KARIUS® | STUDY SUMMARY

Karius Test for Detection of Pulmonary Invasive Mold Infections

548 Retrospective Case-Control Study of the Performance of Cell-Free Plasma Sequencing to Detect Invasive Mold Infections in Hematopoietic Cell Transplant Recipients with Pneumonia

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POSTER SESSION II - Infectious Diseases and Cytotoxic T Lymphocytes
Saturday, February 23rd: 6:45 - 7:45 PM

The Karius® Test provides a non-invasive means of identifying pulmonary invasive mold infections - a significant cause of morbidity and mortality in HCT recipients.

PATIENT POPULATION / STUDY DESIGN

This retrospective case-control study included 57 HCT recipients with proven/probable pulmonary invasive mold infection and 19 controls with non-fungal pulmonary infections.

Plasma samples were obtained within 14 days of diagnosis and analyzed with the Karius Test. The diagnostic workup also included chest CT scans, fungal stains,cultures of BAL and biopsied tissue samples, and galactomannan testing of BAL and serum.

RESULTS

Overall, the Karius Test identified pathogenic molds in 15 out of 57 patients with proven and probable invasive mold infections (IMI) and 14 out of 44 patients when testing was done within 7 days of diagnosis.

In non-*Aspergillus* proven IMI, the Karius Test identified 5 out of 6 molds (83%). For *Aspergillus* proven/probable disease, *Aspergillus fumigatus* was identified in 7 out of 51 patients and *Rhizomucor* and *Cunninghamella* species were identified in three additional patients. By optimizing analytical sensitivity, additional cases had *Aspergillus* and other pathogenic molds identified, increasing the detection rate of pathogenic molds to 16 out of 51.

Session II
#548

Retrospective case-control study of the performance of cell-free plasma DNA sequencing to detect invasive mold infections in HCT recipients with pneumonia

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Background and Methods

Background

- Pulmonary invasive mold infections (IMI) remain a significant cause of morbidity and mortality after hematopoietic cell transplant (HCT).
- Non-invasive diagnostic options are limited, particularly for non-Aspergillus molds.
- Given differences in spectrum of activity and toxicities associated with mold-active therapy, early diagnosis and targeting of specific IMI is important.
- We evaluated the performance of the Karius cell-free plasma next-generation sequencing (NGS) test for detecting IMI in HCT recipients with pneumonia.

Methods

- We conducted a retrospective case-control study of 114 HCT recipients with **1)** proven/probable pulmonary aspergillosis (n=51), **2)** possible pulmonary aspergillosis (n=20), **3)** proven/probable non-Aspergillus pulmonary IMI (n=24), and **4)** non-IMI pneumonia (controls, n =19).
- All subjects had frozen plasma samples obtained within 14 days of diagnosis (79% within 7 days).
- Diagnostic workup included computed tomography chest imaging and bronchoalveolar lavage (BAL) and/or biopsy.
- Fungal stains and culture were performed on BAL fluid and tissue samples, and galactomannan testing was performed on the majority of BAL and serum samples.
- Cell-free DNA was extracted from plasma and NGS performed (Karius, Redwood City, CA).
- Human reads were removed and remaining sequences aligned to a curated database including over 300 fungi.
- Organisms present above a predefined significance threshold were reported.
- Analysis of sequencing data was blinded to all clinical data.
- For the research-use only pipeline, lower significance thresholds were applied

The Karius® Test

- The Karius NGS assay identifies microbial cell-free DNA (cfDNA) in plasma from bacteria, DNA viruses, yeasts, mold, and protozoa.
- Next day results are reported from a single blood draw processed at CAP-accredited and CLIA-licensed laboratory.

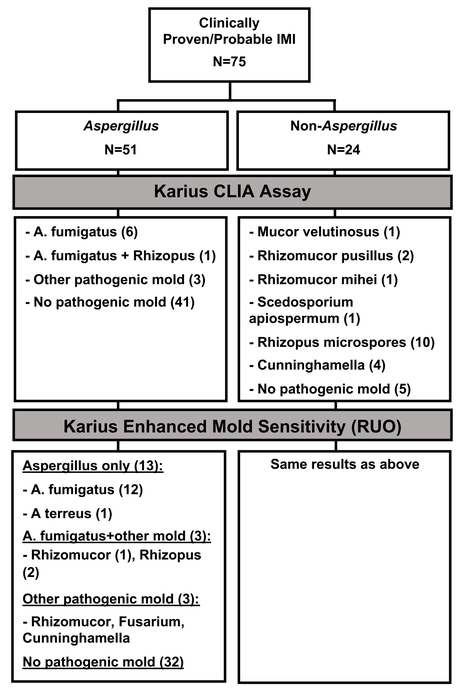
Results and Conclusions

Demographics

Variable	All subjects (N=114)
Median age, years (range)	51 (16-74)
Male sex	61 (54)
Caucasian	97 (85)
Stem cell source	
BM/PBSC	105 (92)
Cord blood	9 (8)
HLA-match	
Matched related	29 (25)
Matched unrelated	44 (39)
Mismatched related	5 (4)
Mismatched unrelated	36 (32)
Days b/w HCT and diagnosis, median (IQR)	72 (30-134)
Days b/w plasma and diagnosis, median (IQR)	3 (1-6)
Anti-mold agent at time of tested plasma[a]	36 (38)
BAL GM tested[a]	58 (60)
Serum GM tested[a]	79 (82)

Data are presented as number (%) unless otherwise indicated.
[a]Not including subjects with non-Aspergillus pulmonary IMI.

Microbiologic Findings



Performance Characteristics

Clinical Diagnosis	Karius Test (restricted to invasive mold)			
	CLIA		Higher Sens (RUO)	
	Pos	Neg	Pos	Neg
Aspergillus (proven/probable)	7 (14) (+3 subjects with non-asp mold)	44 (86)	16 (31) (+3 subjects with non-asp mold)	35 (69)
Non-IMI pneumonia	0	20 (100)	0	20 (100)

	CLIA		Higher Sens (RUO)	
	Pos	Neg	Pos	Neg
Non-aspergillus IMI	19 (79)	5 (21)	19 (79)	5 (21)
Non-IMI pneumonia	0	20 (100)	0	20 (100)

- Among 20 subjects with possible pulmonary aspergillosis, the Karius test detected aspergillus in 1 subject with the higher sensitivity pipeline.
- After restricting to plasma obtained -/+7 days from IMI diagnosis (prov/prob Asp &/or non-Asp), total IMI sensitivity increased from 29/75 (39%) to 27/61 (44%) for the CLIA test.

Conclusions

- The Karius cell-free plasma NGS test is a non-invasive means of detecting pulmonary IMI in HCT recipients.
- The test performance has high sensitivity and specificity for non-Aspergillus IMI pneumonia.
- Plasma samples obtained within 7 days of invasive mold infection diagnosis were more likely to identify mold.
- The Karius test may be a useful adjunct for diagnosing pulmonary IMI in specific clinical contexts.

DISCLOSURES
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