

Implementation of a new antifungal prophylaxis pathway in alloHCT patients resulted in reduced adverse effects and drug costs while maintaining efficacy



Optimising antifungal prophylaxis in allogeneic stem cell transplantation – a cohort study of two different approaches

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Introduction

Limited consensus exists on the optimal use of antifungal agents to prevent invasive fungal infection in the early post allogeneic haematopoietic stem cell transplant (alloHCT) period.

Major issues include:

- How to maximise antifungal cover while minimising toxicity
- Practical difficulties of administration due to mucositis and other chemotherapy toxicities
- High drug costs

Aim

Can implementation of a new antifungal prophylaxis pathway for patients in the early post-allogeneic stem cell transplantation period reduce antifungal associated adverse effects without increasing drug costs and compromising efficacy?

Methods

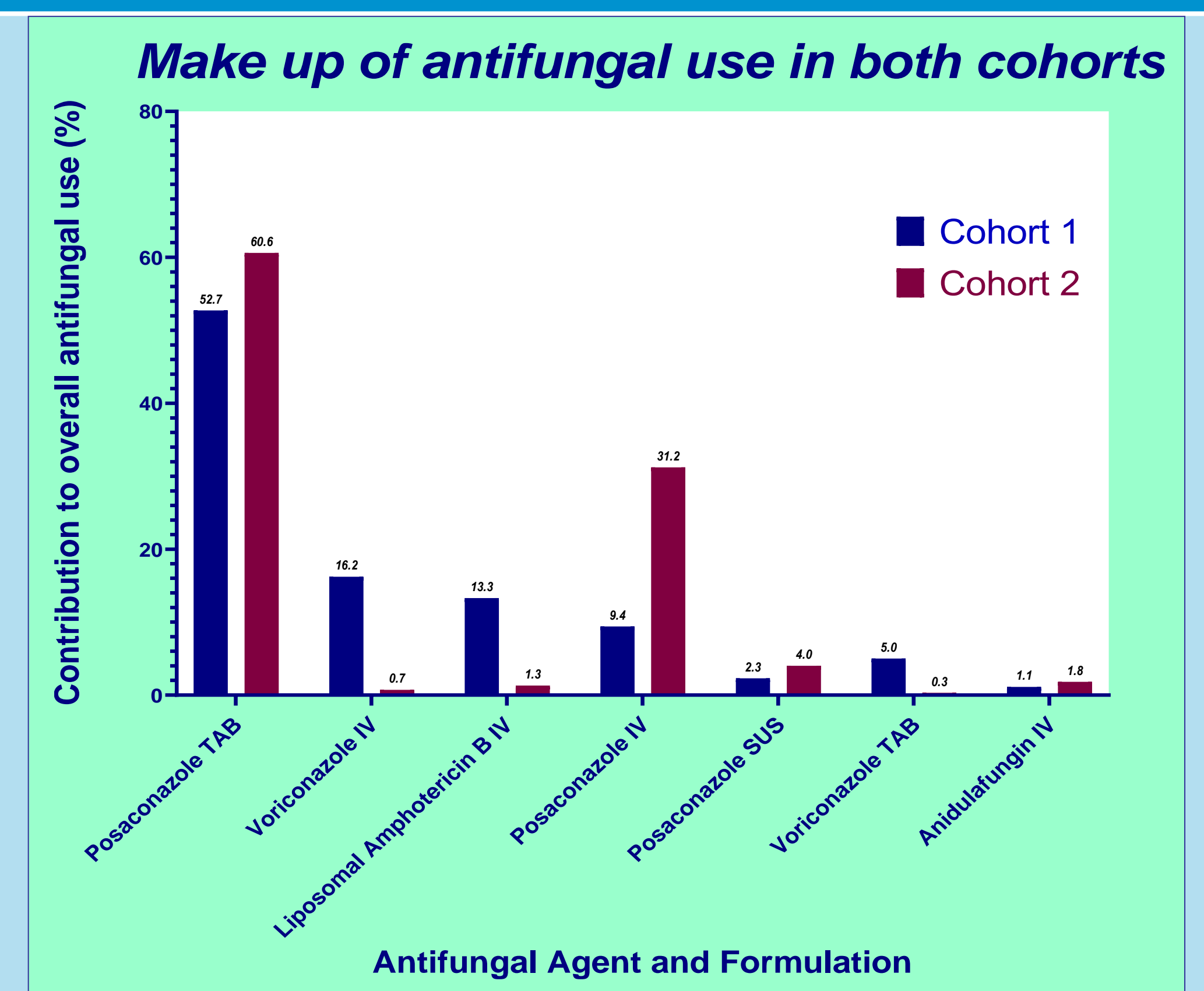
Cohort 1 (n=71)	VS	Cohort 2 (n =71)
Historical control		Post intervention
Feb 2018 – Oct 2019		Apr 2020 – Nov 2021
Antifungal prophylaxis pathway: 1st line Posaconazole modified release tablets 2nd line Voriconazole intravenous 3rd line Liposomal Amphotericin B intravenous 4th Line Posaconazole intravenous		Antifungal prophylaxis pathway: 1st line Posaconazole modified release tablets 2nd line Posaconazole intravenous 3rd line Voriconazole intravenous 4th Line Liposomal Amphotericin B intravenous

