Global Fungal Infection Registry
Initiated in 2003

Interim Report April 2023

Working group of the

Under the auspices of

Has been and is supported by unrestricted grants from Amplyx Pharmaceuticals, Astellas, Cidara Therapeutics, Basilea Pharmaceutica, F2G Ltd., Matinas BioPharma, MSD, Pfizer Inc., Pfizer Pharma GmbH and Scynexis.
# TABLE OF CONTENTS

## INTRODUCTION

3

## FUNGISCOPE REGISTRY WORKFLOW

4

## RESULTS

7

## ACHIEVEMENTS AND GOALS

13

### PROJECT PRESENTATIONS

13

### FULL PUBLICATIONS

15

### PRESENTATION OF RECENT PUBLICATIONS

21

### CURRENT ACTIVITIES

35

## CENTRAL LABORATORIES

36

## CONTACT INFORMATION

37

## REFERENCES

39
Introduction

Due to the intensification of cytotoxic chemotherapy, the growing number of transplantation procedures and the extensive use of immunosuppressive drugs for various clinical conditions, invasive fungal infections (IFI) are an emerging problem worldwide. *Candida* species and *Aspergillus fumigatus* remain the most frequent cause of IFI in immunocompromised patients but less common IFI caused by rare fungi are reported with increasing frequency. Mucormycosis has been an emerging disease only few decades ago, today it is recognized as a considerable threat in respective patient populations. Therapeutic standards have been developed for the most frequent IFI, i.e. candidiasis, aspergillosis and cryptococcosis, for rarer IFIs less robust treatment strategies or no effective treatment options are available. Clinicians are facing infections due to a variety of different fungi, still without reliable treatment recommendations. In a global effort, guidelines on the clinical management of uncommon IFI are developed, where recommendations - especially for the rarest IFI – are based on expert opinions and single center experiences only 1-3. Therapeutic decision making on rare IFIs is not evidence-based as comprehensive data are not available to date.

In order to help alleviate the lack of knowledge on epidemiology, clinical course, biology and pathomechanisms, and finally to aid in facilitating an evidence-based diagnostic-therapeutic integrated approach of IFI caused by rare fungi, FungiScope® - A Global Invasive Fungal Infection Registry has been created in 2003. Via a web-based electronic case form (www.clinicalsurveys.net) physicians, scientists and others contribute clinical cases.

With the increasing knowledge on the epidemiology, diagnostics and therapeutic management of fungal infections, improved strategies for early diagnosis and prompt optimized treatment will eventually be identified. Only through this joint and global effort it will be possible to improve patient care.

In this report, an overview on current results, achievements, future goals and ongoing developments of FungiScope® are presented.
FungiScope® Registry Workflow

Everyone is welcome to join the effort and become a partner within the FungiScope® network and actively support our common goal of improving the clinical management of patients with invasive fungal infections.

Via a web-based questionnaire, anonymized clinical information of proven and probable IFI cases are retrospectively collected. Documented data includes information on underlying conditions and risk factors for IFI, diagnostic procedures (radiological and mycological), clinical manifestation of the IFI, antifungal treatment and response, and outcome. Cases are centralized reviewed by ID specialists of the FungiScope® team in Cologne, Germany (Figure 1a).

Registration and Password Acquisition: fungiscope@uk-koeln.de

Document your case
Anonymized, retrospective

- Demographics
- Risk Factors
- Diagnostic Procedures
- Clinical Signs and Symptoms
- Site of Infection
- Treatment
- Outcome

Send us the clinical fungal isolate
(if available)

- Species Identification
- Therapeutic Drug Monitoring
- In Vitro Susceptibility Testing
- Biobanking
- Share isolates for research purposes with collaborators

*caused by e.g. Aspergillus fumigatus and other Aspergillus species, Mucorales, Alternaria, Cladosporium, Curvularia, Exophiala, Fusarium, Geotrichum, Lomentospora, Penicillium, Scedosporium, Trichosporon species

Joint analysis and publication
Biobank of rare fungal pathogens
Networking and collaboration on other studies

Figure 1a. Project structure
Ideally, the respective clinical fungal isolates are collected, examined and stored in a biobank in Cologne, Germany (Figure 1b). The clinical and biological data are subsequently evaluated and analysed in a joint effort with the partners. Anonymized data of cases entered in the registry are easily accessible via the web-based search engine FungiQuest (www.fungiquest.net), a tool for clinicians who are confronted with similar cases, to evaluate respective treatment and outcome patterns that may guide individual treatment strategies, where valid recommendations are not available to date (Figure 2).

