11th Advances Against Aspergillosis & Mucormycosis Conference

25th-27th January 2024, Milano

SESSION 4: ANTIFUNGALS IN THE CRITICALLY ILL

Chair: Sarah Hammond & Katrien Lagrou

Optimal antifungal strategies to prevent mould infections deaths in solid organ transplant recipients

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Advances Against Aspergillosis & Mucormycosis

Conflicts of interest

- **Speaker and/or consultant**
  - Speaker for Pfizer, ViiV, Merck Sharp & Dohme (MSD), Shionogi.
  - Different Scientific Societies
- **Research**
  - Research grant from Instituto de Salud Carlos III and Fundación Mutua Madrileña.
- **Continuos Medical Education**
  - Travel grants for congresses from Pfizer and MSD.
  - Funding for congresses from MSD, Pfizer, Gilead, Takeda, Menarini, Angellini
- **None for this presentation**

Agenda

- 1. Are there some changes in the epidemiology of IFI? Are there any special situations and new challenges in IFI in SOT?
- 3. Prophylaxis: To whom should it be given, with which antifungals and for how long?
- 4. American vs European Guidelines
- 5. What are we doing: International survey of AF prophylaxis in SOT.
- 6. Problems to be solved
- 7. Take home messages

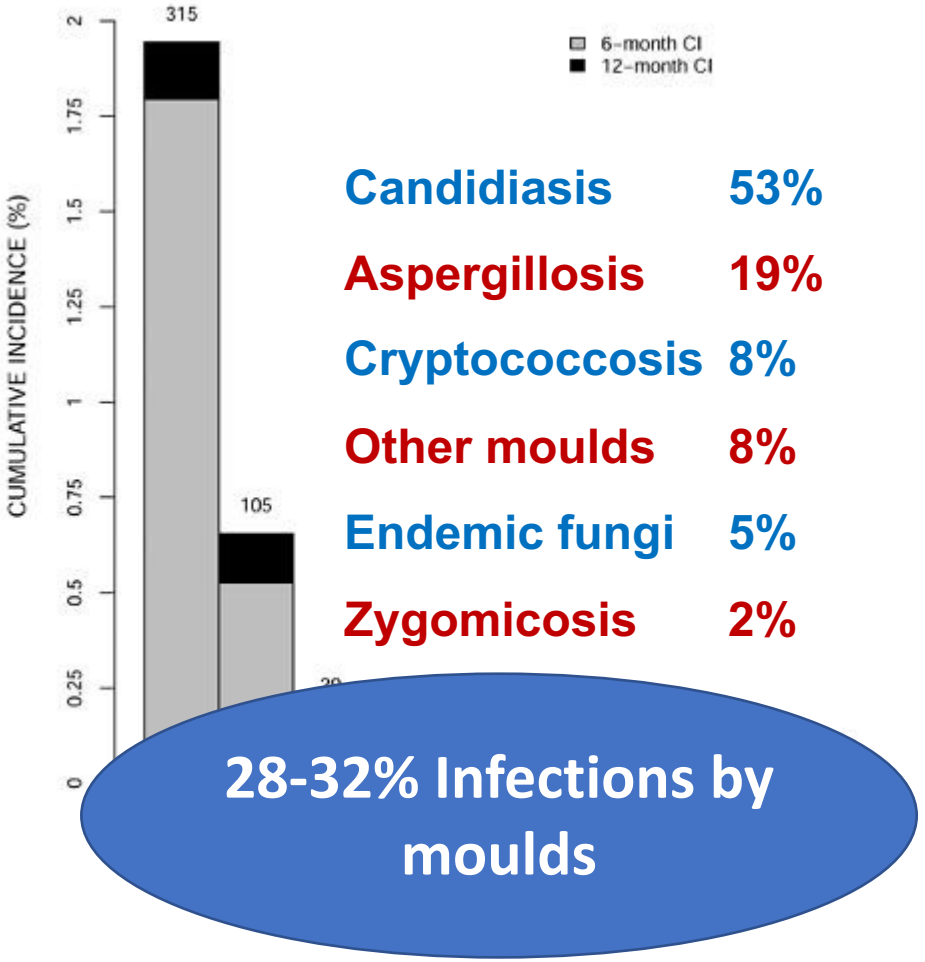
Are there some changes in the epidemiology of IFI?

Are there any special situations and new challenges in IFI in SOT?

Invasive Fungal Infections among Organ Transplant Recipients: Results of the Transplant-Associated Infection Surveillance Network (TRANSNET)

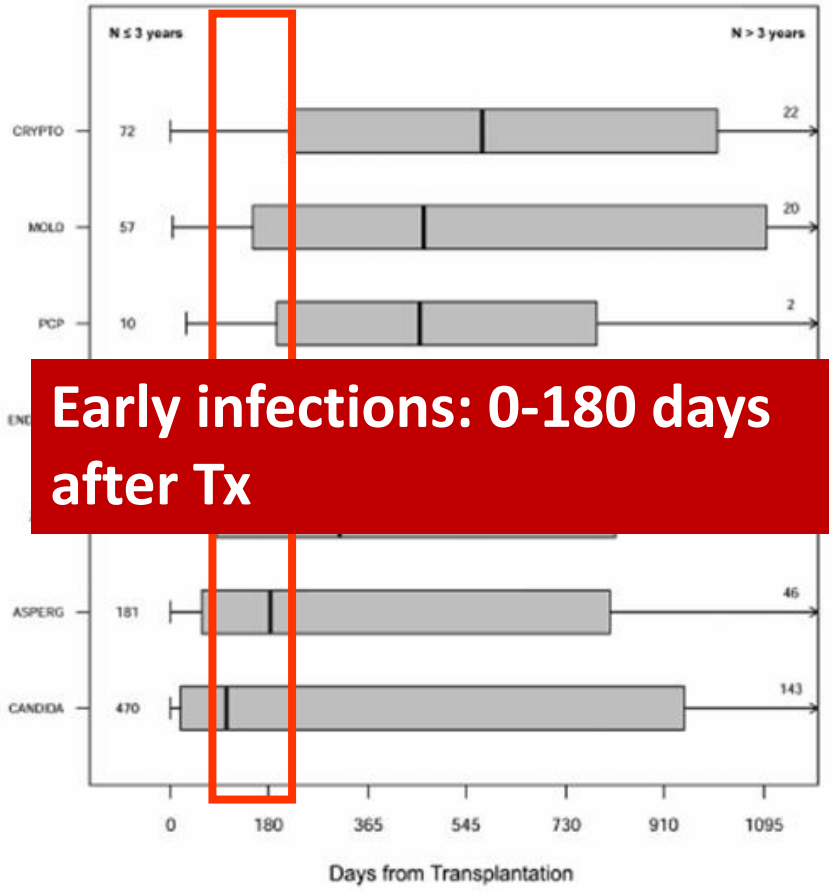
1208 IFIs among 1063 SOT recipients.

