Received: 1 April 2022 | Revised: 1 July 2022 | Accepted: 7 July 2022

DOI: 10.1111/myc.13496

ORIGINAL ARTICLE

mycoses Diagnosis, Therapy and Prophylaxis of Fungal Diseases WILEY

When and how do we stop antifungal treatment for an invasive mould infection in allogeneic haematopoietic cell transplant recipients?

Romain Samuel Roth[1] | Stavroula Masouridi-Levrat[2] | Federica Giannotti[2] | Anne-Claire Mamez[2] | Sarah Morin[2] | Christian van Delden[1] | Yves Chalandon[2] | Dionysios Neofytos[1]

[1]Division of Infectious Diseases, University Hospital of Geneva, Geneva, Switzerland

[2]Bone Marrow Transplant Unit, Division of Hematology, University Hospital of Geneva and Faculty of Medicine, University of Geneva, Geneva, Switzerland

Correspondence
Romain Samuel Roth and Dionysios Neofytos, Division of Infectious Diseases, University Hospital of Geneva, Rue Gabrielle-Perret-Gentil 4, 1211 Geneva, Switzerland.
Email: romain.roth@bluewin.ch (R.S.R.); dionysios.neofytos@hcuge.ch (D.N.)

Funding information
Pfizer, Grant/Award Number: WP2485056 and 59276319

Abstract

Background: Limited data exist to describe end-of-treatment (EOT) parameters of antifungal therapy for invasive mould infections (IMI).

Methods: In a 10-year cohort of consecutive adult allogeneic haematopoietic cell transplant recipients with proven/probable IMI, we describe treatment duration and patient profile at EOT.

Results: There were 61 patients with 66 proven/probable IMI identified: 47/66 (71%) invasive aspergillosis (IA), 11/66 (17%) mucormycosis, and 8/66 (12%) other-IMI. Excluding 5 (8%) patients lost to follow-up, treatment was prematurely discontinued due to death or palliative care in 29/56 (51.8%) patients. Antifungal treatment was completed in 27 (48.2%) patients, for a median duration of 280 days (IQR: 110, 809): 258 (IQR: 110, 1905) and 307.5 (99, 809) days in IA and non-IA IMI, respectively. Treatment was continued after 90 and 180 days in 43/56 (76.8%) and 30/56 (53.6%) patients, respectively. At EOT, most patients were not neutropenic (ANC: 2.12 G/L, IQR: 0.04, 5.3), with CD4+ counts at 99 cells/μl (IQR: 0, 759) and immunoglobulins at 5.6 g/L (IQR: 2.3, 10.6). Most patients (16/27, 59.3%) were not receiving steroids at EOT, while 14/27 (53.9%) were on another type of immunosuppression. Amongst 15 patients with imaging at EOT, 12 (80%) had complete/partial radiologic response. Any chart documentation or an infectious disease consultation on treatment discontinuation was observed in 12/56 (21%) and 11/56 (20%) patients, respectively.

Conclusions: Long treatment courses are observed in patients with IMI, due to prolonged immunosuppression. Although immune reconstitution and radiological response were frequently observed at EOT, consistent documentation of treatment discontinuation based on well-defined parameters is lacking.

KEYWORDS
allogeneic haematopoietic cell transplant recipients, antifungal treatment discontinuation, antifungal treatment stop, invasive mould infections

1 | BACKGROUND

Antifungal treatment duration for invasive mould infections (IMI) is not well defined. Historically, duration of antifungal treatment for IMI has been as long as 12 weeks in the context of clinical trials.[1–5] Recent guidelines suggest that treatment for invasive aspergillosis (IA) should be administered for a minimum of 3 months and based on clinical response and the patient's immune status at the end of treatment (EOT).[6,7] For patients with non-IA IMI, such as mucormycosis, treatment duration may last for up to 6 months, also depending on treatment response and immune status at the EOT.[8,9] However, most of those recommendations are based on experts' opinion, as there is lack of data on the time-point, reasons and documentation of discontinuing antifungal treatment in high-risk haematology patients with IMI.

