NHS
London North West University Healthcare
NHS Trust

Candida glabrata in the kidney: A COpAT Conundrum

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Quality at our HEART

Candida spp.

- Common commensals of skin and GI tract
- Cause both superficial infection (mucosal/cutaneous) and invasive disease
- Candidiasis most common human fungal infection
- *C. albicans* responsible for ~90% of human Candida infections and 40-50% of candidaemias
- Non albicans – *C. glabrata*, *C. parapsilosis*, *C. tropicalis*, *C. krusei*
- IC = blood stream +/- deep seated invasive infections
- IC assoc with high mortality 10-47% for candidaemia, >50% for endocarditis

Table 1. Reports of fungaemia by yeast species in England, 2020 to 2024

Species	2020		2021		2022		2023		2024	
	Number	%	Number	%	Number	%	Number	%	Number	%
Candida	**1311**	(100)	**1387**	(100)	**1404**	(100)	**1431**	(100)	**1475**	(100)
C. albicans	865	(66)	874	(63)	853	(61)	862	(60)	909	(62)
C. dubliniensis	40	(3)	51	(4)	62	(4)	60	(4)	57	(4)
C. metapsilosis	2	(<1)	4	(<1)	6	(<1)	5	(<1)	7	(<1)
C. orthopsilosis	1	(<1)	2	(<1)	3	(<1)	2	(<1)	3	(<1)
C. parapsilosis	219	(17)	274	(20)	261	(19)	278	(19)	280	(19)
