptoms

Pilot study

Breast cancer survivors (BCSs) on aromatase inhibitor (AI) therapy often experience musculoskeletal symptoms (joint pain and stiffness, bone and muscle pain, and muscle weakness), and these musculoskeletal symptoms may be related to low serum levels of vitamin D. The primary purpose of this pilot exploratory study was to determine whether serum levels of 25-hydroxyvitamin D (25[OH]D) concentration were below normal (<30 ng/mL) in 29 BCSs on AI therapy and if musculoskeletal symptoms were



# High-dose Vitamin D Relieves Joint Pain/ Fatigue

## Methods

- Women were started on LET + standard calcium and vitamin D supplementation (1200 mg/d calcium and 600 IU/d vitamin D)
- 4 weeks later, women with 25OHD <40 ng/mL at baseline were given 50,000 IU of oral vitamin D3 every week for 12 weeks

## Results

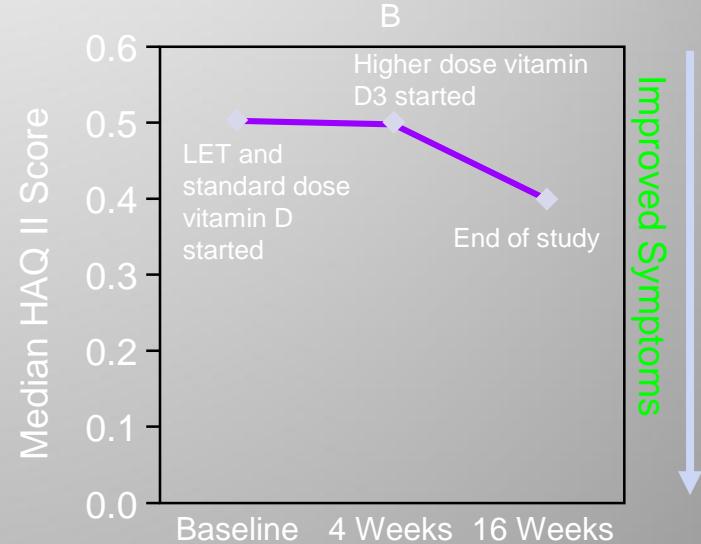
- 64% of postmenopausal women starting adjuvant LET have vitamin D insufficiency

## Conclusion

- High-dose vitamin D appears to provide relief from fatigue and joint pain

■ ***Muslimani et al also found that the group receiving AIs with calcium or bisphosphonates had more patients without musculoskeletal symptoms and fewer fractures ( $P <0.001$ )***

**Improvement of Musculoskeletal Symptoms With Supplementation Using 50,000 IU/week of Vitamin D3 for 12 Weeks**



\*Health Assessment Questionnaire II (HAQ II) is a validated musculoskeletal symptom-directed questionnaire designed to study how an illness or intervention affects activities of daily living. Lower scores are better.

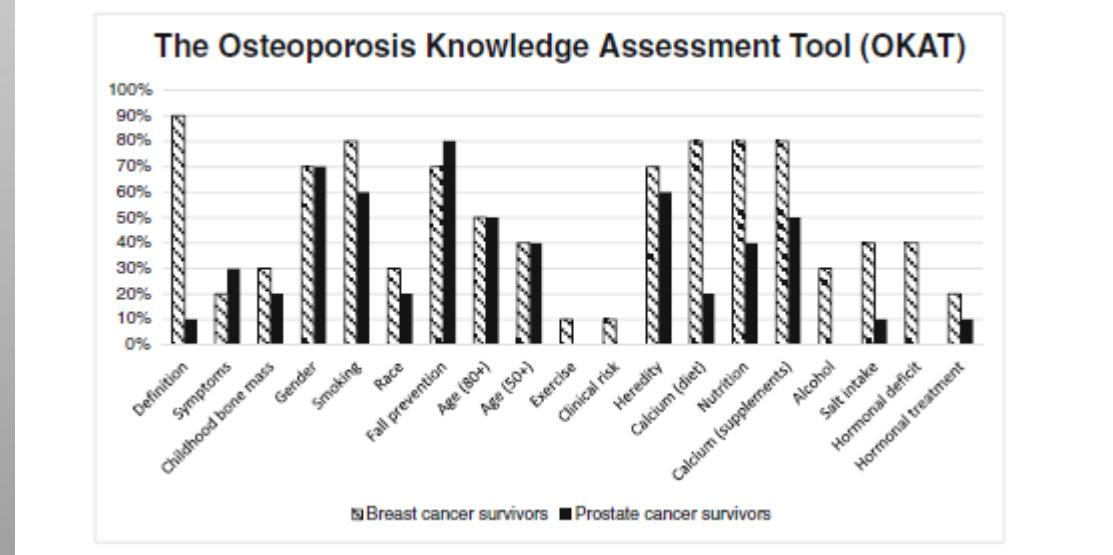
# Encore faut il être au courant ?...

