# POSTER

n. P3398

33rd ECCMID Copenhagen, Denmark 15–18 April 2023

## First case of Candida glabrata prosthetic knee infection treated with rezafungin: case report

*Authors: Matteo Chiurlo[1,3], Giacomo Placella[2,3], Flavia Badalucco Ciotta[1,3], Giovanni Mori[1,3], Marco Ripa[1,3], Chiara Tassan Din[1], Raffaele Dell'Acqua[1], Paolo Scarpellini[1], Vincenzo Salini[2,3], Antonella Castagna[1,3], Chiara Oltolini[1]*

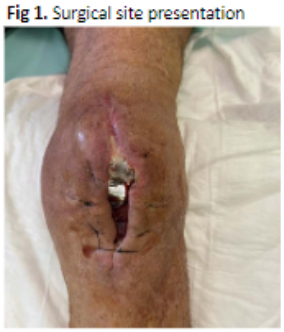
*1) IRCCS San Raffaele Scientific Institute, Milan (Italy), Department of Infectious Diseases*
*2) IRCCS San Raffaele Scientific Institute, Milan (Italy), Department of Orthopedics and Traumatology*
*3) San Raffaele Vita-Salute University, Milan (Italy)*

### Background

Prosthetic joint infections (PJIs) are insidious complications of joint arthroplasties.

Fungal PJIs represents ≤1% of cases with non-albicans Candida species being extremely rare.

**Fig 1.** Surgical site presentation



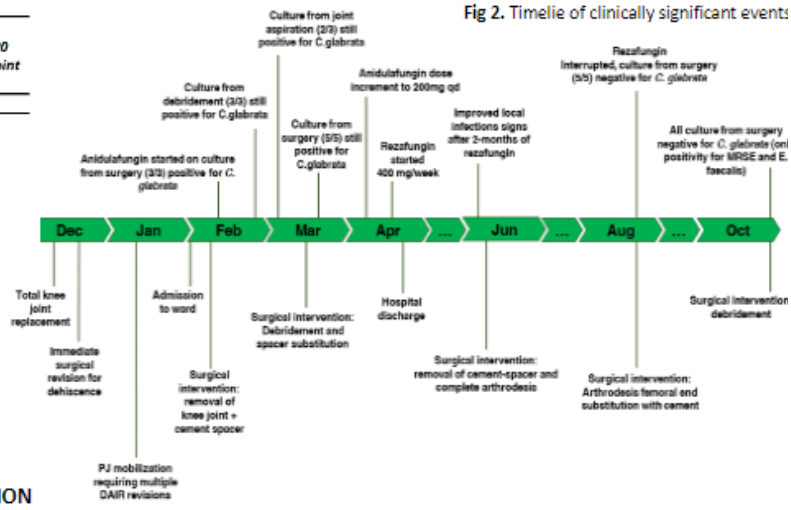
### Case Description

- 75-year-old male presented to our clinic with wound dehiscence and left knee prosthesis exposure (Figure 1)
- Previous (2 month) bilateral total knee joint replacement (requiring early revision and complicated by left patellar tendon detachment and wound dehiscence.
- The patient underwent prosthesis removal, cement spacer insertion and external fixation 45 days after the first surgery.
- Intra-operative cultures turned out positive for ***C. glabrata*** (Table 1) . **Anidulafungin 100 mg daily** was introduced.
- Surgical revisions were performed every two weeks to promote wound healing with intra-operative cultures **persistently positive** for ***C. glabrata.***
- The antibiotic-impregnated spacer was replaced with a **caspofungin-impregnated** device five weeks after starting antifungal treatment and **anidulafungin** was increased to **200 mg daily** due to persistently positive cultures, antibiotics were discontinued.
- Two-months after starting anidulafungin, consolidation therapy with **rezafungin 400 mg weekly** was started.
- After 2-months (local improvement of infection signs) the patient underwent spacer removal and arthrodesis.
- ***C. glabrata*** was **no longer isolated** from cultures
- **No side-effects** were documented, patient displayed good recovery up to 2-months after last surgery.
- Later arthrodesis mobilization was diagnosed, requiring surgical revision with documented infectious aetiology with positive samples for *Staphylococcus epidermidis* and *Enterococcus faecalis.*
- After 6-months of echinocandin treatment (anidulafungin 2-months, rezafungin 4-months), antifungal therapy was stopped, *C. glabrata* has no longer been recovered

