Infecciones en el paciente transplantado de órgano sólido

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Fundació Lluita contra les Infeccions

Pfizer

Jornada intrahospitaria de infecciones en el paciente inmunosuprimido

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1. El estado “neto” de inmunosupresión
2. Cronología de la infección en el TOS
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5. Infecciones víricas
6. Infecciones fúngicas
7. Infecciones Parasitarias

1. El estado “neto” de inmunosupresión

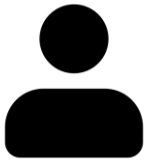
Infecciones en el RECEPTOR

Infecciones en el DONANTE

Complicaciones perioperatorias

Inmunosupresión

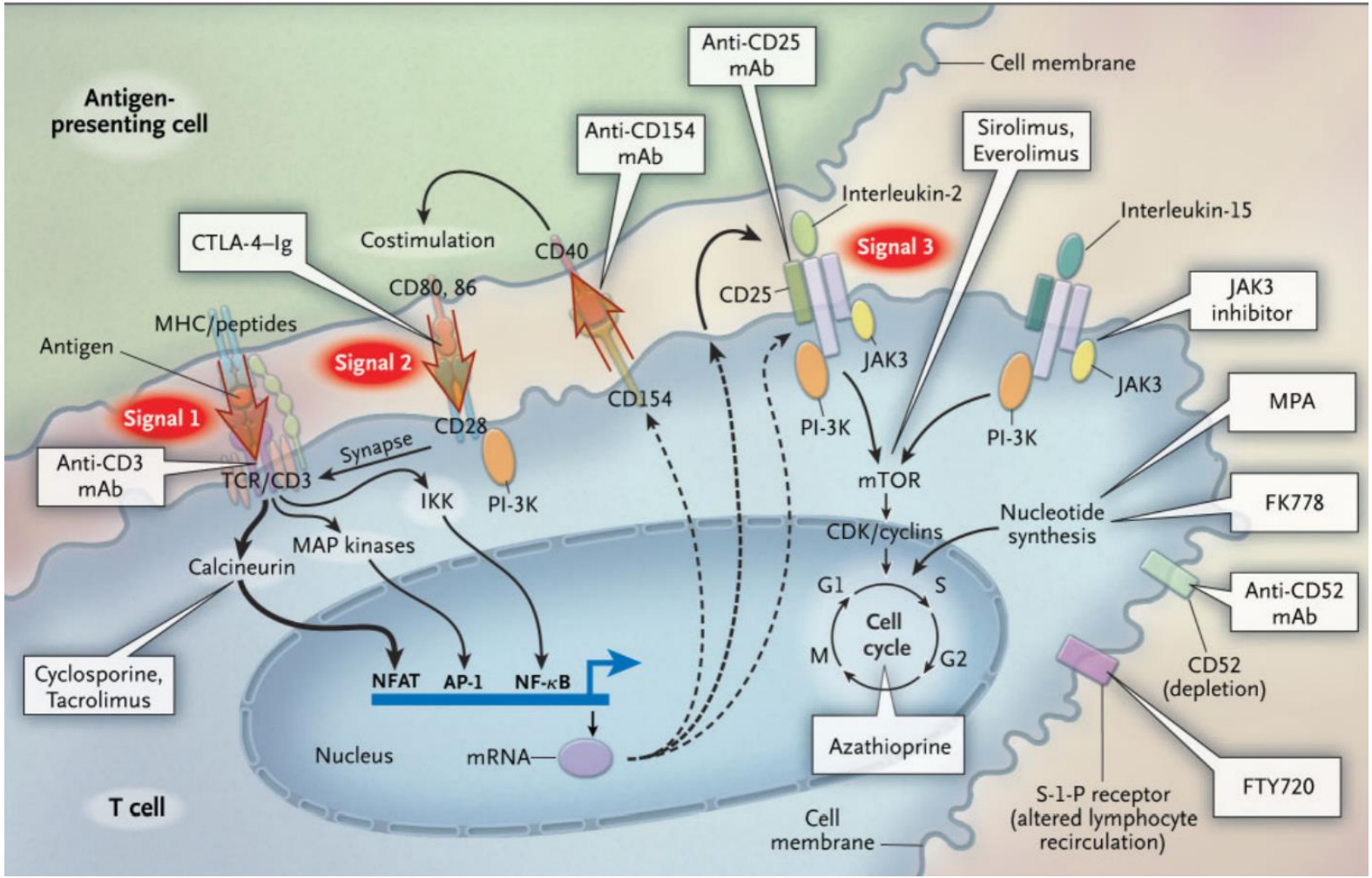
Exposición a Infecciones



1. El estado “neto” de inmunosupresión

- **Enfermedad de base, inmunodeficiencias previas**
- **Complicaciones técnicas** asociadas al trasplante
- **Barrera mucocutánea:** catéteres, drenajes, sondas.
- **Rechazo precoz, disfunción del injerto**
- **Numero de transplantes previos**
- **Complicaciones metabólicas**: uremia/HD, diabetes, desnutrición, miopatía
- **Citopenias:** neutropenia, linfopenia, hipogammaglobulinemia
- **Coinfecciones virales** (CMV, VEB, BKV, etc)

Fernández-Rivera, 2018

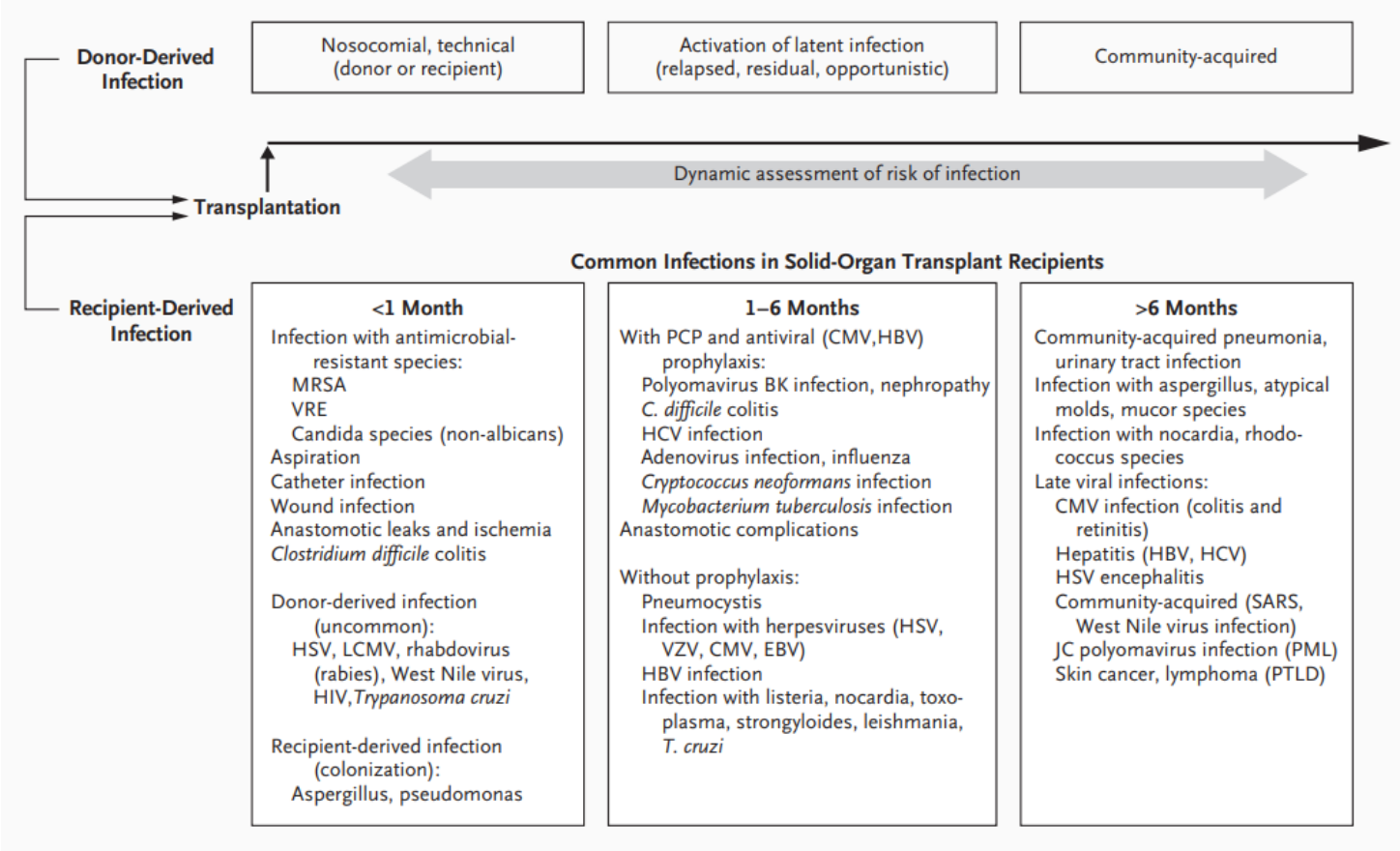


Halloran, NEJM 2004

1. El estado “neto” de inmunosupresión

Glucocorticoides	Inmunoglobulinas Anti-linfocíticas	Inh calcineurina	Inh síntesis nucleótidos	Inh mTOR	Tto rechazo
	Timoglobulina/ATG	*Ciclosporina*	*Micofenolato*	*Sirolimus*	*Plasmaféresis Eculizumab*
	Basiliximab	*Tacrólimus*	*Azatioprina*	*Everolimus*	*Rituximab*
Herida qx Bacterias Hongos	**Virus Bacterias encapsuladas**	**Virus (herpes, gingivitis)**	**Bacterias Víricas (CMV tardío, VPH)**	**Herida qx Menor infección viral?**	**Bacterias Encapsuladas Virus (CMV) Hongos RTX - menor incidencia PTLD**

