Author's response to reviews

Title: Phase II Trial of Sequential Gefitinib After Minor Response or Partial response to Chemotherapy in Chinese Patients with Advanced Non-Small-Cell Lung Cancer

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Author's response to reviews: see over
Answer the comments from Dr. Martin Reck

Major Compulsory Revisions:

1. Yes, the standard of care in chemotherapy of NSCLC is 4-6 cycles of chemotherapy. However, our *in vitro* studies showed that the sequential administration of gefitinib after chemotherapy may enhance/maintain chemotherapy-induced cancer cell damage, and the combination effect is schedule-dependent, the rationale would be to administer the gefitinib when chemotherapy is inducing or has induced maximum tumor damage. Based on our clinical experience, response is usually apparent after the initial two to three cycles of chemotherapy. Thus, in the present trial, only patients with a minor response or partial response to 2-3 cycles of chemotherapy were included.

2. This phase II study is only to explore the value of sequential administration of gefitinib while tumor is responding to chemotherapy. Our purpose is to compare our clinical results (RR, TTP, and OS) with historical data (first-line patients, or second-line patients) reported in literature. Since the response of gefitinib will not be influenced by the different settings, even if it is unfair for our side, we compared our results with first-line data reported in literature is appropriate.

3. All 21 pretreated patients had failed to at least one line of platinum-based chemotherapy since platinum-based chemotherapy is a
standard first-line regimen in my hospital. Before gefitinib, 6 (18.2%) received docetaxel alone, the other 27 (81.8%) received platinum-based regimen. We have added this description to the result section.

4. Yes, in all sections we have changed the description of “response to chemotherapy” to “minor response or partial response to chemotherapy”.

Minor Essential Revisions

1. Yes, we have shortened the discussion section.

2. Ok, we revise the table 2 and omit the statistical comparison between adenocarcinoma and squamous carcinoma in the result section.

3. Do you mean we have to list the items of symptom improvement?

Discretionary Revisions

Yes, we delete the statement since it’s questionable to conclude the advice.

Answer the comments from Dr. David Spigel

1. Since the survival is influenced by so many factors, OS is only a reference factor and the calculations of OS time were different in different studies.

2. Yes, we have corrected the date in the abstract.

3. Yes, we evaluated the response each cycle.
4. Yes, we have added this description in the result section.

5. It’s the first-line chemotherapy we mentioned in the first paragraph of discussion section.

6. Ok, we have added our point why 2-3 cycles is enough in the induction section.

7. Sorry, we did not mean to say gefitinib in patients who did not respond to chemotherapy will not be effective. We were expected to say subsequent synergy will occur if gefitinib was administered to a tumor that is responding to chemotherapy. The purpose of this study is to explore if there are synergistic effects of sequential combination not only on the greater RR but also on the longer TTP and OS than those attained with continuous chemotherapy regimens.

8. Most of the PRs achieved with chemotherapy did not “lost” with gefitinib treatment. Even if it’s SD during sequential gefitinib treatment, we think the minor or partial response achieved by chemotherapy is being maintained.

9. Yes, we have corrected the description.

10. Yes, we delete this paragraph.

Minor Essential Revision

1. Yes, we have corrected it.

2. Ok.

3. Yes, it’s has.
4. Thanks, we have corrected.
5. Ok, erlotinib.
6. Ok, add “potentially”.
7. Ok, define EGFR
8. Yes.
10. OK.
11. Thanks, delete “s”.
12. Yes, add “the”.
13. Yes, in this regard.
14. Yes
15. Yes
16. Yes
17. OK
18. OK