| | ***Isolate 1*** *prosthesis removal surgery* | ***Isolate 2*** *intermediate surgical revisions* | ***Isolate 3*** *cement-spacer substitution* | ***Eucast 2020 MIC Breakpoint*** |
|---|---|---|---|---|
| | MIC [µg/mL] | MIC [µg/mL] | MIC [µg/mL] | R > |
| Amphotericin B | 2 | 2 | 2 | 1 |
| Anidulafungin | 0.03 | 0.03 | 0.06 | 0.06 |
| Caspofungin | 0.06 | 0.12 | 0.06 | Note[3] |
| Micafungin | 0.015 | 0.015 | 0.03 | 0.03 |
| Fluconazole | 16 | 16 | 32 | 16 |
| Isavuconazole | - | - | 2 | IE |
| Posaconazole | 1 | 2 | 2 | IE[2] |
| Voriconazole | 1 | 0.5 | 1 | IE |
| Itraconazole | 1 | 1 | 4 | IE[2] |

**Table 1.** Susceptibility testing of isolates

**Fig 2.** Timelie of clinically significant events




### Discussion

Non-albicans Candida PJIs management is challenging, requiring prolonged antifungal treatment.

Rezafungin represents an appealing option for long-term intravenous therapy in device-associated infections.

Favourite safety profile and retained activity against bio-films and stationary-phase fungi.

# ABSTRACT

**P3398**

## First case of *Candida glabrata* prosthetic knee infection treated with rezafungin: case report

13. Case reports and case series (n<10)
13c. Fungal infections

M. Chiurlo [1, 2], G. Placella [3, 2], F. Badalucco Ciotta [1, 2], G. Mori [1, 2], M. Ripa [1, 2], C. Tassan Din [1], R. Dell'acqua [1], P. Scarpellini [1], V. Salini [3, 2], A. Castagna [1, 2], C. Oltolini [1].
*[1]IRCCS San Raffaele Scientific Institute, Milan (Italy), Department of Infectious Diseases - Milan (Italy), [2]San Raffaele Vita-Salute University, Milan (Italy) - Milan (Italy), [3]IRCCS San Raffaele Scientific Institute, Milan (Italy), Department of Orthopedics and Traumatology - Milan (Italy)*

### Background

Prosthetic joint infections (PJIs) are insidious complications of joint arthroplasties. Fungal PJIs account for ≤1% of cases with non-*albicans Candida* species being extremely rare.

### Case(s) description

A 75-year-old male underwent bilateral total knee joint replacement, requiring early revision of right knee prosthesis because of its misplacement, further complicated by patellar tendon detachment and wound dehiscence requiring debridement with implant retention and antibiotics (Figure 1 shows surgical site at presentation). The wound healing process was again unsatisfactory with prosthesis exposure. The patient underwent prosthesis removal, cement spacer insertion and external fixation 45 days after the first surgery. Intra-operative cultures turned out positive for *C. glabrata* (Table 1 reports antifungals susceptibility test) and anidulafungin 100 mg daily was introduced. Surgical revisions were performed every two weeks to promote wound healing with intra-operative cultures persistently positive for *C. glabrata.* The antibiotic-impregnated spacer was replaced with a caspofungin-impregnated device five weeks after starting antifungal treatment and anidulafungin was increased to 200 mg daily due to persistently positive cultures, discontinuing antibiotics. Two-months after starting anidulafungin, consolidation therapy with rezafungin 400 mg weekly was instituted and after 2-months, following local improvement of infection signs, the patient underwent spacer removal and arthrodesis with a prosthetic component to favour the possibility of a more physiological gait. *C. glabrata* was no longer isolated. No side-effects were documented and the patient displayed a good recovery up to 2-months after the last surgery, when an arthrodesis mobilization was diagnosed; surgical revision documented an infectious aetiology with positive samples for *Staphylococcus epidermidis*. Therefore, after 6-months of echinocandin treatment (anidulafungin 2-months, rezafungin 4-months), antifungal therapy was stopped and suppressive antibacterial therapy was instated due to PJI not amenable to surgical explant (Figure 2 shows timeline of significant events). Currently, 2-months after rezafungin discontinuation, *C. glabrata* has no longer been recovered from intra-operative cultures, which remain positive for *S. epidermidis* and *Enterococcus faecalis.*

## Discussion

Non-*albicans Candida* PJIs management is challenging, especially due to the necessity of prolonged antifungal treatment. Rezafungin represents an appealing option for long-term intravenous therapy in device-associated infections, thanks to its favourite safety profile and retained activity against bio-films and stationary-phase fungi.