One-year incidence for invasive candidiasis was (1.95%) and for invasive aspergillosis (0.65%).



Candidiasis	53%
Aspergillosis	19%
Cryptococcosis	8%
Other moulds	8%
Endemic fungi	5%
Zygomicosis	2%

28-32% Infections by moulds



Early infections: 0-180 days after Tx

One-year cumulative incidences:

11.6% small bowel
8.6% lung
4.7% liver
4.0% heart
3.4% pancreas
1.3% kidney

Pappas PG, et al. Invasive fungal infections among organ transplant recipients: results of the Transplant-Associated Infection Surveillance Network (TRANSNET). Clin Infect Dis. 2010 Apr 15;50(8):1101-11. doi: 10.1086/651262.

GUIDELINES Open Access

Invasive aspergillosis in solid organ transplant patients: diagnosis, prophylaxis, treatment, and assessment of response

Dionysios Neofytos[1*], Carolina Garcia-Vidal[2], Frédéric Lamoth[3,4], Christoph Lichtenstern[5], Alessandro Perrella[6,7] and Jörg Janne Vehreschild[8,9,10]

Recent epidemiological data

Table 1 Epidemiology of invasive aspergillosis in SOT recipients. The large variations of the overall mortality rates in heart and kidney recipients can be explained by the corresponding variations in follow-up in the different studies (3-months [1, 3, 5] or 12-months [6, 7])

Population	Incidence (%)	Overall mortality (%)	References
Heart	3.5–26.7	36–66.7	[1, 3, 5, 8, 9]
Kidney	1.2–4	4–25	[1, 3, 5]
Liver	1–4.7	83–88	[1, 3, 5]
Lung	8.3–23.3	4.2	[1, 3, 5]

Tabla extraída de Neofytos D, et al. BMC Infect Dis. 2021

Neofytos D, et al. Invasive aspergillosis in solid organ transplant patients: diagnosis, prophylaxis, treatment, and assessment of response. BMC Infect Dis. 2021 Mar 24;21(1):296. doi: 10.1186/s12879-021-05958-3.

Risk factors:

Is there a change on the risk factors for IFI in SOT recipients?

Donor acquired infections

- Early infections: 1-2 months after Tx.
- Less tan 1% of all donor derived infections: *Aspergillus, Scedosporium, Lomentospora.*

Case report

Donor-derived aspergillosis from use of a solid organ recipient as a multiorgan donor

N.J. Mueller, M. Weisser, T. Fehr, R.P. Wüthrich, B. Müllhaupt, R. Lehmann, A. Imhof, J.-D. Aubert, M. Genoni, R. Kunz, M. Weber,

Transpl Infect Dis 2010: **12:** 54–59

Transmission of Invasive Aspergillosis From a Subclinically Infected Donor to Three Different Organ Transplant Recipients*

Michael R. Keating, MD; Marco A. Guerrero, MD; Richard C. Daly, MD; Randall C. Walker, MD; and Scott F. Davies, MD, FCCP

CHEST / 109 / 4 / APRIL, 1996

- Donors were transplanted patients as well (1 HT and 1 LT)
- Cause of death: CNS stroke→IFI
- Tx allografts were: 2 kidneys, 1 heart.
- 2 kidneys, 1 liver, 1 lung and 1 páncreas.
- Median time to symptoms: 33 days after Tx (21-48 days).

Our case

Medical Mycology Case Reports 22 (2018) 24–26

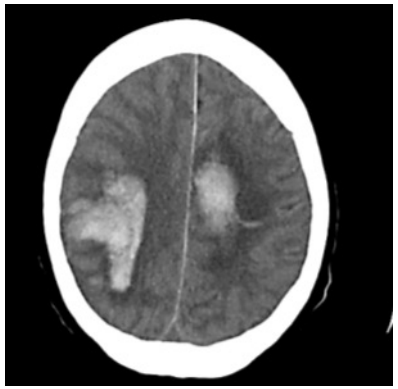
Contents lists available at ScienceDirect

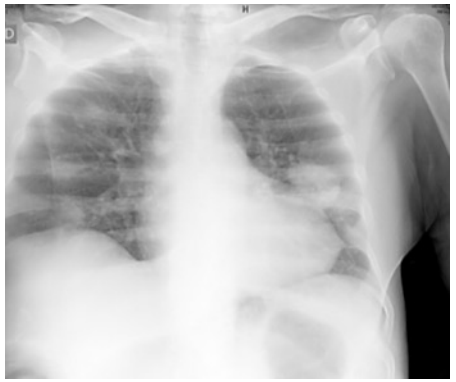
Medical Mycology Case Reports

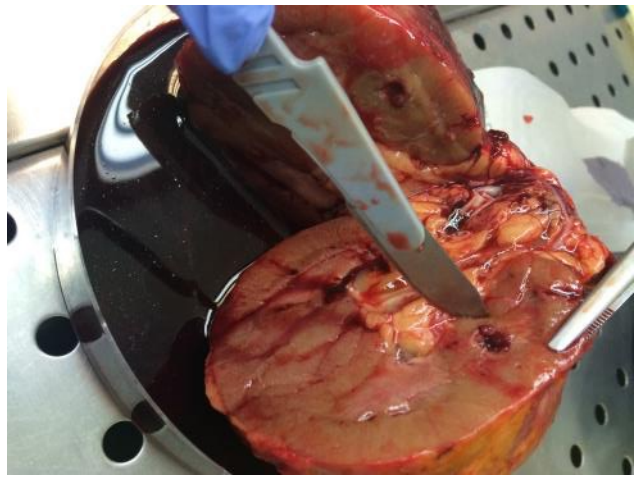
journal homepage: www.elsevier.com/locate/mmcr