C. tropicalis	52	(4)	45	(3)	79	(6)	75	(5)	80	(5)
Candida spp., sp. not recorded	113	(9)	122	(9)	125	(9)	131	(9)	117	(8)
Candida spp., other named	19	(1)	15	(1)	15	(1)	20	(1)	22	(1)
Candidozyma	**1**	(100)	**4**	(100)	**1**	(100)	**5**	(100)	**2**	(100)
C. auris ¥	1	(100)	4	(100)	1	(100)	5	(100)	2	(100)
Clavispora	**28**	(100)	**38**	(100)	**33**	(100)	**27**	(100)	**34**	(100)
C. lusitaniae ¥	28	(100)	38	(100)	33	(100)	27	(100)	34	(100)
Nakaseomyces	**465**	(100)	**470**	(100)	**552**	(100)	**576**	(100)	**613**	(100)
N. glabratus ¥	463	(>100)	469	(>100)	552	(100)	576	(100)	611	(>100)
N. nivariensis ¥	2	(<1)	1	(<1)	0	(0)	0	(0)	2	(<1)

2024 – *C. albicans* (43%), *C. glabrata* (29%), *C. parapsilosis* (13%) of candidaemia

Clin Microbiol Infect 2012; **18** (Suppl. 7): 19–37

ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

Clinical Infectious Diseases® 2016;62(4):e1–50

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America

Lancet Infect Dis 2025; 25: e280–93

Global guideline for the diagnosis and management of candidiasis: an initiative of the ECMM in cooperation with ISHAM and ASM

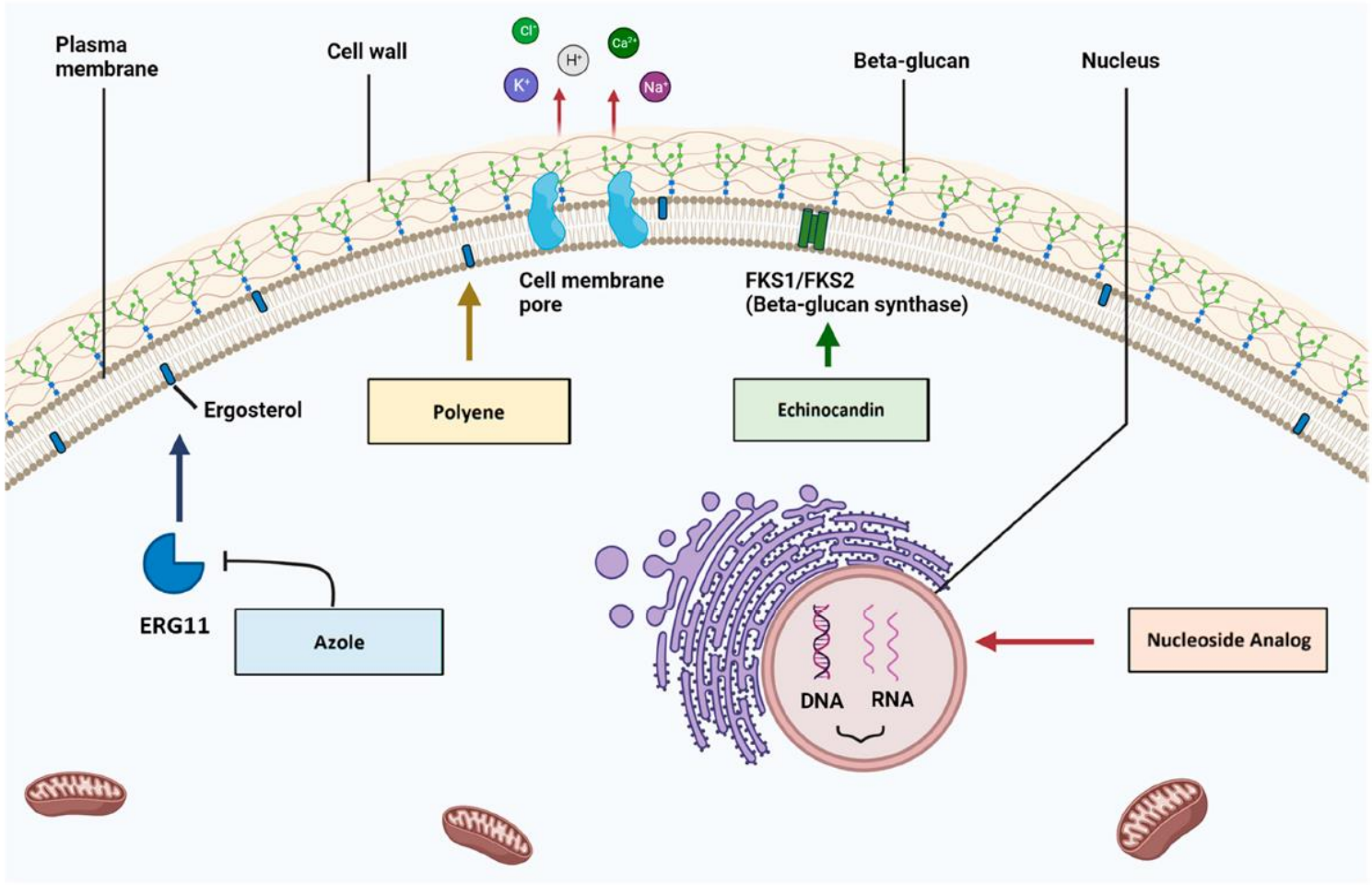
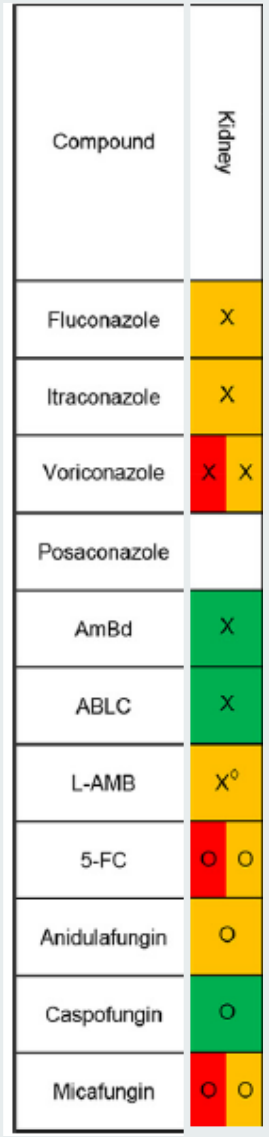


