Diagnostics of Invasive Aspergillosis: From Experimental Models to Clinical Evaluation

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Panel Discussion plus Q&A

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Is there utility of evaluation of *Aspergillus* specimen based on source of sample? Serially monitoring specimens from patient at risk vs taking specimen from patient with clinical syndrome that could be Invasive *Aspergillosis*. Is there utility in testing for *Aspergillus* based on a single specimen? Can therapy according to *Aspergillus* guidelines have an impact on the diagnostic testing? Testing or specimen type collected may need to be modified in response to this process.

Prior to seeking FDA approval / or submitting an application, there are many things to look at: Are there additional studies to determine if the patient can be monitored? What kind of treatment has the patient received? Were tests performed after therapy was initiated? Is a new medical practice being introduced that increases medical risk? – that is – is there a new intended use? Clinical prospective studies may still be required when significant risk is involved. Classifications were made in 1976 and 1980, and some organisms were of little risk at that time. At that time, *Aspergillus* was already in Class 1. Multiple test results may have more value that a single time result. FDA has looked at regulation of *Aspergillus* testing based on a classification system that is now dated. With increased risk to patient, higher level of classifications may be needed.

Do considerations exist between two types of tests – that is – quantitative tests vs qualitative tests? There are differences on whether the assay is for screening or for diagnosis. Quantitation is tricky and will remain so until signal detection improves. The specimen may dictate what is trying to be achieved with the assay, that is – the utility of a test may be to provide a surrogate marker for treatment response. The question is: Do clinical studies exist that can show this? Or can they be designed? Can these studies show beyond a reasonable doubt that these test can be preformed safely and accurately?

How important is the ability of a test to perform speciation of *Aspergillus* or other moulds? That depends on the total impact of the organism on disease, for instance, how many total cases are there? Is a “black box” warning label needed in situations that specific identifications are not made by a test system? New treatment options beyond the one formerly available mean that this makes a clinical difference. Good tests that lack speciation ability can be augmented with other methods that can speciate

an organism. Still, in regard to quantitative tests vs qualitative tests, what question are we trying to answer? It's better to ask a specific question and then develop a test that actually answers the initial question. It makes sense to have both types of tests – and a lot depends on the pretest risk probability. Screening procedures are of little use when the patient is at low risk, whereas for patients at high risk, a good screening test is helpful. In a laboratory setting, two types of tests may be very helpful, particularly since there are dramatic differences in the specimen types.

Should we ignore drug resistance? Or develop more tests to detect drug resistance? What drug should the clinician use? Can we use virology data and studies in the realm of HIV a s model for resistance testing in *Aspergillus*? What is the impact of host response?

What are the necessities for product labeling and study design from a regulatory standpoint? We know that biomarkers vary according to the host. The intended use section will describe the study population. The indications will actually drive the intended studies. The clinical study is very important aspect of the approval process. Do the repository samples continue to have utility in this setting? This needs to be noted in the "indications" section.