

# Early positive results of the MycoMEIA Urine Assay Employed as a Screen to Diagnose Invasive Aspergillosis

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## BACKGROUND

Early therapy improves outcomes of invasive aspergillosis (IA), but available diagnostics are limited in performance and require invasive sampling (blood or BAL). We previously described novel antibodies recognizing galactofuranose (galF)-containing antigens that aid diagnosis of IA when testing urine. Published data demonstrate proof of concept for urine diagnostics in a lateral flow format.<sup>2</sup> An ultrasensitive EIA, MycoMEIA™ has been developed with performance data showing sensitivity of 95.2% (95% CI 76.2–99.9) and specificity of 94.2% (95% CI 89.3–97.3) in people with proven or probable IA, before receipt of <3 days mold-active antifungals or with clinical advancement despite antifungals (data presented in this meeting, Poster #443). Here, we tested MycoMEIA to evaluate sequential urine samples from 49 of 50 people enrolled during high-risk periods after treatment for acute myeloid leukemia (AML) or receipt of allogeneic bone marrow transplant (BMT) at JHU.

## STUDY DESIGN & METHODS

- People with high risks for IA after therapy for AML/MDS and/or receipt of BMT were consented for urine collection at JHU in 2015. Urine and sera were collected weekly until hospital discharge, or for up to 12 weeks in BMT recipients. Sampling frequency increased to twice weekly in people with suspected infections. Samples were stored frozen until testing.
- Management and diagnostic evaluations were performed independent of study activity. Typically, people received fluconazole prophylactically during periods of neutropenia or a mold-active azole or liposomal amphotericin B with suspected invasive fungal infections.
- Results are shown from 49 of 50 people who consented for urine & blood collection and had at least one urine sample obtained.
- Clinical adjudication was performed by a reviewer blinded to urine assay results, to determine certainty of diagnosis after 3-month clinical follow-up, using MSG/EORTC consensus definitions that consider clinical risks, radiology, microbiology, and histopathology. Proven IA requires microbiologic and histopathologic confirmation. Probable IA requires positivity of antigen or culture from non-sterile site (bronchoalveolar lavage or serum galactomannan). Possible IA includes people with consistent clinical and radiographic findings but without microbiologic confirmation. Other diagnoses, including other infections, were also characterized.
- MycoMEIA assays were performed by an investigator blinded to clinical diagnosis. Results were reported as an index value relative to a cut-off control, in which EIA Index  $\geq 1$  is considered positive. Performance was calculated as per-case sensitivity of subjects with sub-analyses considering diagnosis and receipt of mold-active antifungals.
- BioRad's Platelia® galactomannan enzyme immunoassays were performed in sera obtained on the same day positive MycoMEIA assays to test concordance of the two antigens.

## ACKNOWLEDGEMENTS

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## PRINCIPAL FINDINGS

- 383 urine samples were obtained from 49 subjects, with a median of 8 samples collected per subject (range 1–16).
- 23 subjects were enrolled with new or relapsed AML and 26 had undergone haploidentical BMT for AML (n=13) and other diagnoses listed in Table 1.
- Median duration of screening was 9 (range 3–12) and 4 (range 1–10) weeks for BMT and non-BMT subjects, respectively.
- In 37 (75.5%) subjects, 1<sup>st</sup> samples were obtained after start of regimen, at a median 5 days (range 0–21). 22/49 (44.9%) subjects were already receiving mold-active antifungals for possible IA when the first sample was obtained. Diagnoses and sample results are shown in Table 2.
- Per-case sensitivity for MycoMEIA as an aid to diagnose proven or probable IA was 100% (95% CI 39.8–100), and specificity was 90.9% (95% CI 58.7–99.8). When considering possible IA as cases, sensitivity decreased to 91.4% (95% CI 76.9–98.2).
- Test results typically decreased with mold-active antifungals. In 8 people who had positive tests on or before antifungal therapy, MycoMEIA was positive a median of 5 (range 0–23) days prior to clinical suspicion.

