

BIO-RAD PLATELIA ASPERGILLUS EIA DETECTION OF ASPERGILLUS GALACTOMANNAN ANTIGEN IN HUMAN SERUM PERFORMANCE EVALUATION IN A LARGE BONE MARROW TRANSPLANT CENTER.

*McLaughlin L³, Balajee A¹, Leisenring W¹, Tabouret M², Bentsen C³, Ferrera C³, Marr K¹
¹Division of Clinical Research, Fred Hutchinson Cancer Research Center, Seattle, Wa. USA,
²Bio-Rad Laboratories, Steenvoorde, France, ³Bio-Rad Laboratories, Redmond, Wa. USA

Background: Invasive aspergillosis (IA) is a common life-threatening invasive fungal infection in patients undergoing hematopoietic stem cell transplantation (HSCT). Establishing a definitive, early diagnosis is difficult, as it requires invasive procedures and the sensitivity of both microbiology and histopathology tests are often low. The Bio-Rad Laboratories Platelia Aspergillus EIA is a one-stage immunoenzymatic sandwich microplate assay that uses rat monoclonal antibody EBA-2 to detect circulating galactomannan (GM). We evaluated the utility of the GM EIA for the detection of IA using sera collected prospectively from allogeneic HSCT recipients. Methods: A total of 986 sera, collected from 67 patients, were analyzed. Patients were defined as having proven IA (178 sera from 13 patients), probable IA (201 sera from 11 patients), or no IA (472 sera from 35 patients) using NIH MSG/EORTC standardized definitions, by an investigator blinded to GM results. Sera were tested for GM with the Platelia EIA, utilizing the manufacturer's directions. Negative, positive and 2 threshold controls were run on each plate to validate the test results. An Index was calculated as the ratio of sample GM relative to mean optical density of the threshold controls. As we hypothesized that the power of the assay may be impacted by clinical factors that decrease circulating fungal burden (antifungals), analyses were performed utilizing variable index cutoffs to define positivity. Results: Utilizing an index cutoff of 1.5, sensitivity for detection of proven IA was 46.2% (6/13), probable IA 45.5% (5/11), and 45.8%

(11/24) for both groups combined. Utilizing an index cutoff of 0.5, sensitivity increased to 92.3% (12/13), and 72.7% (8/11) in patients with proven and probable IA, respectively, with a loss of specificity from 99.7% (605/607) to 97% (589/607). Utilizing the index cutoff of 1.5, the assay was less sensitive in patients with proven and probable IA receiving mould-active antifungals (30.8%), compared to patients who received fluconazole (63.6%). With an Index cut-off set at 0.5, antifungal therapy did not appear to affect sensitivity in patients receiving antifungal therapy (84.6% vs. 81.8%). Conclusion: The Platelia Aspergillus EIA demonstrated excellent specificity ranging from 97% to 99.7% in patient samples at the three cut-offs evaluated. Sensitivity ranged from 45-92% depending on the cut-off chosen. Sensitivity of the assay can be improved if the index cutoff is adjusted in patients who receive mould-active antifungal therapy prophylactically or empirically.