Title: Cardiac damage after treatment of childhood cancer: A long-term follow-up

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Version: 3 Date: 3 March 2008

Dear editor,

Thank you very much for your letter of 30 January 2008 regarding our manuscript "Cardiac damage after treatment of childhood cancer: A long-term follow-up" (manuscript MS: 1082597227164779). We read comments of reviewer carefully and we revised the manuscript according to his comments. Herein we provide a detailed list of changes performed in the revised manuscript. We believe that revision only strengthened the message of the manuscript.

Comments No.1 and 2:

According to our results the time period of the patient’s treatment emerged as an important risk factor for injury of the heart. Our finding of multivariate analysis show that patients treated latest, in the years 1989-98 are at highest risk for any injury of the heart. These patients were treated with intensive multiagent chemotherapy. They received larger cumulative doses of anthracycline (more than 200 mg/m2) and they received more aggressive chemotherapy. They were treated often concomitantly with anthracycline and alkylating agents. We added this explanation in the Discussion section (page 13, paragraph 2).

3. It is reported by some authors in similar studies that female gender is a predictor for cardiac damage. We were not able to confirm this observation with the results of our study. We added this statement in the Discussion section (page 13, paragraph 3).

4. In Slovenia all children with cancer are treated at the Pediatric Cancer Center at the University Children Hospital, Department of Hematology and Oncology and at the Institute of Oncology. When the childhood cancer survivors reaches the age of 18 years and are at least 5 years posttreatment, they are eligible for further follow up at the outpatients Clinic for Late Effect at the Institute of
Oncology. Of the 874 survivors, 399 were regularly followed at the outpatients Clinic for Late Effects. All were at least 18 years old and at least 5 years after treatment. 235 survivors who were younger than 18 years old and less than five years after treatment of childhood cancer were followed at the University Children Hospital. Of the remaining survivors who had surgery only 95 were followed by surgeons or they refused regular follow up. There were 72 patients originally from other parts of former Yugoslavia, who were not followed after 1991 when Slovenia became independent state.

The patients were systematically sent to the cardiologist for evaluation, when they came to the outpatient Clinic for late effects. There was no selection. We included this explanation in the section Patients and methods (page 5, paragraph 2).

Minor Essential Revisions

1. We added the number of pages
2. We deleted bold words in abstract
3. We corrected the reference on page 14, paragraph 1
4. We deleted »?« on page 14, last paragraph
5. We added explanation for the low level of anthracycline (≤ 200 mg/m2) in tables 1, 3 and in figure 3
6. We translated words in English in table 3
7. We changed reference 16 in pediatr hemtol oncol

We hope that the revised manuscript will fulfill the criteria for publication. However, if there is need, we would appreciate an opportunity for additional revision.

Sincerely,

Veronika Velen±ek, MD, PhD