Figure 1b. FungiThek: Clinical fungal isolates can be send 1.) to the FungiScope® Central Lab in Cologne, Germany for formal identification and biobanking in the FungiThek or 2.) to the designated reference lab in your country (please see in section Study Coordinators below).

Reference analyses from biopsies will be performed at the Robert Koch Institute in Berlin, Germany.
FungiQuest
Check for similar cases at www.fungiquest.net

Go to www.fungiquest.net
Type the name of the fungus and specify your search

Browse through FungiScope cases with the same kind of fungal infection

Figure 2. FungiQuest database search engine.
Results

In the FungiScope® registry, 3,448 cases of invasive fungal infection (IFI) diagnosed between 1997 and 2023 have been documented, 2,670 cases of these are already finalized and considered valid for analysis. Eighty-five percent of cases were diagnosed in 2010 or later.

Main causative pathogens registered were Mucorales (n=930, 34.8%), yeasts (n=261, 9.8%), dematiaceae (n=201, 7.5%), and Fusarium spp. (n=192, 7.2%) followed by Scedosporium spp. (n=440, 16.5%) and Penicillium, Paecilomyces, Purpureocillium spp. (n=80, 3%) (Figure 3a). Between 7% (Dematiaceae) and 16% (Mucorales) of the cases had concomittant infections with other fungal pathogens (not shown).

Mucormycosis is the most frequent IFI in FungiScope®, with Rhizopus, Mucor, Lichtheimia, and Rhizomucor species being the main causative pathogens in this group (Figure 3a and b). Aspergillosis with galactomannan follow up and non-fumigatus Aspergillus-related infections as well as COVID-19-associated fungal infections have been a focus of research since 2019 and 2020, respectively. Currently, 453 (16.9%) cases of Aspergillus-related infections are included, about 300 more cases are related to mixed fungal infections. Two-hundred cases were associated to COVID-19, most of them COVID-19-associated aspergillosis (CAPA).

The majority of cases (78.5%) were contributed from partners in Japan, China, Germany, the United States, South Korea, Thailand, Australia, Spain, India and Malaysia. The contribution of cases by country is shown in Figure 4.

Main sites of infection differed between fungal pathogens (Figure 5) but also between risk groups and geographical regions (data not shown). Patients with invasive mucormycosis most commonly had lung infection (57%), but also frequent involvement of paranasal sinuses (25%) and central nervous system (15%). Lung was also commonly affected in infections caused by rare Yeast, Dematiaceae, Fusarium, Scedosporium and Aspergillus-associated infections (23.3%, 20.2%, 28.0%, 33.8% and 76.6%, respectively) but sinuses were comparably less frequently involved (1%, 16.6%, 10.6%, 8% and 10.5%, respectively). Fusarium, rare Yeast and Scedosporium were commonly identified in blood (35.9%, 72.2% and 15%, respectively), for mucormycosis, aspergillosis and dematiaceae only rare cases of blood stream infections were noted (both <2% and <5, respectively). Infections due to dematiaceae mostly involved deep soft tissue and skin, lungs, paranasal sinuses, and the central nervous system (range between 13.5% and 30%).

Frequent risk factors for the development of IFI are presented for the main fungal groups in Figure 6.
Chemotherapy and allogeneic haematopoietic stem cell transplantation (HSCT) for treatment of underlying malignancy and intensive care unit (ICU) stay were the most common risk factors for mucormycosis, fusariosis, dematiaceae, aspergillosis and yeast-related infections. Diabetes mellitus was frequently reported as a comorbidity overall (20.3%) and was the most common underlying condition in Dematiaceae-associated infections (27%). Chronic renal disease was comparably frequent in patients with yeast and Dematiaceae-associated infections (12% and 11%, respectively).

![Figure 3a. Distribution of main fungal pathogens causing invasive infections in FungiScope® (including mixed infections).](image)

![Figure 3b. Distribution of pathogens causing mucormycosis by genera.](image)
Figure 4. Number of cases per country contributed by FungiScope® partners.
Figure 5. Main sites of infection for major groups of fungi.
CNS, Central Nervous System
Figure 6. Main risk factors for major groups of fungi.

