

## Invasive fungal infections: what is new?

**Economic evaluation of voriconazole versus posaconazole as primary prophylaxis for the prevention of invasive fungal infections in patients undergoing allogeneic haematopoietic cell transplant**

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**OBJECTIVE:** Antifungal prophylaxis (AFP) is commonly used in allogeneic hematopoietic stem-cell transplant (alloHSCT) recipients to prevent invasive fungal infection (IFI), which can have high morbidity, mortality and economic burden. In this study, we evaluated the cost-effectiveness of oral voriconazole (VOR) compared with oral posaconazole (POS) as primary AFP in patients undergoing alloHSCT.

**METHODS:** A decision-analytic model simulated treatment and associated outcomes over a 180-day period in a hypothetical cohort of 1000 patients undergoing alloHSCT. In the absence of head-to-head trials, a network meta-analysis of randomized clinical trials (RCTs) using oral azoles was conducted to derive the probability of developing proven/probable breakthrough invasive aspergillosis (IA), invasive candidiasis (IC), or other IFI, and the proportions of patients requiring other licensed antifungal treatment (OLAT). The previously published meta-analysis included 5 RCTs of oral azoles for AFP in which  $\geq 50\%$  patients underwent alloHSCT. The duration of POS prophylaxis was assumed to be the same as for VOR (from Marks et al, Br J Haematol. 2011;155:318-27). Mortality rates by type of IFI (IA 77.2%, IC 57.1%, other IFI 40.0%) and costs of treating breakthrough IFI (€ 18,354 for IC; € 68,307 for IA) were based on published literature and confirmed by clinical expert opinion. The model considers direct costs associated with drug acquisition, IFI monitoring, and IFI treatment from the Spanish national health system perspective. Model outcomes include number of IFI events, number needed to treat to avoid IFI or IFI death, total costs and incremental cost per IFI avoided.

**RESULTS:** Based on the meta-analysis, VOR was associated with the lowest number of breakthrough IFIs (VOR: n=36, POS: n=60). Consequently, the model predicts fewer deaths from breakthrough IFI (VOR: n=24; POS: n=33), and the lowest predicted costs associated with OLAT and IFI treatment in a cohort of 1000 patients. Compared with POS, VOR had a cost savings of €4,707,391 (€4,707 per patient), along with 23 fewer IFIs, 7 fewer deaths from IFI, and 7 fewer total deaths. In terms of incremental cost-effectiveness ratio, POS was less effective and more costly than VOR in cost per additional IFI avoided, and per additional death avoided.

**CONCLUSION:** In this model, VOR was less costly and more effective than POS as primary AFP in alloHSCT patients 180 days post-transplant.

**Table 1. Outcomes and Costs Summary – VOR vs. POS**

	VOR	POS	VOR vs. POS
<b>Costs per 1000 patients, €</b>			
Prophylaxis	6,849,737	8,627,520	-1,778,783
IFI monitoring	3,272,657	3,272,657	0
IFI treatment	1,953,971	3,353,255	-1,399,285
OLAT	3,286,712	4,817,036	-1,530,323
<b>Total cost</b>	<b>15,363,077</b>	<b>20,070,468</b>	<b>-4,707,391</b>
<b>Outcomes per 1000 patients, n</b>			
Episodes of invasive aspergillosis	22	19	3
Episodes of invasive candidiasis	11	14	-4
Episodes of other IFI	4	27	-23
<b>Total IFI</b>	<b>36</b>	<b>60</b>	<b>-23</b>
<b>Deaths from all IFI</b>	<b>24</b>	<b>33</b>	<b>-7</b>

Numbers have been rounded.