

Reviewers Comments:-

I have read some data about the treatment of leukemia and consulted colleagues , if single **Doxorubicin** treatment of acute lymphoblastic leukemia, it is not in line with international guidelines, there is a big problem in the study.

Author's feedback:-

We followed in our study the published guidelines for diagnosis and treatment of ALL in children and also for diagnosis of DOX induced cardiotoxicity. We just focused on the cardiotoxic chemotherapeutic DOX and the potential cardioprotective GSE and referred to the other drugs when we said that we obtained twice samples from each patient, at the end of induction (phase- I) following four doses of DOX chemotherapy, and at the end of CNS intensification (phase II) at section 2, subsection 2.3. And when we said that" Doxorubicin hydrochloride was provided as Adriamycin vials (25mg/m²) according to BFM protocol" in section 2, subsection 2.2. We presumed that, it is an international protocol and it was known that DOX was given in combination with other chemotherapeutic drugs in each phase. We did not say group I received DOX only. However we revised our MS and tried to clarify this point in the following :

Abstract, place & duration, lines15&16, page no1." **They were divided into two groups; group I received Doxorubicin-containing chemotherapy while Group II was treated with Doxorubicin-containing chemotherapy plus GSE all over the study period "**.

Materials & methods section, subsection 2.2, lines 113& 114, page 3 "**Group I received chemotherapy containing cardiotoxic DOX, and Group II received chemotherapy containing cardiotoxic DOX plus proanthocyanidin GSE "**. Subsection2.3, lines 121-124, page 3 " **Doxorubicin hydrochloride was provided as Adriamycin vials (25mg/m² per dose for 4 doses weekly), in combination with other chemotheraputics according to modified BFM protocol (prednisone 60 mg/m²,**

vincristine 1.5 mg/m², L- asparaginase 6000u/m², cyclophosphamide 1000 mg/m², 6- mercaptopurine 60 mg/ m², ARA-c 75mg/ m² and age dependent dose of methotrexate) ".We hope that all comments were replied and our MS was clear & informative.