Author’s response to reviews

Title: Fast Track Multi-Discipline Treatment (FTMDT trial) Versus Conventional Treatment In Colorectal Cancer - The Design of A Prospective Randomized Controlled Study

Authors:

Jiao-Jiao Zhou (doctor.iojozhou.forwork@gmail.com)
Jun Li (jia6088@gmail.com)
Xiao-Jiang Ying (lg_sx@sina.com)
Yong-Mao Song (zsypanda@yahoo.com.cn)
Rong Chen (cr13806887833@163.com)
Gang Chen (chengang120@hotmail.com)
Yan Min (yanminnina@hotmail.com)
Ke-Feng Ding (dingkefeng@zju.edu.cn)

Version: 3 Date: 26 September 2011

Author’s response to reviews: see over
Title: Fast Track Multi-Discipline Treatment (FTMDT trial) Versus Conventional Treatment In Colorectal Cancer – The Design of A Prospective Randomized Controlled Study (Study protocol, ID: 1167830824551850)

Authors: Jiao-Jiao Zhou, Jun Li, Xiao-Jiang Ying, Yong-Mao Song, Rong Chen, Gang Chen, Min Yan, Ke-Feng Ding

Dear Dr. Christna Chap,

Thanks for your review. All of the authors think that the comments are valuable. We have revised and uploaded the manuscript according to the comments. The point-to-point responses and changes are listed below.

All the lines and pages indicated below are in the revised manuscript. And each change in the manuscript was highlighted, with the amendments present in the comment boxes.

Part A. Response to Editor:

1. The editor’s comments: Please structure the abstract according to the guidelines.

Response: We have read the BMC authors' checklist and revised the manuscript formatting conforms to the journal style. The abstract was less than 350 words, and was restructured into separate sections as suggested: Background, Methods, and Conclusions. Because it’s the study protocol, we didn’t involve the Results in the manuscript.

Changes in the manuscript: Page3, Abstract
Part B. Response to Reviewer:

1. The reviewer’s comments: The authors mentioned that the numbers of patients of one arm is 80 and total 320 patients. Is the number of patients of one arm enough?

Response: Thank you for reminding us the sample size. Our statistician carefully estimated the sample size for the trial before the trial started and consider that 340 patients in total are enough. With the standard deviation of 6 days of mean hospitalization days, a total sample size of 218 would have a power of > 0.85 to detect a minimum reduction of 2 days in hospital stay among the 4 groups, using a 5% significance level.

And adjuvant chemotherapy will be needed for III stage or high-risk II stage pathologically established colorectal cancer. According to the Li M*, the III stage or high-risk II stage account for 64% of the total colorectal cancer patients in China, therefore it totally needs 340 patients (218 ÷ 64% = 340) to reach the sample size of 218. And each group needs 85 patients.

Changes in the manuscript: None


2.

1) The reviewer’s comments: The Inclusion Criteria was regulated as patients who are 18 years and older. But, did the authors want to include the high aged patients such as over 75 years old?

Response: All the authors agree to your advice. Since there were lack of
evidence-based researches on the efficacy and safety of the chemotherapy on older patients of colorectal cancer, our reason of not setting the age upper limit was aim to further explore the feasibility and safety of the Fast Track Multi-Discipline Treatment Model on the older patients of colorectal cancer. Some publications (Schmoll HJ etc.**) also involved the older patients even ≥75 years. So, patients older than 18 who agree to participate with the informed consent obtained, will be included in the trial.

Changes in the manuscript: None


2) The reviewer’s comments: The authors excluded tumors which can be resected by endoscopic mucosal resection (EMR). Were the submucosal tumors included? Adjuvant chemotherapy may not be needed for patients with Stage I colorectal cancer. Did the authors want to include Stage II and III colorectal cancers?

Response: All the authors agree your comments that we should also exclude the tumors, which can be resected by endoscopic submucosal dissection (ESD).

For adjuvant chemotherapy, we mentioned it will be needed for III stage or high-risk II stage pathologically established colorectal cancer in Page10, Adjuvant Chemotherapy, Line1-2. However, we didn’t present it in the Eligibility, and now we add it in the revised manuscript as suggested.
3) The reviewer’s comments: Chemotherapy should not be performed for such patients with leucopenia, renal failure, or inflammation.

Response: The exclusion criteria before surgery include American Society of Anesthesiologists (ASA) score $\geq$ IV. Then, performance status of the patients after surgery will be also evaluated with the Zubrod-ECOG-WHO score, before the chemotherapy start. Patients with Zubrod-ECOG-WHO score sustain $\geq 2$ within 3 months after surgery will be excluded and not have the chemotherapy.

Changes in the manuscript: Page8, Line4

3. The reviewer’s comments: The authors should clarify the discontinuance criterion of this clinical trial. Or the authors should mention the reduction rate of XELOX or FOLFOX treatment.

Response: All the authors agree to add the discontinuance criterion of this clinical trial as followings: 1) the trial appears causing unexpected harm or severe adverse events to participants, or the evidence that the risks outweigh the benefits, with the discontinuance decision of the ethics committees. 2) the enrollment indicates the trial can’t be finished in the period of 4 years. 3) chemotherapy will be suspended for the patients with the chemotherapy adverse events more than grade 3 according to NCI-CTC AE 3.0 (National Cancer Institute Common Terminology, Criteria for Adverse Events 3.0). And the dose will be adjusted to 75% after adverse events reduce to grade 2 or lower. The chemotherapy will be withdrawn once the severe adverse events
appear again.

**Changes in the manuscript:** Page8, Line5

4. The reviewer’s comments: The period of this study is not clarified. To investigate the patients’ QOL, it takes long follow-up time.

**Response:** The primary endpoint of this study is the hospital stays. And the main investigation of the hospital stays for surgery and chemotherapy will need approximately half a year. The patient quantity of trial will also be enough, because each center (Hangzhou, Shaoxing, Wenzhou center) conducted ≥300 colorectal cancer surgeries per year.

The recruitment of the trial has begun since April 2010, and the study will take 4 years for the investigation and follow-up of the patients.

**Changes in the manuscript:** None

**Part C. Corrections:**

1. **Correction:** We miswrote the hospital stay of III and IV group as 46 and 48 days and it was corrected as 48 and 50 days.

**Changes in the manuscript:** Page11, final line

Thank you and reviewer for all the kind advice!

We hope that the revised manuscript is acceptable for publication in BioMed Central, Cancer.

Sincerely yours,
Prof. Ke-Feng Ding

Department of surgical oncology, Second Affiliated Hospital, and The Key Laboratory of Cancer Prevention and Intervention, China National Ministry of Education, Zhejiang University College of Medicine, Hangzhou 310009, China.
Tel: 86-571-87784760.
Fax: 86-571-87783458.
Email: dingkefeng@zju.edu.cn

Authors’ E-mail
Jiao-Jiao Zhou, doctor.jojozhou.forwork@gmail.com
Jun Li, lj6088@gmail.com
Xiao-Jiang Ying, lg_sx@sina.com
Yong-Mao Song, zsypanda@yahoo.com.cn
Rong Chen, cr13806887833@163.com
Gang Chen, chengang120@hotmail.com
Min Yan, yanminnina@hotmail.com