Voriconazole as secondary antifungal prophylaxis in stem cell transplant recipients (reply)

I do agree with Cordonnier and colleagues who in this issue of the Journal underline the importance of a proper definition of secondary antifungal prophylaxis (SAP) in patients with a previous invasive fungal disease (IFD).[1] The term secondary prophylaxis is only applicable to a population with inactive or apparently resolved disease.

With this premise, their recently published prospective, non-comparative study of SAP with voriconazole in allogeneic hematopoietic stem cell transplant (HSCT) recipients demonstrated that the triazole is an effective option in SAP of IFDs after HSCT.[2] This was strongly evident in patients with an *aspergillus* infection, considering that none of the 31 patients with a previous proven or probable invasive *aspergillosis* experienced recurrence of the disease after transplant. For the first time, a prospective study confirmed retrospective evidence showing that the probability of posttransplantation invasive *aspergillosis* and overall survival among patients who had resolution of radiographic abnormalities and receive SAP was no different from that of patients without prior invasive *aspergillosis* under primary antifungal prophylaxis.[1,3]

In my editorial on prophylaxis of IFDs in patients with hematologic disorders, I underlined the fact that the efficacy of SAP in patients with active infection or with persistent radiological abnormalities remains unclear.[4] As suggested by Cordonnier and colleagues, strictly speaking, the treatment with antifungal drugs of a controlled but not resolved IFD should not be defined as SAP. In these cases, other terms such as suppressive or continuous antifungal therapy may be more appropriate. On the other hand, an evidence-based antifungal approach in patients with an IFD not in complete remission who require urgent antileukemic treatment remains even more challenging. In real life, a large number of patients with hematologic malignancies undergo allogeneic HSCT despite unresolved IFD. When the underlying malignancy is at high risk of relapse or progression, an early transplant procedure may be required without time for a prolonged antifungal therapy and complete remission of the infection before transplant. This is being seen with increasing frequency in clinical practice and is a challenging issue. In retrospective studies of patients with prior IFD undergoing allogeneic HSCT, the infection was in partial remission, stable phase or progression in about half of the cases and persistent radiographic abnormalities were associated with increased risks of posttransplantation IFD.[3,5] Preliminary data of an ongoing prospective, multicenter epidemiological survey of IFDs in allogeneic HSCT recipients among transplant centers of the Gruppo Italiano Trapianto di Midollo Osseo (GITMO) report 84 patients with an IFD diagnosed within the12 months before transplant. In about 40% of these cases, the infection was in partial remission or active at the time of transplant, and the probability of relapse or progression of the infection and of IFD-related death was significantly higher compared to patients with prior IFD in complete clinical response at the time of transplant (C Girmenia and A Locasciulli on behalf of the GITMO, unpublished data, 2010).

Prior IFD is no longer a contraindication of allogeneic HSCT. However, while SAP in patients with a resolved infection is able to minimize the risk of relapse after transplant, patients with an active/not resolved IFD at the time of transplant continue to be at risk of a potentially fatal reactivation. The role of suppressive/continuous antifungal treatment and of preventive surgical resection of residual pulmonary lesions should be properly investigated in order to identify a tailored antifungal prevention strategy.

Corrado Girmenia

Dipartimento di Ematologia, Oncologia, Anatomia Patologica e Medicina Rigenerativa, Azienda Policlinico Umberto I, Rome, Italy.

Correspondence: Corrado Girmenia, Dipartimento di Ematologia, Policlinico Umberto I Rome, Italy

Key words: voriconazole, antifungal prophylaxis, stem cell transplant.

Citation: Girmenia C. Voriconazole as secondary antifungal prophylaxis in stem cell transplant recipients. Haematologica 2011; 96(02):e11. doi:10.3324/haematol.2010.038810

The information provided by the authors about contributions from persons listed as authors and in acknowledgments is available with the full text of this paper at www.haematologica.org.

Financial and other disclosures provided by the authors using the ICMJE (www.icmje.org) Uniform Format for Disclosure of Competing Interests are also available at www.haematologica.org.

References

1. Cordonnier C, Rovira M, Maertens J, Cornely OA, Ljungman P, Einsele H. Voriconazole as secondary antifungal prophylaxis in stem cell transplant recipients. Haematologica. 2010;96(2):e1-e9.
2. Cordonnier C, Rovira M, Maertens J, Olavarria E, Faucher C, Bilger K, et al. Voriconazole for Secondary prophylaxis of invasive fungal infection in allogeneic stem cell transplant recipients: results of the VOSIFI Study. Haematologica. 2010;95(10):1762-8.
3. Fukuda T, Boeckh M, Guthrie K, Mattson DK, Owens S, Wald A, et al. Invasive aspergillosis before allogeneic hematopoietic stem cell transplantation: 10 year experience at a single transplant center. Biol Bone Marrow Transplant. 2004;10(7):494-503.
4. Girmenia C. Prophylaxis of invasive fungal diseases in patients with hematologic disorders. Haematologica. 2010;95(10):1630-2.
5. Martino R, Parody R, Fukuda T, Maertens J, Theunissen K, Ho A, et al. Impact of the intensity of the pretransplant conditioning regimen in patients with prior invasive aspergillosis undergoing allogeneic stem cell transplantation: A retrospective survey of the Infectious Diseases Working Party of the European Group for Blood and Marrow Transplantation. Blood. 2006;108(9):2928-36.