2. Cronología de la infección en TOS



3. Screening donante/receptor

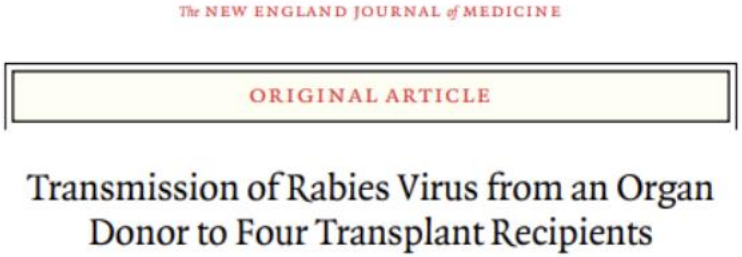
- **Infecciones transmitidas por el donante**

TABLE 1 Potential donor-derived disease transmission as reported to the OPTN: 2005-2017

	Reports (Donors)	Recipients potentially involved[a]	Recipients with proven/ Probable transmission	Donor-derived disease attributable deaths (Recipients)	Liver recipients[a] with proven or Probable transmissions	Heart recipients[a]	Kidney/ Pancreas[a]	Lung or heart/Lung recipients[a]
Malignancy	577	1342	164	43	17	1	26	3
Viruses[b]	463	1463	216	27	26	6	41	14
Bacteria[c]	467	1524	230	21	12	3	39	24
Fungi[d]	299	1043	179	26	10	5	18	15
Mycobacteria[e]	136	468	35	7	0	0	0	3
Parasites[f]	118	385	103	17	8	6	12	5
Other Disease	121	402	68	3	8	0	10	6
Total	1980	5688	908 (15.9%)	135 (14.9%)	81	21	146	70

3. Screening donante/receptor

- **Screening en donante**


The NEW ENGLAND JOURNAL of MEDICINE

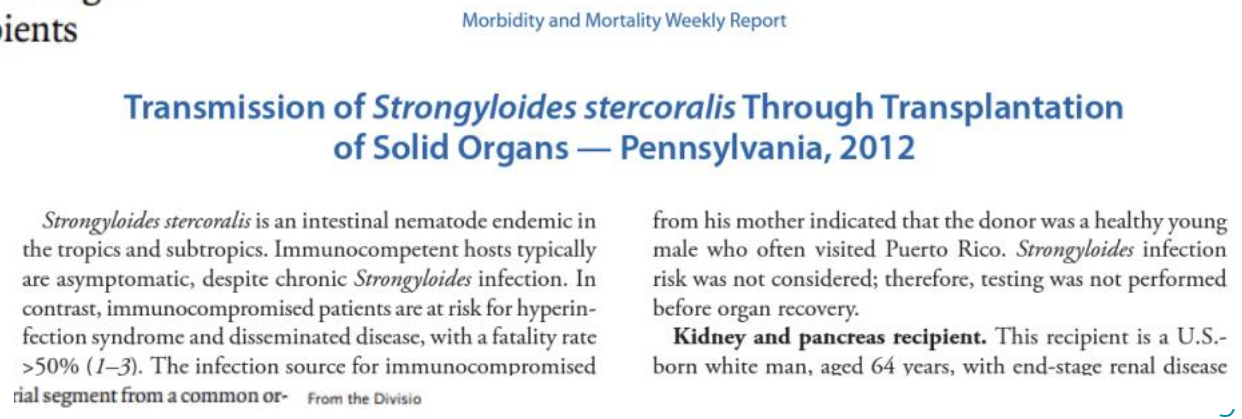
ORIGINAL ARTICLE

Transmission of Rabies Virus from an Organ Donor to Four Transplant Recipients


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transmission of West Nile Virus from an Organ Donor to Four Transplant Recipients


Morbidity and Mortality Weekly Report

Transmission of *Strongyloides stercoralis* Through Transplantation of Solid Organs — Pennsylvania, 2012

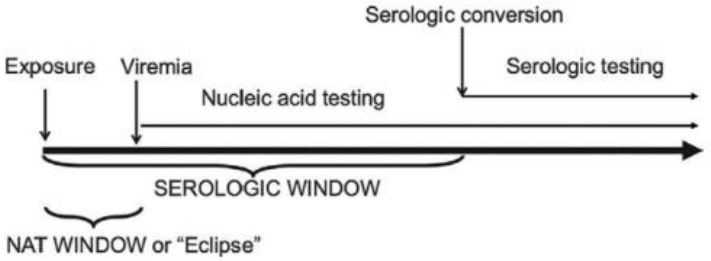
Strongyloides stercoralis is an intestinal nematode endemic in the tropics and subtropics. Immunocompetent hosts typically are asymptomatic, despite chronic *Strongyloides* infection. In contrast, immunocompromised patients are at risk for hyperinfection syndrome and disseminated disease, with a fatality rate >50% (*1–3*). The infection source for immunocompromised

rial segment from a common or- From the Divisio

from his mother indicated that the donor was a healthy young male who often visited Puerto Rico. *Strongyloides* infection risk was not considered; therefore, testing was not performed before organ recovery.

Kidney and pancreas recipient. This recipient is a U.S.-born white man, aged 64 years, with end-stage renal disease

Test	Candidate	Deceased donor	Living donor
Viral			
HIV			
Human immunodeficiency virus (HIV) antibody/antigen (fourth Generation HIV screening test)	x	x	x
HIV nucleic acid amplification testing (NAT)		x[b]	x[b]
Cytomegalovirus (CMV) IgG antibody	x	x	x
Hepatitis B virus (HBV)			
HBV surface antigen (HBsAg)	x	x	x
HBV core antibody (HBcAb-IgM and IgG, or total core antibody)	x	x	x
HBV surface antibody (HBsAb)	x		
HBV NAT		x[b]	x[b]
Hepatitis C virus (HCV)			
HCV antibody	x	x	x
HCV NAT	x[c]	x	x
Epstein-Barr virus (EBV) antibody (EBV VCA IgG, IgM)	x	x	x
West Nile virus serology or NAT (seasonal)			x
Parasitic			
Toxoplasma IgG antibody	x	x	x
Strongyloides IgG (if from endemic areas)	x	x	x
Trypanosoma cruzi serology (if from endemic areas)	x	x	x
Fungal			
Coccidioides serology (if from endemic areas)	x	x	x
Bacterial			
Syphilis (any of the following)	x	x	x
Fluorescent treponema antibody absorption (FTA-ABS)			
T. pallidum particle agglutination (TPPA)			
T. pallidum enzyme immunoassay (TP-EIA)			
Rapid plasma reagin (RPR)			
Venereal Disease Research Laboratory (VDRL)			
Tuberculosis (any of the following)	x		x
Purified protein derivative (PPD)			
Interferon gamma release assay (IGRA)			



Virus	Serology	NAT
HIV	22 days	5-10 days
HBV	38 - 50 days	20 – 26 days
HCV	38 - 94 days	6 - 9 days

FIGURE 1 Schematic of viral infection and detection by serology and nucleic acid testing

4. Infecciones bacterianas en SOT

Infecciones de la herida quirúrgica

- Alta morbilidad y mortalidad
- Incidencia 3-53%
- Alta incidencia en intestinal, multivisceral, hígado, páncreas.
- Ingreso prolongado, reingreso,
- Riesgo de MDR
- El órgano en sí puede ser un foco de infección

Organ transplant type	Incidence of SSIs (%)	Predominant pathogens causing SSIs	Secondary pathogens causing SSIs
Renal	3-11	*Staphylococcu aureus*	Gram-negative organisms (Enterobacteriaceae, Pseudomonas)
		CoNS	Yeast
		Enterococci	
Pancreas and pancreas-kidney	9-45	*Staphylococcu aureus*	Gram-negative organisms (Enterobacteriaceae, Pseudomonas)
		CoNS	*Streptococci*
		Enterococci	*Candida* spp *Mycoplasma hominis*

4. Infecciones bacterianas en SOT

TABLE 2 Risk factors for SSI by organ transplant type

Organ transplant type	Risk factor categories			
	Host factors	Surgical factors	Donor/allograft factors	Immunosuppression
Renal	DM	Ureteral leak	DGF	Azathioprine
	Obesity	Hematoma	Contamination of kidney perfusate	ATG
	Chronic GN	Blood transfusion	Acute graft rejection	MMF
	Re-operation			Sirolimus
Pancreas, pancreas-kidney	Re-operation	Prolonged operative time	Donor > 55 y old	
		Prolonged ischemic time	ATN in transplanted kidney	
		Enteric drainage	Graft rejection	
		Post-transplant fistula		
		Hand sewn anastomosis		
		Blood transfusion		

AST 2019

4. Infecciones bacterianas en SOT

- **ITU en el paciente trasplantado renal**

Risk Factors for Urinary Tract Infections During the First Year After Kidney Transplantation

R. Sorto [a], S.S. Irizar [a], G. Delgadillo [a], J. Alberú [b], R. Correa-Rotter [a], L.E. Morales-Buenrostro [a]

35 – 68%
E. Coli
Principales FR:
- Mujeres
- Días de sondaje
- ITU en el mes previo al trasplante
- Alteraciones genitourinarias
- 14 días de tratamiento

- **Bacteriuria asintomática**

Cochrane Database of Systematic Reviews | Review - Intervention

Antibiotics for asymptomatic bacteriuria in kidney transplant recipients

Julien Coussement, Anne Scemla, Daniel Abramowicz, Evi V Nagler, Angela C Webster Authors' declarations of interest

Version published: 01 February 2018 Version history
https://doi.org/10.1002/14651858.CD011357.pub2

4. Infecciones bacterianas en SOT

- **Tuberculosis latente y activa**
  - Riesgo de TB activa en SOT x20-75
  - Pulmón ++.
  - Incidencia TR
    - 0.5-6% en países desarrollados,
    - 15% en países endémicos
  - Primeros 6 meses postrasplante
  - PPD + IGRA

