WHO EDL Secretariat

Sent by email to: WHO EDL Secretariat (edlsecretariat@who.int)
Cc: Maria Mercedes Pérez Gonzalez (perezgonzalezm@who.int)
Lucy Hattingh (lucy.hattingh@dxmarketinginsight.com)

Estoril (Portugal), February 25th 2019

Subject: IPOPI’s response to the review questions relating to the submission to EDL of differential diagnosis of primary antibody deficiency (rule out multiple myeloma) ID 41_15

Dear Sir, dear Madam,

Thank you for sending the question raised by the reviewer on the differential diagnosis of primary antibody deficiency (rule out multiple myeloma) that we submitted for its inclusion in the next version of the WHO Essential Diagnostics List.

Please find below the answer required to the following question: “If the authors believe a significant number of patients with multiple myeloma will benefit from protein electrophoresis being performed in patients suspected of primary immunodeficiencies, please submit estimates of the number of patients along with references.”

There is no age limit to diagnose a patient with an antibody failure (including low serum levels of immunoglobulin A -IgA-, IgG and IgM). In the case of Common Variable Immunodeficiency Disorder (CVID), the diagnosis is made on the basis of exclusion – including that of multiple myeloma and other haematological malignancies.

Patients with a CVID diagnosis have a range of 4 to 80+ years of age (for supporting references, please see below), so other causes of low serum immunoglobulins have to be excluded. In this sense, electrophoresis is essential for such exclusions to be made in older adults.

Free light chain analysis is useful to confirm myeloma but probably not essential for a PID; the reviewer comments that urine electrophoresis may be sufficient. The reviewer also recommends that protein electrophoresis and presumably urine electrophoresis also, should be included for haematological diseases and we submit that this also applies to adults presenting with PIDs – especially low serum Igs, to exclude immunodeficiency secondary to haematological malignancies.

Contrary to the question posed, the immunologists that are also supporting this application do not think that “a significant number of patients with multiple myeloma will benefit from protein electrophoresis being performed in patients suspected of primary immunodeficiencies” but they need protein electrophoresis to exclude a secondary cause of low Igs in order to diagnose a primary immunodeficiency in adults.

Supporting references:
- Chapel, H and Cunningham-Rundles, C. Update in understanding common variable immunodeficiency disorders (CVIDs) and the management of patients with these conditions. British Journal of Haematology, 145, 709–727

We hope that with the information provided above, we have answered the question raised by the examiner. We remain at your disposal should there be a need to provide any clarification or additional information.

With kind regards,

Johan Prévot
Executive Director