We have previously reported long treatment durations of antifungal treatment, at a median of 200 and 293 days for IA and non-IA IMI, respectively, in a single-centre cohort study of allogeneic haematopoietic cell transplant (HCT) recipients.[10,11] Our findings suggest that in clinical practice, antifungal treatment duration of IMI may be longer than currently recommended. This may, in part, be attributed to the more complex cases observed, frequently not included in randomised clinical trials, but also based on institutional protocols and clinical experience. Using the same 10-year cohort, we sought to describe the profile of allogeneic HCT recipients with IMI at EOT and identify variables that could be important in the decision-making of when to stop IMI treatment.

2 | METHODS

2.1 | Study design

This was a retrospective observational single-centre cohort study performed over a 10-year period from 1 January 2010 through 1 January 2020. All adult (≥18-year-old) allogeneic HCT recipients who were treated for a proven or probable IMI during the study period were included, as previously described.[10,11] The study was approved by the institutional Ethics Committee (2020–01072).

2.2 | Study objectives

The primary objective of this study was to describe the profile of allogeneic HCT recipients with IMI at the EOT. As secondary objectives, we sought to describe the following: (i) number of patients and reasons to prolong IMI treatment beyond 3 and 6 months post-treatment initiation, and (ii) documentation of EOT decision by the primary haematology service and by the Infectious Disease service in the patient's chart.

2.3 | Data collection

Allogeneic HCT recipients were identified through the institutional HCT database and pertinent HCT and IMI data were collected, as previously described.[10,11] The following data were also collected at 90 (±7), 180 (±7) and EOT (±7) day: (i) laboratory data: leucocyte count, absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelet count, absolute CD4+ count, immunoglobulin (Ig) G level, glomerular filtration rate (GFR), alanine aminotransferase (ALT) and γ-glutamyl-transferase (γ-GT), (ii) immunosuppression: prednisone (<10, 10–20, 21–30, >30 mg/day), other (tacrolimus, sirolimus, cyclosporine, mycophenolate mofetil, cyclophosphamide, ruxolitinib, rituximab), (iii) reasons for treatment continuation beyond day 90 and 180 of treatment, including lack of clinical/radiological response, continued immunosuppression, disease relapse and (iv) reasons for treatment discontinuation: death, palliative care, loss to follow-up and treatment completion. The following variables were included for the EOT: (i) imaging findings, (ii) documentation in haematology notes of a discussion with the Infectious Disease service, and (iii) Infectious Disease consultation to address treatment discontinuation.

2.4 | Definitions

Proven and probable IMI were defined based on revised consensus guidelines.[12] Pre-HCT IMI were defined as all proven or probable IMI that were diagnosed during the administration of induction chemotherapy for acute myelogenous leukaemia (AML) and prior to an allogeneic HCT. Clinical and radiologic response were defined as previously described.[13]

2.5 | Statistical analysis

Continuous variables were described as median with interquartile range (IQR). Categorical and continuous variables were compared with the Fisher's exact and a two-tailed Student's *t*-test, respectively. Data were analysed using STATA 16.0 (StataCorp).

3 | RESULTS

3.1 | Patient population

There were 61 patients with 66 proven/probable IMI identified: 47/66 (71%) IA, 11/66 (17%) mucormycosis and 8/66 (12%) other IMI, including 3 *Fusarium* spp., and 1 each: *Hormographiella aspergillata*, *Alternaria* spp., *Schizophyllum commune*, *Scedosporium* spp. and *Scopulariopsis* spp. Overall, 14 (23%) and 43 (70%) patients were diagnosed before and after HCT, respectively; 4 (7%) patients had an IMI diagnosed both pre- and post-HCT. The majority of patients were male (39, 64%) and the median age was 56-year-old (IQR: 26, 69; Table 1). Reduced-intensity conditioning was reported in 47 (77.1%) patients and stem cell source was peripheral stem cells in 49 (80.3%) patients. A total of 37 (60.7%) patients developed acute ≥grade 2 GvHD. All 61 patients had an infectious disease consultation documented in their chart at the time and during the initial treatment of all 66 IMI.

