Reviewer’s report

Title: Phase II randomized study of neoadjuvant METformin plus letrozole vs placebo plus letrozole for estrogen receptor positive postmenopausal breast cancer (METEOR)

Version: 3 Date: 10 June 2013

Reviewer: Lev Berstein

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Actually, it is not scientific paper while description of study protocol or intentions of the author’s.

In case editorial politics accepts such approach (intentions instead of results), let’s it be so.

Authors will combine in a blind multicenter neoadjuvant study letrozole (2.5 mg/day) with metformin (1.5 g/day 1 week, 1.75 g/day 1 week and 2.0 g/day remaining 22 weeks) in 104 postmenopausal BC patients with ER+, Stage II-III tumors vs placebo in the same number of patients.

Criteria of evaluation are mostly clinical, pathological and instrumental.

Although it is underlined in Introduction that effect of Metformin may be dual (‘antiproliferative’ at target level and ‘anti-insulinic’ at systemic level), and Bonnani et al. [Ref 11] showed that BC patients with insulin resistance responded to metformin positively in opposite to the patients without insulin resistance, the authors did not include systemic criteria into their protocol.

Also, is not 24 weeks too long time for evaluation and is not it too risky for the patients with II-III stage of disease? Is not, say 14-16 weeks as often recommended, enough?

In addition, this reviewer cannot agree, that this study will be ‘The first study evaluating direct anti-tumor effect of Metformin in Breast Cancer’ (Discussion, paragraph).

Minor issues: In the text one can find a lot of technical errors (‘breat’ instead of ‘breast’ in Methods/Design in Abstract, ‘respone’ instead of ‘response’ in Study Goal, etc in different places).