CITY ST GEORGE'S UNIVERSITY OF LONDON

NHS St George's Healthcare NHS Trust

Use of the novel antifungal rezafungin in outpatient parental antibiotic therapy:

1-year experience from St George's

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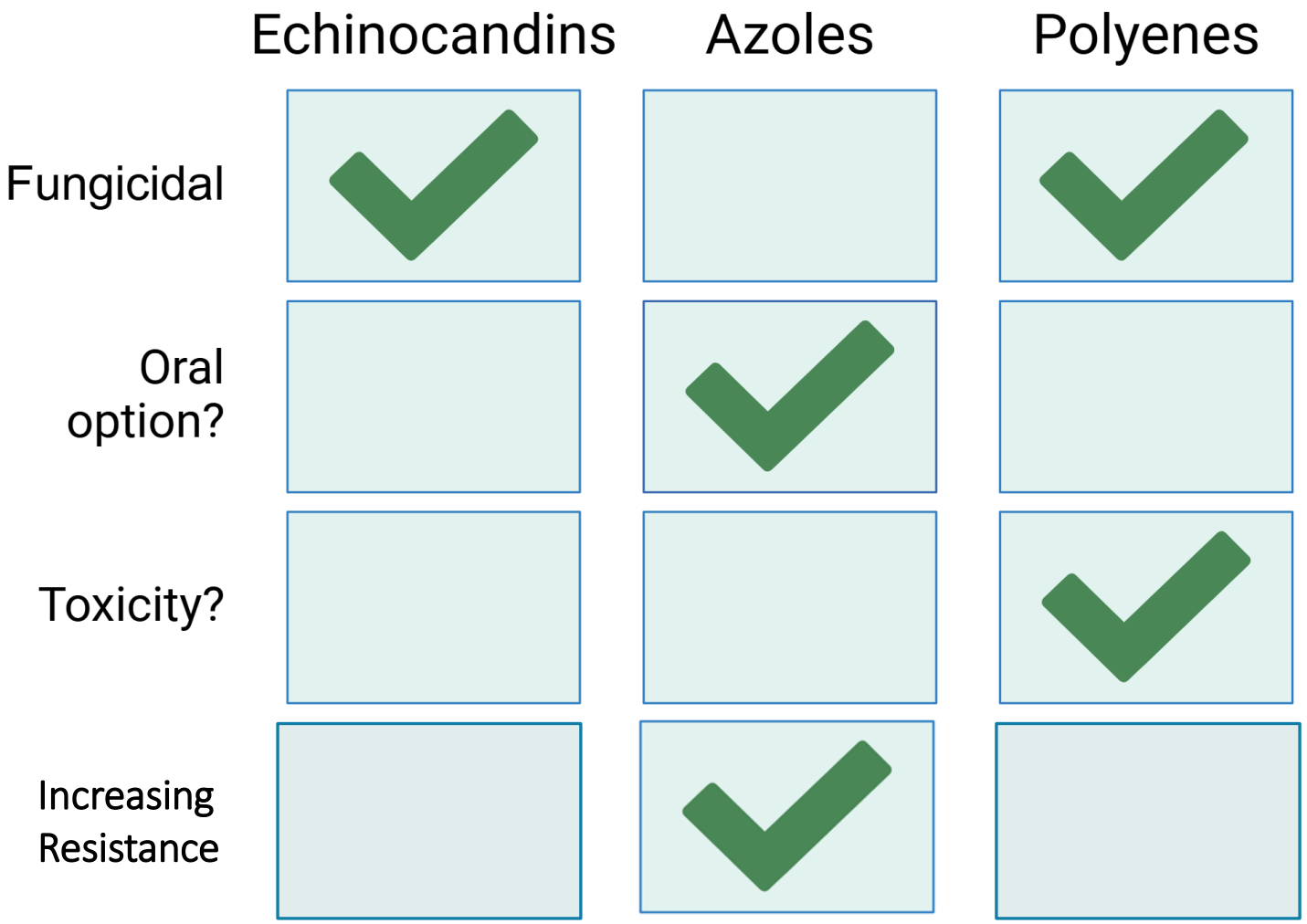
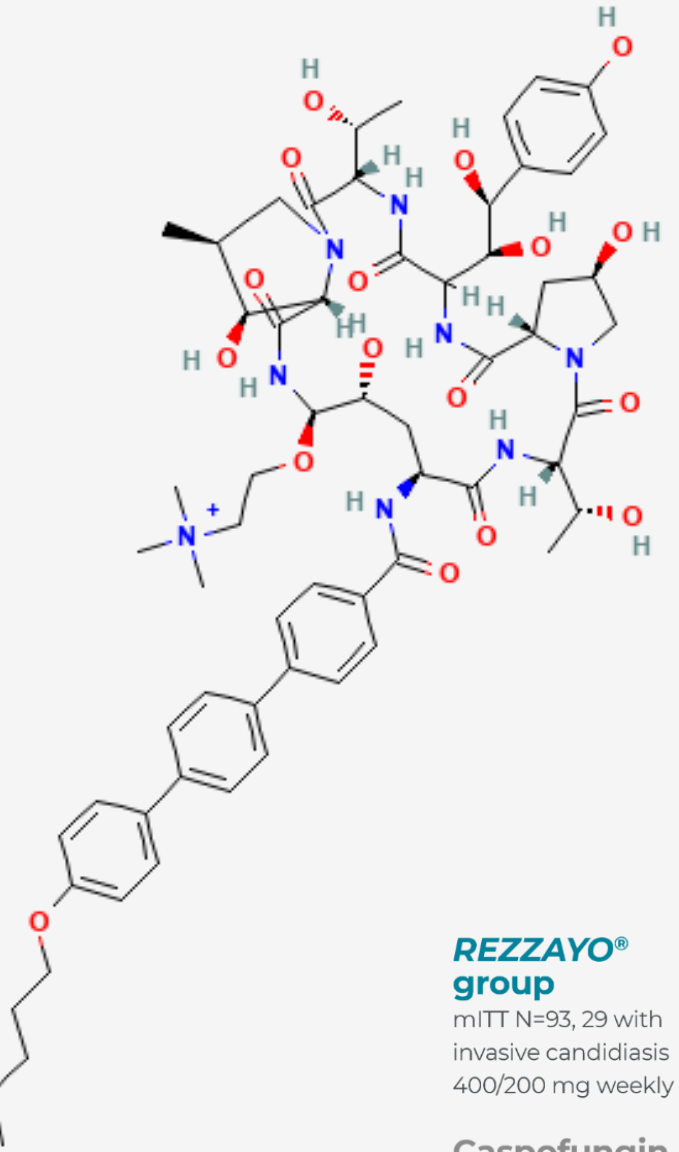
Antifungal therapy