Donor-derived invasive aspergillosis after kidney transplant

Maricela Valerio[a,b], Marina Machado[a,b,d,*], Santiago Cedeño[c], Maria Luisa Rodríguez[c], Fernando Anaya[c], Antonio Vena[a,b], Jesús Guinea[a,b,d,e], Pilar Escribano[a,b,d], Emilio Bouza[a,b,d,e], Patricia Muñoz[a,b,d,e]







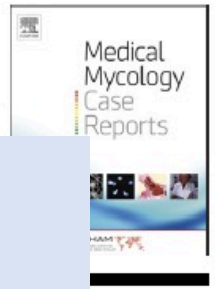
2 kidney recipients
1 previous Heart Tx/ CRD /HD
1 CRD /HD
Both kidneys explanted
Positive culture: *Aspergillus*
Secondary prophylaxis

Deceased donor due to cerebral hemorrhage in ICU
Alcoholic liver disease who received corticosteroids
Bacterial pneumonia

Our case

Medical Mycology Case Reports 22 (2018) 24–26

Contents lists available at ScienceDirect



What we learned:

1. To always keep in mind donor derived infections, especially during the first weeks after transplant.
2. If there is a clinical suspicion: assess the clinical charts of the donor (cause of death, epidemiological and demographic data).
3. Include an infectious disease specialist and a clinical microbiologist in the transplant team in charge of evaluating potential donors.
4. Improve the microbiological assessment of respiratory samples (calcofluor stain and fungal cultures) and other clinical samples of potential donors.

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Aspergillus
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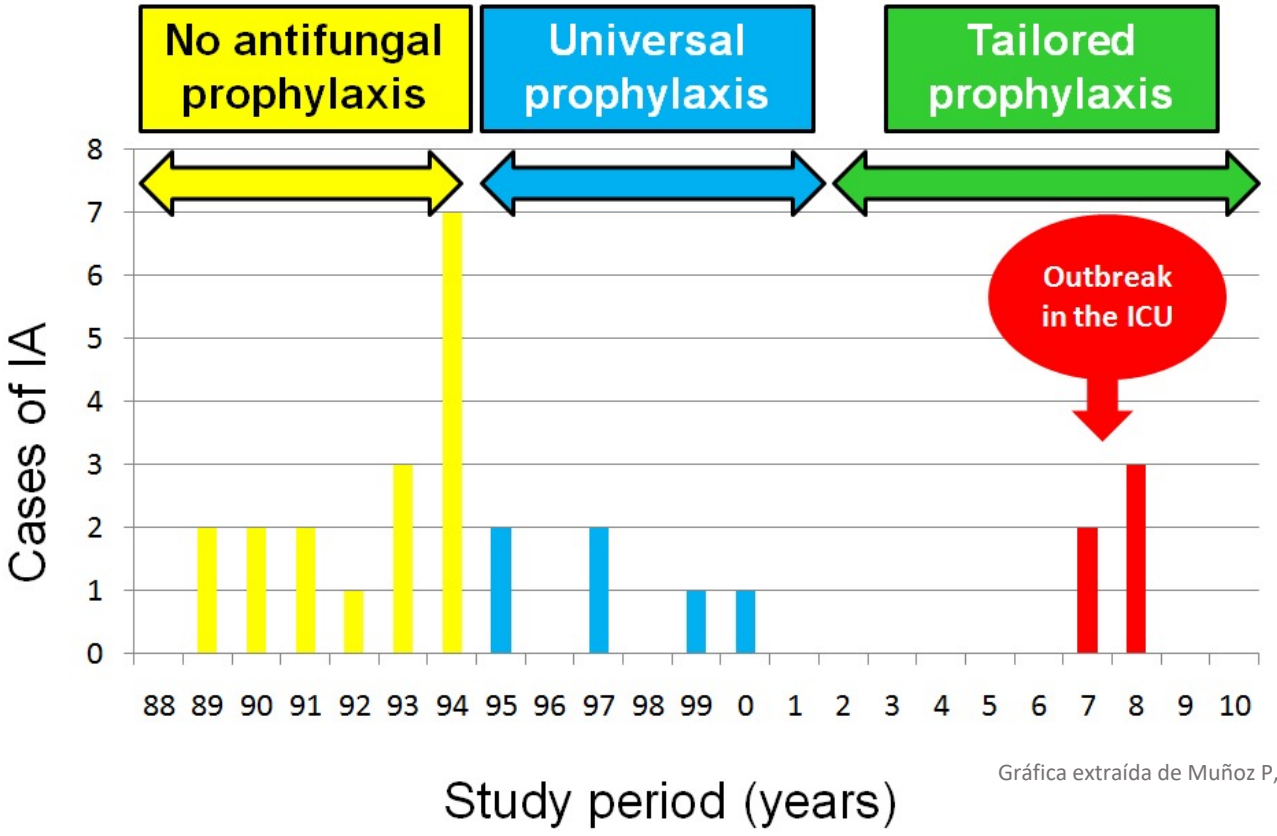
Dece
Alcoholic liver disease who received corticosteroids
Bacterial pneumonia

Invasive aspergillosis among heart transplant recipients: A 24-year perspective

Patricia Muñoz, MD, PhD,[a,b,c,d] Ines Cerón, MD,[a,b] Maricela Valerio, MD,[a,b] Jesús Palomo, MD,[e] Adolfo Villa, MD, PhD,[e] Alia Eworo, MD,[a,b] Juan Fernández-Yáñez, MD,[e] Jesús Guinea, MD, PhD,[a,b,c,d] and Emilio Bouza, MD, PhD,[a,b,c,d]

Invasive Aspergilosis cases (1988-2010)