**HSCT** Hematopoietic stem-cell transplantation, **ICU** Intensive Care Unit
All-cause-mortality, mortality due to fungal infection and response to treatment differed among individual pathogens and are shown in Figure 7. The highest all-cause-mortality was observed in patients with infection caused by Mucorales (53.2%). Similar mortality was reported for patients with aspergillosis (46.2%), yeast (48.7%), and Fusarium-related infections (42.9%). Reported mortality attributable to fungal infections was highest in patients with mucormycosis (31.1%), similar for yeast-related infections (25.4%), and fusariosis (23.6%). Dematiaceae infection was associated with the lowest all-cause and attributable mortality (21.5% and 12.1%, respectively).

Favorable outcome considering partial and complete response to antifungal therapy was achieved in two thirds of patients with Dematiaceae-associated infections. Fungal infections caused by any other fungal pathogen, including Mucorales, Aspergillus, Scedosporium and Fusarium were associated with less favorable outcome overall, half of the patients in each group had partial or complete response at day of final assessment (Figure 7).

**Figure 7.** Mortality rates and clinical response at final assessment for major causative pathogen groups in FungiScope®. Favorable response is defined by complete or partial response assessed by the treating physician.
# Achievements and Goals

## Project presentations

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
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<tbody>
<tr>
<td>Sep 21, 2022</td>
<td>Interna Society for Human and Animal Mycology (ISHAM 2022) (Talk, Poster), New Delhi, India</td>
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<tr>
<td>Sep 15-17, 2022</td>
<td>Sociedad Argentina de Infectología (SADI) XXII Coference (Talk), Buenos Aires, Argentina</td>
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<tr>
<td>Sep 12-14, 2022</td>
<td>56. Wissenschaftliche Tagung der Deutschsprachigen Mykologischen Gesellschaft (Myk2022), Vienna, Austria (Talk)</td>
</tr>
<tr>
<td>Mar 10, 2022</td>
<td>Live Webinar, Pfizer Ireland 'Recent Publication on Covid-19 - Associated Pulmonary Aspergillosis', Virtual Event (Talk)</td>
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<td>Mar 4, 2022</td>
<td>Hot Topics in Infectious Diseases (HTIDE)-Conference 5th Edition (Talk)</td>
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<tr>
<td>Nov 9, 2021</td>
<td>Approaching The Severely Infected Patient (ATHENA)-International Conference 2021 (Talk)</td>
</tr>
<tr>
<td>Oct 12, 2021</td>
<td>Zealands University Hospital Roskilde, Denmark, Virtual Event (Talk)</td>
</tr>
<tr>
<td>Oct 8 - 11, 2021</td>
<td>10th Trends in Medical Mycology (TIMM), Aberdeen, United Kingdom (Talk, Poster)</td>
</tr>
<tr>
<td>Sep 27, 2021</td>
<td>55. Wissenschaftliche Tagung der Deutschsprachigen Mykologischen Gesellschaft (DMykG) (Talk)</td>
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<tr>
<td>Jul 9 – 12, 2021</td>
<td>31st European Congress of Clinical Microbiology &amp; Infectious Diseases (ECCMID) (Talk, Poster)</td>
</tr>
<tr>
<td>Jun 16 – 19, 2021</td>
<td>15. Kongress für Infektionskrankheiten und Tropenmedizin (KIT), Virtual Event (Talk, Poster)</td>
</tr>
<tr>
<td>Mar 20, 2021</td>
<td>Taiwan Infectious Disease Society Annual Meeting (Lecture)</td>
</tr>
<tr>
<td>Jan 29, 2021</td>
<td>Pfizer Medical Affairs India Virtual Train The Trainer Cresemba Launch Symposium (Talk)</td>
</tr>
<tr>
<td>Oct 21-25, 2020</td>
<td>IDWeek Virtual Event (Poster)</td>
</tr>
<tr>
<td>Sep 23 – 25, 2020</td>
<td>ECCVID ESCMID Conference on Coronavirus Disease, Virtual Event (Poster)</td>
</tr>
<tr>
<td>Sep 23, 2020</td>
<td>Mycology Week 2020, Antioquia University, Medellín, Colombia, Virtual Event (Talk)</td>
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Full Publications