Rezafungin

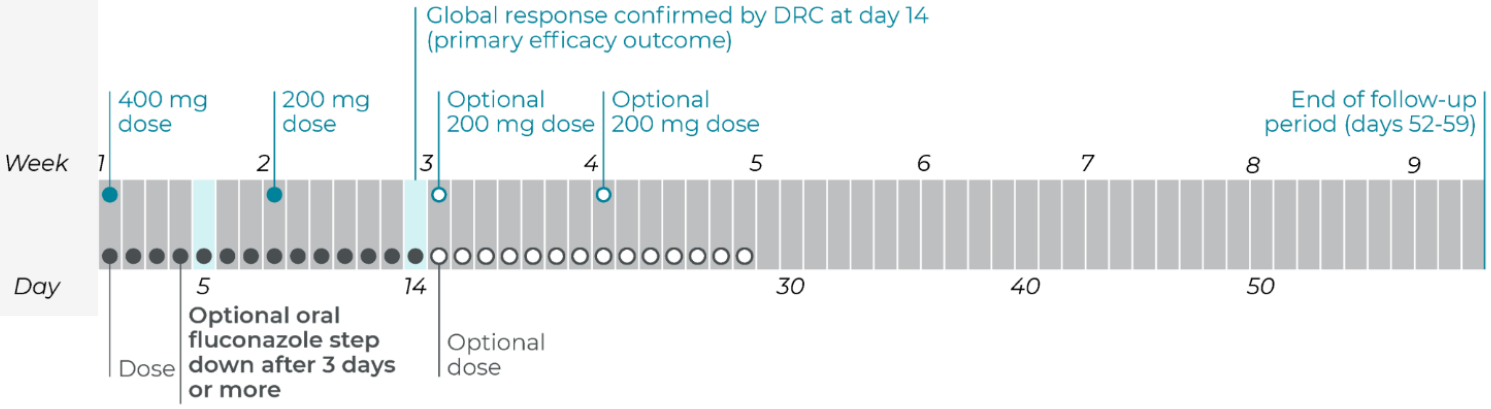
Next-generation long-acting echinocandin