J Cancer Surviv  
DOI 10.1007/s11764-015-0491-6



## Assessing information needs on bone health in cancer survivors

Jude K. A. des Bordes<sup>1</sup> • Noha Abdel-Wahab<sup>1</sup> • Maria Suarez-Almazor<sup>1</sup> •  
Maria A. Lopez-Olivo<sup>2</sup>





# Chez les patients traités pour cancer ???

- Jacobs E.T. Thomson C.A. Flatt S.W. Al-Delaimy W.K. Hibler E.A. Jones L.A. LeRoy E.C. Newman V.A. Parker B.A. Rock) (Thomson) Department of (Jones) University of Texas MD Anderson Cancer Center, Houston, TX, United States

Vitamin D and breast cancer recurrence in the Women's Healthy Eating and Living (WHEL) Study.

- Source American Journal of Clinical Nutrition. 93 (1) (pp 108-117), 2011. Date of Publication: 01 Jan 2011.

*There is a paucity of research evaluating the relation between vitamin D and recurrence of breast cancer after treatment*

**Conclusion:** These results *do not provide* support for a relation between concentrations of 25(OH)D after treatment and the recurrence of breast cancer.



# Effets thérapeutiques sur la tolérance des traitements??

- Effect of vitamin D supplementation on serum 25-hydroxy vitamin D levels, joint pain, and fatigue in women starting adjuvant letrozole treatment for breast cancer

**Qamar J. Khan  $\text{\AA}$  Pavan S. Reddy  $\text{\AA}$  Bruce F. Kimler  $\text{\AA}$**   
Breast Cancer Res Treat (2010) 119:111–118

- \* Vitamin D threshold to prevent aromatase inhibitor-induced arthralgia: a prospective cohort study

Daniel Prieto-Alhambra • M. Kassim Javaid • Sonia Servitja •  
Breast Cancer Res Treat (2011) 125:869–878

- \* High Prevalence of Low Vitamin D and Musculoskeletal Complaints in Women with Breast Cancer

Nicola Napoli, MD, PhD,\* Swapna Vattikuti, MD, Cynthia Ma, MD,  
The Breast Journal, Volume 16 Number 6, 2010 609–616



# Chimiothérapie néoadjuvante et vitamine D

- une étude très intéressante rapportée par WJacot, pour le CRLCC de Montpellier, s'intéresse au taux de la Vitamine D en cours de traitement néo adjuvant chez des patientes avec cancer du sein localement avancé
- Mise en évidence d' une vraie déficience majorée en fin de traitement, faisant évoquer une dérégulation des mécanismes de régulation fonctionnelle.

Breast Cancer Res Treat  
DOI 10.1007/s10549-012-2084-7

CLINICAL TRIAL

**Increased prevalence of vitamin D insufficiency in patients with breast cancer after neoadjuvant chemotherapy**

William Jacot · Stéphane Pouderoux · Simon Thezenas ·  
Angélique Chapelle · Jean-Pierre Bleuse ·  
Gilles Romieu · Pierre-Jean Lamy



# AU QUOTIDIEN....

- Dosages effondrés ( 4 et 10 ) plusieurs fois par semaine
- On y croit ..; effet placebo ?
- À suivre sous hormonothérapie ....
  - Surtout si plus longue et plus toxique !!