Figure 1. Mechanisms of antifungal action for the four main drug types. (1) **Azoles** bind to and inhibit the Erg11 enzyme and subsequent ergosterol production. (2) **Polyenes** bind to ergosterol and induce the formation of cell membrane pores, which cause intracellular ion leakage. (3) **Echinocandins** bind to and inhibit beta-glucan synthase, which disrupts cell wall architecture. (4) **Nucleoside analogues** are incorporated into nucleic acid molecules and disrupt DNA/RNA biosynthesis (created with BioRender.com, accessed on 16 October 2023).

Limited armamentarium…

- Asymptomatic candiduria is common
- Upper urinary tract infection can occur via
  - Haematogenous spread
  - Ascending infection associated with renal stones
  - Challenging to treat as only FLZ + D-AMB + 5FC achieve high concentrations in kidneys + urine



Felton et al. *Clinical Microbiology Reviews* 2014;27:68-88

Concentrations in kidney for antifungal agent relative to its concentration in plasma

Red, from below level of detection to <0.5X the plasma concentration

Yellow, from >0.5X to <5X the plasma concentration

Green, >5X the plasma concentration

Candida and the urinary tract

JG 65M

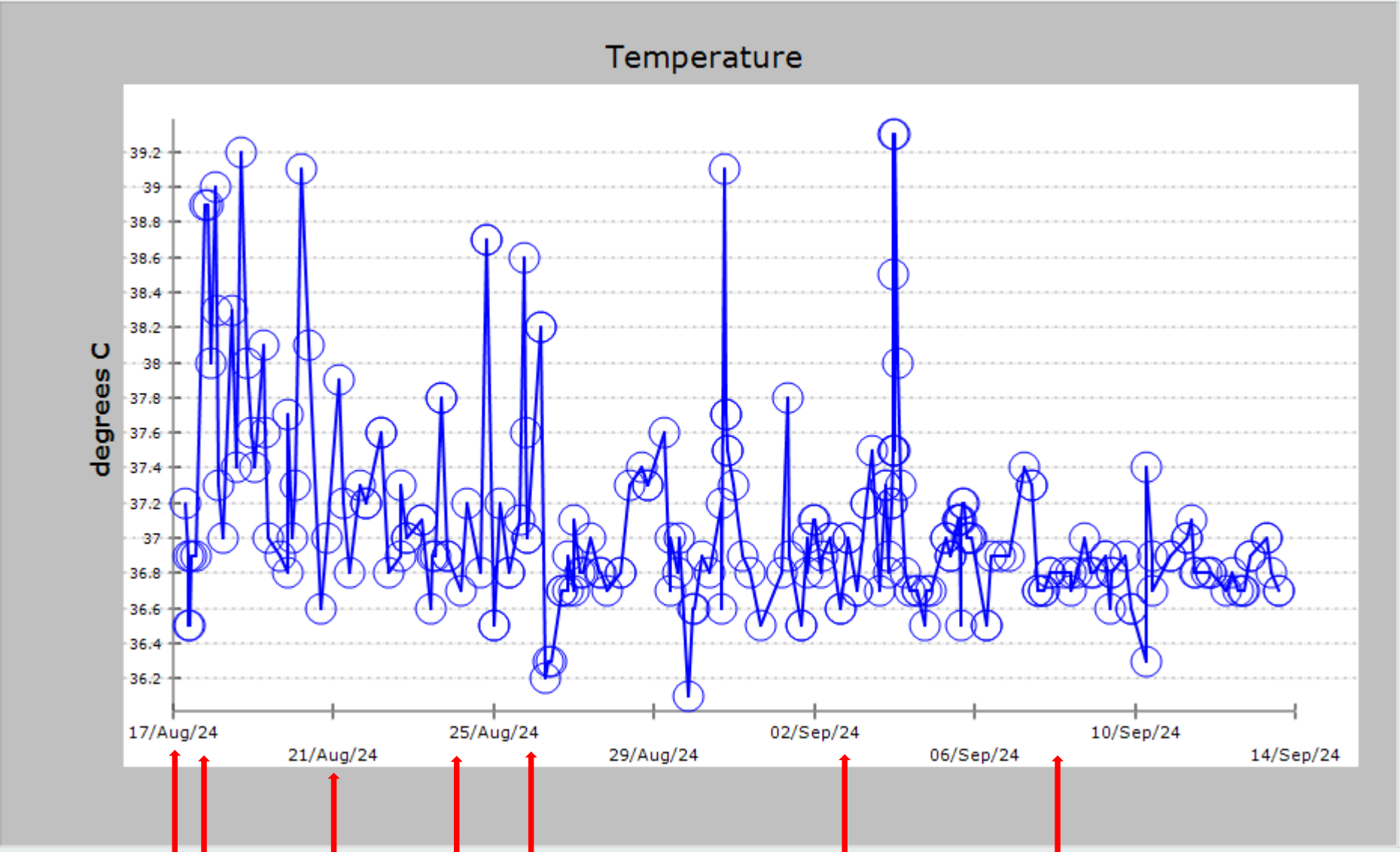
- 2/8/24 2wk rule urology – 5wk haematuria, 2x Abx
- 7/8 OP Flexi cystoscopy
  - Patchy erythematous mucosa; free floating FB
  - For rigid cystoscopy to evaluate FB, Cipro 2wk
- 12/8 Ongoing haematuria, R flank pain
  - CTKUB, urology SpR R sided stone, home with analgesia, SAU next day
- 13/8 Rigid cystoscopy + R ureteric stent insertion, TCI URS + laser fragmentation + stent exchange/removal (28/8)

Urological history

- HPC
  - Fevers (39C overnight) and shivering 3/7, not E+D
- PMH
  - T2DM, inflammatory erosive OA, lap chole 2022, TURP 2020, appendicectomy 1970
- DH
  - Atorvastatin, Metformin, Ramipril, Novorapid + Lantus, Ciprofloxacin; NKDA
- SH
  - Married, Independent, ex-smoker

- O/E
  - NEWS 5, no flank tenderness
- Ix
  - wcc 17.5, neut 16.2, crp 200
  - HbA1c 64 (48-64)
  - BC + MSU sent
- Impression
  - ‘Urosepsis post JJ stent’
  - Stat Amik + IV Coamox

Admission 17/8



BC 17/8, 21/8, 27/8 NG

MSU 17/8 *C spp*

MSU 20/8 *C spp*

MSU 27/8 *C spp*

MSU 30/8 *C glabrata*

(**FLZ/AMB/5-FC sens**)

