Author's response to reviews

Title: Immunophenotypic Identification of High-Risk Monoclonal Gammopathy of Undetermined Significance

Authors:

Horatiu Olteanu (holteanu@mcw.edu)
Huan-You Wang (Huan-You.Wang@UTSouthwestern.edu)
Weina Chen (Weina.Chen@UTSouthwestern.edu)
Robert W McKenna (mcken138@umn.edu)
Nitin J Karandikar (Nitin.Karandikar@UTSouthwestern.edu)

Version: 2 Date: 30 July 2008

Author's response to reviews:

Reply to reviewers

Dear Dr. Emunds,

We thank you, Dr. Rawstron and Dr. Johnsen for reviewing our manuscript. We hope we were able to address them in a satisfactory manner and are looking forward to your reply. Following are the specific changes made to the manuscript based on the reviewers’ comments:

Reviewer: Andy C. Rawstron

Major compulsory revisions:
1) We included in the “Results” section the progression-free survival and the time from diagnosis until progression for the MGUS patients. Also added was a reference for the criteria used to define progression of disease and information on the treatment the patients with ROTI received.
2) We added the specific antibody combinations and the corresponding fluorochrome conjugates, in the “Methods” section.

Discretionary revision:
1) We deleted Figure 6 and combined Figures 4 and 5 in a single figure, formatted as requested.
2) We agree with Dr. Rawstron on the importance of CD138 for gating plasma cells and added a comment regarding this in the “Discussion” section, including the reference to the report of the European Myeloma Network. We also acknowledge the difference in CD19(+) plasma cells in MGUS cases reported by us (<10%) and by the Salamanca group (<5%), and agree with the comment regarding the importance of this difference for defining MGUS at risk for progression vs. identifying minimal residual disease. Of note, both our study and the study by Perez-Persona et al. were independently performed and preliminary
result were reported the same year at different venues (2006 EAH Annual Congress and 2006 USCAP Annual Meeting, respectively).

Minor essential revisions:
1) The wording of the last sentence on page 3 was changed as suggested by Dr. Rawstron.
2) The wording of the sentence on page 6, Clinical and laboratory characteristics section, was changed as suggested by Dr. Rawstron.

Reviewer: Hans E. E. Johnsen

We respect Dr. Johnsen’s opinion of not considering this manuscript worthy of publication. However, we feel the data presented in our study are interesting enough to warrant dissemination in the research community. In terms of data analysis and methodology, our initial hypothesis was based on the findings of Ocqueteau et al. (reference 10 in the manuscript), corroborated with our personal observations, that there are immunophenotypic differences between MGUS and plasma cell myeloma. We undertook a similar approach to that reported in the study of Perez-Persona et al (reference 27 in the revised version of the manuscript) and arrived at similar conclusions. We acknowledge that our cohort does not match the size and length of follow-up of the Salamanca studies and that the CD19(+) plasma cell cut-off used to define MGUS cases at risk for progression are slightly different (10% vs. 5%). However, as mentioned in the reply to Dr. Rawstron, we would like to point out that both our study and the study by Perez-Persona et al. were independently performed and preliminary result were reported the same year at different venues (2006 EAH Annual Congress and 2006 USCAP Annual Meeting, respectively). Together with the data from the Leeds group, they represent only a very limited number of studies that addresses an important issue and as such, we felt our results warrant consideration for publication.

There were no specific items to address otherwise in Dr. Johnsen’s review.

Regards,
Horatiu Olteanu, MD, PhD