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Results

Comparison of Baseline Characteristics	Cohort 1	Cohort 2	Significance (P-Value)
Age (years), median (range)	54 (16 – 69)	51 (17 – 71)	0.53
Sex, n (%)			
Male	45 (63)	40 (56)	0.49
Female	26 (37)	31 (44)	0.49
Haematological Diagnosis, n (%)			
Acute Myeloid Leukemia	28 (33)	33 (46)	0.5
Acute Lymphoblastic Leukemia	9 (13)	16 (23)	0.19
Myelodysplastic Syndrome	12 (17)	7 (10)	0.32
Myelofibrosis	9 (13)	1 (1)	0.017
Other	13 (18)	14 (20)	>0.99
Stem Cell Source, n (%)			
Matched Sibling Donor	14 (20)	18 (25)	0.55
Matched Unrelated Donor	43 (61)	34 (48)	0.18
Umbilical Cord Blood Donor	9 (13)	8 (11)	>0.99
Haploidentical Donor	5 (7)	11 (15)	0.18
Conditioning Intensity, n (%)			
Myeloablative Conditioning (MAC)	17 (24)	15 (21)	0.84
Intermediate Intensity Conditioning (MIDI)	8 (11)	8 (11)	>0.99
Reduced Intensity Conditioning (RIC)	46 (65)	48 (68)	0.86
HCT-CI score, n (%)			
0	27 (38)	23 (32)	0.6
1	13 (18)	7 (10)	0.23
2	9 (13)	15 (21)	0.26
3	10 (14)	13 (18)	0.65
>3	12 (17)	13 (18)	0.83
Overall median (range)	1 (0 - 6)	2 (0 - 8)	0.35



Comparison of Outcomes

	Cohort 1	Cohort 2	Significance (P-Value)	Odds Ratio/95% Confidence Interval
Antifungal Use				
No of lines of antifungal prophylaxis per patient n (%):				
1	16 (23)	28 (39)	0.045	0.45 (0.22 – 0.94)
2	28 (39)	42 (59)	0.029	0.45 (0.23 – 0.89)
3	21 (30)	1 (1)	<0.0001	29.4 (4.9 – 310)
4	6 (8)	0 (0)	0.028	-
Total changes in antifungal agent or route of administration (n)	175	96	-	-
Reason for patients requiring change in antifungal therapy or route of administration:				
Oral route unavailable† n (%)	51 (72)	42 (59)	0.16	1.76 (0.88 – 3.36)
Escalation to treatment antifungal n (%)	26 (37)	9 (13)	0.0016	3.98 (1.71 – 9.42)
Neuropsychiatric toxicity n (%)	20 (28)	0 (0)	<0.0001	-
Hepatotoxicity n (%)	2 (3)	2 (3)	>0.99	1 (0.15 – 6.52)
Nephrotoxicity n (%)	7 (10)	0 (0)	0.013	-
Physician choice n (%)	2 (3)	1 (1)	>0.99	2.03 (0.23 – 29.77)
Adverse Events				
Neuropsychiatric adverse events – total, n (%)	35 (49)	14 (20)	0.0004	3.96 (1.87 – 8.03)
Visual Hallucinations‡, n (%)	21 (30)	3 (4)	<0.0001	9.52 (2.88 – 31.18)
Delirium‡, n (%)	14 (20)	11 (15)	0.66	1.34 (0.55 – 3.1)
Probably due to antifungal§, n (%)	19 (26)	0 (0)	<0.0001	-
Nephrotoxicity: Patients experiencing Acute Kidney Injury ≥ grade 2† - total, n (%)	44 (62)	36 (51)	0.24	1.58 (0.8 – 3.04)
Hepatotoxicity: Patients experiencing potential Drug Induced Liver Injury¶, n (%)	22 (31)	15 (21)	0.25	1.68 (0.80 – 3.47)
Invasive Fungal Infections				
Proven††, n (%)	2 (3)	5 (7)	0.44	0.38 (0.07 – 1.89)
Probable†††, n (%)	3 (4)	1 (1)	0.62	3.09 (0.45 – 40.61)
Possible††††, n (%)	20 (28)	3 (4)	0.0002	8.89 (2.67 – 29.2)
Antifungal drug costs				
Overall Drug cost (AUD)	830 486	477 149	-	-
Drug cost per day of admission (AUD)	238.20	154.47	-	-
Drug cost per patient (AUD)	11 697	6 720	-	-

KEY FINDINGS

The antifungal prophylaxis pathway used in cohort 2 when compared to cohort 1 resulted in:

- Reduced antifungal associated neuropsychiatric adverse events
- Less patients requiring progression to 3rd and 4th line antifungal prophylaxis options
- Reduced antifungal drug costs

For more information

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