3.2 | Patient profile at EOT

Treatment completion was not recorded in 5 (8%) patients, because they were lost to follow-up. Hence, results are presented for the remaining 56 patients (Table 2). Treatment was prematurely discontinued due to death or palliative care in 29/56 (51.8%) patients. Antifungal treatment was completed in 27/56 (48.2%): 17 (70.4%) and 8 (29.6%) with IA and non-IA IMI, respectively. Antifungal treatment was continued for a median of 280 days (IQR: 110, 809): 258 (IQR: 110, 1905) and 307.5 (99, 809) days in patients with IA and non-IA IMI, respectively (Figure 1). At EOT, most patients were not neutropenic (ANC > 0.5 G/L; 21/24 with available data, 87.5%), with a median ANC at 2.12 G/L (IQR: 0.04, 5.3) and platelet counts at 69 G/L (IQR: 3, 193). In contrast, the majority of patients at EOT were lymphopenic (ALC < 1 G/L; 19/24 with available data, 79.2%), with a median ALC at 0.31 G/L (IQR: 0, 2.2). The median CD4+ count was 99 cells/μl (IQR: 0, 759) and immunoglobulins at 5.6 g/L (IQR: 2.3, 10.6). Eleven (of 27, 42.3%) patients were still receiving steroids at EOT: 7 and 4 patients at < and ≥ 30 mg of prednisone daily, respectively. Overall, 14 (of 27, 53.9%) patients were receiving another type of immunosuppression at EOT. More than half (15/27, 56%) of patients had a repeat CT scan at EOT. The majority of them (12/15, 80%) had complete or partial radiologic response on their repeat imaging test at the EOT.

3.3 | Reasons to prolong IMI treatment

Treatment was continued after 90 and 180 days in 43/56 (76.8%) and 30/56 (53.6%), respectively (Table 3). Amongst 41 patients with IA, treatment was continued beyond 90 and 180 days in 32 (78.0%) and 22 (53.7%) patients, respectively. Similarly, amongst 15 patients with non-IA IMI, treatment was continued beyond 90 and 180 days in 11 (73.3%) and 8 (53.3%) patients, respectively. Treatment was predominately prolonged beyond 90 days due to an underlying immunosuppression in 39/43 (90.7%) patients, including continued administration of immunosuppression (27/43, 62.8%), an allogeneic HCT for the underlying haematological malignancy (11/43, 25.1%), or underlying disease relapse (1/43, 2.3%; Figure 2), followed by lack of radiologic response (5/43, 11.6%), while the reason was not recorded in the chart of 3 (6.9%) patients. Neutrophil and lymphocyte counts were 0.52 G/L (IQR: 0.2, 2.1) and 2.16 G/L (IQR: 0.8, 4.3), respectively. The median CD4+ count at 73 cells/μl (IQR: 9, 98) and immunoglobulins were at a median of 5.99 g/L (IQR: 2.7, 12.8). More than half of the patients (25/43, 58.1%) were receiving some type of non-steroid immunosuppressive therapy, while only one-third of patients were on a steroid treatment (13/43, 30.2%): 6 and 7 patients on < and ≥ 30 mg of prednisone daily, respectively. Similar results were observed in patients whose treatment was continued beyond 180 days (Table 3).

TABLE 1 Baseline characteristics of 61 allogeneic haematopoietic cell transplant recipients who received antifungal treatment for 65 proven/probable invasive mould infections

	Patients *N*: 61 (%)
Demographics	
Age, Median years (IQR)	56 (26, 69)
Gender, Male	39 (63.9)
HCT-related variables	
Conditioning, Reduced intensity	47 (77.1)
HCT source, Peripheral blood stem cells	49 (80.3)
Donor	
Matched related	15 (24.6)
Matched unrelated	27 (44.3)
Haplo-identical	14 (23.0)
Mismatched unrelated	5 (8.2)
Acute GvHD ≥grade 2	37 (60.7)
Chronic GvHD	14 (23.0)
Infectious disease consultation[a]	61 (100)

Abbreviations: GvHD, graft versus host disease; HCT, haematopoietic cell transplant; IQR, interquartile range; *N*, number.

[a]Infectious disease consultation was obtained and documented in patient's chart at the time of and during the initial treatment of IMI.