MSU 2/9 mixed growth

Coamox

Meropenem
18/8-24/8

FLZ 400mg
21/8-25/8

Ciprofloxacin
24/8-13/9

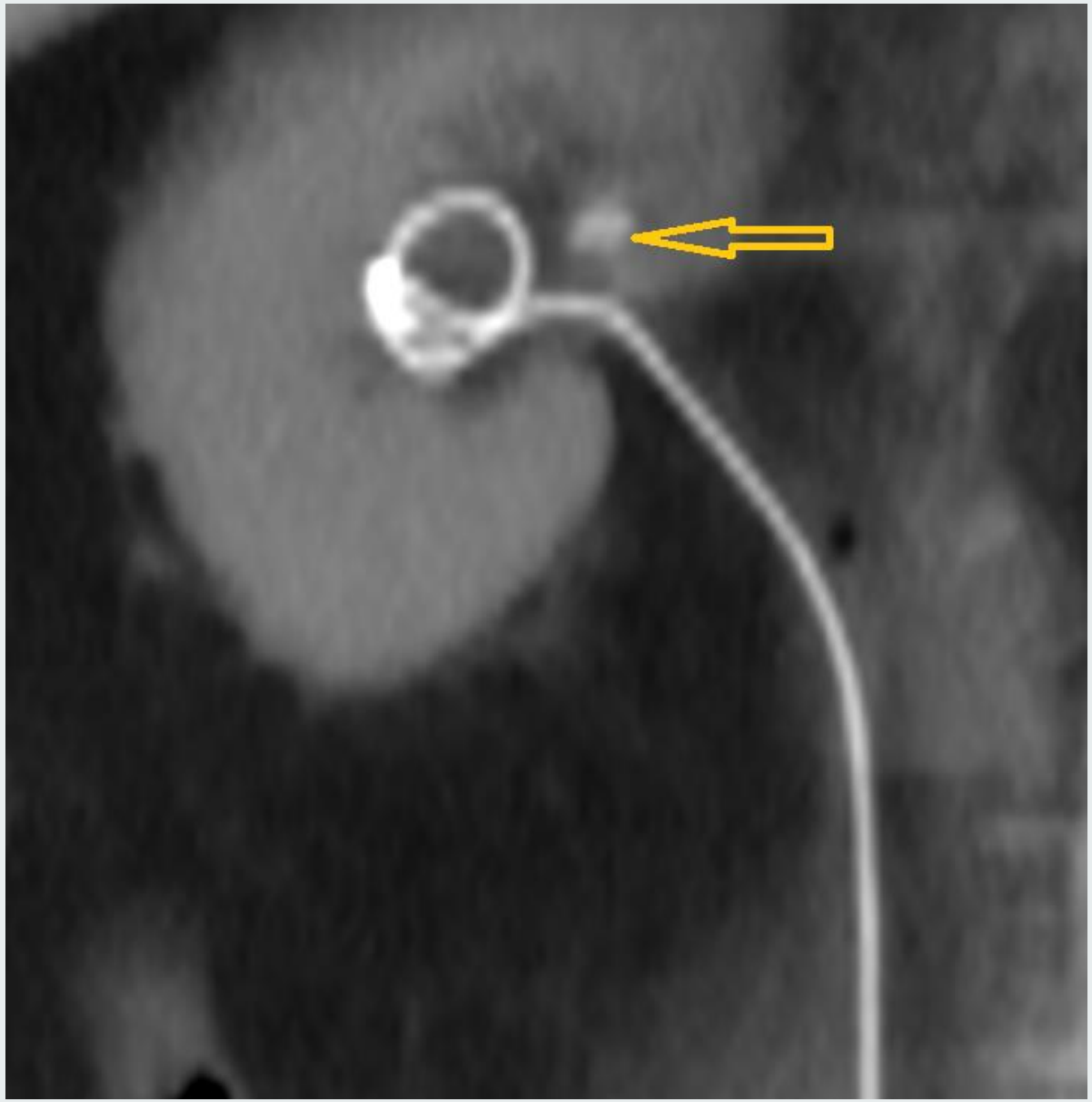
FLZ 800mg
26/8-13/9

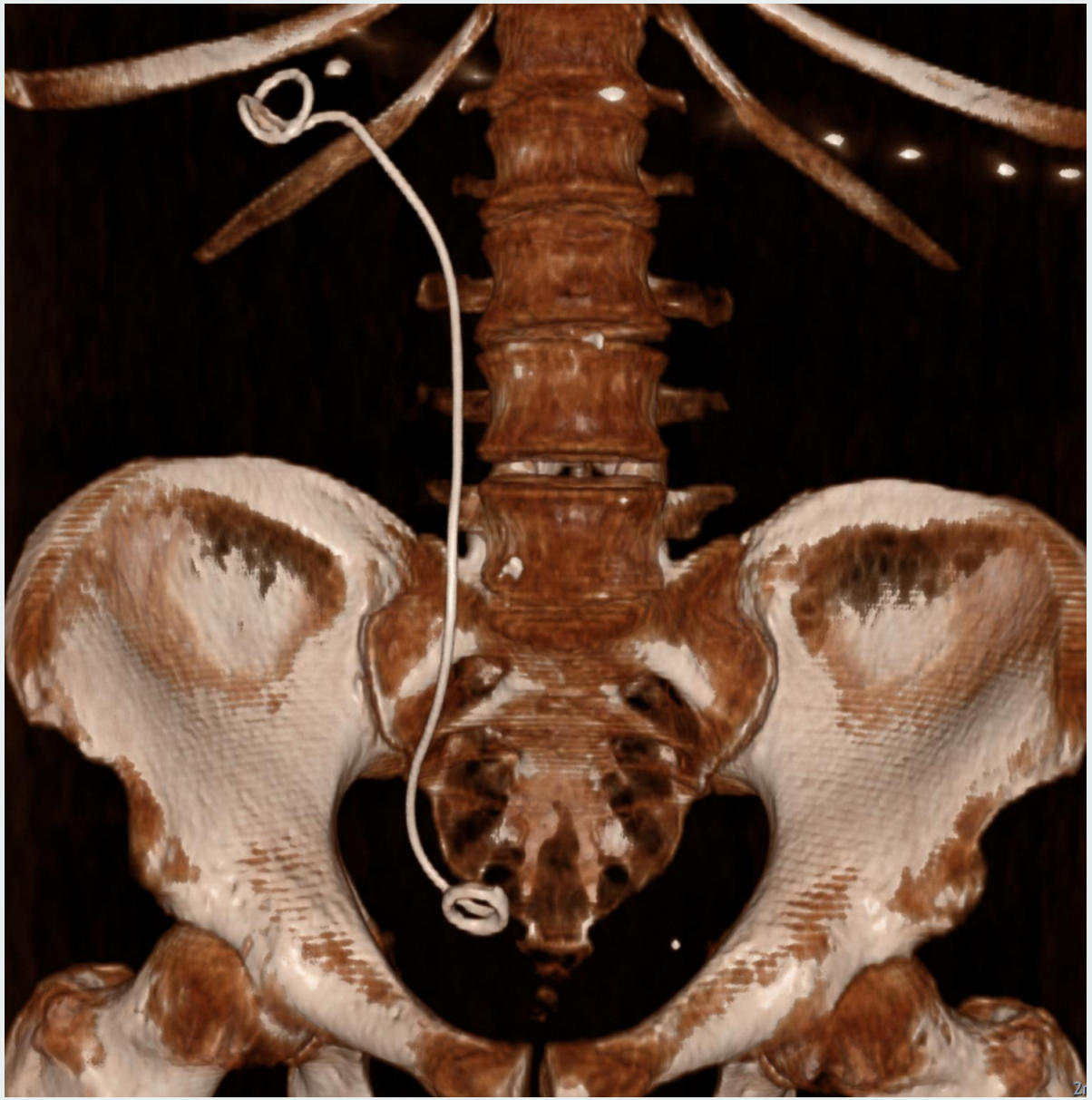
D-AMB ADR
Stat 3/9+5/9

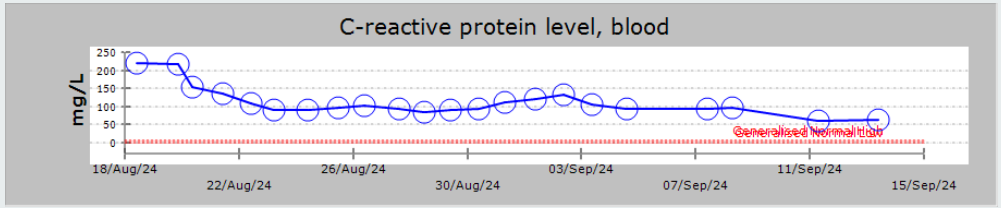
Flucytosine
8/9-13/9

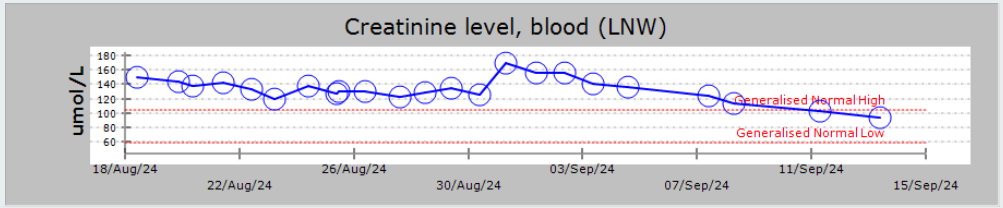