Structural configuration: extended-interval dosing (weekly) based on PK profile

Based on non-inferiority (+ safety) cf caspo in phase II and III trials (ReSTORE)- Licensed in UK for treatment of **invasive candidiasis** in January 2024

REZZAYO® group
mITT N=93, 29 with invasive candidiasis
400/200 mg weekly

Caspofungin group
mITT N=94, 27 with invasive candidiasis
70/50 mg daily*



*Dose may be adjusted for hepatic impaired and obese patients.

Why rezafungin?

Echinocandins: first line therapy for invasive candida infections, stepdown to azoles- to which resistance is increasing (*C glabrata, C parapsilosis, C auris*)

in vitro/ in vivo activity against common *Candida spp,* including *Candida auris;* broad tissue penetration (except brain)

Weekly administration facilitating earlier discharge/ admission avoidance

Low toxicity, no drug-drug interactions; no dose adjustment for elderly, hepatic or renal impairment or weight extremities

Pappas et al. 2018. Nat. Rev. Dis. Prim., Vol 4
Winkler et al. 2024. Mycoses, Vol 67 (11)

Safety Profile from RESTORE trial

Most frequently reported adverse reactions:

- Pyrexia
- Diarrhoea
- Hypokalaemia

Common reactions

- Hypotension
- Wheezing
- Nausea, abdominal pain, constipation
- ↓ Hb
- Electrolyte disturbances
- Increased liver enzymes
- Skin reactions

Uncommon

- Phototoxicity

Implementation Process

New Drug Application submitted to Formulary Committee in May 2024

Cost-effectiveness highlighted

14 day caspofungin course on OPAT via elastomeric devices = £8599 – 9964

14 day rezafungin course (3 vials over 2 clinic appointments) = £2178

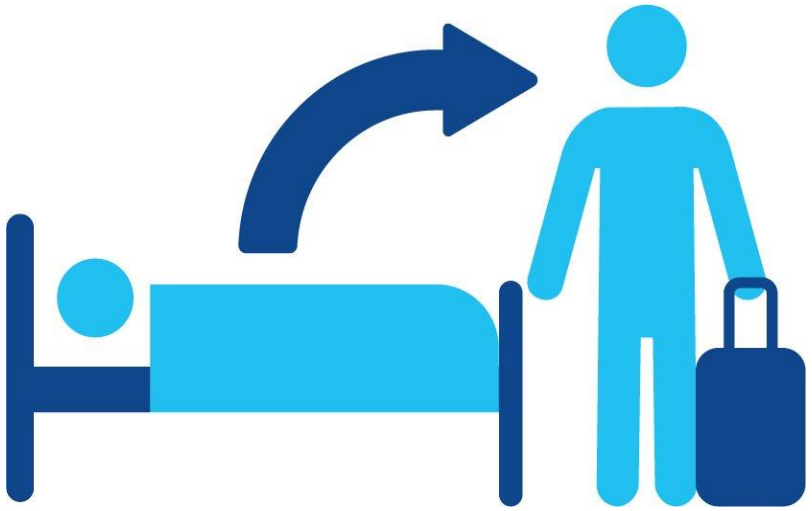
Application approved in July 2024

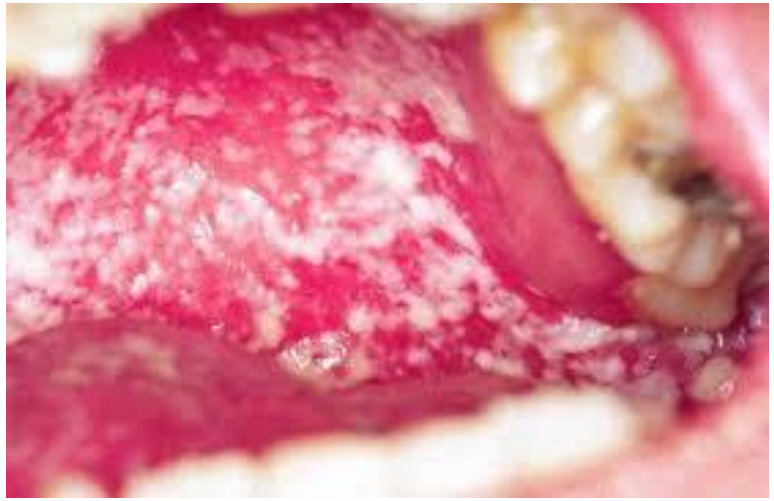
First patient started on rezafungin July 2024

All patients received rezafungin through the OPAT team

Infusions given in ambulatory assessment unit

	Risk factors	Infection diagnosis	Species	Reason for rezafungin therapy	No. of courses	Total duration (wks)	Outcome
4F	Sarcoidosis/**steroids**	Pulmonary aspergilloma (azole refractory)	*Aspergillus* (presumed)	**Admission avoidance**	4 x 2 dose	Cyclical for 11 months (7 months reza)	Clinical improvement, radiological stability, decreased precipitins, ongoing posa
0M	**DM**, GORD with stricture	Severe refractory mucosal candidiasis with stricture	*C albicans (Flu refractory); C glabrata (Flu I)*	CAS failure / **admission avoidance**	2	4	Failed-Refractory to high dose daily Rx, eventual PEG
0M	STAT1 GOF mutation	Chronic mucocutaneous candidiasis	*C albicans (pan azole R)*	Patient compliance with CAS, **azole R**	3 x 1-2 dose	5 doses over 12 months	Response- relapse- requiring 2-dose courses 3 monthly
2M	**DM** with S aureus foot infection	Osteomyelitis	*C albicans*	Metalwork in situ, **earlier D/C**	1	4	Polymicrobial infection- BKA (no Candida in bone)
6F	Liver transplant, UC, SLE, CMV reactivation Tacrolimus & high dose **steroids** for rejection	Oesophageal candidiasis	*C glabrata*	**Azole R**, drug interactions w tacrolimus; admission avoidance	3	7	Resolved on OGD; relapsed x 2 requiring further courses over 1 year
4M	Previous laminectomies, **steroid** injections	Spondylodiscitis	*C glabrata (Flu I, Vori R)*	**earlier D/C-** stepdown from ANI	1	4	Resolved (clinical and radiological improvement)





Challenges & Lessons Learned

- Used predominantly in O/p mucosal candida infections in patients with underlying I/S
- Appears to be well tolerated
- repeat courses required- Lasting cure only achieved in one patient so far
- useful to have monitoring / input from specialist with interest in Mycology but risk separating out from standard OPAT monitoring systems

Comparing cost of rezafungin to OPAT caspofungin

Caspofungin at 70mg OD, outpatient 14-day course	Cost (GBP)
Caspofungin 70mg elastomeric device	£7770 (£555/device)
Nurse visits	£1820 (£130/visit)
Fridge delivery	£150
Consumables for daily infusions	£224 (£112/week)
Total	**£9964**
Rezafungin at 400mg/200mg weekly outpatient x 2 doses (14-day effective course	
Cost of drug: 2 infusions (400mg loading, then 200mg dose on Day 8)	£2178 (£726/vial x 3)
Nurse administration time 2h per infusion@£20/h	£80 (£40/visit)
Total	**£2258**

Days with IV catheter:

- 18 days vs 126 days
  - 108 days saved

Author, year	Country	Diagnosis	Age/ gender	Relevant comorbidity	Fungal species	Previous antifungal therapy	Antifungal treatment duration; adjunctive surgery	Outcome
Abdominal								
Pechacek, 2022[18]	USA	Intra-abdominal candidiasis	65/F	Liver transplant	*Pichia kudriavzevii* (formerly *Candida krusei*)	ANI, MICA	12 weeks	Resolved
Bone and joint								
Ponta, 2024[19]	Italy	Sacral osteomyelitis	79/F	Rectal carcinoma	*Candida tropicalis* (azole resistant); *N. glabratus* (FLU-resistant)	CAS	8 weeks+surgery	Resolved
Lahouati, 2024[20]	France	Spondylodiscitis	63/M	Diabetes mellitus, renal stones	*N. glabratus* (azole resistant)	CAS	10 weeks	Resolved
Viceconte, 2024[21]	Italy	Spondylodiscitis	68/M	Paraplegia and spinal stabilization (metalwork *in situ*), short bowel syndrome, home TPN	*C. parapsilosis* (reduced susceptibility to azoles and FLU-resistant)	ANI, VORI, AmB	26 weeks	'Satisfactory'
Chiurlo, 2023[22]	Italy	Prosthetic knee joint infection	75/M	None stated	*N. glabratus* (FLU-resistant)	ANI, CAS	4 months+revision surgery	Resolved
Trapani, 2025[23]	Germany	Spondylodiscitis	46/M	Diabetes mellitus, major surgery, end-stage renal failure, haemodialysis	*C. albicans, N. glabratus*	CAS	19 months, ongoing	Radiological response, treatment ongoing
Keck, 2025[24]	USA	Prosthetic joint infection	—	Total hip arthroplasty	*C. parapsilosis*	None	12 weeks	Resolved
Endovascular								
Adeel, 2021[25]	USA	Mediastinal/vascular graft infection	49/M	No significant medical history	*N. glabratus* (MDR)	MICA, FLU, POSA, AmB, 5FC	>1 year t	Radiological resolution
Trapani, 2025[23]	Italy	Prosthetic valve IE with EVAR	69/M	CVC line candidaemia, TPN, major surgery	*C. tropicalis* (azole-resistant)	CAS, FLU, AmB, ISA	10 months (with ISA)	Died with septic embolism after ISA stopped
Mori, 2024[26]	Italy	Native valve IE	70/F	Diabetes mellitus, polymyalgia rheumatica on steroids	*N. glabratus*	ANI	8 weeks	Resolution of aortic vegetations, died (sepsis)
Trapani, 2023[27]	Italy	Native AV IE	48/M	Marfan syndrome	*C. albicans*	CAS, azoles	>1 year	Ongoing at time of publication
Trapani, 2023[27]	Italy	Native MV IE	64/M	Severe COVID-19	*C. parapsilosis*	CAS, azoles	8 months	Resolved
Trapani, 2025[23]	Italy	Prosthetic AV IE, endophthalmitis	66/M	None	*C. parapsilosis*	FLU, CAS, AmB	12 weeks (with FLU)	Resolved
Trapani, 2025[23]	Italy	Prosthetic valve IE	74/M	CVC, major surgery	*C. parapsilosis*	FLU, ANI	5 weeks	Discontinued due to patient choice
Keck, 2025[24]	USA	Central venous port infection	—	Mantle cell lymphoma, chemotherapy	*C. auris*	FLU, MICA	1 week; port removed	Resolved
Skin and soft tissue								
Lötsch, 2025[28]	Austria	Limb abscesses	71/M	Bilateral lung transplant, immune suppression, ravulizumab therapy	*Candida dubliniensis*	CAS	5 months, ongoing; FLU added after 4 weeks	Resolution of candidaemia, soft tissue lesions regressed
Mucocutaneous								
Melenotte, 2023[29]	France	Chronic mucocutaneous candidiasis	19/M	STAT1-GOF mutation	*C. albicans* (azole-resistant)	ITRA, FLU, griseofulvin; CAS, terbinafine, VORI	5 weeks	Episode resolved
Keck, 2025[24]	USA	Chronic mucocutaneous candidiasis	F	STAT3 deficiency, AD hyper IgE syndrome, renal transplant, immune suppression	*C. albicans* (FLU, ISA-resistant)	POSA, CLOT, nystatin, ANI, terconazole	6 weeks	Episode resolved

Published experience

22 cases to date

Complex IC- abdo/ SST/ bone/joint/ endovascular/ prosthetic

2 mucocutaneous

Most pts azole and echinocandin-experienced

12/22 risk factors (i/s and DM predominant)