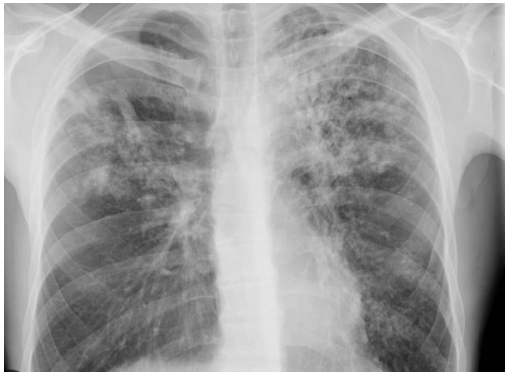


TABLE 2 Efficacy of short-term treatment with isoniazid and rifampicin for latent tuberculosis infection in lung transplant candidates

	No LTBI	Untreated LTBI	LTBI treated with 6H	LTBI treated with 3HR
Patients, No.	277	62	8	22
Median follow-up, days (range)	572 (1-6636)	741 (1-6138)	754 (1-2344)	175 (3-1560)
TB cases, No. cases (%)	3 (1%)	3 (4.8%)	0	0
TB incidence density, No. cases/10^5 patients-year (confidence interval 95%)	270 (60-800)	1200 (250-3490)	0 (0-16770)	0 (0-14190)

No., number; LTBI, latent tuberculosis infection; TB, tuberculosis; 6H, 6 months of isoniazid; 3HR, 3 months of isoniazid and rifampicin.

Guirao-Arrabal E et al. Clin Transplant 2016

4. Infecciones bacterianas en SOT

Tuberculosis latente: pautas de tratamiento

	Drug	Dose	
INH	9 months	5mg/kg/d (300mg max)	85-93%
INH	6 months	5mg/kg/d (300mg max)	80%
INH/RMP	3-4 months	5mg/kg (300mg max) 10mg/kg (600mg max)	80-85%
RMP	4 months	10mg/kg (600mg max)	80-95%
Levo or moxifloxacin	9 months	500mg/d // 400mg/d	LT, Weak evidence

- **Indicaciones de tratamiento de la ITL**

Tuberculin reactivity of ≥5mm before transplantationPositive interferon-gamma release assays (IGRAs)
History of tuberculin reactivity/positive IGRA without adequate prophylaxis
Recent conversion of tuberculin skin test or IGRA to positive
Radiographic evidence of old TB without prior prophylaxis; a chest CT scan should be performed in these patients to look for disseminated disease and to serve as a baseline study
History of inadequately treated active TB
Close contact with an individual with active pulmonary TB
Receipt of an allograft from a donor with latent TB or with a remote history of untreated or inadequately treated active TB

3. Infecciones perioperatorias en TOS

- **Clostridium difficile**

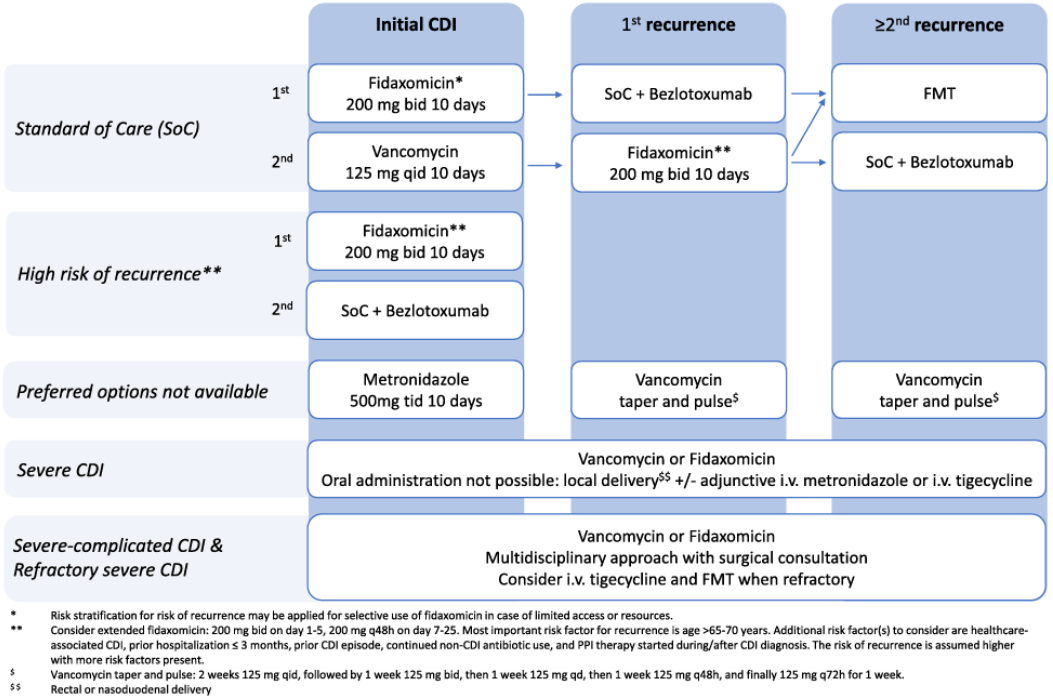


Fig. 1. Suggested treatment algorithm.

Factores de riesgo de recidiva
- **Edad > 65a**
- **TOS**
- **Neoplasia hematológica**
- **Hospitalización < 3m**
- **Uso de PPI**

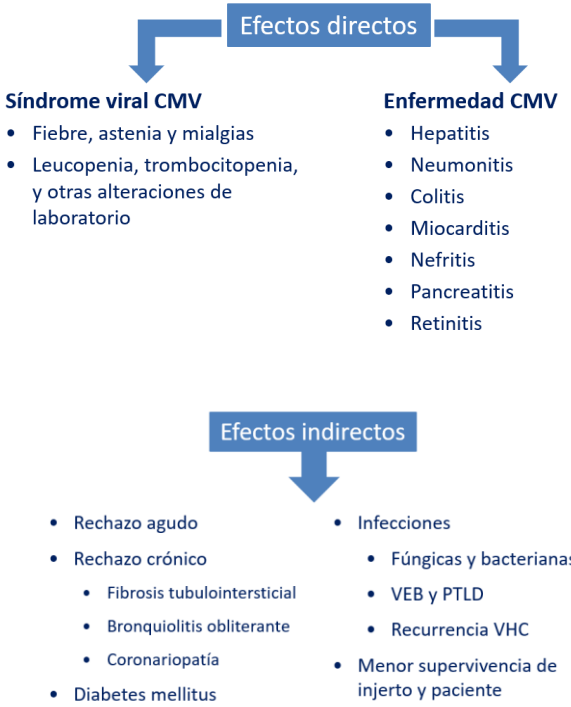
Criterios de gravedad
- Megacolon/ileo
- Leucocitosis / leucopenia
- Insuficiencia renal
- Lactato sérico > 2.2

ECCMID guidelines 2021

4. Infecciones virales en TOS

CMV

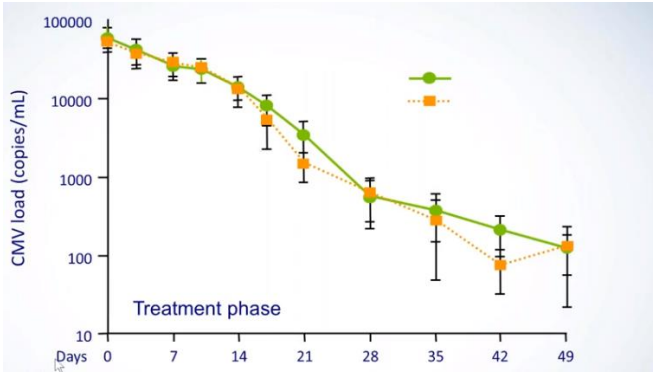
- Es la infección viral más prevalente en el paciente TOS.
- Virus inmunomodulador
- **Presentación en**
  - **Alto riesgo: D+ / R-**
  - **Riesgo moderado D + o -/ R+***
  - **Bajo Riesgo D-/R-**



4. Infecciones virales en TOS

CMV

- Oral VGCV
- IV si presentación grave o problemas de absorción
- Monitorización semanal de la viremia y hemograma + función renal
- Tratar mínimo dos semanas o hasta su negativización.
- Monitoring
- ¿Profilaxis secundaria?



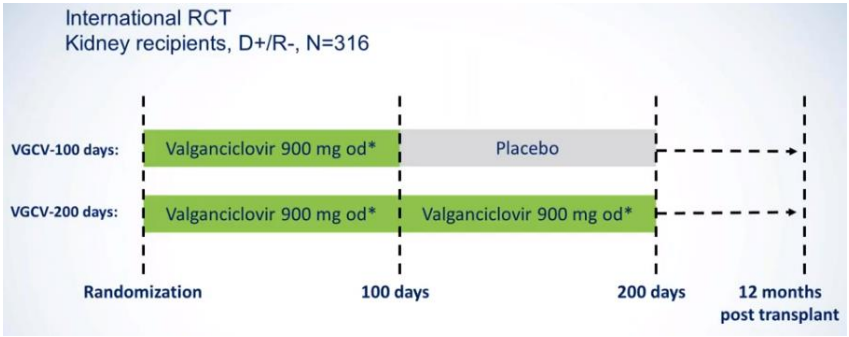
American Journal of Transplantation 2010; 10: 1–10
Wiley Periodicals Inc.