23/8 CTKUB stent in situ + stone, no hydronephrosis

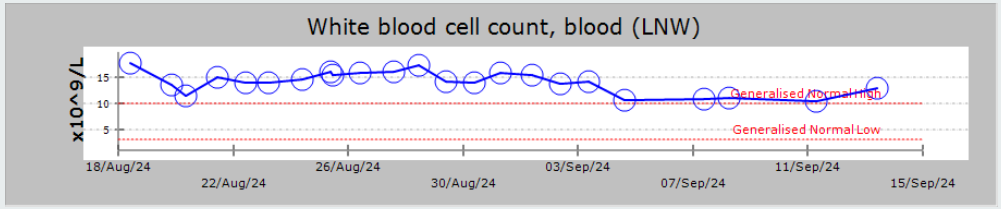
29/8 Cystoscopy + exchange stent (pus insertion guide wire)

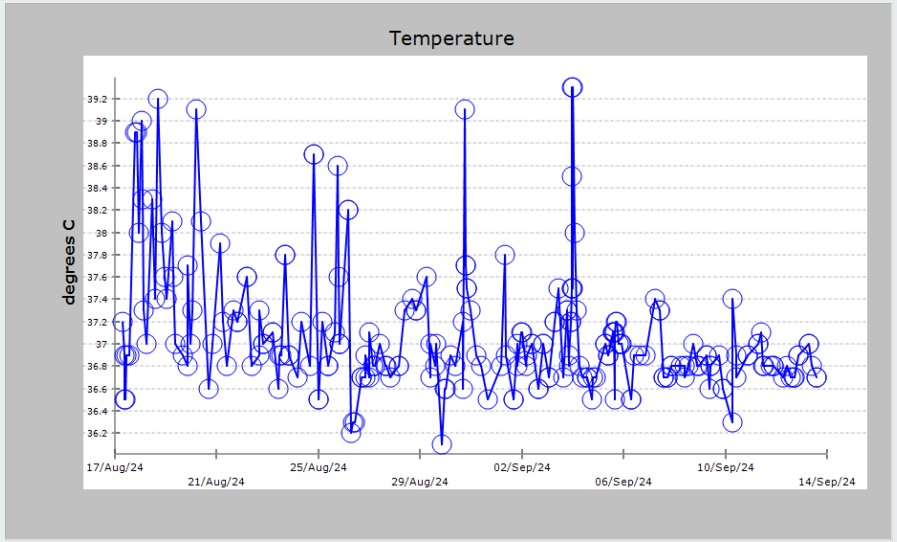





C-reactive protein level, blood
mg/L
250
200
150
100
50
0
Generalised Normal High
18/Aug/24
22/Aug/24
26/Aug/24
30/Aug/24
03/Sep/24
07/Sep/24
11/Sep/24
15/Sep/24