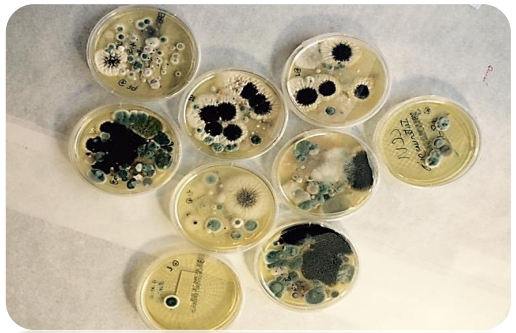
Gráfica extraída de Muñoz P, et al. J Heart Lung Transplant. 2014

Comparison between **tailored prophylaxis** era and previous era (1988 – 2002):

- Patients who received **AF prophylaxis**: 9.8% vs 33.4%; P= 0.001
- **Invasive aspergillosis incidence:** 2.2% vs 8.6%; P= 0.01
- **IA related mortality:** 1.5% vs 5.75% vs; P= 0.06

Muñoz P, et al. Invasive aspergillosis among heart transplant recipients: a 24-year perspective. J Heart Lung Transplant. 2014 Mar;33(3):278-88. doi: 10.1016/j.healun.2013.11.003.

Air control for the prevention of mould infections



- Establish air control routine at your center
- If any outbreak of high counts of cfu is detected, contact preventive health department,

Hospital authorities and technical staff.

- Increase cleaning and vacuum cleaning of filters
- Hepa filter must be change in outbreaks
- If renovations, construction or demolitions are

Ocurring nearby→increase number of measurements

Documento de consenso

Recomendaciones sobre la prevención de la infección fúngica invasora por hongos filamentosos de la Sociedad Española de Microbiología Clínica y Enfermedades Infecciosas (SEIMC)

Isabel Ruiz-Camps [a], Jose María Aguado [b], Benito Almirante [a], Emilio Bouza [c], Carmen Ferrer Barbera [a], Oscar Len [a], Lorena López-Cerero [d], Juan Luis Rodríguez-Tudela [e], Miguel Ruiz [f], Amparo Solé [g], Carlos Vallejo [h], Lourdes Vázquez [i], Rafael Zaragoza [j], Manuel Cuenca-Estrella [e,*] y Grupo de Estudio de Micología Médica de la SEIMC (GEMICOMED)

Guidelines for the prevention of invasive mould diseases caused by filamentous fungi by the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC)

I. Ruiz-Camps[1], J. M. Aguado[2], B. Almirante[1], E. Bouza[3], C. F. Ferrer-Barbera[1], O. Len[1], L. Lopez-Cerero[4], J. L. Rodríguez-Tudela[5], M. Ruiz[6], A. Solé[7], C. Vallejo[8], L. Vazquez[9], R. Zaragoza[10] and M. Cuenca-Estrella[5] GEMICOMED (Medical Mycology Study Group of SEIMC)

Ruiz-Camps et al. CMI 2011

Ruiz-Camps et al. EIMC 2010

Outdoor air

Range 0-105

c.f.u. / m³

Unprotected hospital air

5-25 c.f.u. / m³

HEPA filtered air

<0.1 c.f.u. / m³

Received: 17 February 2021 | Revised: 18 April 2021 | Accepted: 26 April 2021
DOI: 10.1111/myc.13298

ORIGINAL ARTICLE

mycoses WILEY

Invasive aspergillosis in solid organ transplantation: Diagnostic challenges and differences in outcome in a Spanish national cohort (Diaspersot study)

Francesca Gioia[1] | Eta Filigheddu[1] | Laura Corbella[2,3] | Mario Fernández-Ruiz[2,3] | Francisco López-Medrano[2,3] | Ana Pérez-Ayala[4] | Jose María Aguado[2,3] | Maria Carmen Fariñas[3,5] | Francisco Arnaiz[5] | Jorge Calvo[6] | Jose Maria Cifrian[7] | Claudia Gonzalez-Rico[3,5] | Elisa Vidal[3,8] | Julian Torre-Cisneros[3,8] | Maria Mar Ras[9] | Sandra Pérez[9] | Nuria Sabe[3,9] | Leyre Monica López-Soria[10] | Regino Jose Rodríguez-Alvarez[11] | José Miguel Montejo[3,11] | Maricela Valerio[12] | Marina Machado[12] | Patricia Muñoz[12] | Laura Linares[3,13] | Marta Bodro[3,13] | Asuncion Moreno[3,13] | Ana Fernández-Cruz[14] | Rafael Cantón[3,15] | Santiago Moreno[1] | Pilar Martin-Davila[1,3] | Jesús Fortún[1,3]

- DIASPERSOT: 9 spanish centers during 10 years (2010- 2019).

Objetives:

- Analyze the impact of IA in SOT in Spain.
- Evaluate diagnostic criteria, treatment, mortality factors and prophylaxis.

Gioia F, et al. Invasive aspergillosis in solid organ transplantation: Diagnostic challenges and differences in outcome in a Spanish national cohort (Diaspersot study). Mycoses. 2021 Nov;64(11):1334-1345. doi: 10.1111/myc.13298.

DIASPERSOT Study: General characteristics

TABLE 1 Baseline conditions

	n: 126 (%)
Type of transplant	
Lung	54 (42.8)
Kidney	25 (19.8)
Liver	24 (19.1)
Heart	16 (12.7)
Intestinal	1 (0.8)
Combined	6 (4.7)
Transplant time	
2010–2014	64 (50.8)
2015–2019	62 (49.2)
Age at transplant time (median and SD)	54.6 (18.2)
Previous tumour	14 (11.1)
Previous surgery for tumour	9 (7.1)
Previous chemotherapy	4 (3.2)
Uncontrolled tumour	4 (3.2)
Hepatopathy (in no-liver transplant)	3 (2.3)
Nephropathy (in no-kidney transplant)	27 (21.4)
COPD (in no-lung transplant)	13 (10.3)
Other pneumopathy (in no-lung transplant)	10 (7.9)
Diabetes	37 (29.3)
Previous tuberculosis infection/disease	8 (6.3)
Previous tuberculosis infection in no-lung transplant	3 (2.3)

Tabla extraída de Gioia F, et al. Mycoses. 2021

- 126 IA cases (proven/probable).
- Half of the cases ocurred in **Lung Tx**.
- Cumulative anual incidence:
  - Lung Tx 6.5%
  - Bowel Tx 5.5%
  - Heart Tx 2.9%,
  - Liver Tx 1.8%
  - Kidney Tx 0.6%.