3.4 | Documentation of EOT decision

Chart documentation of IMI treatment discontinuation by the haematology service was observed of 12/56 (21%) patients. An infectious disease consultation and chart documentation by the infectious disease service pertaining to treatment discontinuation was documented in 11/56 (20%) patients (Figure 3). Amongst 27 patients who completed antifungal treatment for an IMI, an infectious disease consultation to discuss treatment discontinuation at EOT was documented in 11 (40.7%) patients.

4 | DISCUSSION

In this real-life, single-centre cohort study, we sought to describe the profile of allogeneic HCT recipients with IMI at the time of antifungal treatment discontinuation. This is one of the few studies to describe in a consistent and detailed manner the duration of antifungal treatment in high-risk haematology patients and the reasons that prompted treatment discontinuation. Although current guidelines suggest that treatment courses between 3 and 6 months should be considered and tapered based on the type of IMI, clinical response, and the overall immune status of patients, real-life evidence describing in detail the course of antifungal treatment in high-risk haematology patients with proven or probable IMI is lacking.[6–9] We report prolonged treatment courses, for both IA and non-IA IMI, at an average duration of 9 months. In fact, treatment was continued beyond 90 days in the majority of patients with IA (and non-IA IMI), with more than half of patients having their treatment prolonged even beyond 180 days. In nine out of 10 cases, longer treatment durations were due to persistent immunosuppression, either due

TABLE 2 Detailed description of clinical and immunologic status, immunosuppressive treatments, and clinical response at end of treatment for 56 proven/probable invasive mould infections (after excluding five patients lost to follow-up)

	Overall	Death or palliative care[a]	Treatment completion
	N: 56 (%)	*N*: 29 (%)	*N*: 27 (%)
IMI type			
IA	41 (73.2)	22 (75.9)	19 (70.4)
Non-IA	15 (26.8)	7 (24.1)	8 (29.6)
Treatment duration, Median days (IQR)	140.5 (14, 740)	48 (11,246)	280 (110, 809)
IA	133 (14, 432)	64 (11, 224)	258 (110, 1′905)
Non-IA	166 (14, 809)	29 (14, 675)	307.5 (99, 809)
Laboratory, Median (IQR)			
WBC (G/L)	3.25 (0.1, 8.2)	2.15 (0.1, 10.7)	4.15 (0.2, 6.7)
ANC (G/L)	1.67 (0.02, 5.9)	1.5 (0.02, 9.4)	2.12 (0.04, 5.3)
ALC (G/L)	0.31 (0, 2.4)	0.32 (0.05, 2.4)	0.31 (0, 2.2)
PLT (G/L)	36.5 (3, 334)	24 (7, 365)	69 (3, 193)
Absolute CD4+ (cells/μl)	124 (0, 759)	149 (0, 385)	99 (0, 759)
IgG (gr/L)	5.5 (2.3, 10.6)	5.2 (2.3, 14.3)	5.6 (2.3, 10.6)
ALAT (IU/L)	33.5 (9, 159)	39 (8, 138)	30 (13, 159)
gGT (IU/L)	97.5 (16, 659)	109 (24, 526)	73 (11, 659)
eGFR (ml/min/m[b])	60 (31, 116)	60 (31, 113)	60 (33, 116)
Immunosuppression			
Steroids	27 (49.1)	16 (55.2)	11 (42.3)
Non-steroid immunosuppression[b]	34 (61.8)	20 (69.0)	14 (53.9)
Radiologic response			
CT scan performed at EOT	25 (44.6)	10 (34.5)	15 (55.6)
Complete/Partial resolution[c]	19 (76.0)	7 (70.0)	12 (80.0)
Stable[c]	4 (16.0)	2 (20.0)	2 (13.3)
Deterioration[c]	2 (8.0)	1 (10.0)	1 (6.7)

Note: Results are presented for all patients and based on whether patients died or required palliative care before the end of their treatment or completed their treatment course.

Abbreviations: ALAT, alanine aminotransferase; ALC, absolute lymphocyte count; ANC, absolute neutrophil count; CT, computed tomography; eGFR, estimated Glomerular Filtration Rate; gGT, gamma-glutamyltransferase; IA, invasive Aspergillosis; Ig, immunoglobulin; IMI, invasive mould infection; IQR, Interquartile Range; PLT, platelets; WBC, white blood cell count.