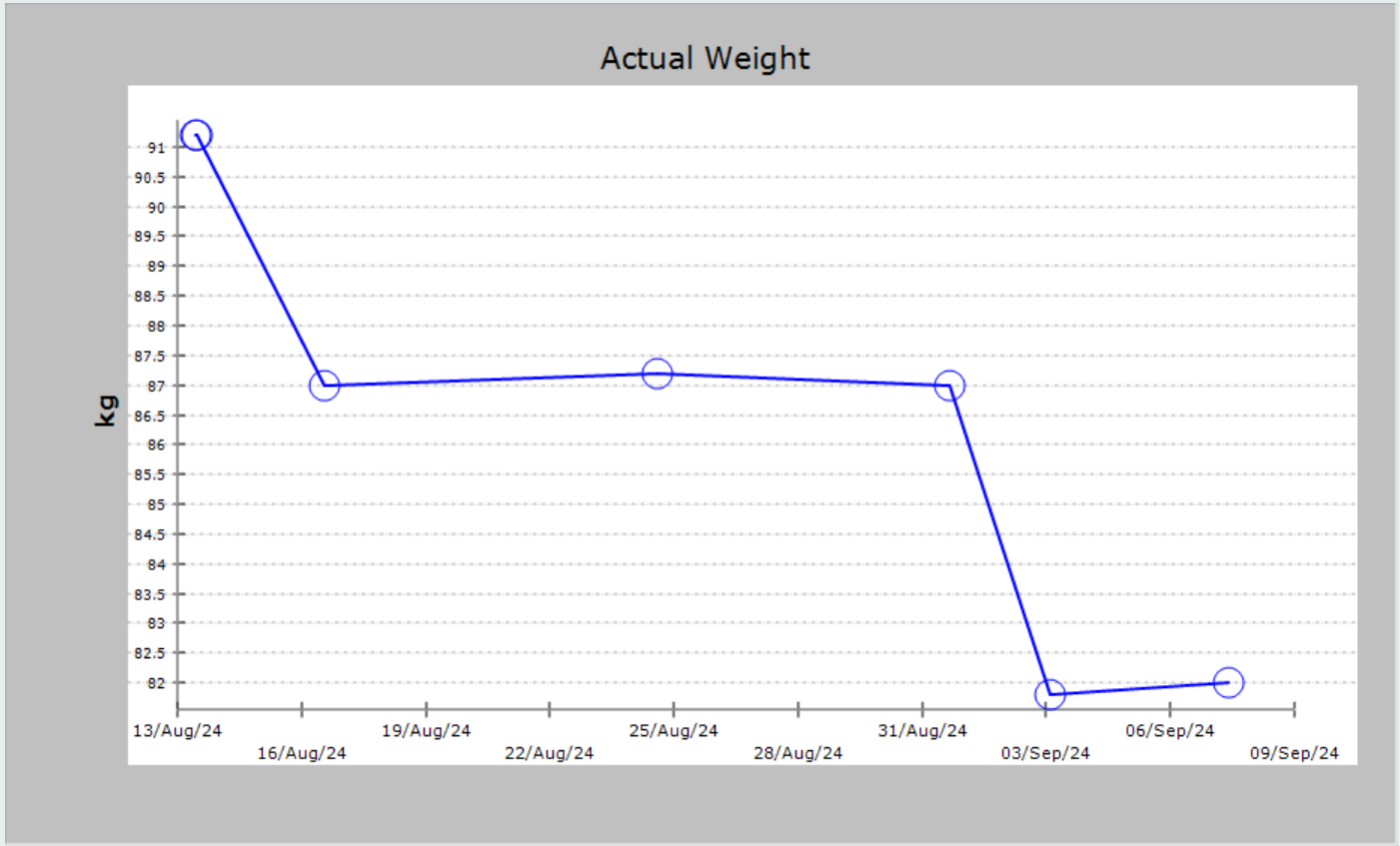

Creatinine level, blood (LNW)
umol/L
180
160
140
120
100
80
60
Generalised Normal High
Generalised Normal Low
18/Aug/24
22/Aug/24
26/Aug/24
30/Aug/24
03/Sep/24
07/Sep/24
11/Sep/24
15/Sep/24


White blood cell count, blood (LNW)
x10^9/L
15
10
5
Generalised Normal High
Generalised Normal Low
18/Aug/24
22/Aug/24
26/Aug/24
30/Aug/24
03/Sep/24
07/Sep/24
11/Sep/24
15/Sep/24


Temperature
degrees C
39.2
39
38.8
38.6
38.4
38.2
38
37.8
37.6
37.4
37.2
37
36.8
36.6
36.4
36.2
17/Aug/24
21/Aug/24
25/Aug/24
29/Aug/24
02/Sep/24
06/Sep/24
10/Sep/24
14/Sep/24

Discharged 13/9

- Fevers settled
- Tired and lethargic
- TTO FLZ + 5-FC + Cipro
- Urology plan
  - 4/52 antimicrobials, stent exchange, then 2/52 more
- OPAT clinic f/u



Fatigue

16 Sep.

18 Sep.

Runs out of 5-FC (national shortage)

FLZ MIC 8 (sens) monotherapy

‘absolutely exhausted’