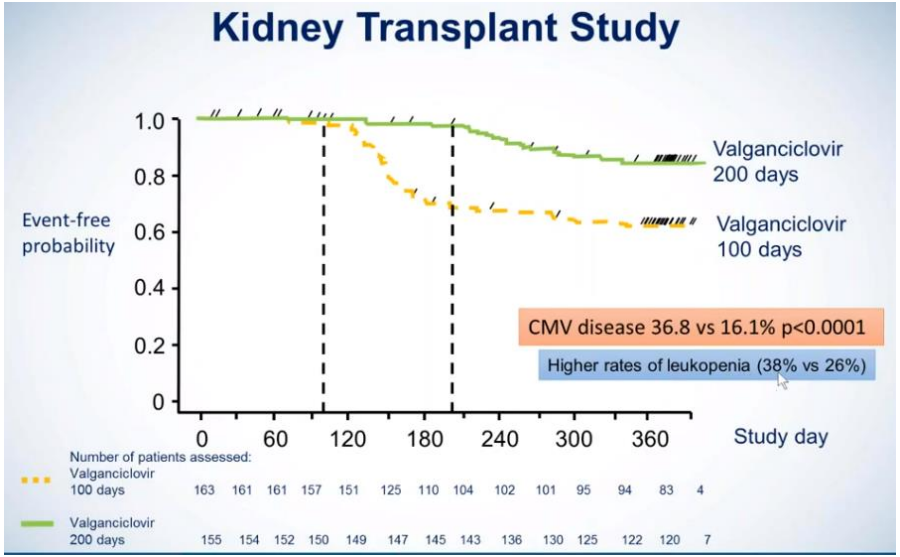
doi: 10.1111/j.1600-6143.2010.03074.x

The Efficacy and Safety of 200 Days Valganciclovir Cytomegalovirus Prophylaxis in High-Risk Kidney Transplant Recipients

A. Humar[a,*], Y. Lebranchu[b], F. Vincenti[c], E. A. Blumberg[d], J. D. Punch[e], A. P. Limaye[f], D. Abramowicz[g], A. G. Jardine[h], A. T. Voulgari[i], J. Ives[j], I. A. Hauser[j] and P. Peeters[k]

Humar, A (2010)





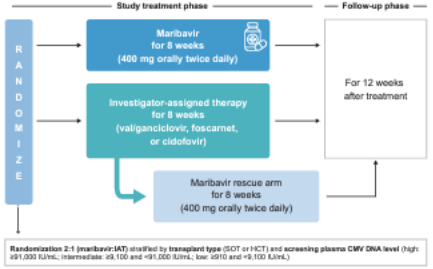
Maribavir for Refractory Cytomegalovirus Infections With or Without Resistance Post-Transplant: Results from a Phase 3 Randomized Clinical Trial

Robin K. Avery, Sophie Alain, Barbara D. Alexander, Emily A. Blumberg, Roy F. Chemaly, Catherine Cordonnier, Rafael F. Duarte, Diana F. Florescu, Nassim Kamar, Deepali Kumar, Johan Maertens, Francisco M. Marty, Genovefa A. Papanicolaou, Fernanda P. Silveira, Oliver Witzke, Jingyang Wu, Aimee K. Sundberg, and Martha Fournier, for the SOLSTICE Trial Investigators

INTRODUCTION

This was a phase 3, multicenter, randomized, open-label, **active-controlled study to assess the efficacy and safety of** maribavir compared with IAT in HCT and SOT recipients with CMV infections refractory to most recent treatment, with or without resistance to ganciclovir/valganciclovir, foscarnet, and/or cidofovir.

STUDY DESIGN



STUDY ENDPOINTS

The primary endpoint was confirmed CMV viremia clearance at the end of Week 8 (regardless of premature treatment discontinuation).

The key secondary endpoint was a composite of confirmed CMV viremia clearance and symptom control at the end of **Week 8, maintained through Week 16 after receiving exclusively** study-assigned treatment.

RESULTS

352 patients were randomized (maribavir, n=235; IAT, n=117)

PRIMARY ENDPOINT (WEEK 8)

Adjusted difference (95% CI): 32.8 (22.80–42.74)

A significantly higher proportion of patients treated with maribavir achieved the primary endpoint of confirmed CMV viremia clearance at Week 8 compared with IAT.

KEY SECONDARY ENDPOINT (WEEK 16)

Adjusted difference (95% CI): 9.5 (2.02–16.88)

A greater proportion of patients treated with maribavir achieved the composite key secondary endpoint of CMV viremia clearance and symptom control at Week 8, with maintenance through Week 16 compared with IAT.

SAFETY

Median (range) duration of exposure was 57 (2–64) days with maribavir and 34 (4–64) days with IAT.

Fewer patients discontinued maribavir than IAT due to TEAEs (13.2% vs 31.9%).

Dysgeusia was the most frequently reported TEAE in the maribavir group (maribavir: 37.2%; IAT: 3.4%).

Maribavir was associated with less acute kidney injury versus foscarnet (8.5% vs 21.3%) and neutropenia versus valganciclovir/ganciclovir (9.4% vs 33.9%).

One patient per treatment group had fatal treatment-related TEAEs.

CONCLUSIONS

Maribavir was superior to IAT for cytomegalovirus viremia clearance, and viremia clearance plus symptom control, **with maintenance of these effects post-therapy in transplant** recipients with refractory cytomegalovirus infections with or without resistance.

Maribavir demonstrated an improved safety profile versus valganciclovir/ganciclovir for myelotoxicity and versus foscarnet for nephrotoxicity, with fewer patients discontinuing maribavir than IAT.

The availability of an orally bioavailable therapy without the tolerability issues associated with current therapies may confer patient management benefits.

CMV, cytomegalovirus; HCT, hematopoietic-cell transplant; IAT, investigator-assigned therapy; SOT, solid-organ transplant; TEAE, treatment-emergent adverse event.

ClinicalTrials.gov: NCT02931539
This study was funded by Takeda Development Center Americas, Inc., Lexington, MA

JAMA | Original Investigation

Letermovir vs Valganciclovir for Prophylaxis of Cytomegalovirus in High-Risk Kidney Transplant Recipients
A Randomized Clinical Trial

Ajit P. Limaye, MD; Klemens Budde, MD; Atul Humar, MD, MSc; Flavio Vincenti, MD; Dirk R. J. Kuypers, MD, PhD; Robert P. Carroll, BM, BCh, DM; Nicole Stauffer, BS; Yoshihiko Murata, MD, PhD; Julie M. Strizki, PhD; Valerie L. Teal, MS; Christopher L. Gilbert, BS; Barbara A. Haber, MD

Figure 2. Primary Outcome of Cytomegalovirus (CMV) Disease With Letermovir vs Valganciclovir Prophylaxis Through Week 52 in the Full Analysis Set

	No./total No. (%)		Difference (95% CI), %[b]
	Letermovir[a]	Valganciclovir	
Primary outcome			
CMV disease[c]	30/289 (10.4)	35/297 (11.8)	-1.4 (-6.5 to 3.8) (noninferior)
Sensitivity analysis			
Investigator-reported CMV disease[d]	50/289 (17.3)	51/297 (17.2)	0.1 (-6.1 to 6.3)
Subgroup analysis			
Sex			
Men	25/210 (11.9)	24/209 (11.5)	0.5 (-5.8 to 6.8)
Women	5/79 (6.3)	11/88 (12.5)	-6.3 (-15.5 to 2.9)
Age, y			
<65	26/242 (10.7)	23/242 (9.5)	1.2 (-4.2 to 6.7)
≥65	4/47 (8.5)	12/55 (21.8)	-12.5 (-27.0 to 2.1)
Race[e]			
Non-White	2/37 (5.4)	6/53 (11.3)	-5.7 (-18.1 to 6.7)
White	28/250 (11.2)	29/243 (11.9)	-0.7 (-6.4 to 5.0)
Region			
US	15/118 (12.7)	16/116 (13.8)	-1.3 (-10.0 to 7.5)
Non-US	15/171 (8.8)	19/181 (10.5)	-1.7 (-8.0 to 4.6)
Lymphocyte-depleting induction immunosuppression			
Use	18/131 (13.7)	17/138 (12.3)	1.4 (-6.7 to 9.6)
Nonuse	12/158 (7.6)	18/159 (11.3)	-3.7 (-10.3 to 2.8)

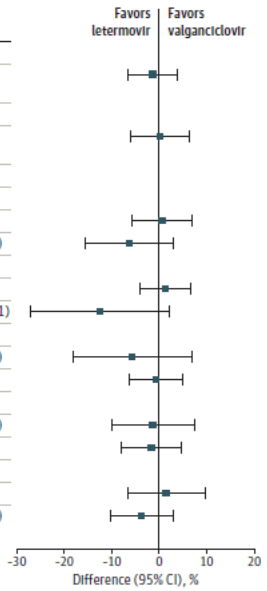
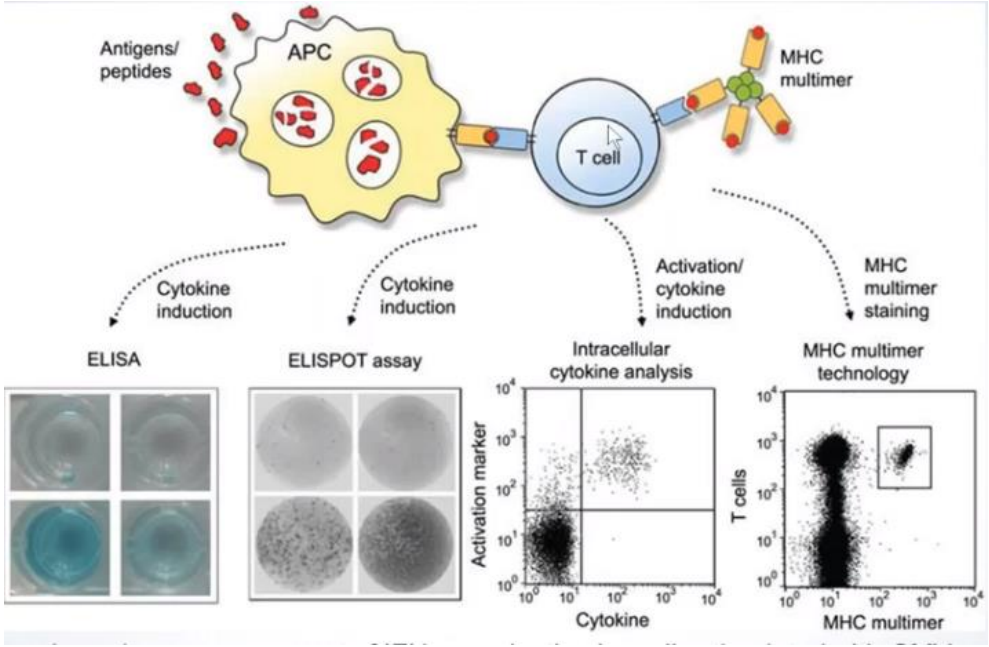