[a]Two patients were in palliative care when treatment was stopped.

[b]Non-steroid immunosuppression included: cyclosporine, tacrolimus, mycophenolate mofetil, sirolimus, and cyclophosphamide. One patient could receive >1 agents.

[c]Percentages were calculated based on the number of CT scans performed at end of treatment.

to ongoing administration of immunosuppressive treatments or because patients received an allogeneic HCT. It is not clear at which point the administered antifungal agent represented continued primary targeted antifungal treatment versus secondary prophylaxis, particularly for those patients who were subsequently transplanted or had a relapse of their underlying malignancy. Nevertheless, our findings show that clinicians tend to adjust antifungal treatment duration based on the overall immune status of their patients, with patients with IMI often receiving treatment courses which last beyond the traditional 3 months of treatment as described in clinical trials. This is pertinent, considering the fact that patients are thus susceptible and prone to treatment-associated adverse events and complications.[10]

Based on the retrospective nature of this study, we were not able to document the rationale based on which clinicians might have decided to discontinue antifungal treatment. However, we carefully reviewed the bone marrow reconstitution and administered immunosuppressive agents at EOT. Patients appeared to have reconstituted blood counts, mainly leucocytes and ANC at the time of EOT, with only a few patients remaining neutropenic. Robust lymphocyte reconstitution, as documented by ALC and CD4+ counts, was not observed in a large number of patients at EOT. This suggests that while clinicians are attentive to neutropenia resolution, they may not always consider lymphocyte reconstitution as a major determinant for antifungal treatment discontinuation. In terms of immunosuppression, a minority of patients were on steroids at EOT and amongst those

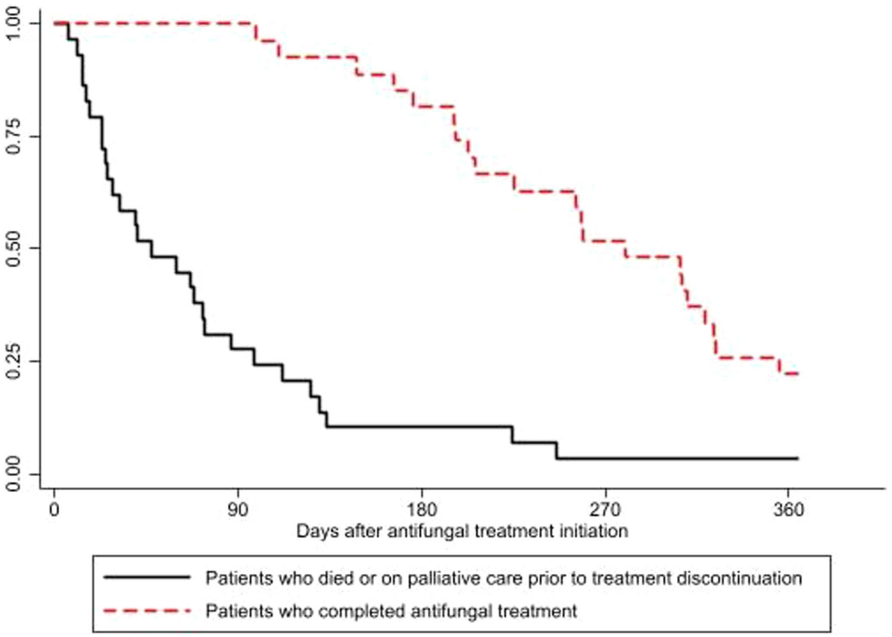

FIGURE 1 Time to treatment discontinuation for patients whose treatment was considered completed and for those patients whose treatment was discontinued due to death or palliative care during the first year after treatment initiation

TABLE 3 Detailed description of clinical and immunologic status and immunosuppressive treatments at 90 and 180 days of treatment for 43 and 30 proven/probable invasive mould infections amongst patients whose therapy was continued beyond 90 and 180 days, respectively