23 Sep.

30 Sep.

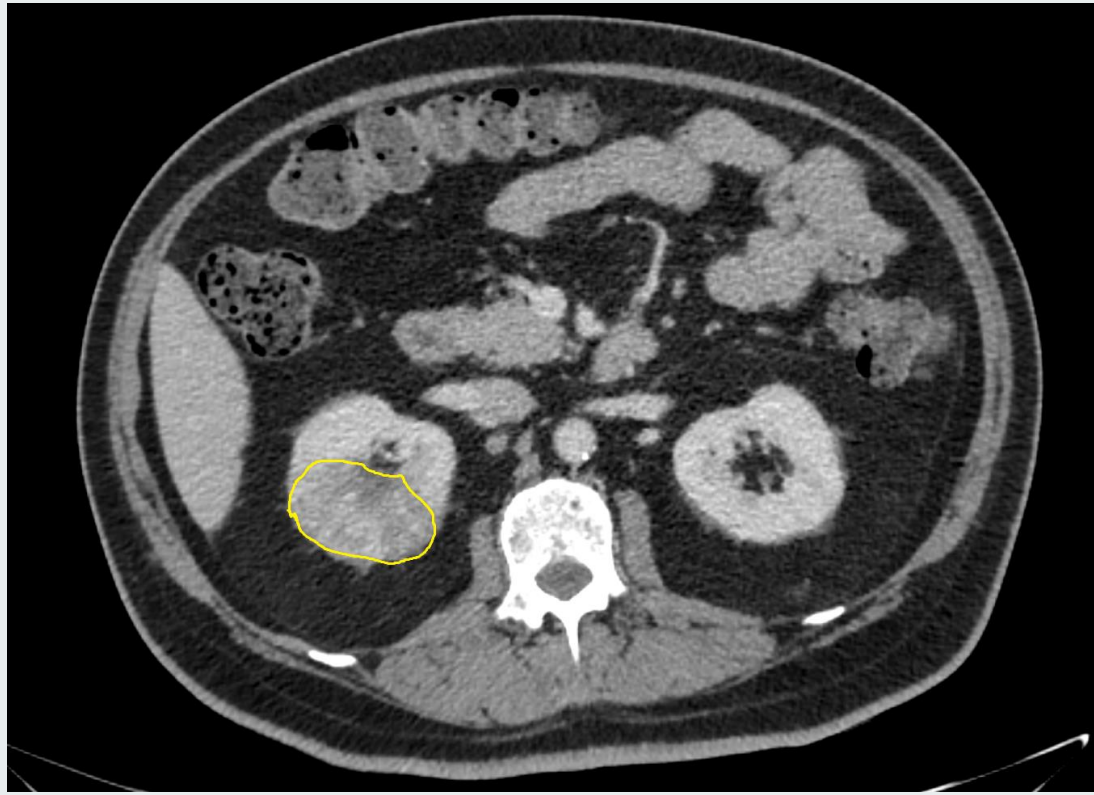
Still tired

no clinical/biochem improvement

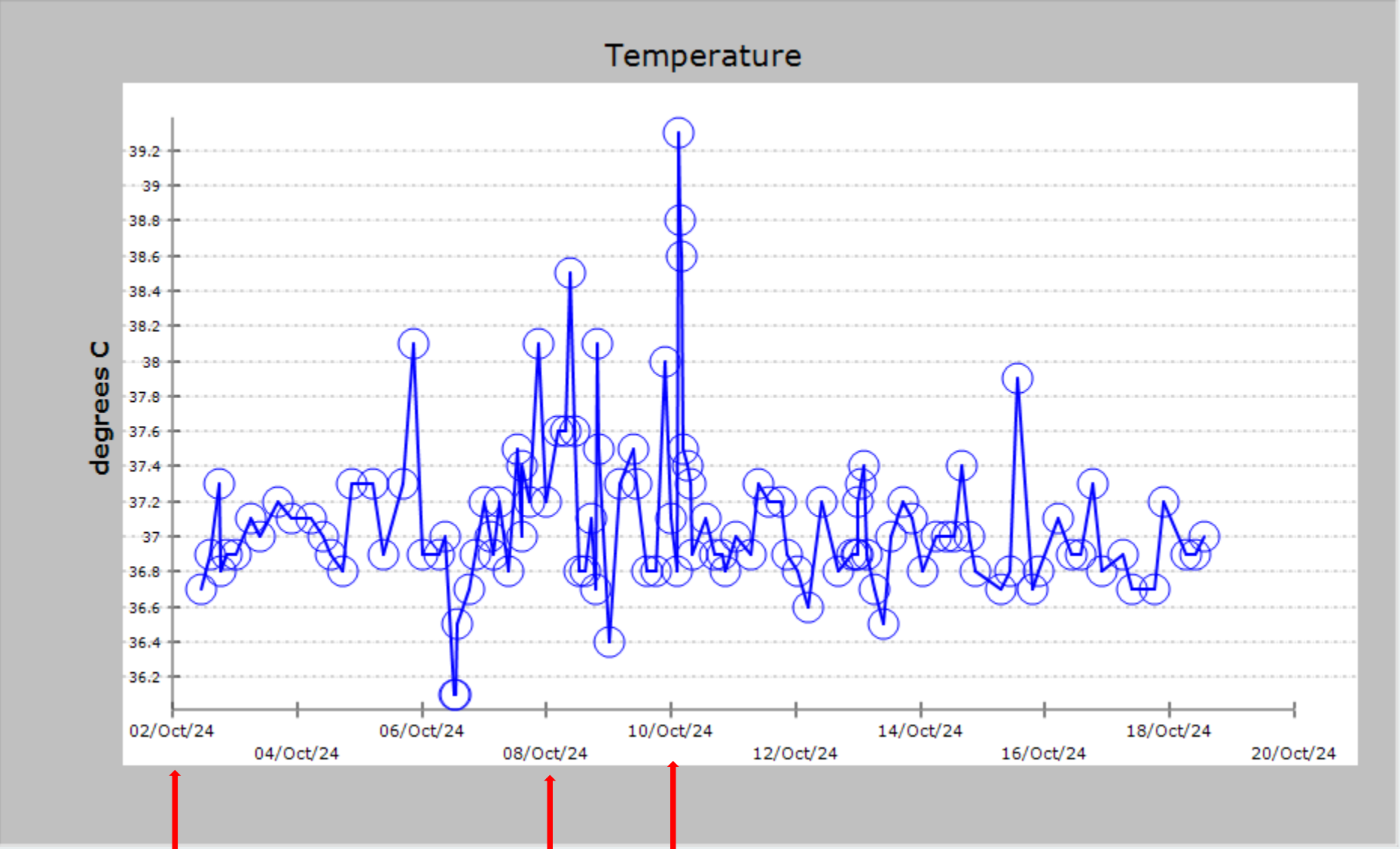
Urgent CTAP (1/10)