Chetrit E, Roth Y, Cornely OA. *Mucormycosis in the Middle East and North Africa: Analysis of the FungiScope® registry and cases from the literature.* Mycoses. 2020 Oct;63(10):1060-1068


Presentation of recent publications

- NEW Trichosporon EQUAL Scorecard
- Contains 18 items with a max. score of 39 points

Link:

Rosanne Sprute, MD
Oliver.Cornely@uk-koeln.de

- NEW CPA EQUAL Scorecard
- Contains 27 items with a max. score of 51 points

Link:

Rosanne Sprute, MD
Oliver.Cornely@uk-koeln.de
- 40% of *Magnusiomyces*-associated infections occurred during antifungal prophylaxis
- First-line antifungal therapy with azoles, alone or in combination, was associated with improved response
- Overall day-30 mortality rate: 43%
- Factors associated with higher mortality: septic shock, corticosteroid treatment ≥14 days, lack of neutrophil recovery

**Link:**
Del Principe et al. *Mycoses*. 2022 Sep 19
Maria Ilaria Del Principe; Danila Seidel, PhD
del.principe@med.uniroma2.it; Danila.Seidel@uk-koeln.de
- Overview of the main projects regarding Medical Mycology at the University Hospital Cologne (ECMM Excellence Center)
- One World One Guideline Project – Summary

<table>
<thead>
<tr>
<th>Year of publication</th>
<th>Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td>Mucormycosis (with MSG-ERC)</td>
</tr>
<tr>
<td>2022</td>
<td>CAPA (adapted methodology)</td>
</tr>
<tr>
<td>2021</td>
<td>Rare Molds Endemic Mycoses Rare Yeast</td>
</tr>
<tr>
<td>~2022</td>
<td>Cryptococcus</td>
</tr>
<tr>
<td>~2023</td>
<td>Candida</td>
</tr>
<tr>
<td></td>
<td>Aspergillus</td>
</tr>
</tbody>
</table>

- Overview of Treatment Algorithms throughout the University Hospital of Cologne
- Presentation of EQUAL Score Cards and translations

- Clinical Trials at the ECMM EC Cologne
- YoungECMM
- YouTube Channel “IDIM – Infectious Diseases in Motion” and YouKu Channel
- ECMM Consulting Service
- Overview on Publications

Link:
Danila Seidel, PhD
Danila.Seidel@uk-koeln.de
Most CAM presented as pulmonary infection (11/13)
Most had severe/critical COVID-19 (12/13), 11 required intensive care involving mechanical ventilation
Median time between diagnosis of COVID-19 and CAM: 10 (range 0 – 62) days
All-cause mortality: 53.8%

Link:
Danila Seidel, PhD
Danila.Seidel@uk-koeln.de
Interim Report April 2023
Patients: 310 cases of mucormycosis in the MENA region

Risk: Diabetes mellitus (49.7%)  
Conditions associated with immunosuppression (46.5%)

Mortality:

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhino-orbital-cerebral</td>
<td>145 (46.8)</td>
<td>56 (38.6)</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>38 (12.3)</td>
<td>17 (44.7)</td>
</tr>
<tr>
<td>Curaneous</td>
<td>35 (11.3)</td>
<td>8 (22.9)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>6 (1.9)</td>
<td>5 (83.3)</td>
</tr>
<tr>
<td>Disseminated</td>
<td>59 (19.0)</td>
<td>36 (61.0)</td>
</tr>
</tbody>
</table>

Conclusions: Increase of reports of mucormycosis in the MENA region over the past few decades  
Treatment with antifungals and surgery is associated with improved outcome  
Mortality rates decreased from 47.8% before 1990 to 32.3% in the 2010s

Link:  
Jannik Stemler, MD  
Jannik.Stemler@uk-koeln.de
Invasive Scedosporium spp. and Lomentospora prolificans infections in pediatric patients: Analysis of 55 cases from FungiScope® and the literature