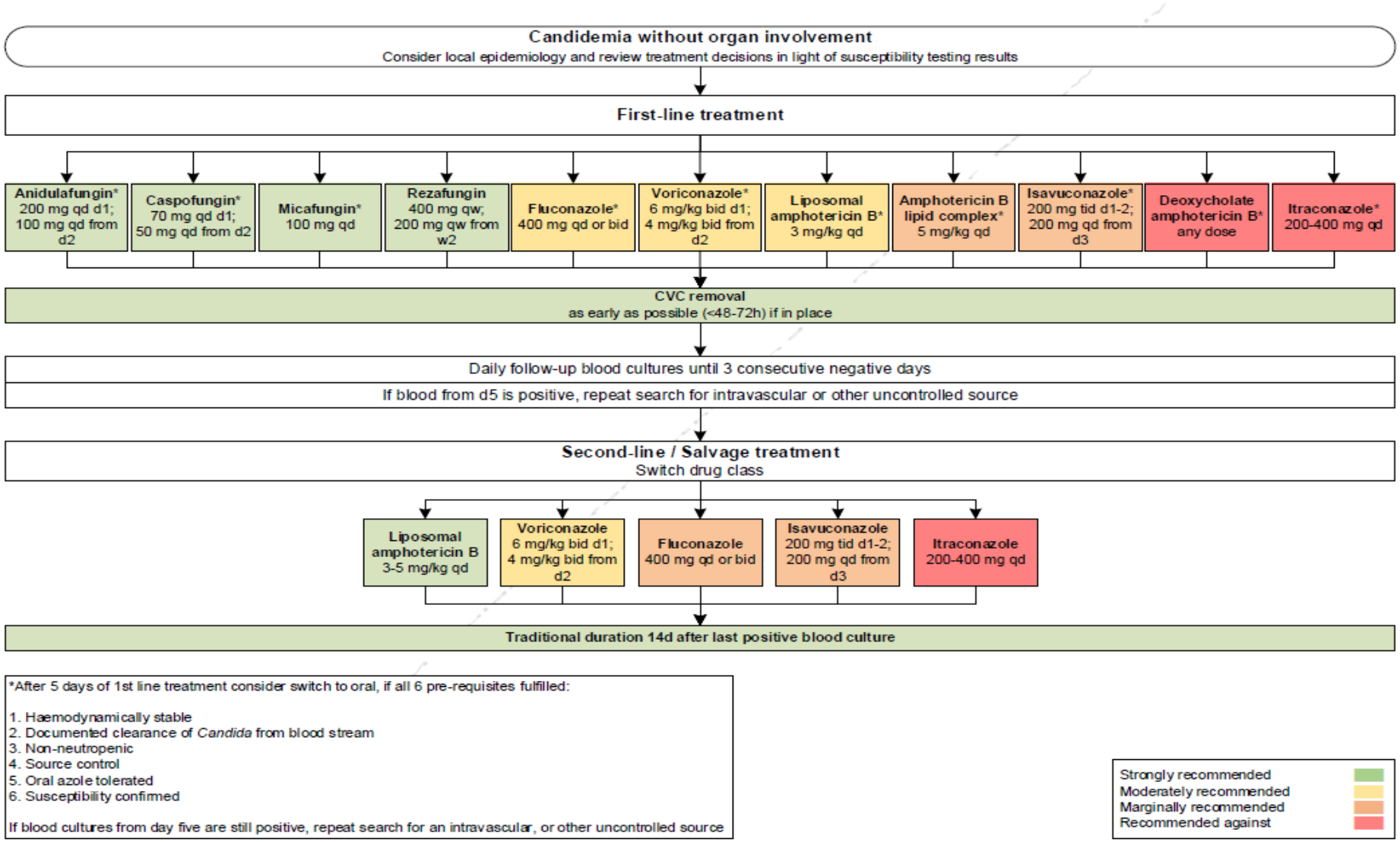
Duration 1 week-19 months

AE inconsistent reporting- rash x 1

Favourable response in 17/20 where outcome reported

Davidson H JAC 2025 July 80 (7): 1885-92
4 cases since

Figure 11. Optimal treatment pathway for candidaemia without organ involvement in adults when all treatment modalities and antifungal drugs are available.



Summary

- First long-acting echinocandin
- Easy to implement
- Convenient for patients and well tolerated
- Potentially Cost effective in OPAT setting
- In IC- consider for complex IC (bone and joint, endovascular, prosthetic material) in patients ready for discharge
- Our experience- only 2/6 of our cases had IC- 3/6 mucosal in immunocompromised patients (with an irreversible deficit); first report of use in CPA

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