Table 2. Adverse Events Through Week 28 in the Safety Population[a]

Adverse event	No. (%) Letermovir (n = 292)	Valganciclovir (n = 297)	Difference (95% CI), %[b]
Adverse event summary			
≥1 adverse event	271 (92.8)	276 (92.9)	−0.1 (−4.4 to 4.2)
Serious adverse events[c]	106 (36.3)	113 (38.0)	−1.7 (−9.5 to 6.1)
Drug-related adverse events[d]	58 (19.9)	104 (35.0)	−15.2 (−22.2 to −8.0)
Serious drug-related adverse events[c,d]	4 (1.4)	15 (5.1)	−3.7 (−7.0 to −0.9)
Death	2 (0.7)	1 (0.3)	0.3 (−1.3 to 2.2)
Discontinued due to adverse events	12 (4.1)	40 (13.5)	−9.4 (−14.1 to −4.9)
Discontinued due to serious adverse events[c]	6 (2.1)	14 (4.7)	−2.7 (−5.9 to 0.3)
Discontinued due to drug-related adverse events[d]	8 (2.7)	26 (8.8)	−6.0 (−10.1 to −2.4)
Discontinued due to serious drug-related adverse events[c,d]	2 (0.7)	7 (2.4)	−1.7 (−4.2 to 0.4)
Adverse events in ≥10% of participants			
Diarrhea	92 (31.5)	85 (28.6)	2.9 (−4.5 to 10.3)
Tremor	53 (18.2)	52 (17.5)	0.6 (−5.6 to 6.9)
Urinary tract infection	41 (14.0)	42 (14.1)	0.1 (−5.8 to 5.6)
Peripheral edema	39 (13.4)	38 (12.8)	0.6 (−4.9 to 6.1)
Hypomagnesemia	37 (12.7)	39 (13.1)	−0.5 (−5.9 to 5.0)
Leukopenia	33 (11.3)	110 (37.0)	−25.7 (−32.3 to −19.1)
Hypertension	33 (11.3)	36 (12.1)	−0.8 (−6.1 to 4.5)
Increased creatinine	30 (10.3)	41 (13.8)	−3.5 (−8.9 to 1.8)
Hypophosphatemia	30 (10.3)	35 (11.8)	−1.5 (−6.7 to 3.6)
Hyperkalemia	27 (9.2)	32 (10.8)	−1.5 (−6.5 to 3.4)
Nausea	25 (8.6)	33 (11.1)	−2.5 (−7.5 to 2.3)
Fatigue	18 (6.2)	32 (10.8)	−4.6 (−9.3 to −0.1)
Neutropenia	8 (2.7)	49 (16.5)	−13.8 (−18.7 to −9.3)

Leukopenia 13% vs 37%
Neutropenia 2% vs 16%

4. Infecciones virales en TOS



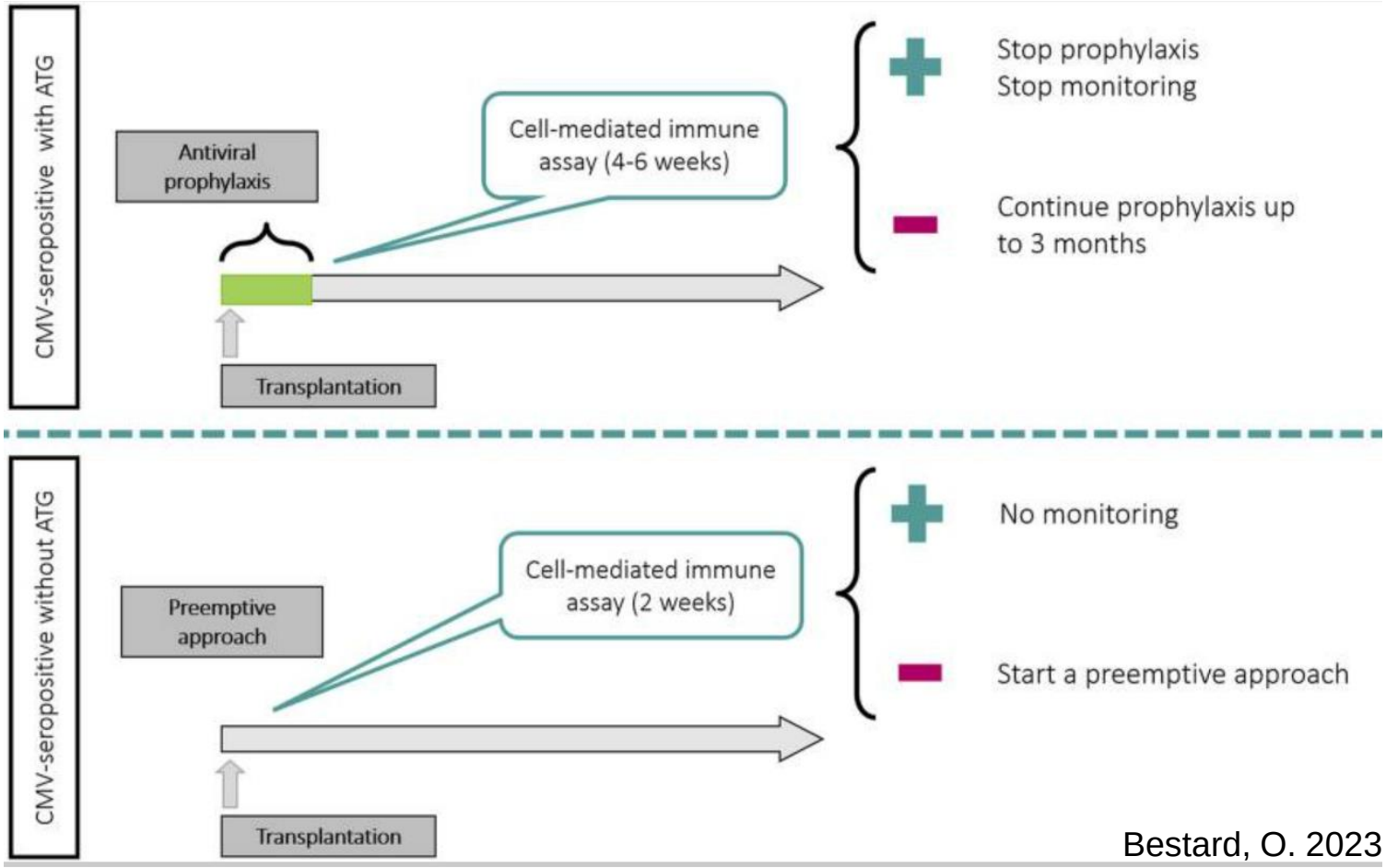
O. Manuel. CMI (2013)

4. Infecciones virales en TOS

Immune monitoring–guided vs fixed duration of antiviral prophylaxis against cytomegalovirus in solid–organ transplant recipients. A Multicenter, Randomized Clinical Trial

O. Manuel. CID (2023)

- Open label – RCT in adult kidney and liver Tx
- 193 randomized (D+/R- and R+ATG)
  - Control group: fixed duration valgancyclovir 3 or 6 months
  - Interventional group: Guided by CMI (monthly – T track - CMV). If positive, they stopped the prophylaxis.
- Primary endopoint: % of patients with clinically significant CMV infection
- Results:
  - Monitoring group 30.9% vs 31% in the control group
  - Reduction of duration of antiviral prophylaxis (MD -26 days, p<0.001)



Bestard, O. 2023

Casos clínicos

Infecciones en trasplante de órgano sólido

Fundació Lluita contra les Infeccions

Pfizer

Jornada intrahospitaria de infecciones en el paciente inmunosuprimido

Caso 1

- 77 años
- Tx renal 25/08/2023 por nefropatía diabética
- Serology CMV +/+ VEB +/+
- Inducción: timoglobulina >> FK, MMF, PDN
- Profilaxis: septrim, VGCV, nistatina
- Excelente evolución renal, retirada catéteres
- Alta 01/08/2023 (Cr 1.3mg/dl)

Caso 1

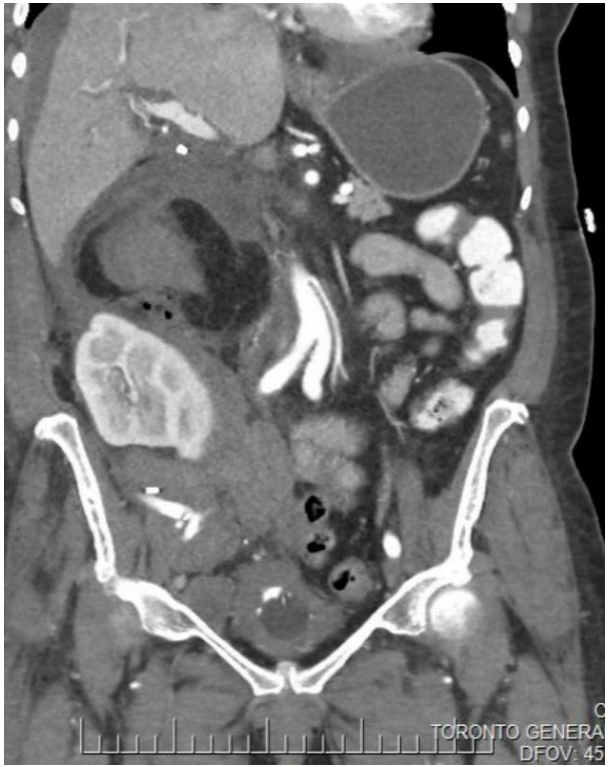
Reingreso el 14 días después por dolor abdominal y caída de Hb hasta 6.1g/dl y empeoramiento de función renal (Cr 2.8mg/dl)

