Reviewer's report

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

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Reviewer: Shunji Takahashi

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Fasching et al. reported the randomized phase II study comparing clinical response of primary breast cancer patients to neoadjuvant therapy with letrozole alone or letrozole and zoledronic acid. This is the first study to compare endocrine therapy with or without zoledronic acid in the neoadjuvant setting, so is very interesting. But in addition to the small number of the patients, there are some problems to be fixed.

Major points
1. The eligibility criteria seem too simple. The patients did not have to be ER and/or PgR positive? How about Her2? Tumor had be measurable by the RECIST criteria?
2. Number of per protocol patients (131) seems low compared with that of randomized patients (168). For instance, ‘unsatisfactory treatment effect’ might be PD and those patients might be included in the per protocol group.
3. Efficacy endpoint is only the clinical (radiological) response. The authors had better show other endpoints such as pathological response or rate of patients with breast-conserving surgery, considering unreliability of the clinical response rate.
4. The measurement methods for clinical response are not clearly described. In how much of the patients MMG, MRI or ultrasonography were used? And as the authors described, the response rates are too dissociated between local and central assessment, making the measurement methods seem very unreliable.

Minor points
1. p4 L25 chemotherapy#endocrine therapy

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I had fees and funding from Novartis.