9th EUROPEAN CONFERENCE on INFECTIONS in LEUKAEMIA

▶ IN-PERSON CONFERENCE
From September
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Revised Guidelines
slide set
September 2022

Update on fungal diagnostics ECIL-9,2022

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ECIL-9: suggested changes for GM

- There is good evidence to support the use of serum/plasma* or BAL GM (Platelia assay) for the diagnosis of IA in high-risk hemato-oncological patients
  - AII for BAL in all patients (neutropenic and non-neutropenic)
  - AII for serum/plasma in (prolonged = more than 7 days) neutropenic (less than 500 neutrophils/microliter) patients; BII for non-neutropenic patients
  - Confirmed positivity in blood (≥ 2 ODI above 0.5) and use of a higher threshold (≥ 1.0) in BAL improves specificity with an acceptable loss in sensitivity (AII)

  * Plasma has not been validated by the manufacturer
- A diagnosis-driven strategy that incorporates serum GM monitoring (combined with appropriate clinical and microbiological evaluation, including other biomarkers as appropriate, and high-resolution CT imaging) every 3-4 days (twice weekly) is proposed in prolonged neutropenic patients not receiving mold-active prophylaxis (AI; kids AII_t)
- Prospective monitoring of serum GM in the presence of mold-active prophylaxis: DII.
  - However, a positive sample may still be diagnostic for a breakthrough Aspergillus infection (AII).
- The course of the serum GM index during antifungal therapy is predictive of outcome (AII)
  - ≥2 serum galactomannan measurements elevated compared with baseline after 2 weeks of therapy or rising GM antigenemia after 7 days of therapy is a poor prognostic sign and should prompt clinical reassessment: AII
- GM in CSF* with an ODI > 0.5 is an adjunctive method for the diagnosis of central nervous system aspergillosis (AII)

  * CSF has not been validated by the manufacturer
- The combined use of blood GM and PCR for screening is highly recommended: AI
- Recommendations for pediatric use have been proposed in ECIL-8 (Groll et al. Lancet Oncol 2016); the performance appears to be similar in children and adults

ECIL-9 recommendations for alternative *Aspergillus* antigen detection assays

- The Virclia monotest and the mannoprotein assay (Euroimmune)
- No grading or recommendations given the lack of sufficient data.

Aspergillus PCR Recommendations

- Aspergillus PCR alone (screening and diagnosis): **AII**
- Combined Aspergillus PCR and GM
  - Screening of blood (**AI**) – Multiple RCT including PCR
  - Diagnostic confirmation (**AII**): needs to be supported by additional evidence (clinical and/or imaging)
  - Prognostic marker (no grade)
    - Limited data, Strong positive = poor prognosis, persistent PCR positivity despite antifungal therapy = poor sign)
- High-risk hosts – AML, allogeneic SCT
- Genetic Markers of resistance – (no grade - further evaluation required – comment on Dutch/Belgian study demonstrating link with resistance/mortality Chong et al JAC 2016) vary
- CT values vary between centres and assays

Mucorales PCR Recommendation

- Mucorales PCR is highly specific and recommend for the diagnosis of mucormycosis in the presence of suggestive features when testing serum/plasma, fluids and tissue (**AII**)
- Serial detection in serum/plasma is recommended to confirm PCR positivity (increase confidence in diagnosis).
- Upon antifungal therapy, qPCR follow up is recommended to monitor response (**AIII**)
- While PCR negativity in BAL fluid means mucormycosis is less likely, further evaluation is required
- A negative PCR on serum/plasma samples does not exclude invasive mucormycosis
- Serial detection in serum/plasma is recommended in PCR negative patients with persistent suspicion: **AIII**

Fusarium PCR Recommendation

- Fusarium PCR seems highly specific for the diagnosis of fusariosis when testing blood, fluids and tissue
- Prospective trials to be implemented

Histoplasma PCR Recommendation

- Histoplasma PCR seems highly specific for the diagnosis of histoplasmosis when testing Blood, fluids and tissue
- Interesting in patients from endemic area for diagnosis histo among IFD

Panfungal PCR Recommendation

- Pan-fungal PCR testing is recommended on tissue biopsies where fungal elements have been demonstrated by histology/microscopy but culture is negative in an attempt to provide an genus/species level ID (**AIII**)
- Any attempt to demonstrate the presence of fungi using pan-fungal PCR without species or genus identification is discouraged (**DIII**)
- Pan-fungal PCR on blood samples or on culture-negative, histopathology-negative tissue requires further research.

Recommendations for BDG testing for IFI diagnosis in hematologic cancer patients

Objective	Grading	Comment
To screen for IFI (serial monitoring, e.g. 2/week)	D II	Limited sensitivity [1] Concern for specificity (e.g. concomitant IVIG administration) [2, 3]
To diagnose IFI	C II	Lack of specificity of type of fungal species Limited sensitivity [1, 4] No plus values compared to galactomannan (IA) and culture (IC) No detection of mucormycosis

BDG testing for the detection of IFI (except for PcP) in hematologic cancer patients is marginally recommended (**CII**) because of its limited sensitivity and specificity, and limited added value compared to other fungal diagnostic tests (GM, qPCR).
According to the clinical context, local epidemiology and other mycological evidence, BDG testing might be useful to aid in the diagnosis of chronic disseminated candidiasis or non-Aspergillus non-Mucorales invasive mold infections (e.g., invasive fusariosis or scedosporiosis/lomentosporosis) (**BIII**).

IFI: invasive fungal infection, IVIG: intravenous immunoglobulins

1. Lamoth et al. Clin Infect Dis 2012; 54:633-43 2. Tschopp et al. Clin Infect Dis 2022 (in press) 3. Bougnoux et al. Clin Microbiol Infect 2020; 26:1101-2 4. Angebault et al. Open Forum Infect Dis 2016; 3:ofw128

ECIL-9: Serum beta-D-glucan in HIV-negative patients

- We recommend the use of b-D-glucan in serum as a contributively laboratory diagnostic tool for the diagnosis of PCP, but confirmation should be performed with another test (BAL or non-invasive respiratory sample qPCR) when serum BDG is positive (specificity 83% - false positive results): **AII**
- Consider a significant rate of false positivity with low correlation between BDG titre and qPCR loads (good correlation in HIV patients)
- Despite the high negative predictive value, a negative serum BDG does not exclude PCP in at risk non-HIV patients with unexplained or refractory radiological findings compatible with pulmonary infection: **B-II**

ECIL-9 recommendations

- *Aspergillus*-specific lateral flow assays (IMMY and OLM), used as an alternative to GM to diagnose IA on serum samples or BAL fluid are useful (BII)

You can send your comments about the update on fungal diagnostics group revised guidelines before Octobre 31st to the group leader: Johan Maertens johan.maertens@uzleuven.be