- **¿Qué sospechamos?**
  - **Una dehiscencia de la sutura ureteral**
  - **Una apendicitis aguda**
  - **Un hematoma periinjerto con sangrado activo de la sutura arterial**
  - **Una malaria transmitida por el donante**

Caso 1

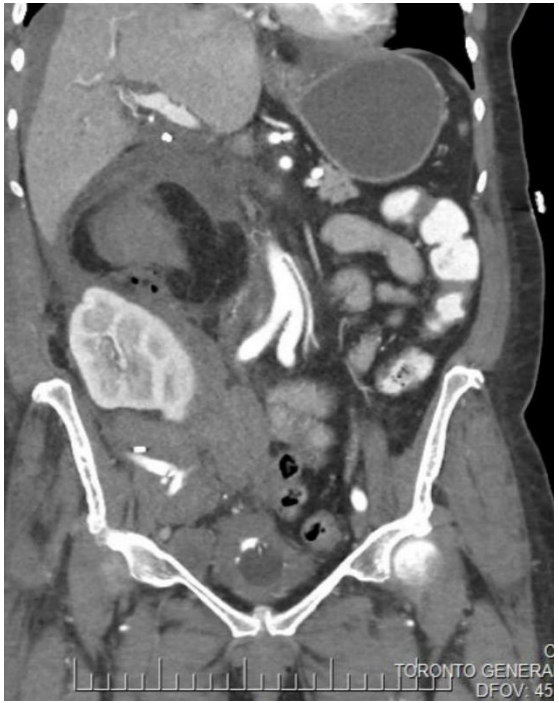
- **Angio- CT** hematoma perirrenal que mide 10,5 x 7,1 cm con gran cantidad de extravasación de contraste en consonancia con sangrado activo de la arteria ilíaca externa.
- **Evacuación qx urgente.**
- **Cultivos aspirado y urocultivo:**

  S. epidermidis



Caso 1

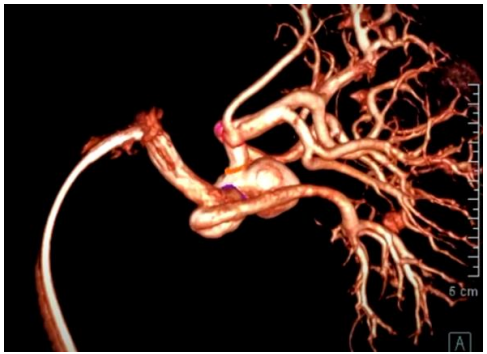
- Cobertura con vancomicina + meropenem ev.
- Después de 48h, la Hb continúa cayendo hasta 6.5g/dl.
- Nuevo angio-TC:



*There is a **focal outpouching noted involving the proximal renal artery of the transplant kidney** at the level of the **anastomosis** with the right external iliac artery (series 16, image 131), measuring up to 10 mm (series 18, image 105), not definitely seen on prior imaging.*
Additional smaller outpouching more proximally measuring up to 7 mm (series 18, image 103) is stable from prior day imaging.

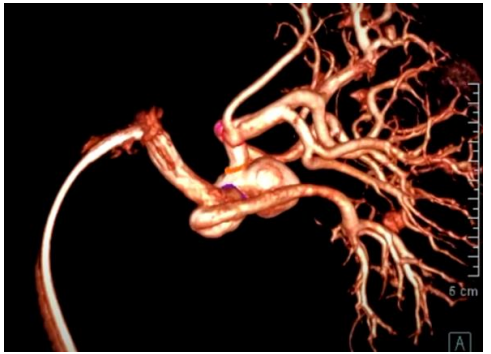
Caso 1

- Re-IQx urgente
- Transplantectomía y reparación vascular de **aneurisma micótico de la arteria renal**.



Caso 1

- **¿Qué microorganismo da más típicamente aneurismas postquirúgicos de la a. renal?**
  - ***S. epidermidis* (si salió en el primer cultivo!)**
  - ***S. Aureus***
  - ***Pseudomonas Aeruginosa***
  - ***Candida Albicans***



Caso 1

Misc Asp/Tis/Bx	**Coagulase negative staphylococcus (not S. lugdunensis) !** Scant growth Gram Stain: 1+ pus cells No bacteria seen.

Misc Asp/Tis/Bx	**Candida albicans !** Heavy growth Gram Stain: Few pus cells Few yeast with pseudohyphae seen.

Aneurisma micótico de la a. renal

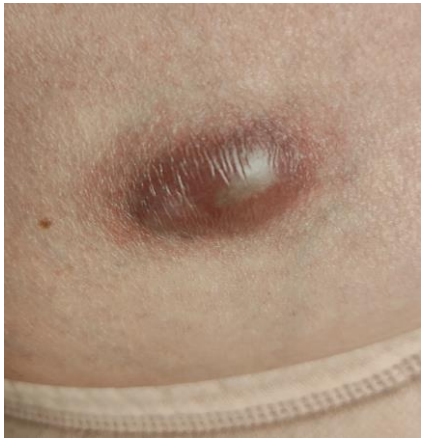
- Complicación rara (<1%) pero potencialmente mortal
- Después de 10 a 15 días después del Tx
- Puede ser anastomótica o intrarrenal. Causado por infecciones > errores técnicos
- Más frecuentes: *S Aureus, Pseudomonas Aeruginosa, Candida*
- La mayoría requiere nefrectomía por adherencias, rechazo, disminución de la función del injerto o infección persistente.
- Tratamiento:
  - Escisión del tejido infectado y la cirugía de reconstrucción arterial.
  - Procedimientos endovasculares: experiencias decepcionantes.
- Tratamiento: atb dirigido/terapia antifúngica durante 4-6 semanas

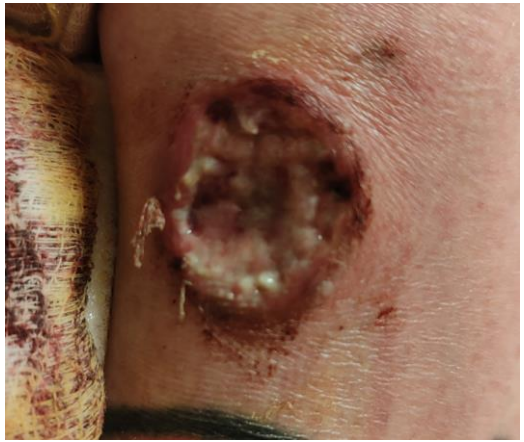
Caso 2

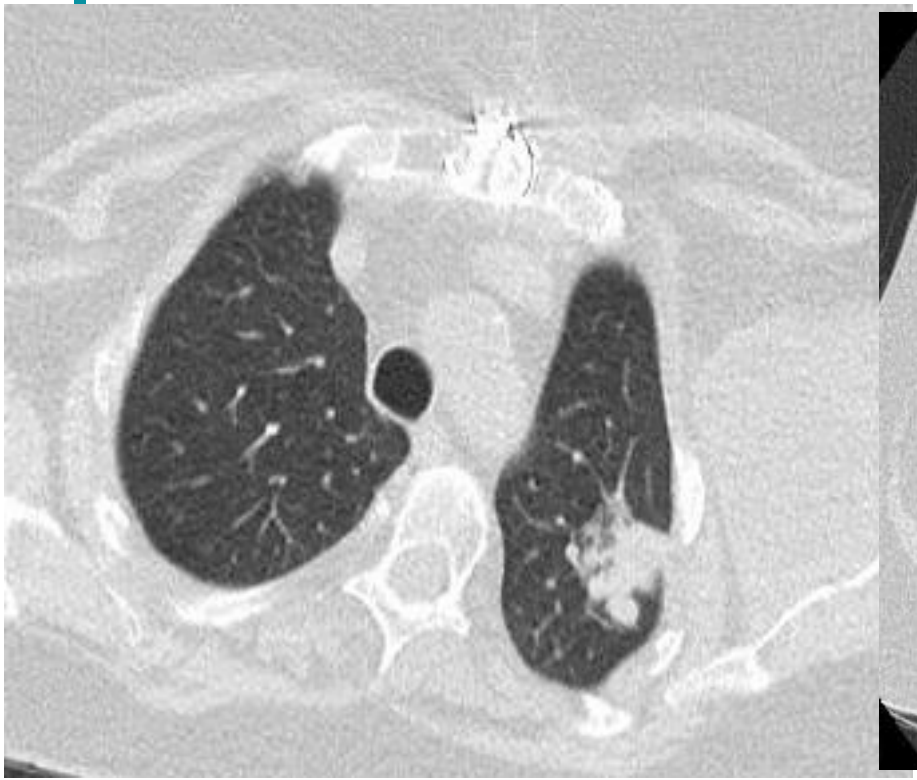
- Mujer de 52 años
- Tx renal en abril 2023 por NAE
- IS: ATG 3mg/kg → MMF 540, Tacrolimus 5 mg, PDN 2.5
- Serologías CMV D+/R+
- Natural de Ontario, Canadá. Vive en una casa con dos gatos y un perro.
- Trabaja de dependienta en Winners.