	90 days *N*: 43 (%)	180 days *N*: 30 (%)
IMI type		
IA	32 (74.4)	22 (73.3)
Non-IA	11 (25.6)	8 (26.7)
Treatment continuation reasons[a]		
Lack of radiographic response	5 (11.6)	2 (6.7)
Continued immunosuppression	27 (62.8)	17 (56.7)
Allogeneic HCT	11 (25.1)	5 (16.7)
Disease relapse[b]	1 (2.3)	1 (3.3)
Not recorded	3 (7.0)	3 (10)
Laboratory, median number (IQR)		
WBC (G/L)	4 (1.2, 12.4)	3.5 (1.2, 6.4)
ANC (G/L)	2.51 (0.6, 10.8)	2.16 (0.8, 4.3)
ALC (G/L)	0.44 (0.08, 1.9)	0.52 (0.2, 2.1)
PLT (G/L)	64 (10, 196)	77 (19, 282)
Absolute CD4+ (cells/μl)	65 (8, 4.9)	73 (9, 98)
IgG (g/L)	5.85 (2.9, 12.8)	5.99 (2.7, 12.8)
Immunosuppression		
Steroids	13 (30.2)	11 (36.7)
Non-steroid immunosuppression[c]	25 (58.1)	17 (56.7)

IMI: Invasive Mould Infection, IA: Invasive Aspergillosis, HCT: Haematopoietic Cell Transplant, IQR: Interquartile Range; WBC: White Blood Cell Count, ANC: Absolute Neutrophil Count, ALC: Absolute Lymphocyte Count, PLT: Platelets, Ig: Immunoglobulin.

[a]More than one treatment continuation reasons could be present.

[b]Relapse refers to the underlying haematologic malignancy.

[c]Non-steroid immunosuppression include tacrolimus, sirolimus, cyclosporine, MMF, cyclophosphamide and ruxolitinib amongst others. One patient could receive >1 agents.

patients still on steroids, most were receiving a daily dose of prednisone at <30 mg. Considering the detrimental role of high-dose steroid treatments in the risk and management of opportunistic infections, including IMI, it is likely that clinicians tend to wait until patients are tapered off steroids or receiving lower steroid doses, before making the decision to discontinue antifungal treatment. Based on the

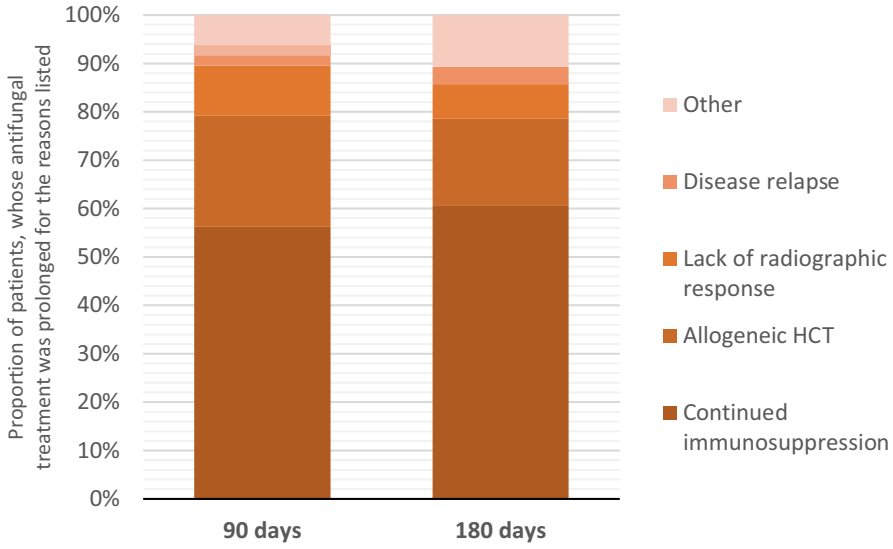

FIGURE 2 Reasons to prolong antifungal treatment for the treatment of invasive mould infections beyond 3- and 6-month post-treatment initiation

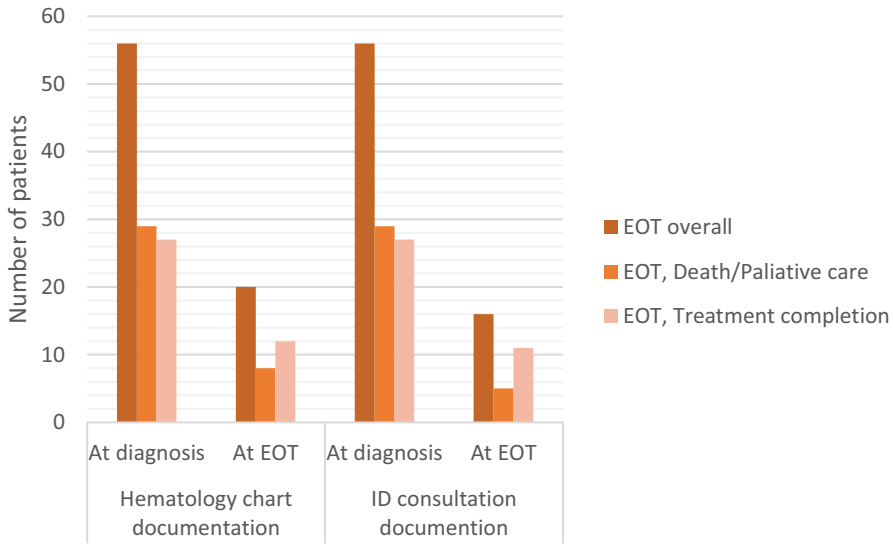

FIGURE 3 Documentation of end-of-treatment decision by the primary Haematology service and by the Infectious Disease service in patient charts

retrospective nature of this study and inconsistencies in patient chart documentation, we were not able to discern a certain threshold in bone marrow reconstitution and/or the daily dose of steroids above which clinicians may be more likely to decide to stop or continue antifungal treatment in allogeneic HCT recipients. Based on our findings, a large variability seems to exist in the way immune status is assessed in the management of high-risk patients with IMI, even in one centre, suggesting that stopping antifungal treatment criteria may differ amongst clinicians and different transplant centres.

In addition to immune reconstitution, clinical and radiologic response in patients with IMI play a significant role in the treatment discontinuation decision-making. Although routinely performed in the context of clinical trials, a repeat imaging test at the EOT was performed in a small minority of patients in this cohort. This may, in part, be due to the fact that treatment was prolonged due to immunosuppression reasons and at that point clinicians were convinced or had already documented clinical and/or radiologic responses in their patients. Nevertheless, amongst those patients with repeat imaging test at EOT, radiologic documentation showed complete or partial response in most cases, further supporting clinicians' decision to proceed with treatment discontinuation.

We also sought to describe whether treatment discontinuation was well documented in patient charts either by the haematology and/or infectious disease teams. Overall, chart documentation by haematology specialists and infectious disease consultants at the time of diagnosis and treatment initiation for an IMI was present for all patients. In contrast, the decision to stop treatment was documented in only one in five patients by the primary haematology team. Similarly, an infectious disease consultation documenting treatment discontinuation and the reasoning of this decision was present in the chart of only one in five patients. Although absence of chart documentation does not necessarily exclude a possible communication between haematology and infectious disease services about treatment continuation, this observation remains noteworthy and further supports the lack of definitive guidance as to when and how antifungal treatment should be discontinued.

The observations made in this study are limited by the small number of patients, single-centre and retrospective nature of the study.

Data might have not always been available and retrospective chart review might have prevented us from fully appreciating the reasoning and decision-making process in most cases. However, this study represents a snapshot of everyday real-life management of patients with IMI. In conclusion, we report prolonged treatment courses in allogeneic HCT recipients with IMI, beyond the traditional 3- or 6-months post-infection diagnosis and treatment initiation. Continued prolonged immunosuppression appears to be the major driver of prolongation of antifungal treatment in this cohort. Blood count parameters and administration of immunosuppressive treatments play an important role in the decision-making of clinicians treating patients with such infections. However, documentation of variables leading to treatment discontinuation, including an infectious disease consultation, is limited. Our findings clearly suggest that there is lack of definitive guidance to drive clinicians' decisions on antifungal treatment discontinuation. Better defined criteria for treatment discontinuation documentation could be useful in clinical practice, to help in decision-making and ascertain a certain degree of homogeneity across centres.

ACKNOWLEDGEMENTS

The authors would like to thank all our colleagues, nurses, and physicians for taking care of the patients in the transplant inpatient and outpatient units. Open access funding provided by Universite de Geneve.