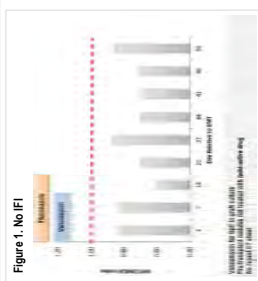
Table 1. Subject Characteristics (n=49)

| Variable                            | N (%)      |
|-------------------------------------|------------|
| Clinical Risk for Aspergillosis     | 23 (46.9%) |
| AML/MDS (no BMT)                    | 26 (53.1%) |
| BMT (non-maleobalve haploidentical) | 26 (53.1%) |
| Underlying Disease                  |            |
| AML / MDS                           | 36 (73.4%) |
| Lymphoma                            | 4 (8.2%)   |
| ALL                                 | 3 (6.1%)   |
| Stickle Cell Disease                | 2 (4.1%)   |
| CLL                                 | 1 (1.1%)   |
| CML                                 | 1 (1.1%)   |
| Adjudicated Fungal Infection        |            |
| Proven invasive mold, NOS           | 1 (1.1%)   |
| Probable IA                         | 3 (6.1%)   |
| Possible IA                         | 31 (63.2%) |
| Possible histoplasmosis             | 1 (1.1%)   |
| Candidemia                          | 1 (1.1%)   |
| No IFI                              | 10 (20.4%) |

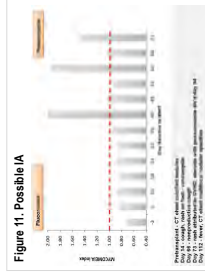
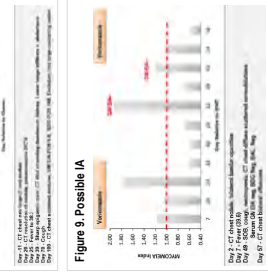
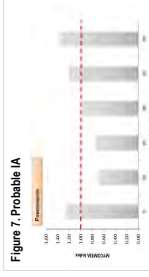
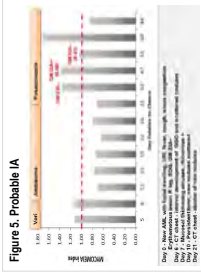
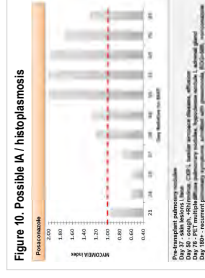
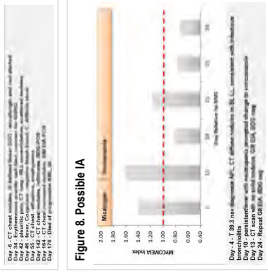
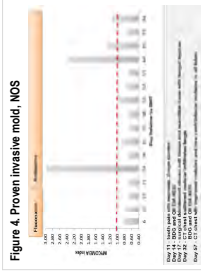
Table 2. MycoMEIA Results classified by IFI Diagnosis

| Diagnosis                                     | Positive / Subjects (%) | Negatives / Subjects (%) | Positive / Samples (%) | Negative / Samples (%) |
|---|-------------------------|--------------------------|------------------------|------------------------|
| Controls – No IFI                             | 1/10 (10%)              | 9/10 (90%)               | 156 (1.8%)             | 55/56 (98.2%)          |
| Controls – Candidemia                         | 1/1 (100%)              | 0/1 (0)                  | 1/5 (20%)              | 4/5 (75%)              |
| <b>Controls, Total</b>                        | <b>3 (21.4%)</b>        | <b>11 (78.6%)</b>        | <b>3 (3.8%)</b>        | <b>76 (96.2%)</b>      |
| Cases – Proven IMI, NOS                       | 1/1 (100%)              | 0/1 (0)                  | 4/16 (25%)             | 12/16 (75.0%)          |
| Cases – Probable IA                           | 3/3 (100%)              | 0/1 (0)                  | 14/35 (40.0%)          | 21/35 (60.0%)          |
| <b>Cases, Total</b>                           | <b>4 (100%)</b>         | <b>0</b>                 | <b>18 (35.3%)</b>      | <b>33 (64.7%)</b>      |
| Possible IA                                   | 28/31 (90.3%)           | 3/31 (9.7%)              | 71/263 (27.0%)         | 192/263 (73.0%)        |
| Possible histoplasmosis                       | 1/3 (33.3%)             | 2/3 (66.7%)              | 1/18 (5.6%)            | 17/18 (94.4%)          |
| <b>Ambiguous (possible) diagnoses – Total</b> | <b>29 (85.3%)</b>       | <b>5 (14.7%)</b>         | <b>72 (25.6%)</b>      | <b>209 (74.4%)</b>     |

## NARRATIVES: CONTROLS



## NARRATIVES: CASES



## CONCLUSION

This, and results of other presented studies show that MycoMEIA is sensitive and specific as an aid to diagnose IA in people with suspected disease. This screening study demonstrates good sensitivity with signs of possible, radiographic IA. Urine tests appear to be a more common positive indicator of IA compared to the currently used BioRad Platelia® serum GM EIA. Early positivity here suggests potential utility as a screen in people with high risks.

## CONTACTS

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## REFERENCES

(1) Dufresne SF, et al. PLoS One. 2012;7(8):e42736. (2) Marr KA, et al. Clin Infect Dis. 2018 Nov 13;67(11):1705–1711.