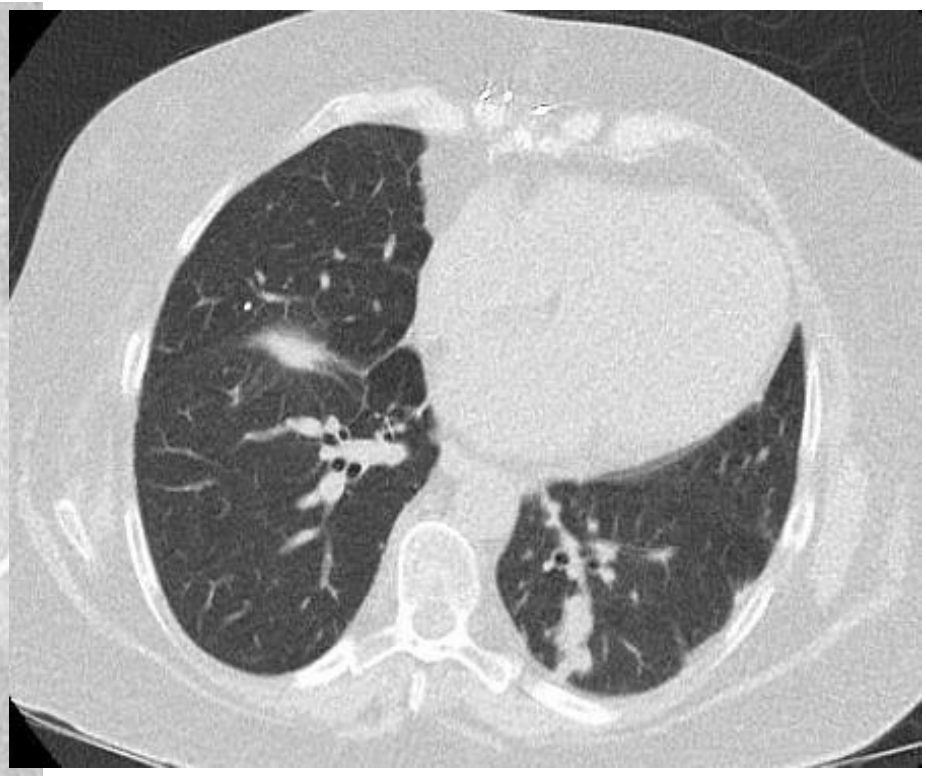
Caso 2

- Lesiones nodulares dolorosas desde hace 2 semanas en tobillo, y abdomen, junto a febrícula de 37.5°C









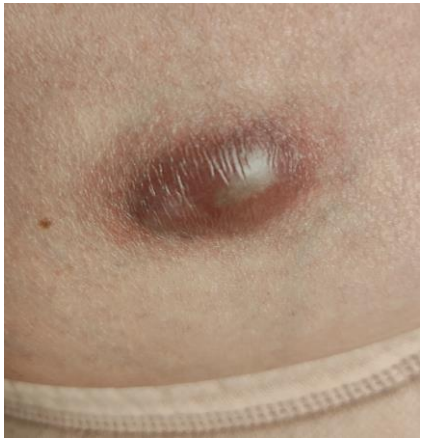
Caso 2

- ¿Qué más pruebas diagnósticas haríais?
  - **Hemocultivos seriados incluyendo bacterias, micobacterias, hongos**
  - **BAL + Biopsia de lesión cutánea, examen directo + cultivo**
  - **Antígeno Galactomannano + BDG**
  - **TC craneal con contraste**

Caso 2

- El TC craneal descartó colecciones intracraneales, tampoco mostró signos de rinosinusitis.

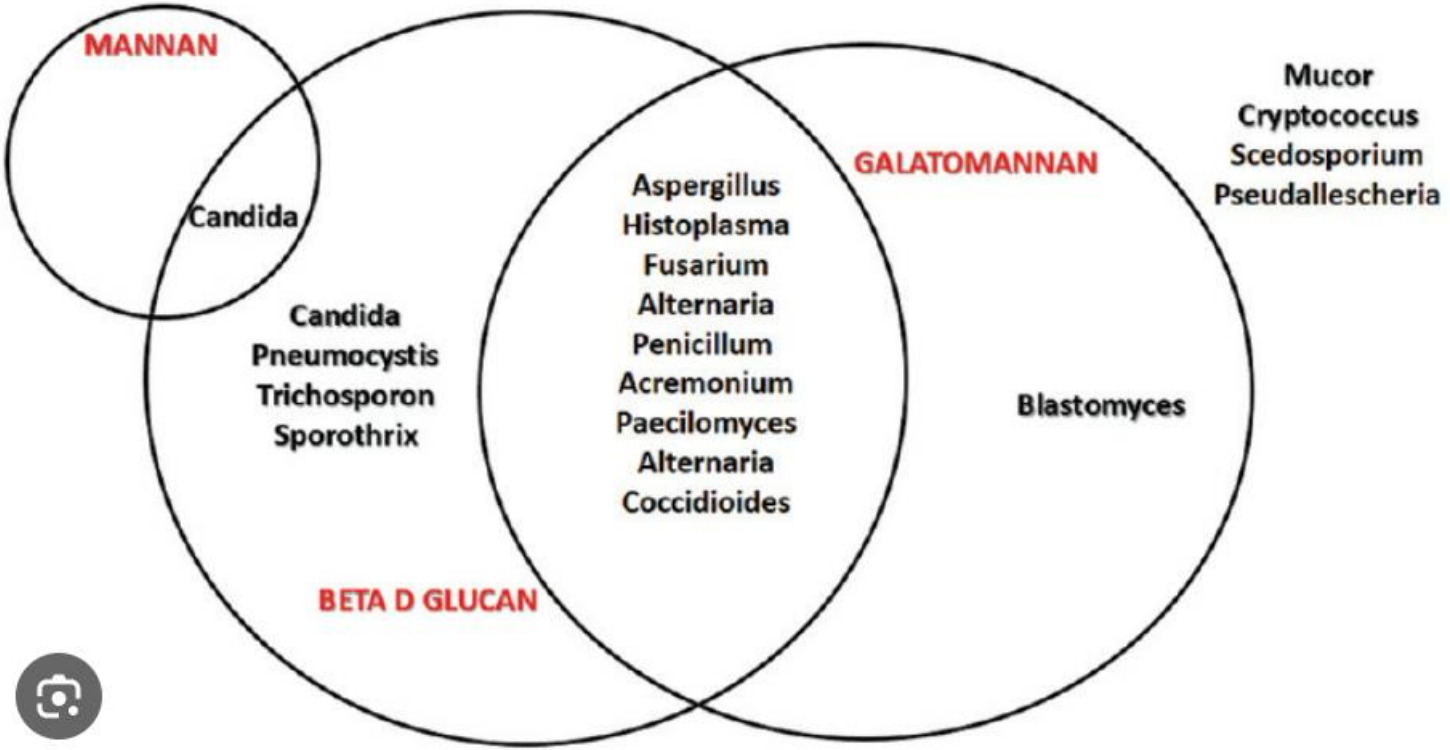
- Galactomanano
  - En suero: negativo (x3)
  - En BAL: negativo
  - Ag de cryptococo: negativo



Caso 2

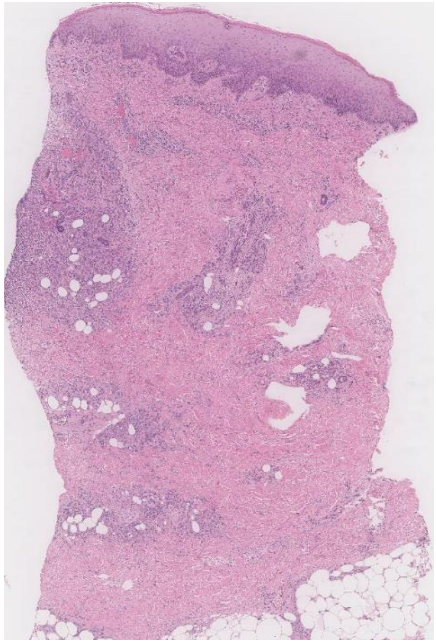
- **¿Cuál sería vuestra primera opción diagnóstica?**
  - **Ectima gangrenoso por Pseudomonas Aeruginosa**
  - **Micobacteria no tuberculosa**
  - **Infección fúngica diseminada**
  - **No tengo ni idea de lo que puede ser… UMI, ayuda!**