Surgical site presentation at admission

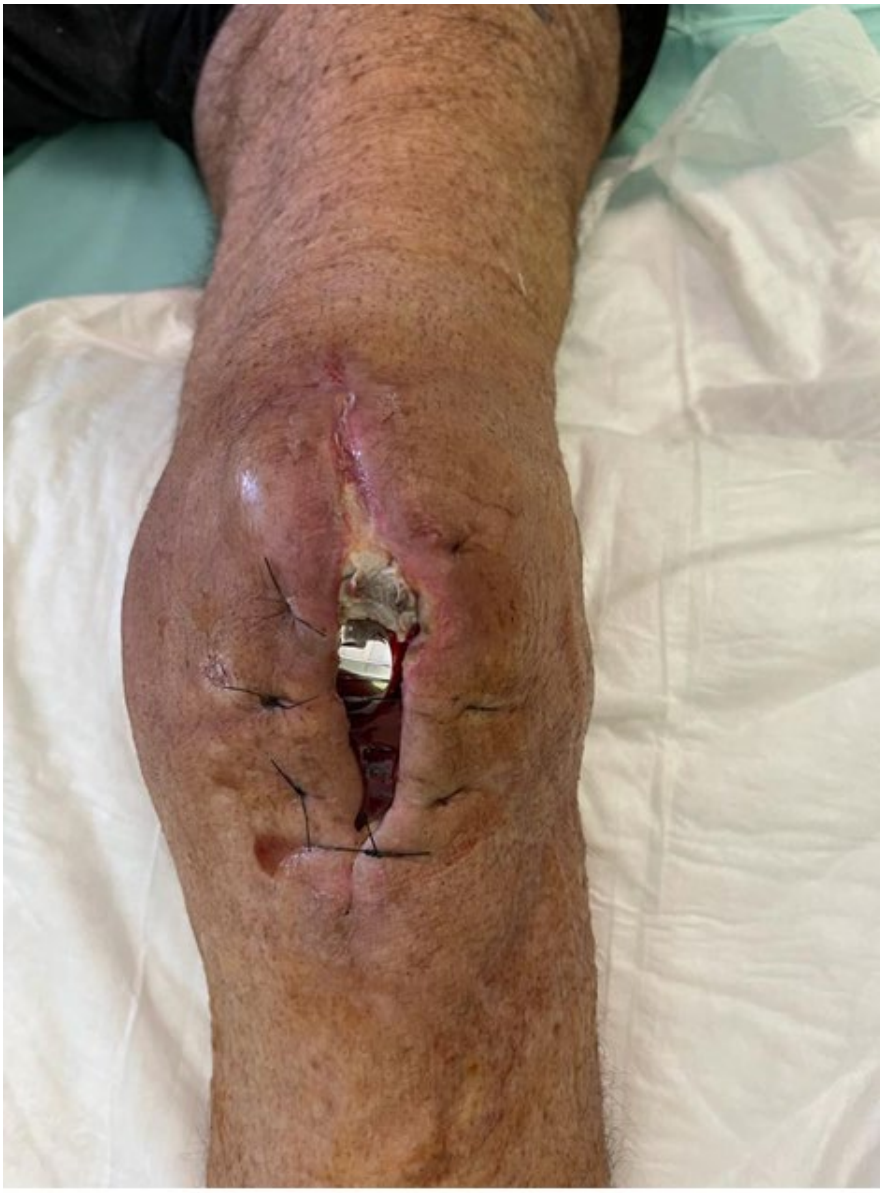


**Figure 1.** Surgical site presentation at admission before explant: exposition of prosthesis femoral component and patellar tendon detachment.

Antifungal susceptibility testing of isolates

| | ***Isolate 1*** *prosthesis removal surgery* | ***Isolate 2*** *intermediate surgical revisions* | ***Isolate 3*** *cement-spacer substitution* | ***Eucast 2020 MIC Breakpoint*** |
|---|---|---|---|---|
| | **MIC [µg/mL]** | **MIC [µg/mL]** | **MIC [µg/mL]** | **R >** |
| Amphotericin B | 2 | 2 | 2 | 1 |
| Anidulafungin | 0.03 | 0.03 | 0.06 | 0.06 |
| Caspofungin | 0.06 | 0.12 | 0.06 | Note[3] |
| Micafungin | 0.015 | 0.015 | 0.03 | 0.03 |
| Fluconazole | 16 | 16 | 32 | 16 |
| Isavuconazole | - | - | 2 | IE |
| Posaconazole | 1 | 2 | 2 | IE[2] |
| Voriconazole | 1 | 0.5 | 1 | IE |
| Itraconazole | 1 | 1 | 4 | IE[2] |

**Table 1.** Antifungal susceptibility testing of *C. glabrata* isolates and MIC breakpoints according to EUCAST 2020 data.
IE= insufficient evidence; [2] The ECOFFs for these species are in general higher than for C. albicans; [3] Isolates that are susceptible to anidulafungin as well as micafungin should be considered susceptible to caspofungin, until caspofungin breakpoints have been established.

Timeline of clinically significant events

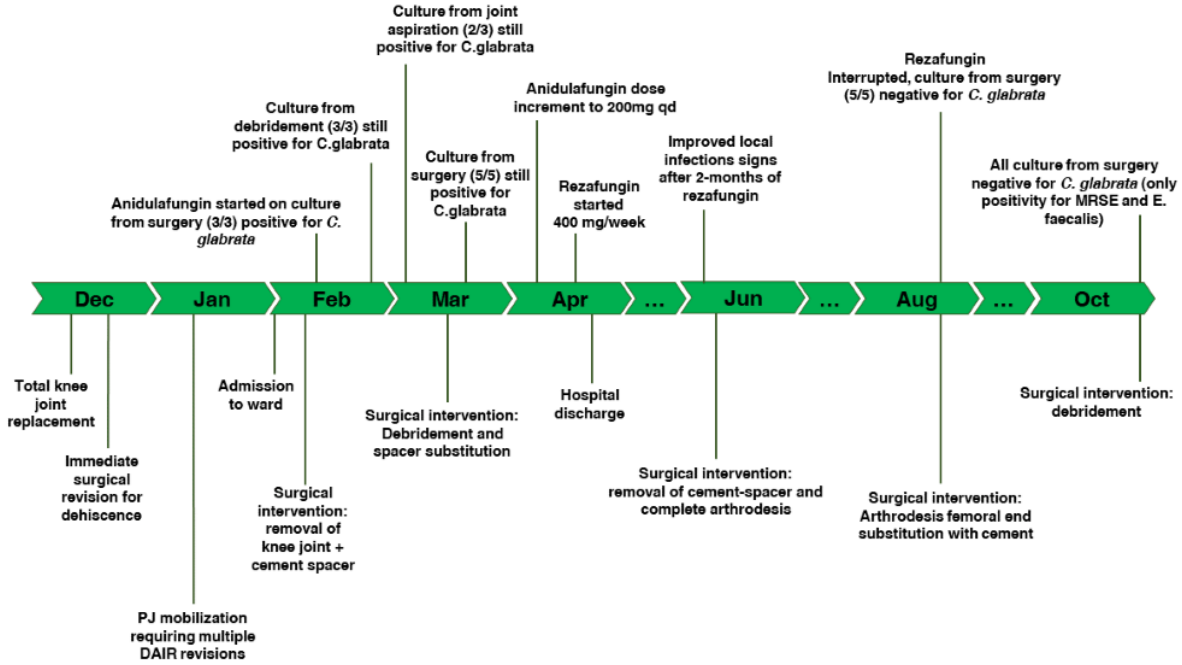



**Figure 2.** Timeline of clinically significant events: surgeries, microbiological isolates and antifungal therapies

**O1225**

# Successful treatment of *Candida* endocarditis with rezafungin: a case series

13. Case reports and case series (n<10)
13c. Fungal infections

F. Trapani [1], R. Pascale [2, 1], A. Amedeo [1], G. Beci [1], G. Menotti [1], D. Riccucci [1], S. Tedeschi [1, 2], M. Bartoletti [3, 4], M. Gatti [2, 5], M. Giannella [2, 1], P. Viale [2, 1].
*[1]Infectious Diseases Unit, Department of Integrated Management of Infectious Risk, IRCCS Azienda Ospedaliero-Universitaria di Bologna - Bologna (Italy), [2]Department of Medical and Surgical Sciences, University of Bologna - Bologna (Italy), [3]Department of biomedical sciences, Humanitas University - Milan (Italy), [4]Infectious Disease Unit, IRCCS Humanitas Research Hospital - Milan (Italy), [5]Clinical Pharmacology Unit, Department of Integrated Management of Infectious Risk, IRCCS Azienda Ospedaliero-Universitaria di Bologna - Bologna (Italy)*

## Background

Endocarditis is a rare but frightened type of Candida spp intravascular infections, especially when it occurs in patients with prosthetic valve. A combined antifungal administration and surgical valve replacement is the recommended approach by Guidelines to treat Candida endocarditis. If high perioperative risk contraindicates surgery, a suppressive antifungal treatment could be needed. The novel echinocandin rezafungin, with an extended half-life and a weekly administration, is a promising treatment option for long term antifungal treatment.

