Reviewer’s report

Title: Safety and feasibility of adjuvant chemotherapy with S-1 in Japanese breast cancer patients after primary systemic chemotherapy: a feasibility study

Version: 2
Date: 26 November 2014

Reviewer: Luca Porcu

Reviewer’s report:

Major Compulsory Revisions
1. ‘Design of the Study’ section: the primary endpoint is not clear; is it the percentage of the eligible patients completing the 18-course treatment or the cumulative percentage of administration for 365 days? If the primary endpoint is the former a simple percentage (22 out of 43 (51.2%) pts) was calculated and the Kaplan-Meier method is non-sense; otherwise the definition of the primary endpoint should be modified in this section; because the cumulative rate of S-1 administration is a time-to-event endpoint is mandatory to specify the starting time (it should be the first day of the first S-1 administration), the event (it should be the constrained interruption of S-1 administration, patient withdrawal from treatment) and the right-censoring mechanism (data should be right-censored when adjuvant chemotherapy was completed per protocol).

Because no statistical hypothesis was planned it’s possible to use a couple of primary endpoints (e.g. the percentage of the eligible patients completing the 18-course treatment and the cumulative percentage of administration for 365 days); for the same reason lines n°259,260,261 of the ‘Results’ section should be better reported; both endpoints (the cumulative percentage of administration at 365 days from the date of first administration and the percentage of the scheduled adjuvant chemotherapy completed) should be defined and reported as primary or secondary endpoints in this section

Minor Essential Revisions:
1. ‘Design of the Study’ section: I suggest to stress that this is a multicenter trial; the statement ‘This was a non-blinded, open-label, feasibility study’ should be replaced by the statement ‘This was a multicenter, non-blinded, open-label, feasibility study’

2. ‘Design of the Study’ section: the Kaplan-Meier method shouldn’t be reported in the ‘Design of the Study’ section but only in the ‘Statistical analysis’ section

3. ‘Design of the Study’ section: Safety evaluation was an objective of the trial; the endpoint used to evaluate safety should be clearly defined and reported; as showed in table 3 it could be the percentage of patients having a particular adverse event

4. ‘Patient Eligibility Criteria’ section: the applied staging system should be reported (for instance AJCC Cancer Staging Manual. 7th ed.)
5. ‘Treatment schedule’ section: the following statement was reported in the ‘Discussion’ section: ‘Thus, in this study, we chose an anthracycline-based regimen followed by a taxane regimen as the standard PSC’; the standard PSC used in this feasibility study should be reported; the statement ‘All patients received PSC consisting of an anthracycline-based regimen and/or a taxane regimen’ doesn’t support the presence of a standard PSC

6. ‘Dose modification’ section: it should be reported if just a single dose reduction was permitted before treatment interruption

7. ‘Statistical analysis’ section: this section should be better formulated; as reported in the unique ‘Major Compulsory Revision’ the percentage of patients completing the scheduled adjuvant chemotherapy was calculated without the Kaplan-Meier method; a 95% confidence interval for this point estimate should be combined with the point estimate in the ‘Results’ section; the cumulative percentage of administration from the date of first administration was estimated by the Kaplan-Meier method and a 95%CI at 365 days from the starting date was calculated

8. ‘Results’ section: Table 1 should be improved in the following points: BSA should be splitted in three categories: <1.25, >=1.25 and <1.5, >= 1.5; Surgery labels ’Bt’ and ’Bp’ should be explained; assessment system for clinical and pathological response should be reported (for instance RECIST version 1.1)

9. ‘Results’ section: a 95%CI should be reported with the percentage point estimate (51.2%) of patients completing the 18-course treatment

10. ‘Results’ section: the absolute frequencies for patients discontinuing treatment (e.g. 9, 7 and 5 pts) should be combined with percentage frequencies

11. ‘Results’ section: in Fig.1 censoring ticks should be explained in a legend; number of patients at risk should be reported below the survival curves in order to evaluate the reliability of point estimates (this number should be reported at least for the following time-points: 100, 200, 300 days)

12. ‘Discussion’ section: the following methodological limitations should be reported: a. because no statistical hypothesis was planned this feasibility study was exploratory, generating and not demonstrating an hypothesis of safety and feasibility of adjuvant chemotherapy with S-1; b. because of the small sample size and the wide eligibility criteria it was impossible to identify patients at particularly high/low risk of bad/good feasibility

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

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests