

# THE LANCET Oncology

[\[Close\]](#)

## Articles

---

The Lancet Oncology, [Volume 10, Issue 2](#), Pages 135 - 146, February 2009  
doi:10.1016/S1470-2045(08)70341-3

## Safety and efficacy of tibolone in breast-cancer patients with vasomotor symptoms: a double-blind, randomised, non-inferiority trial

Prof [Peter Kenemans MD](#) <sup>a</sup> , Prof [Nigel J Bundred MD](#) <sup>b</sup>, Prof [Jean-Michel Foidart MD](#) <sup>c</sup>, Prof [Ernst Kubista MD](#) <sup>d</sup>, Prof [Bo von Schoultz MD](#) <sup>e</sup>, Prof [Piero Sismondi MD](#) <sup>f</sup>, Prof [Rena Vassilopoulou-Sellin MD](#) <sup>g</sup>, Prof [Cheng Har Yip MD](#) <sup>h</sup>, [Jan Egberts MSc](#) <sup>i</sup>, [Mirjam Mol-Arts MD](#) <sup>i</sup>, [Roel Mulder](#) <sup>i</sup>, [Steve van Os MD](#) <sup>i</sup>, Prof [Matthias W Beckmann MD](#) <sup>j</sup>, on behalf of the LIBERATE Study Group<sup>†</sup>

## Summary

---

### Background

Vasomotor symptoms and bone loss are complications frequently induced by adjuvant treatment for breast cancer. Tibolone prevents both side-effects, but its effect on cancer recurrence is unknown. The aim of this study was to show non-inferiority of tibolone to placebo regarding risk of recurrence in breast-cancer patients with climacteric complaints.

### Methods

Between July 11, 2002, and Dec 20, 2004, women surgically treated for a histologically confirmed breast cancer (T<sub>1-3</sub>N<sub>0-2</sub>M<sub>0</sub>) with vasomotor symptoms were randomly assigned to either tibolone 2.5 mg daily or placebo at 245 centres in 31 countries. Randomisation was done by use of a centralised interactive voice response system, stratified by centre, with a block size of four. The primary endpoint was breast-cancer recurrence, including contralateral breast cancer, and was analysed in the intention-to-treat (ITT) and per-protocol populations; the margin for non-inferiority was set as a hazard ratio of 1.278. This study is registered with [ClinicalTrials.gov](#), number [NCT00408863](#).

### Findings

Of the 3148 women randomised, 3098 were included in the ITT analysis (1556 in the tibolone group and 1542 in the placebo group). Mean age at randomisation was 52.7 years (SD 7.3) and mean time since surgery was 2.1 years (SD 1.3). 1792 of 3098 (58%) women were node positive and 2185 of 3098 (71%) were oestrogen-receptor positive. At study entry, 2068 of 3098 (67%) women used tamoxifen and 202 of 3098 (6.5%) women used aromatase inhibitors. The mean daily number of hot flushes was 6.4 (SD 5.1). After a median follow-up of 3.1 years (range 0.01–4.99), 237 of 1556 (15.2%) women on tibolone had a cancer recurrence, compared with 165 of 1542

(10·7%) on placebo (HR 1·40 [95% CI 1·14–1·70];  $p=0\cdot001$ ). Results in the per-protocol population were similar (209 of 1254 [16·7%] women in the tibolone group had a recurrence *vs* 138 of 1213 [11·4%] women in the placebo group; HR 1·44 [95% CI 1·16–1·79];  $p=0\cdot0009$ ). Tibolone was not different from placebo with regard to other safety outcomes, such as mortality (72 patients *vs* 63 patients, respectively), cardiovascular events (14 *vs* 10, respectively), or gynaecological cancers (10 *vs* 10, respectively). Vasomotor symptoms and bone-mineral density improved significantly with tibolone, compared with placebo.

### Interpretation

Tibolone increases the risk of recurrence in breast cancer patients, while relieving vasomotor symptoms and preventing bone loss.

### Funding

Schering-Plough (formerly NV Organon, Oss, Netherlands).

To read this article in full you will need to login or make a payment

### Already Registered? Please Login

Username:

Password:

Login

[Forgotten Username or Password?](#)

Remember me on this computer until I logout

### Payment Options

[Purchase this article for \\$31.50](#)

Online access for 24 hours. The PDF version can be downloaded as your permanent record.

[Subscribe to The Lancet Oncology](#)

Options include:

- Personal print + online subscription
- Personal online-only subscription

### ScienceDirect Access

[Check ScienceDirect](#) to see if you have access via your institution, or login with your Athens, Shibboleth or remote ScienceDirect username and password.

### Already a Print Subscriber?

[Claim online access](#)

[Renew your print subscription](#)

### Have a Free Trial Code?

[Activate your free trial](#)

[a](#) Department of Obstetrics and Gynaecology, VU University Medical Centre, Amsterdam, Netherlands

[b](#) Department of Surgery, University of Manchester, Manchester, UK

[c](#) Department of Obstetrics and Gynaecology, University of Liege, Liege, Belgium

[d](#) Medical University, Vienna, Austria

[e](#) Karolinska Institute, Stockholm, Sweden


[f](#) University of Turin, Turin, Italy

[g](#) MD Anderson Cancer Center, Houston, TX, USA

[h](#) University Malaya Medical Centre, Kuala Lumpur, Malaysia

[i](#) Schering-Plough, Oss, Netherlands

[j](#) University Clinic, Erlangen, Germany

 Correspondence to: Prof Peter Kenemans, Department of Obstetrics and Gynaecology, VU University Medical Centre, PO Box 7057, 1007 MB Amsterdam, Netherlands

[‡](#) LIBERATE Study Group participants listed at end of paper