## Case(s) description

The Case 1 is a 48-year-old man affected by Marfan syndrome with multiple aortic prosthesis and aortic valved tube. He was admitted in February 2021 for abdominal pain and fever. A diagnosis of valved tube and aortic prosthesis infection by Candida albicans was made. Surgery was not performed due to the noteworthy extension of the infection. After several weeks of caspofungin treatment, a switch to azole therapy was tried. Azoles treatment was discontinued due to intolerance by the patient (arthralgia, nausea), new embolic events and high levels of beta D glucan (BDG). In March 2022, rezafungin was started and it is ongoing at time of the writing. Rezafungin is well tolerated without any adverse event reported. Also, we observed no further embolic events and a significant drop of BDG levels.

The Case 2 is a 64 year-old man admitted in July 2021 for severe COVID. During ICU stay he developed a Candida parapsilosis bloodstream infection, treated with Liposomal-Amphotericin-B due to a concomitant diagnosis of pulmonary Aspergillosis. Two months later there was a relapse of Candida parapsilosis candidemia. Ecocardiography revelead infective endocarditis of native mitral valve. Surgery was excluded due to the compromised conditions of patient. Caspofungin was administered and then azoles. Azoles treatment was discontinued soon due to gastrointestinal symptoms onset. In March 2022, rezafungin was started and continued for 8 - months with an optimal safety profile and resolution of infection.

## Discussion

We presented the first two patients treated in Europe with rezafungin for Candida endocarditis within a compassionate program. We observed a good clinical and microbiological outcome without safety concerns.

**O1224**

# Succesful rezafungin treatment for an azole-resistant chronic mucocutaneous candidiasis in a STAT1 gain-of-function patient

13. Case reports and case series (n<10)
13c. Fungal infections

C. Melenotte [1], R. Ratiney [2], O. Hermine [3], E. Bougnoux [4], F. Lanternier [1].
*[1]Infectious Diseases and Tropical Medicine, Hôpital Necker-Enfants Malades - Paris (France), [2]Phamacy, Hôpital Necker-Enfants Malades - Paris (France), [3]Hematology and Immunology, Hôpital Necker-Enfants Malades - Paris (France), [4]Mycology and Parasitology, Hôpital Necker-Enfants Malades - Paris (France)*

## Background

STAT1 GOF (gain of function) is the most common genetic cause of inherited chronic mucocutaneous candidiasis (CMC) and is challenging physicians since prolonged antifungal exposure may favor the emergence of *C. albicans* resistant strains (1,2). We report here the first experience of rezafugin in one STAT1-GoF patient with CMC resistant to azoles.

## Case(s) description

A 19-year-old man with STAT1-GoF immunodeficiency (heterozygote mutation E353 mutation MR391311) diagnosed at age 11 years presented to the hospital with persistent CMC evolving since early childhood (one year-old). He was treated alternately with itraconazole, fluconazole and griseofulvin for documented *Candida albicans* CMC. At the age of 13, he presented an azole-resistant *C. albicans* skin and mucosal infection involving his right cheek, right arm and right hand. The *C. albicans* isolated strain presented resistance to voriconazole (CMI : 1,5 mg/L), fluconazole (CMI: 256 mg/L) and isavuconazole, (CMI : 32 mg/L), and was sensitive to caspofungine (CMI : 0,023 mg/L), micafungine (CMI : 0,023 mg/L), amphotericine B (CMI : 0,25 mg/L) and flucytocine (CMI : 0,094 mg/L). He was treated daily with intravenous caspofungin in addition to oral terbinafine during 6 weeks followed by voriconazole as maintenance therapy for 5 months, with favorable clinical outcome. In December 2021, he relapsed with erythematous and pruritic inflammatory lesion of the suprapubic and pubic subumbilical region extended to the prepuce with balanoposthitis treated with itraconazole and terbinafine (Figure 1). To avoid daily intraveinous treatment with caspofungin or micafungin, rezafungin was initiated in September 2022 with a loading dose of 400 mg followed by 200 mg per week for 5 weeks (*i.e.* 5 doses). Clinical outcome was favorable without any adverse event. We decided not to introduce antifungal prophylaxis to avoid development of echinocandin resistant *Candida* strain.

## Discussion

Rezafungin, a novel echinocandin with a prolonged half-life and high activity against *Candida* has the advantage of being administered intravenously once a week (3). Rezafungin was efficient in a STAT1-GoF patients with CMC due to azole-resistant strains of *C. albicans*, which could improve quality of life of this patient avoiding every day intravenous treatment.

Mucocutaneous candidiasis treated with rezafungin