Gioia F, et al. Invasive aspergillosis in solid organ transplantation: Diagnostic challenges and differences in outcome in a Spanish national cohort (Diaspersot study). Mycoses. 2021 Nov;64(11):1334-1345. doi: 10.1111/myc.13298.

TABLE 2 Predisposing conditions according to type of transplant

	Lung Tx. (*n*: 54)	Kidney Tx. (*n*: 25)	Liver Tx. (*n*: 24)	Heart Tx. (*n*: 16)
Unipulmonar	23 (42.6%)	–	–	–
Acute rejection	17 (31.5%)	9 (36.0%)	5 (20.8%)	7 (43.7%)
Chronic organ dysfunction	8 (14.8%)	5 (20.0%)	4 (16.7%)	3 (18.7%)
Previous Aspergillus colonisation	8 (14.8%)	–	–	1 (6.2%)
Ischaemia of bronchial anastomosis	5 (9.2%)	–	–	–
COPD	24 (44.4%)	8 (32.0%)	3 (12.5%)	1 (6.2%)
CMV infection	5 (9.2%)	9 (36.0%)	7 (29.2%)	8 (50.0%)
CMV disease	1 (1.8%)	4 (16.0%)	2 (8.3%)	2 (12.5%)
Continuous dialysis	5 (9.2%)	15 (60.0%)	7 (29.2%)	6 (37.5%)
Bronchial prosthesis	1 (1.8%)	–	–	–
Delayed function	–	12 (48.0%)	–	–
Retransplantation	–	–	5 (20.8%)	–
Biliodigestive anastomosis (y-Roux)	–	–	5 (20.8%)	–
High haemoderivate requirement	–	–	5 (20.8%)	–
MELD >30	–	–	4 (16.7%)	–
Fulminant hepatitis	–	–	3 (12.5%)	–
Reintervention	10 (18.5%)	7 (28.0%)	6 (25.0%)	8 (50.0%)
Hypogammaglobulinaemia	–	–	–	5 (31.2%)
Previous thymoglobulin	2 (3.7%)	3 (12.0%)	0	1 (6.2%)
Diabetes	16 (29.6%)	6 (24%)	6 (25.0%)	7 (43.7%)
Previous/simultaneous bacteraemia	3 (5.5%)	4 (16.0%)	3 (12.5%)	1 (6.2%)
Previous/simultaneous, other infection	15 (27.8%)	7 (28.0%)	8 (33.3%)	6 (37.5%)

- IA in lung tx was commonly one sided (42.6%).
- CMV infecion is a common factor in liver tx (29.2%) and heart (50%).
- Continuous renal replacement therapy (continuous dyalisis) was a common risk factor in most of the transplants.
- Reintervention and diabetes are also common risk factors.

Tabla extraída de Gioia F, et al. Mycoses. 2021

Gioia F, et al. Invasive aspergillosis in solid organ transplantation: Diagnostic challenges and differences in outcome in a Spanish national cohort (Diaspersot study). Mycoses. 2021 Nov;64(11):1334-1345. doi: 10.1111/myc.13298.

Breakthrough fungal infections

GUIDELINES Open Access

Invasive aspergillosis in solid organ transplant patients: diagnosis, prophylaxis, treatment, and assessment of response

Dionysios Neofytos[1*], Carolina Garcia-Vidal[2], Frédéric Lamoth[3,4], Christoph Lichtenstern[5], Alessandro Perrella[6,7] and Jörg Janne Vehreschild[8,9,10]

- Major concern following universal antifungal prophylaxis.
- Caused by filamentous fungi that have been selected due to intrinsic or acquired resistance to the prophylactic agent used, the latter in case of suboptimal absorption and/or tissue concentration of the AF administered.
- There are few data on the incidence of breakthrough IFI in SOT, most studies were on hematologic patients.
- Main breakthrough IFIs are due to mucorales, and azole-resistant *Aspergillus* species.
- Among the *Aspergillus* species, *A. calidoustus* was found to be the predominant cause of gap IFI.

Neofytos D, et al. Invasive aspergillosis in solid organ transplant patients: diagnosis, prophylaxis, treatment, and assessment of response. BMC Infect Dis. 2021 Mar 24;21(1):296. doi: 10.1186/s12879-021-05958-3.

AF prophylaxis To whom? With what? For how long?

Which is the best strategy?

UNIVERSAL

- More expensive
- More risk of drug to drug interactions (particularly with azoles)
- Emerging fungal infections (*Scedosporium, Lomentospora, Fusarium, Mucor*)
- More adverse events related to the antifungals

PREEMPTIVE OR TAILORED

- Cheaper
- Less potential drug to drug interactions
- Less emergent mycosis (in theory)
- **Failures in selecting patients who are candidates for prophylaxis**

Which are the most current guidelines?

2019

2014

AST | AMERICAN SOCIETY OF TRANSPLANTATION

ESCMID MANAGING INFECTIONS PROMOTING SCIENCE

ESGICH

Received: 4 March 2019 | Accepted: 18 March 2019
DOI: 10.1111/ctr.13544

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SPECIAL ISSUE: TRANSPLANT INFECTIOUS DISEASES

Clinical TRANSPLANTATION The Journal of Clinical and Translational Research | WILEY

Invasive Aspergillosis in solid-organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice

Shahid Husain[1] | Jose F. Camargo[2] on behalf of the AST Infectious Diseases Community of Practice

S. Husain, et al. Clin Transplant. 2019 Sep;33(9):e13544.doi: 10.1111/ctr.13544.

REVIEW 10.1111/1469-0691.12660

Invasive fungal infections in solid organ transplant recipients

J. Gavaldà[1], Y. Meije[1], J. Fortún[2], E. Roilides[3], F. Saliba[4], O. Lortholary[5], P. Muñoz[6,7,8,9], P. Grossi[10], M. Cuenca-Estrella[11] on behalf of the ESCMID Study Group for Infections in Compromised Hosts (ESGICH)

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J. Gavaldá, et al. Clin Microbiol Infect. 2014 Sep:20 Suppl 7:27-48. doi: 10.1111/1469-0691.12660.