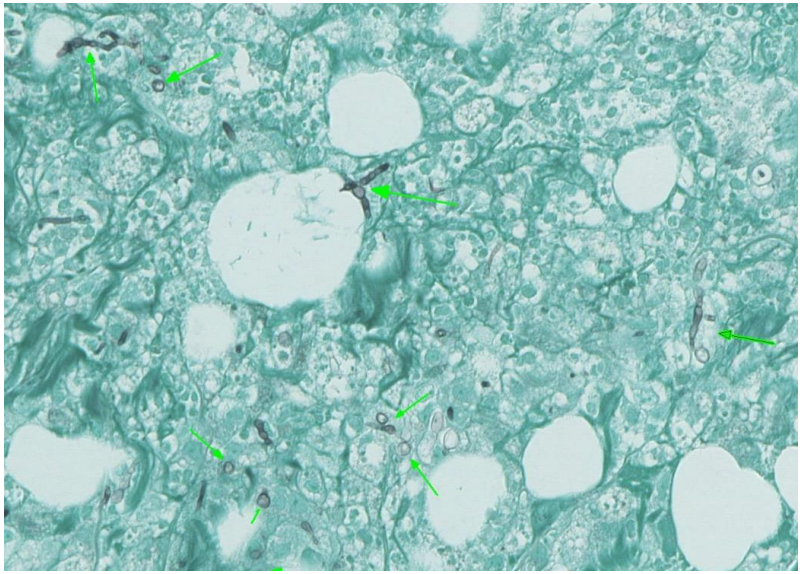
Caso 2

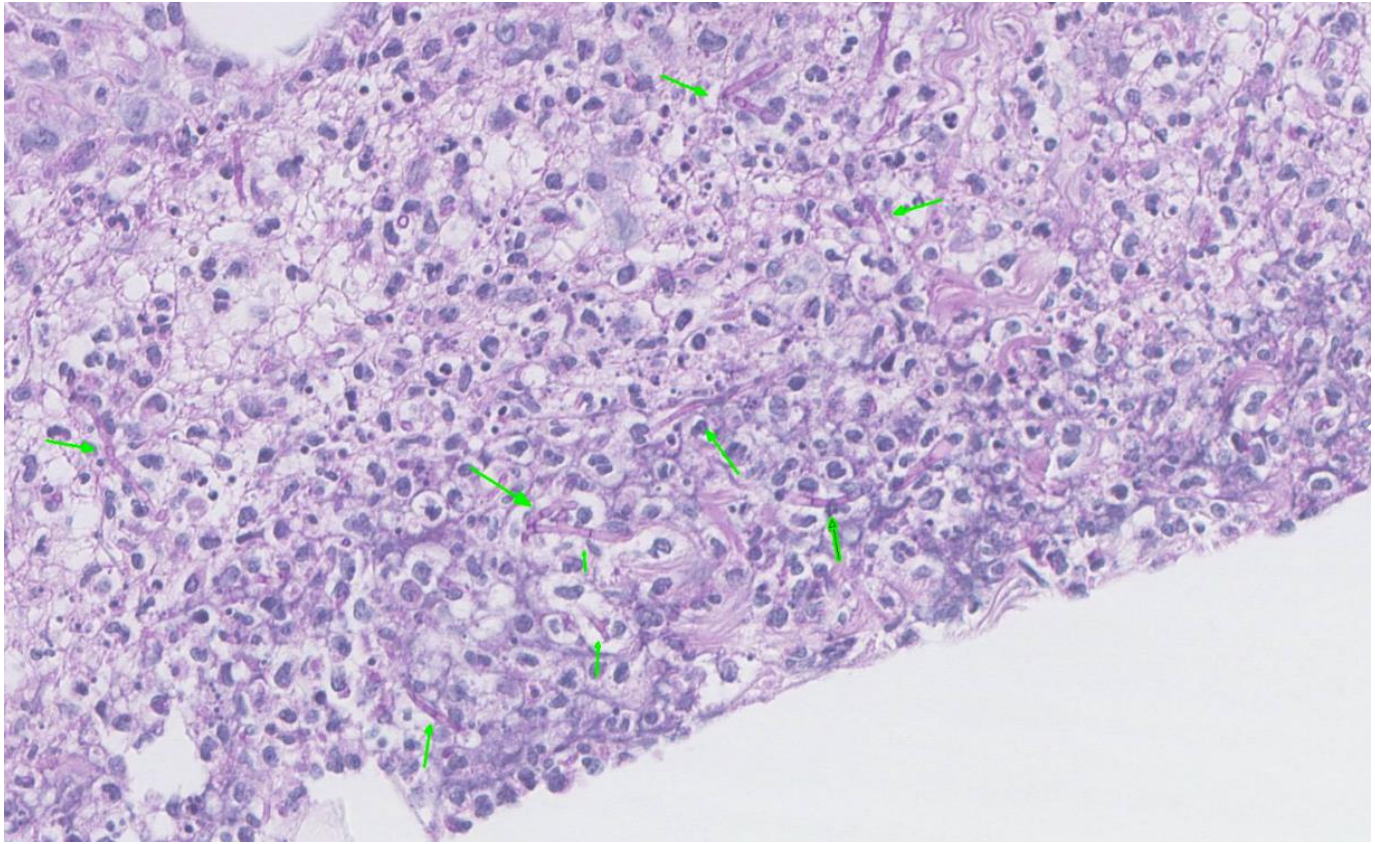

MANNAN
Candida
Candida
Pneumocystis
Trichosporon
Sporothrix
BETA D GLUCAN
Aspergillus
Histoplasma
Fusarium
Alternaria
Penicillum
Acremonium
Paecilomyces
Alternaria
Coccidioides
GALATOMANNAN
Blastomyces
Mucor
Cryptococcus
Scedosporium
Pseudallescheria

Caso 2

- Tinción de BAL, biopsia: formas fúngicas – **hifas septadas**

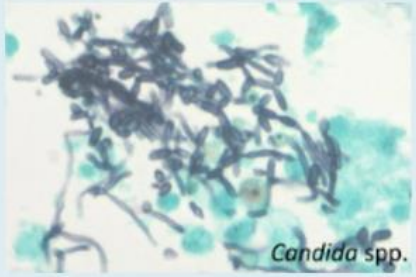






Guarner, 2011

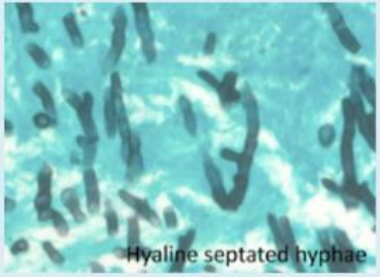
Morphology & descriptions of fungal infections with hyphae or pseudohyphae in tissues



Dx: **Yeasts with pseudohyphae**

Description: Small yeasts (3-5 microns in size) intermingled with pseudohyphae and hyphae

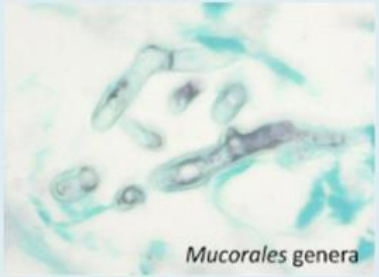
Consistent with ***Candida* spp**, however *Aspergillus* spp. and other hyaline fungi can be confused histologically



Dx: **Non-pigmented (hyaline), septated hyphae**

Description: acute angle branching

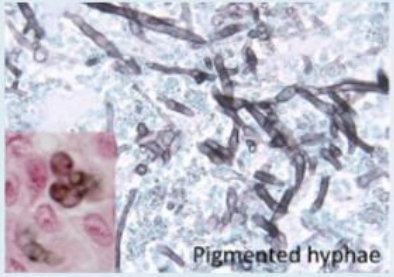
Consistent with ***Aspergillus* spp.**, *Fusarium* spp., *Scedosporium* spp., *Trichoderma* spp., *Paecilomyces* spp. and others.
Mucorales genera can sometimes have this morphology



Dx: **Non-pigmented (hyaline), pauciseptate hyphae**

Description: pauciseptate ribbon-like hyphae with right angle branching

Consistent with ***Mucorales* genera**; however Aspergillus spp. and other septated hyaline hyphae can sometimes have this morphology



Dx: **Pigmented yeasts and hyphae with septations**

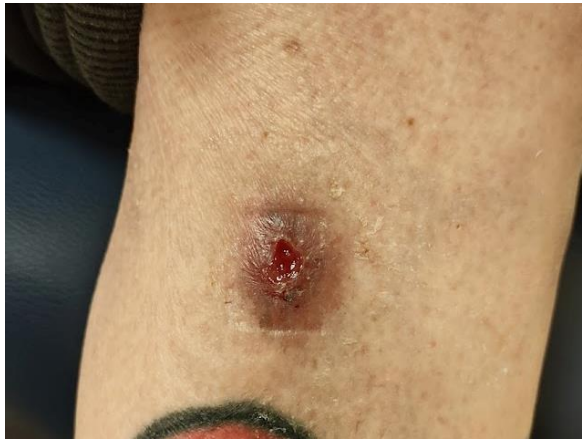
Description: pigmented irregular hyphae and yeast-like structures both with septations

Consistent with **dematiaceous fungi** including: *Madurella* spp, *Fonsecaea* spp, *Cladophialophora* spp, *Exophiala* spp, *Curvularia* spp, *Bipolaris* spp, and others

Caso 2

- Diagnóstico: **Scedosporidiasis diseminada**

- **Tratamiento:**
  - Voriconazol 200mg q 12h
    - Niveles de tacrólimus 32-24ng/ml, náuseas, vómitos
  - Isavuconazol 200mg cada 24h vo
  - 3 meses



Scedosporidiasis diseminada

- También llamado *Lomentospora*
- *S. apiosperpum, S. prolificans*
- Aumento incidencia en pacientes IS junto a Fusarium (primera causa IFI no-aspergillus) y Mucorales (10-19% en SOT).
- Hábitat:
  - Suelo, agua estancada, estiércol
  - Contaminación de heridas
  - Hospedadores: felino, equino. NO se transmite de persona a persona ni de animales a hombre.
- MDR/ Resistencia alta a antifúngicos

Tabla 1
Manifestaciones clínicas de las principales especies del género *Scedosporium*

	S. apiospermum	*S. prolificans*
Colonización	Oído externo Traqueobronquial (fibrosis quística) Bola fúngica pulmonar o paranasal Heridas	
Infección local	Micetoma Piel y partes blandas Artritis y osteomielitis Queratitis	Artritis y osteomielitis Queratitis Herida quirúrgica Onicomicosis
Infección profunda	Sinusitis Neumonía Meningitis y abscesos SNC Endoftalmitis Diseminación multiórgánica	Endoftalmitis Endocarditis (válvula nativa o protésica) Neumonía Diseminación multiórgánica, especialmente al SNC

Pemán, Salavert 2014

- Aislado típicamente en vía respiratoria → Trasplantados pulmonares y con fibrosis quística.
- Típico en síndrome de **asfixia por inmersión** (neumonía o absceso cerebral) o en **traumatismos penetrantes** en aguas contaminadas.
- Tratamiento medico-quirúrgico combinado durante 3-6 meses
  - Azoles/terbinafina
  - Azoles/micafungina.
  - Anfotericina B / micafungina

Muchas gracias

- ¿Preguntas?