CONFLICT OF INTEREST

R.S.R., S.M-L., F.G., A-C.M. and C.v.D.: No conflicts of interest. Y.C. has received consulting fees from MSD, Novartis, Incyte, BMS, Pfizer, Abbvie, Roche, Jazz, Gilead, Amgen, Astra-Zeneka Servier and travel support from MSD, Roche, Gilead, Amgen, Incite, Abbvie, Janssen, Astra-Zeneka, Jazz. D.N. has received research support from MSD and Pfizer and consulting fees from Roche Diagnostics, MSD, Pfizer, Basilea and Gilead.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Romain Samuel Roth https://orcid.org/0000-0003-0394-9636
Dionysios Neofytos https://orcid.org/0000-0001-6970-2869

REFERENCES

1. Herbrecht R, Denning DW, Patterson TF, et al. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. *N Engl J Med*. 2002;347(6):408-415.
2. Marr KA, Schlamm HT, Herbrecht R, et al. Combination antifungal therapy for invasive aspergillosis: a randomized trial. *Ann Intern Med*. 2015;162(2):81-89.
3. Maertens JA, Raad II, Marr KA, et al. Isavuconazole versus voriconazole for primary treatment of invasive mould disease caused by aspergillus and other filamentous fungi (SECURE): a phase 3, randomised-controlled, non-inferiority trial. *Lancet*. 2016;387(10020):760-769.
4. Maertens JA, Rahav G, Lee DG, et al. Posaconazole versus voriconazole for primary treatment of invasive aspergillosis: a phase 3, randomised, controlled, non-inferiority trial. *Lancet*. 2021;397(10273):499-509.
5. Cornely OA, Maertens J, Bresnik M, et al. Liposomal amphotericin B as initial therapy for invasive mold infection: a randomized trial comparing a high-loading dose regimen with standard dosing (AmBiLoad trial). *Clin Infect Dis*. 2007;44(10):1289-1297.
6. Patterson TF, Thompson GR 3rd, Denning DW, et al. Practice guidelines for the diagnosis and management of Aspergillosis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;63(4):e1-e60.
7. Ullmann AJ, Aguado JM, Arikan-Akdagli S, et al. Diagnosis and management of Aspergillus diseases: executive summary of the 2017 ESCMID-ECMM-ERS guideline. *Clin Microbiol Infect*. 2018;24(Suppl 1):e1-e38.
8. Cornely OA, Alastruey-Izquierdo A, Arenz D, et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the mycoses study group education and research consortium. *Lancet Infect Dis*. 2019;19(12):E405-E421.
9. Hoenigl M, Levitz SM, Schuetz AN, Zhang SX, Cornely OA. All you need to know and more about the diagnosis and management of rare mold infections. *MBio*. 2021;12(1):e02920-20.
10. Roth RS, Masouridi-Levrat S, Giannotti F, et al. Frequency and causes of antifungal treatment changes in allogeneic haematopoietic cell transplant recipients with invasive mould infections. *Mycoses*. 2022;65(2):199-210.
11. Roth RSM-LS, Chalandon Y, Mamaze AC, et al. Invasive mold infections in allogeneic hematopoietic cell transplant recipients in 2020: have we made enough progress? *Open forum Infect Dis*. 2022;9:ofab596.
12. Donnelly JP, Chen SC, Kauffman CA, et al. Revision and update of the consensus definitions of invasive fungal disease from the European Organization for Research and Treatment of cancer and the mycoses study group education and research consortium. *Clin Infect Dis*. 2019;71(6):1367-1376.
13. Segal BH, Herbrecht R, Stevens DA, et al. Defining responses to therapy and study outcomes in clinical trials of invasive fungal diseases: mycoses study group and European Organization for Research and Treatment of Cancer consensus criteria. *Clin Infect Dis*. 2008;47(5):674-683.

How to cite this article: Roth RS, Masouridi-Levrat S, Giannotti F, et al. When and how do we stop antifungal treatment for an invasive mould infection in allogeneic haematopoietic cell transplant recipients? *Mycoses*. 2022;65:1061-1067. doi: 10.1111/myc.13496