

Supplementary material. Breakthrough invasive fungal infection among patients with hematologic malignancies: a national, prospective, and multicentre study.

Supplementary results.

Supplementary Table S1. Isolated species and antifungal susceptibility to prior antifungal.

Isolated fungi	Episodes with fungal isolation^a N=65 (%)	Prior antifungal (S, R, NS or NA)
<i>Aspergillus</i>	27 (41.5)	-
<i>A. fumigatus</i>	11 (16.9)	ECHIN (NA x4), FLUC (R x2), ISA (NA x2), L-AmB (NA x2), and VOR (NA)
<i>A. terreus</i>	7 (10.8)	FLUC (R x6), POS (NA)
<i>A. flavus</i>	4 (6.2)	FLUC (R x2), ECHIN (NA), L-AmB (NA)
<i>A. niger</i>	4 (6.2)	FLUC (R), ECHIN (NA x2), POS (NA)
<i>A. calidoustus</i>	1 (1.5)	POS (R)
<i>A. alliaceus</i>	1 (1.5)	ECHIN (R)
<i>A. hiratsukae</i>	1 (1.5)	ECHIN (R)
<i>Candida</i>	23 (35.4)	-
<i>C. krusei</i>	6 (9.2)	VOR (NS), FLUC (R x3), POS (NS), L-AmB (R)

<i>C. parapsilosis</i>	5 (7.7)	POS (S), ISA (S), ECHIN (R x2, NS x1)
<i>C. glabrata</i>	4 (6.2)	FLUC (R) and POS (NS x3)
<i>C. albicans</i>	3 (4.6)	FLUC (S), VOR (S) and L-AmB (S)
<i>C. guilliermondii</i>	2 (3.1)	POS (NS) and ECHIN (NS)
<i>C. tropicalis</i>	1 (1.5)	ECHIN (R)
<i>C. orthopsilosis</i>	1 (1.5)	ECHIN (NS)
<i>C. kefyr</i>	1 (1.5)	ECHIN (S)
Mucorales	7 (10.8)	-
<i>Lichtheimia</i> spp.	2 (3.1)	ECHIN (R) and VOR (R)
<i>Rhizopus</i> spp.	2 (3.1)	FLUC (R), POS (NA)
<i>Rhizomucor</i> spp.	2 (3.1)	ECHIN (R x2)
<i>Cunninghamella</i> spp.	1 (1.5)	FLUC (R)
Other molds	5 (7.7)	-
<i>Fusarium solani</i>	2 (3.1)	FLUC (R), ECHIN (R)
<i>Paecilomyces</i> spp.	2 (3.1)	POS (NA)
<i>Scedosporium</i> spp.	1 (1.5)	ISA (NA)
<i>Purpureocillium lilacinum</i>	1 (1.5)	ECHIN (R)
Other yeasts	5 (7.7)	-
<i>Geotrichum</i> spp.	2 (3.1)	FLUC (R), ECHIN (R)
<i>Rhodotorula</i>	1 (1.5)	FLUC (NS)

<i>mucilaginoso</i>		
<i>Trichosporon asahii</i>	1 (1.5)	ECHIN (R)
<i>Magnusiomyces capitatus</i>	1 (1.5)	ECHIN (R)

Abbreviations. S: susceptible; R: resistant*; NA: not available; ECHIN: echinocandins; FLUC: fluconazole; ISA: isavuconazole; L-AmB: liposomal amphotericin-B; VOR: voriconazole; POS: posaconazole.

^aIncluding 4 episodes with mixed infections caused by two species of mould.

*When breakpoints are not available, we classified the strains as: resistant (R), when they are considered intrinsically resistant or when there is a breakpoint available for a very closely related species; and as non-susceptible (NS), when the species has intrinsically intermediate MICs to the drug and/or there is insufficient evidence that the species is a good target for the compound in question.

Supplementary Table S2. Diagnostic characteristics of probable episodes of breakthrough invasive fungal infection.

	Probable BtIFI
	N=53 (%)
Host criteria^a	
Recent profound neutropenia	42 (79.2)
Hematopoietic stem cell transplantation	27 (50.9)
Prolonged corticosteroid use	22 (41.5)
Treatment with other T-cell immunosuppressants	18 (34)
Clinical criteria^a	
Compatible thoracic CT scan	51 (96.2)
Sinonasal compromise	2 (3.8)
CNS infection	4 (7.5)
Mycological criteria^a	
Positive culture of a mould	19 (35.8)
Positive galactomannan ^b	42 (79.2)
Positive serum galactomannan	24 (45.3)
Mean (SD) serum galactomannan	3.03 (2.12)
Positive BAL galactomannan	31 (58.5)

Mean (SD) BAL galactomannan	4.07 (2.98)
Direct staining with presence of fungal elements indicating a mould	2 (3.8)
Positive fungal PCR for a mould	5 (9.4)

Abbreviations. BtIFI: breakthrough invasive fungal infection; CT: computed tomography; CNS: central nervous system; SD: standard deviation; BAL: bronchoalveolar lavage; PCR: polymerase chain reaction.

^aMore than one criterion could be present.

^bIncluding patients with both serum and/or bronchoalveolar lavage galactomannan positivity.

Supplementary Table S3. Radiological characteristics of breakthrough invasive fungal infection episodes caused by moulds with pulmonary involvement.

	Mould infections with pulmonary involvement
	N=83 (%)
Consolidation or mass	43 (51.8)
Macronodule	45 (54.2)
Single^a	12 (26.7)
Multiple^a	33 (73.3)
Halo sign	38 (45.8)
Necrotizing pneumonia	12 (14.5)
Infarct-shape pneumonia	3 (3.6)
Micronodules	40 (48.2)
Peri-bronchial thickening	29 (34.9)
Ground-glass opacities	56 (67.5)
Other small-airway lesions	24 (28.9)
Pleural effusion	28 (33.7)

^aPercentage among those with macronodules