Reviewer's report

Title: FemZone Trial: a randomized phase II trial comparing neoadjuvant letrozole and zoledronic acid with letrozole in primary breast cancer patients

Version: 2 Date: 14 June 2013

Reviewer: Judith R R Kroep

Reviewer's report:

The role of bisfosfonates in the antitumor effect is still unknown and this trials supports previous findings for a trend in better outcome for postmenopausal woman. The neoadjuvant setting in a homogeneous group of patients treated with letrozole is new.

Major comment:

The authors explain why they have used clinical response as a primary outcome, however pathological response should be known and are valuable data to report.

Minor comment

Abstract, methods: define primary endpoint and how this was measured
Abstract, results: change 'for the treatment arm' in 'for the experimental arm'
Abstract, conclusion: a non-significant increase should be changed in 'no increase' or similar findings etc. Then in second sentence however a trend..

Introduction:

-First sentence, 'neoadjuvant therapy has helped improve health care for breast cancer patients' is rather general statement can you be more specific?
-ZOFAST trial was in postmenopausal pts
-'On the basis of clinical evidence from studies of metastasis': as far as I know data from patients with metastasis are discordant, we currently use bisfosfonates for SRE and osteoporosis but not standard for the antitumor effect.

Patients and Methods:

-2nd paragraph: first sentence belongs to first paragraph -Please define adequate renal function -Treatment and tumor assessment plan, 2nd paragraph: please define how clinical response was measured (palpation/MRI/ultrasound?)

Results:

Patients: please insert reference to Table 1 -Please add pCR (see before)
-Measurement of FACT-B should also be described in methods -Safety, line 4: please delete ' as expected', please add is differences in toxicity were significant.

Discussion:
Consider to add that in the neoadjuvant setting similar results have been found in two trials with neoadjuvant chemotherapy plus/min zoledronic acid presented at last ASCO [abstract 1028 and 1029].