Readmitted 2/10

2 Oct.



OPAT 1



BC 8/10 Staph epi

BC 9/10 Staph epi

BC 10/10 Staph epi

BC 13/10 No growth

MSU 6/10 + 10/10

no bacterial growth

FLZ 800mg
2/10-18/10
ANID ADR
Stat 2/10

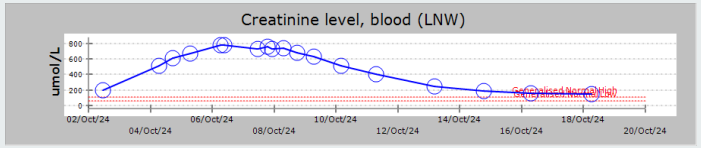
Coamox
8/10-10/10

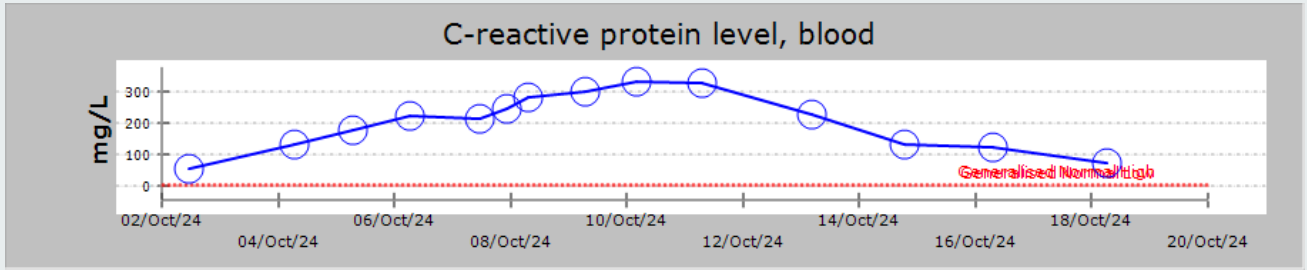
Meropenem
10/10-18/10

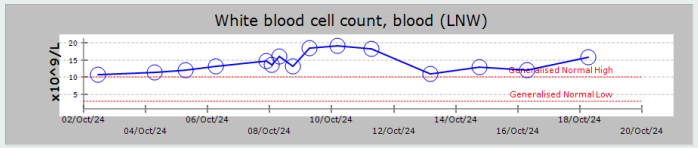
Fevers settled after PICC removal

6/10 R URS + laser stone fragmentation + JJ stent

14/10 CTKUB no stone, JJ stent removed







6/10 R URS + laser stone fragmentation + JJ stent

Home
6/52 FLZ

18 Oct.

28 Oct.

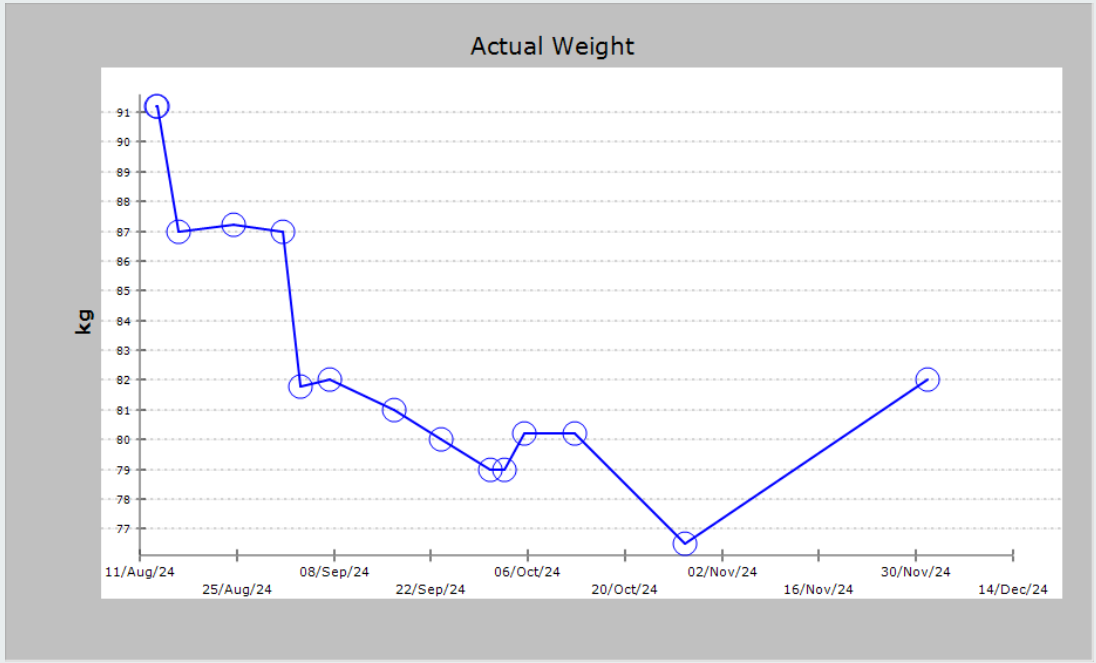
Mental health
Eating more

‘better spirits’
Stop FLZ 16/11
Crp 8.6, wcc12.3, cr 121

12 Nov.

2 Dec.

More energy
Gaining weight
discharge



OPAT 2

Challenges/Lessons learned

- Limited antifungals
  - ADR D-AMB
  - National shortage 5-FC (8/9-18/9)
- Time to get sensitivities back from ref lab
- Convincing Urologists re source control
- Mycology Ref Centre Manchester