What are the antifungal prophylaxis recommendations for each type of transplant?

	Kidney	Liver	Heart	Lung	Pancreas	Bowel
Universal				X	X	X
Tailored based on risk factors	X	X	X			

AF prohylaxis in Lung transplantation

Target population	European		
Lung OR Lung/Heart		**Agents**	**Duration**
All recipients (Recommended)	+	**Nebulised Lip-AmB 25mg (A-II)** Until resolution of bronchial Suture: 3 times a week 2-6 m: once a week >6m: once every 2 weeks	Indefinite or a minimum of 12m
OR Guided Prophylaxis if one RF:			
Induction with alemtuzumab or ATG	+	**Guided prophylaxis (A-II)** Nebulised Lip-AmB Load 25mg 3 times a week For 2 weeks. Then once a week **Nebulised AmB lipid complex** 50mg (B-II) Load once every 2 days for 2 weeks, then 50mg once a week.	A mínimum of 12m
Acute rejection	+		
Single-lung transplant	+		
Aspergillus spp. Colonization pre- Tx or during 1st y post-x	+		
Hypogammaglobulinema (<400mg/dL)	+		

Gavaldá J. Clin Microbiol Infect 2014.
Husain S. Clinical Transplantation 2019.

AF prohylaxis in Lung transplantation

Target population	European			American		
Lung OR Lung/Heart		**Agents**	**Duration**			**Duration**
All recipients (Recommended)	+	**Nebulised Lip-AmB 25mg (A-II)** Until resolution of bronchial Suture: 3 times a week 2-6 m: once a week >6m: once every 2 weeks	Indefinite for a minimum of 12m		Universal prophylaxis or Preemptive Depending on availability of dx tests (strong)	4-6m for universal
OR Guided prophylaxis if one RF						
Induction with alemtuzumab or ATG	+	**Guided prophylaxis (A-II)** Nebulised Lip-AmB Load 25mg 3 times a week For 2 weeks. Then once a week	A mínimum of 12m	+	Targeted If one mayor RF (Green): (strong) **OR** if more tan one of minor (Yellow): (weak).	3-4m for targeted **Duration should be guided by:** -Airway inspection -Respiratory surveillance fungal cultures -Clinical RF
Acute rejection	+			+	**Inhaled AmB** in preemptive (USE with CAUTION)	
Single-lung transplant	+	**Nebulised AmB lipid complex** 50mg (B-II) Load once every 2 days for 2 weeks, then 50mg once a week.		+	**Inhaled AmB in targeted:** 50mg once every 2 days for 2 weeks, Then once per week For at least 13 weeks	
Aspergillus spp. Colonization pre-Tx or during 1st y post-x	+			+		
Hypogammaglobulinema (<400mg/dL)	+			+		
Positive if intraoperative *Aspergillus* culture in CF patients		**Nebulised AmB lipid complex** 50mg (B-II) Load once every 2 days for 2 weeks, then 50mg once a week.		+	Voriconazole, Itraconazole for Universal or preemptive	
Early airway ischemia				+	Alternative: posaconazole or isavuconazole (weak)	

AF prohylaxis in Lung transplantation

Target populat	
Lung OR Lung/	
All recipients (Re	
OR Guided prophyla	
Induction with al ATG	
Acute rejection	
Single-lung transp	
Aspergillus spp. C Tx or during 1st y	
Hypogammaglob (<400mg/dL)	
Positive if intraop *Aspergillus* cultur	
Early airway ische	

- If preemptive is used:
- Recommend GM in BAL and fungal culture in BAL periodically.
- Use BAL GM cutoff point of >1.0
- Serum GM is not recommended for screening

- If azoles are used: monitor liver toxicity, levels, beware of long term effects (squamous cell carcinoma), patient protection measures

- If inhaled amphotericins are used: beware of AEs (coughing, wheezing, nausea)

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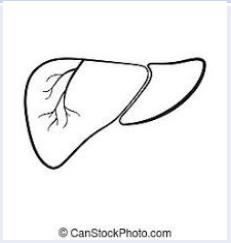
ratory llance cultures
al RF

AF prohylaxis in Liver transplantation

Target population	European			American		
High Risk LTx **Major:**		**If one major or two minor:**	**Duration**			
Retransplantation	+	Micafungin (A-II) Caspofungin (A-II) L-AmB (A-II) Lipid complex AmB (A-II) Anidulafungin (BIII)	2-4 weeks or until RF resolution			
Fulminant hepatic failure	+					
MELD >30	+					
Renal failure requiring replacement therapy	+					
Minor:	+					
MELD score 20-30	+					
Split	+					
Living-donor	+					
Choledochojejunostomy (Roux-en-Y)	+					
High transfusión requirement (>40 units of celular blood products	+					
Renal failure not requiring replacement therapy (CrCL <50)	+					
Early reintervention	+					
Multifocal colonization /infection by *Candida* spp	+					



Gavaldá J. Clin Microbiol Infect 2014.
Husain S. Clinical Transplantation 2019.

AF prohylaxis in Liver transplantation

Target population	European			American		
Major:		**If 1 major or 2 minor:**	**Duration**		**If one RF:**	**Duration**
Retransplantation	+	Micafungin (A-II)	2-4 weeks or until RF resolution	+	Anidulafungin (strong)	14-21 days posTx
Fulminant hepatic failure	+	Caspofungin (A-II)			Micafungin (strong)	
MELD >30	+	L-AmB (A-II)		+	Caspofungin (strong)	
Renal failure requiring replacement therapy	+	Lipid complex AmB (A-II)		+ (7 d postTx)	Voriconazole (strong)	
Minor:		Anidulafungin (BIII)			L-Amb (weak)	
MELD score 20-30	+					
Split	+					
Living-donor	+					
Choledochojejunostomy (Roux-en-Y)	+					
High transfusión requirement (>40 units of blood products)	+					
Renal failure not requiring replacement therapy (CrCL <50)	+			+ Cr>3.3g/dl		
Early reintervention	+			+		
Multifocal colonization /infection by *Candida* spp	+					
CMV				+		

Gavaldá J. Clin Microbiol Infect 2014.
Husain S. Clinical Transplantation 2019.