Danila Seidel<sup>a,b,*</sup>, Angela Hassler<sup>c</sup>, Jon Sal manton-Garcia<sup>a,b</sup>, Philipp Koehler<sup>a,b</sup>, Sibylle C. Mellinghoff<sup>h,b</sup>, Fabianne Carl esse<sup>4</sup>, Matthew P. Cheng<sup>e</sup>, Iker Falces-Romero<sup>f</sup>, Raoul Herbrecht<sup>g</sup>, Alfredo Jover Sáenz<sup>b</sup>, Nikolai Klimko<sup>i</sup>, Mihai Marey<sup>j</sup>, Cornelia Lass-Flörl<sup>k</sup>, Pere Soler-Palacín<sup>l</sup>, Hilmar Wisplinghoff<sup>m,n,p</sup>, Oliver A. Cornely<sup>a,b,p</sup>, Zoi Pana<sup>i</sup>, Thomas Lehmb echer<sup>e</sup>

**Patients:** 55 children with Scedosporium and Lomentospora-related infections

**Risk:** Immunosuppression, malignancy, allogeneic HSCT, trauma, near drowning

**Mortality:**

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Immuno-compromised</th>
<th>Immuno-competent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scedosporium spp.</td>
<td>42%</td>
<td>46%</td>
<td>85%</td>
</tr>
<tr>
<td>Lomentospora spp.</td>
<td>50%</td>
<td>40%</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Conclusions:** Severity of infection predicts worse outcome irrespective of immune status - Localized infection predicts good outcome
Voriconazole use and surgical treatment are associated with improved outcome in children

**Link:**

Danila Seidel, PhD
Danila.Seidel@uk-koeln.de
Patients: 23 Rasamsonia spp. cases

Risk: Chronic granulomatous disease, immunosuppression, malignancy, HSCT

In vitro susceptibility:
- Amphotericin B (S/R)
- Caspofungin (S)
- Micafungin (S)
- Posaconazole (R)
- Voriconazole (R)

Mortality: 39%

Conclusions: No predictors of mortality identified, but frequently misidentified as Paecilomyces spp. (48%) and frequently BT-IFI (56.5%). Species identification by PCR necessary

Link:
Jannik Stemler, MD
Jannik.Stemler@uk-koeln.de
Matched-paired analysis of patients treated for invasive mucormycosis: standard treatment versus posaconazole new formulations (MoveOn)


**Patients:**
- First-POS<sub>new</sub> (n=5) vs First-AMB (n=15)
- First-AMB+POS<sub>new</sub> (n=18) vs First-AMB (n=50)
- Salvage-POS<sub>new</sub> (n=22) vs Salvage-POS<sub>susp</sub> (n=42)

**Matching:**
- Malignancy, Surgery, Severity, Renal dysfunction

**Mortality:**
- First-POS<sub>new</sub> 40% vs First-AMB 60%
- First-AMB+POS<sub>new</sub> 50% vs First-AMB 60%
- Salvage-POS<sub>new</sub> 18% vs Salvage-POS<sub>susp</sub> 33%

**Conclusion:**
Posaconazole tablet or iv is effective against mucormycosis with regard to treatment response and mortality

**Link:**
Jon Salmanton-García, MPH, PHD
Jon.Salmanton-Garcia@uk-koeln.de
Patients: 208 Scedosporium spp., 56 Lomentospora prolificans cases
(34 Scedosporium and 7 Lomentospora cases from FungiScope)
Male 60.6%; Median age 57 years (IQR 40 – 65)

Risk: Malignancy, HSCT, solid organ transplantation

Sites: Fungemia, lung, CNS, heart

In vitro susceptibility:
Scedosporium spp.: Voriconazole (S)
Lomentospora prolificans: All (R)

Mortality:
Scedosporium spp.: 40% vs Lomentospora prolificans: 57%
Malignancy
Scedosporium spp.: 55% vs Lomentospora prolificans: 86%

Conclusions: Predictors for mortality (-) and survival (+):
Scedosporium spp.
Solid organ transplantation: (-) CNS, disseminated disease
Malignancy: (-) Lung
Lomentospora prolificans
(-) Disseminated disease
(+) Surgery

Link:
Danila Seidel, PhD
Danila.Seidel@uk-koeln.de

S.M. Heimann a,*, M.J.G.T. Vehreschild a, b, O.A. Cornely a, b, c, W.J. Heinz d, B. Grüner e, G. Silling f, J. Kessel g, D. Seidel a, J.J. Vehreschild a, b

