Author's response to reviews

Title: Initial partial response and stable disease according to RECIST indicate similar progression-free survival for chemotherapeutical patients with advanced non-small cell lung cancer

Authors:

Lijie He (Hlj0182@sina.com)
Yuee Teng (tenguee517@yahoo.com.cn)
Bo Jin (jinbo@csc.org.cn)
Mingfang Zhao (zhaomf618@yahoo.com.cn)
Ping Yu (yu_ping0182@yahoo.cn)
Xuejun Hu (cmufuture@hotmail.com)
Jingdong Zhang (zqj_0182@yahoo.cn)
Songbai Li (cumlsb1974@yahoo.cn)
Yaling Gao (gylcancer@hotmail.com)
Yunpeng Liu (cmuliuyunpeng@yahoo.cn)

Version: 6 Date: 15 July 2010

Author's response to reviews: see over
July 15, 2010

Dear editor:

Thank you very much for giving us some constructive advice on the manuscript entitled “initial partial response and stable disease according to RECIST indicate similar progression-free survival for chemotherapeutical patients with advanced non-small cell lung cancer”. Your advice is very helpful to researches in this field. Here we address your concerns point-by-point.

Response to editor:

Editorial request:

Please document ethical approval. Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration (http://www.wma.net/e/policy/b3.htm), and any experimental research on animals must follow internationally recognized guidelines. A statement to this effect must appear in the Methods section of the manuscript, including the name of the body which gave approval, with a reference number where appropriate.

Answer: Our research completely complies with the Helsinki Declaration, and has been approved by the medical ethics committee of the First Hospital of China Medical University (No. 200715), which is underlined in the last paragraph in the Methods section.

Response to Dr. Takehito Shukuya:

Comments and answers:

1. In this study, because the number of the patients is too small, it is hard to conclude that there is no difference of progression free survivals between the patients with SD and PR. Moreover, considering that most of the patients experienced tumor shrinkage (100/117) in the patients with SD, there seemed to be some bias.

Answer: As we all agree that big number of the patients is more convincing in any scientific research, and thus is more desirable. But we have consulted with some statisticians that a sample of about 100 is also reliable to conduct such kind of research. Similarly, Birchard KR et. al. conducted their study with a sample of 99[Birchard KR, Cancer 2009], and their result is quite similar to ours. Our sample consists of 179 patients. It has been reported that response rate (CR+PR) of advanced non-small cell lung cancer in the initial assessment after platinum-based
chemotherapy ranged from 20% to 30%, many more patients experience SD [Primo N. Lara Jr, J Clin Oncol 2008. Sirohi B, J Thorac Oncol 2007. Birchard KR, Cancer 2009], and our result is totally in compliance with these studies. Moreover, our result that more patients experienced tumor shrinkage in the patients with SD is just the true outcome of the research which is very similar to the result of a research conducted by Katherine R. Birchard in 2009 [Birchard KR, Cancer 2009].

2. Although the authors describe that PFS can accurately indicate the survival benefit of the first-line therapy, the impact of overall survival is still high. So, the authors should investigate both PFS and overall survival.
Answer: As been known, OS is a widely accepted end-point of all solid tumors. But OS is often significantly affected by other factors, such as the effects of second-line, third-line, best supportive care and other local treatment, thus it is hard to reflect the effectiveness of first-line chemotherapy precisely. We choose PFS as our end-point because we consider PFS more accurate, swift and specific in reflecting effectiveness of first-line chemotherapy, which enables clinicians to modify their treatment project as soon as possible.

3. Because RECIST was revised from ver 1.0 to ver 1.1 in the first of last year, the authors should investigate using ver 1.1.
Answer: In the study, we adopted the revised version of RECIST in the year 2009. The changes are underlined in the first paragraph in the Background section.

4. In "Methods, Dosage Adjustment Scheme", I think it is not common to reduce the dosage of chemotherapy when only grade 3 hematological toxicity occurs.
Answer: According the Medical Ethics Committee of the First Hospital of China Medical University, when grade 3 or greater hematological toxicity occurs, dosage for the next course should be reduced to 75%-85% of the original dosage. And some clinical trials abroad also adopt this principle.

5. In "Results, Distribution of Response Categories and Patient Characteristics", the authors should show the reason of 9 withdrawals after completing their first cycle of chemotherapy.
Answer: We agree with you totally. As for the reason for the 9 withdraw from the study, it has been underlined in “Results, Distribution of Response Categories and Patient Characteristics”.
Response to Dr. Maria Werner-wasik:

Comments and answers:

1. When defining RECIST, please make it clear it is based on the CT scans and does not include any modalities which assess a metabolic response

Answer: Upon the request of referee 2, when defining RECIST, we make it clear in the manuscript that stratification of patients into CR, PR, SD or PD has been carried out solely on the basis of CT scans.

2. The statement that the PFS is predictive of survival (OS) is not universally accepted in all solid tumors, even though it may be true for colorectal cancer. The clinical trials continue to use OS as an endpoint, at least in lung cancer.

Answer: Just as the answer above, PFS is more accurate in reflecting the effectiveness of first-line chemotherapy for the patients who did not receive any maintenance treatment after first-line therapy.

3. It would be an interesting analysis to see if percentage tumor shrinkage in patients examined in this study correlates with PFS and/or OS, when examined as a continuous variable (as done in "waterfall plots")

Answer: Upon the request of referee 2, we have added the “waterfall plots” in the distribution of change in tumor size of initial SD patients, which is underlined in “Result, Distribution of Change in Tumor Size of Initial SD Patients”.

Thank you very much for your attention and consideration.

Sincerely yours

Yunpeng Liu