AF prohylaxis in Liver transplantation

Target population	European			American		
Major:		**If 1 major or 2 minor:**	**Duration**		**If one RF:**	**Duration**
R						
Fu						
M						
R re						
M						
M						
Sp						
Li						
C er						
H (>						
R re						
Ea						
Multifocal colonization /infection by *Candida* spp	+					
CMV				+		

- Tailored prophylaxis for patients with one major or 2 minor RFs
- Duration 14-21 days or until RF resolution.
- At our center, candins are the first option for prophylaxis because of their low potential for drug interaction, less frequent adverse events and no need for dosage adjustment according to renal function.
- Other centers choose prophylaxis with L-AmB
- Screening with GM or BDG is not recommended to guide preemptive treatment (lack of evidence).

Gavaldá J. Clin Microbiol Infect 2014.
Husain S. Clinical Transplantation 2019.

AF prohylaxis in Heart transplantation

Target population	European			American	
Acute rejection		**If one RF**	**Duration**		
Hemodialysis /CRRT	+	Itraconazole (A-II)	At least 3months		
Re-exploration after transplant	+	Voriconazole (B-III)			
Aspergillus spp. Heavy colonization of air	+	Posaconazole (B-III)			
Renal failure requiring replacement therapy	+	Candins (BIII)			
CMV	+				

Gavaldá J. Clin Microbiol Infect 2014.
Husain S. Clinical Transplantation 2019.

AF prohylaxis in Heart transplantation

Target population	European			American		
Acute rejection		**If one RF**	**Duration**		**If one RF**	**Duration**
Hemodialysis /CRRT	+	Itraconazole (A-II)	At least 3months	+	Itraconazole	50-150 days
Re-exploration after transplant	+	Voriconazole (B-III)		+	Candins (Strong)	Up to 120 days
Aspergillus spp. Heavy colonization of air	+	Posaconazole (B-III)		+		
Renal failure requiring replacement therapy	+	Candins (BIII)		+		
CMV	+			+		
Existence of an episode of IA in The unit 2mo before or after HT				+		
ECMO (Swiss cohort)	+					

- Prophylaxis directed to patients with one or more RFs.
- Do not forget patients with ECMO, Levitronix, Berlin-Heart peritransplantation.
- Duration 14-21 days or until resolution of the risk factors.
- We prefer candin because of low interaction with other drugs, AE, no need to adjust to renal function.
- With candins there is no need to monitor levels (CRRT, ECMO)

Gavaldá J. Clin Microbiol Infect 2014.
Husain S. Clinical Transplantation 2019.

AF prohylaxis in Kidney transplantation

Target population	European			American		
		Prophylaxis	**Duration**		**Prophylaxis**	**Duration**
Do not establish RF	+	No prophylaxis (B-III)			Data insufficient to recommend prophylaxis	
Pre-tx diagnosis of COPD				+		
Acute rejection episode in the last 3 m				+		
Graft failure				+		
High and prolonged duration of corticosteroids				+		

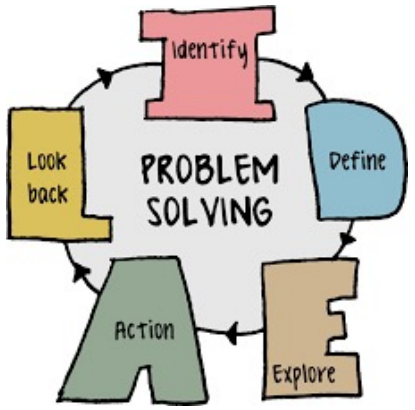
- Individualize each case
- Consider if preservation fluid cultures are positive for *Candida.*
- Consider it in cases of suspected IFI in the donor.
- Consider in cases of CMV /Corticoresistant rejection /Thymoglobuline
- Consider in cases of hospital outbreaks /high colony count in ambient air (individualize)

Gavaldá J. Clin Microbiol Infect 2014.
Husain S. Clinical Transplantation 2019.

Is there still a problem for guideline implementation?

- Last update: 2019 (american), 2014 (european).

  - There has been some changes in epidemiology
  - New biomarkers (change from universal prophylaxis → guided prophylaxis → preemptive therapy)
  - Due to the extended use of prophylaxis→Emergent fungal infections
  - New antifungal drugs with different spectrum, profile and drug-to-drug interactions
  - New real-life experience regarding prophylaxis in transplant centers



European survey→ International survey

Objective: To have more information regarding actual ideas and practices of AF prophylaxis in SOT

- Ongoing work
- **Participants:** 50 centers
- **Completed:** 41 centers

If you want to participate, just follow this link:

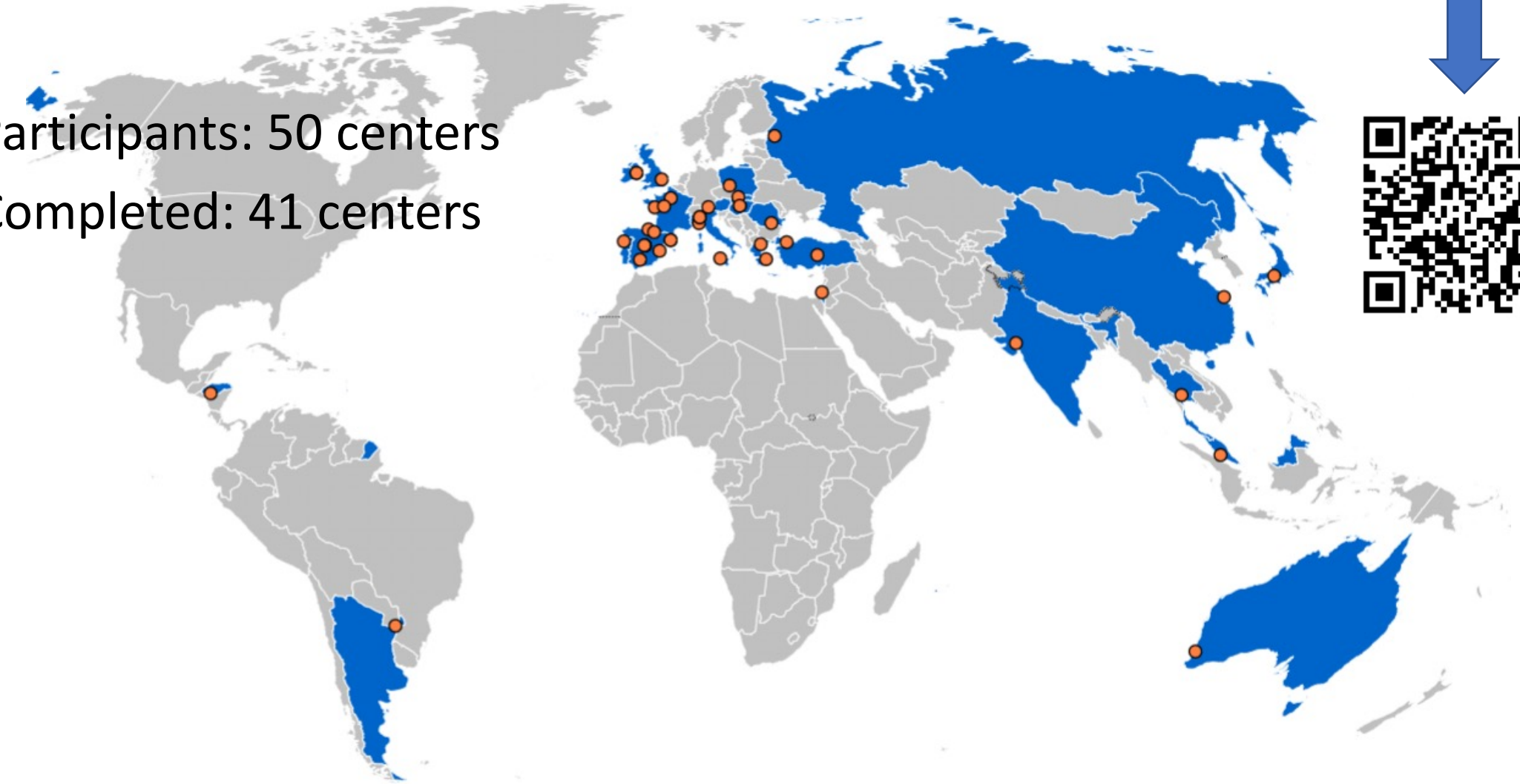
https://www.clinicalsurveys.net/uc/AFprophylaxisSOT/

International survey

https://www.clinicalsurveys.net/uc/AFprophylaxisSOT/

QR code directs to the survey:

- Participants: 50 centers
- Completed: 41 centers

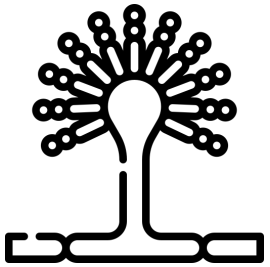


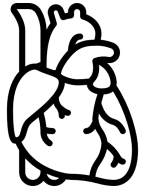
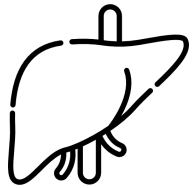
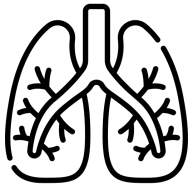
Are we following the guidelines?

- No because of the differences in local epidemiology.
- No because we lack of clinical trials (Grade A evidence) that support them.
- No because of problems in the access to new antifungals.
- No because no information regarding its performance in SOT population.
- No because risk factors already change in our centers, and we don´t rely on outdated guidelines.
- No because there is NO consensus between ID physicians, clinical mycologists and transplant physicians (nephrologists, cardiologists, hepatologists, neumologists, surgeons, critical care physicians).
- No because there is not an accepted guideline backed by the different transplant societies and ID and clinical microbiologist societies.

Ideas to take home

- The recognition of risk factors in each type of TOS together with the optimization of AF prophylaxis strategies has significantly reduced morbidity and mortality caused by IFIs and changed their epidemiology (late IFIS, emerging and resistant pathogens, etc).
- There are still situations of special risk: ECMO, CRRT, Ventricular assist devices, allograft rejection in which more studies are needed.
- It is important to remember donor-transmitted fungal infections, the possibility of regional infections in travelers and migrants and horizontal transmission.
- Do not forget the importance of environmental air quality control (air sampling and HEPA-filtered rooms), a high burden of spores in the air could be the explanation for hospital outbreaks in patients without known risk factors for IFIs.
- Close collaboration between transplantologists, clinical microbiologists and infectious diseases specialist is essential to continue adapting antifungal prophylaxis.
- Clinical trials and real life experience with the new AF drugs in SOT prophylaxis is needed.



Acknowledgments

- Alessandro Giacinta, Marina Machado, Agustin Estévez, Patricia Muñoz, **Clinical Microbiology and Infectious Diseases Department**.

- **Jon Salmanton-García**, Danila Seidel, Olivier Cornely, **University Hospital Cologne, Germany.**

- Maddalena Gianella, **ESGCIH, ESCMID.**

- All the members of the Spanish group for the study of infections in transplant and immunocompromised patients **(GESITRA-IC) from the Spanish Society of Clinical Microbiology and Infectious Diseases (SEIMC).**

- **ECMM** organizing committee for inviting me to this conference.

Thank you very much!

- International Survey of Antifungal prophylaxis in solid organ transplant:
  - Participants from all the world are welcome
  - If you are interested in participate here is the link:

Link

https://www.clinicalsurveys.net/uc/AFprophylaxisSOT/

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