Patients: 46 Mucorales
Male 67%; Median age 53 years (range 11 – 88)

Risk: Malignancy, HSCT

Mortality: 41%

Extra costs:

<table>
<thead>
<tr>
<th></th>
<th>Invasive Mucormycosis FungiScope n=46</th>
<th>Control German central health care database</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay median days (IQR)</td>
<td>46.5 (30.3 – 83.3)</td>
<td>25.6 (17.9 – 40.4)</td>
<td>+ 20.9 days</td>
</tr>
<tr>
<td>direct treatment costs €; median (IQR)</td>
<td>35,765 (18,090 – 69,350)</td>
<td>12,587 (6,601 – 30,762)</td>
<td>+ 23,178 €</td>
</tr>
</tbody>
</table>

Conclusions: Lower overall costs if
- No chemotherapy
- Surgical treatment of mucormycosis
- Antifungal prophylaxis

Link:
Sebastian Wingen-Heimann, PhD
Sebastian.Wingen-Heimann@uk-koeln.de
Invasive infections due to *Saprochaete* and *Geotrichum* species: Report of 23 cases from the FungiScope Registry

Luisa Durán Graeff1  |  Danila Seidel1  |  Maria J. G. T. Vehreschild1  |  Axel Hamprecht2,3  
| Anupma Kindo3,6  |  Zdenek Racil3  |  Judit Demeter5  |  Sybren De Hoog4,6  |  Ute Aurbach7  
| Maren Ziegler7  |  Hilmar Wisplinghoff2,7,8  |  Oliver A. Cornely1,9,10,11,13  |  FungiScope Group†

**Patients:** 23 cases, Female 48%, Median age 49 years (18 - 78)

**Risk:** Malignancy, HSCT, diabetes mellitus, treatment in ICU

**Sites:** Fungemia, lung, liver, spleen, CNS

**In vitro susceptibility:**
- Amphotericin B (I)
- Echinocandins (R)
- Triazoles (S)

**Mortality:** 65%

**Conclusions:** Treatment with echinocandins predicts worse outcome

**Link:**

Luisa Durán Graeff, MD
Invasive mucormycosis in children: an epidemiologic study in European and non-European countries based on two registries

Zoi Dorothea Pana¹, Danila Seldi², Anna Skliadá³, Andreas H. Groll⁴, Georgios Petrikos⁵, Oliver A. Comely², Emmanuel Rollides⁶ and Collaborators of Zygomycos.net and/or FungiScope™ Registries⁷

**Patients:** 63 children: 34 girls, Median age: 13 years

**Risk:** Malignancy, HSCT, solid organ transplantation, trauma/surgery, diabetes mellitus

**Treatment:**
- 31% monotherapy AMB
- 48% combination AMB
- 14% no systemic antifungals
- 54% + surgery

**Mortality:** 33%

**Conclusions:**
- Predictor for mortality (-) and survival (+)
- (-) HSCT
- (-) Disseminated IFI
- (+) Combination antifungal therapy + surgery

**Link:**
Zoi Pana, MD
Current Activities

- FungiScope® expanded its inclusion criteria to invasive Aspergillus spp. infections
- COVID-19 associated fungal infections are enrolled
- Publication on Purpureocillium and Paecilomyces-associated infections, on COVID-19 associated aspergillosis and mucormycosis
- Participation in global guidelines on clinical management of mold and yeast infections
- Prof. Yingchun Xu and Prof. Yao Wang at the Peking Union Medical College Hospital joint FungiScope® as the reference lab for the People’s Republic of China
- Extending and renewal of the FungiQuest® platform [www.fungiquest.net](http://www.fungiquest.net)
- Web presence on the Research for Rare website [www.research4rare.de](http://www.research4rare.de)
- Web presence as an Expert center for rare mycosis on the Orphanet - The portal for rare diseases and orphan drugs website [www.orpha.net](http://www.orpha.net)

ECMM Excellence Center Symposium October 10th, 2017

The University Hospital of Cologne was awarded with the ECMM Excellence Center Diamond status in 2017, certifying Excellence in the mycological fields of clinical microbiology and infectious diseases and acknowledging participation in ECMM endorsed clinical and epidemiological studies. The Excellence Diamond status was reevaluated in 2021.
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