Oral Bisphosphonates and Breast Cancer: Prospective Results from the Women's Health Initiative (WHI)

Presentation discussed in this issue:

Chlebowski RT et al. **Oral bisphosphonate and breast cancer: Prospective results from the Women's Health Initiative (WHI).** San Antonio Breast Cancer Symposium 2009;**Abstract 21**.

Slides from a presentation at SABCS 2009

Introduction

- Bisphosphonate administration in metastatic breast cancer has been shown to reduce skeletal related complications (*JCO* 1998:16;2038).
- Results from phase III trials ABCSG-12 and ZO-FAST suggest that bisphosphonate use in the adjuvant setting in breast cancer may lower loco-regional disease recurrence (*NEJM* 2009;360:679, *Oncologist* 2008;13:503).
- Evidence suggests that women with low bone mineral density (BMD) are at a lower breast cancer risk (*Cancer* 2008:113:907).
- **Current study objective:**
  - Assess the relationship between oral bisphosphonate use and breast cancer incidence while controlling for differences in BMD, using hip fracture risk score.

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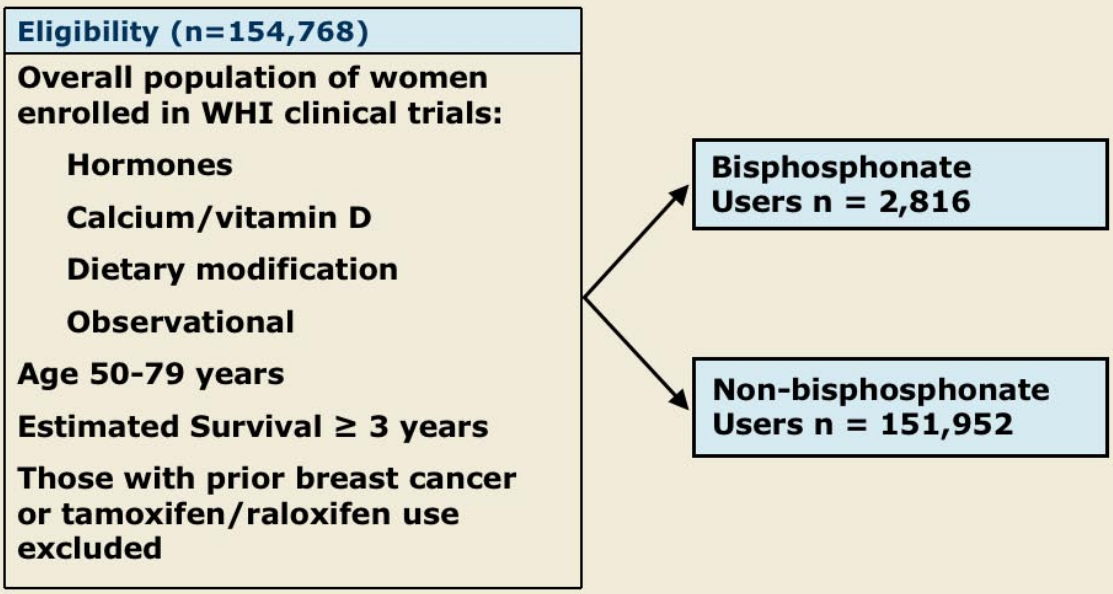
Bisphosphonates and Breast Cancer: Women's Health Initiative (WHI) Clinical Trials Cohort



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Methods

- Medication use details were collected at baseline and at 3 years for all patients.
- Medical histories were updated annually (observational study) or semi-annually (clinical trials).
- BMD determined by DXA bone densitometry in ancillary study at three WHI clinical centers (n=10,693).
- Five-year risk of hip fracture calculated using algorithm developed in the WHI cohort (*JAMA* 2007;298:2389).
- Hip fracture risk score used to adjust for potential BMD differences between bisphosphonate users and non-users.

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Baseline Characteristics

	Bisphosphonate Users		Non-Bisphosphonate Users	
	N	%	N	%
5 year breast cancer risk (Gail) > 1.7%	1,633	58%	57,581	37.9%
Family history of breast cancer	586	22.1%	26,123	18.2%
Benign breast disease	760	27.3%	30,592	21.3%

All differences, $p < 0.01$.

Types of Bisphosphonate Use:
- **Alendronate = 89.7% (n = 2,527)**
- **Etidronate = 10.1% (n = 285)**

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Breast Cancer Incidence by Bisphosphonate Use

Breast Cancer Type	Bisphosphonate Use		Multivariate	
	Yes (rate/1,000 person-years)	No (rate/1,000 person-years)	HR*	P value
Invasive Breast Cancer	3.29	4.38	0.68	< 0.01
ER-positive	2.56	3.28	0.70	0.02
ER-negative	0.41	0.61	0.66	0.27
Carcinoma In Situ†	1.53	0.92	1.59	0.002

** HR = hazard ratio adjusted for age, ethnicity, smoking, alcohol use, physical activity, BMI, mammograms, prior hormone use, calcium, vitamin D, hip fracture risk, Gail risk and stratified on WHI trial randomization arm*

† Lobular carcinoma in situ tumors excluded

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Conclusions

- Oral bisphosphonate use is associated with a lower incidence of invasive breast cancer in postmenopausal women after adjustment for potential BMD differences.
- The hazard ratios for ER-positive and ER-negative invasive breast cancers among bisphosphonate users versus non-users were similar, although statistical significance was not seen with the ER-negative breast cancers.
- Carcinoma in situ (DCIS) incidence is higher among bisphosphonate users.

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