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Assessment of the budget impact of increased micafungin use in the treatment of systemic *Candida* infections in France

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Background

- Micafungin is an echinocandin with a broad spectrum of activity against *Candida* spp., including fluconazole-resistant species[1] and the most commonly isolated non-*albicans Candida* species.[2]
  - in Phase III studies, micafungin (100 mg or 150 mg daily) was non-inferior to liposomal amphotericin B (L-AmB; 3 mg/kg daily) or caspofungin (70 mg followed by 50 mg daily) for the treatment of invasive candidiasis/candidaemia.[3,4]
- Micafungin has demonstrated efficacy against invasive *Candida* infections in a range of patients/settings,[3,4] including patients in intensive care units (ICUs),[5] those with underlying malignant disease[6] and paediatric patients.[7]
  - Also, in a pooled safety analysis in >3000 patients, micafungin was well tolerated in a broad range of patients with severe and life-threatening underlying conditions.[8]
- This analysis evaluated the budget impact of increased use of micafungin therapy for invasive candidiasis/candidaemia in the ICU setting in France.

Methods

Decision-tree model

- A decision-tree model was developed to compare the costs associated with proposed and current prescribing patterns in patients >16 years of age with confirmed invasive candidiasis/candidaemia in French ICUs. Patients entered the model and received either micafungin or caspofungin. Overall treatment duration was 14 days, with a time horizon of 19 days. The treatment strategy is shown in Figure 1.
  - At Day 5, if echinocandin treatment was unsuccessful, patients were switched to either L-AmB or an alternative echinocandin. (The proportion of patients switching to an alternative therapy is a user input. In the base case, 80% switch to L-AmB and 20% switch to an alternative echinocandin).
  - At Day 10, for patients in whom treatment is working, those with confirmed susceptibility were switched to fluconazole for the remaining 4 days of treatment; patients with resistant isolates continue to receive echinocandin.

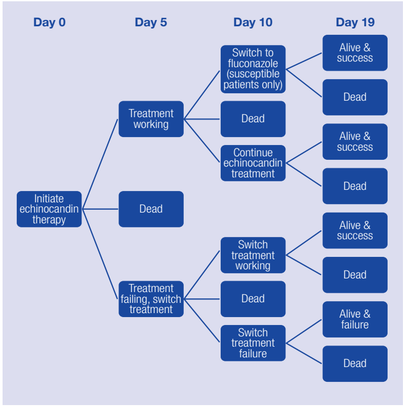
Outcomes

- Comparative efficacy data were sourced from an indirect treatment comparison using a network meta-analysis, following a systematic review of the literature.[9] This information was used to calculate the number needed to treat (NNT) to achieve one additional clinical cure (defined as resolution of all signs and symptoms of infection) or mycological cure (defined as eradication or presumed eradication of baseline pathogen).
- Overall treatment costs: medication and hospital care costs.
- Five-year budget impact: assessed at the hospital level based on user-inputted market share and epidemiological data. Default data were a current market share of 4% with micafungin and 19% with caspofungin.

Assumptions

- Patients receiving successful treatment were moved onto a general ward at Day 10. Patients receiving L-AmB or an alternative echinocandin were assumed to remain on the ICU for the duration of their therapy.
- It was assumed that the incidence of systemic *Candida* infections remained constant during the 5-year period.
- Cumulative budget impact was assessed assuming an increase in micafungin use of 4% in year 1 and 1% in each of the next 4 years, and decreasing caspofungin use of 4% in year 1 and then 1% in each year thereafter.

Figure 1. Decision-tree model.



Inputs

All were from French published sources and were user changeable.

Epidemiology

- *Estimated incidence of candidaemia in France in 2015*: 4.3 per 100,000 population, based upon linear extrapolation of retrospective incidence data from 2001–2010 published by the Programme de Médicalisation du Système d'Information.[10]
- *Candida profile*: the typical *Candida* profile observed in France was derived from a prospective, observational, French multicentre study[11] as follows: *C. albicans* 57%, *C. glabrata* 16.7%, *C. parapsilosis* 7.5%, *C. krusei* 5.2%, *C. tropicalis* 4.9%, *C. Kefyr* 3.6%, and other 4.9%. The fluconazole susceptibility of each *Candida* spp. was taken from the ARTEMIS DISK Global Antifungal Surveillance Study[12] as follows: *C. albicans* 1.3%, *C. glabrata* 16.3%, *C. parapsilosis* 2.6%, *C. krusei* 80.8%, *C. tropicalis* 2.9%, *C. Kefyr* 1.7%, and other 0%.

Market share

- Market share of echinocandins was sourced from a prospective, observational, multicentre study of European ICU patients.[13]

Efficacy

- *Probability of achieving additional clinical or mycological cure* (Table 1): odds ratios and clinical cure rates for micafungin versus caspofungin were obtained from a network meta-analysis following a systematic review of the literature.[9] Micafungin 100 mg was used as the baseline treatment to which the odds ratios of caspofungin and L-AmB were applied.

Table 1. Model base case efficacy inputs.[9]

	Micafungin	Caspofungin	L-AmB
Odds ratio of clinical cure	–	0.81	0.83
Probability of clinical cure	74%	60%	62%
Odds ratio of mycological cure	–	0.69	0.83
Probability of mycological cure	82%	57%	68%

Mortality

- *Mortality data associated with candidaemia in ICU patients*: mortality rates were 21% at Day 5, 16% at Day 10 and 8% at Day 14. In unsuccessfully treated patients, the odds ratio for death was 3.83.[14] Rates were sourced from a hospital-based surveillance programme carried out in the Paris area, France between October 2002 and September 2010.[14]

Costs

- *Drug costs*: micafungin €430 per 100 mg vial, caspofungin €599.36 per 70 mg vial and €439.76 per 50 mg vial, L-AmB €608 per dose, and fluconazole €24.24 per 400 mg dose; taken from Hospital list price, Journal Officiel de La République Française 29 July 2009.
- *Hospital costs*: general ward €1,252 per day, ICU €2,757 per day. Costs sourced from daily rates set for public hospitals in Paris (Agence Regionale de Sante, 2012) and uplifted to 2014 prices using healthcare-specific inflation indices.

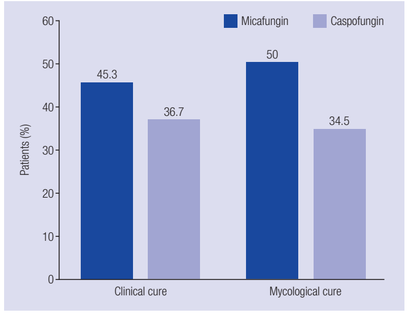
Sensitivity analyses

- One-way sensitivity analyses were carried out to assess the impact of changes in each model input on the estimated cost difference between micafungin and caspofungin. Each parameter was varied between upper and lower 95% confidence bounds calculated from standard distributions assigned around each model input.

Results

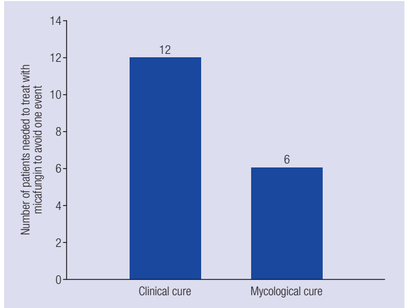
- More patients treated with micafungin achieved clinical or mycological cure compared to those treated with caspofungin (Figure 2).

Figure 2. Clinical or mycological cure following treatment with micafungin or caspofungin.



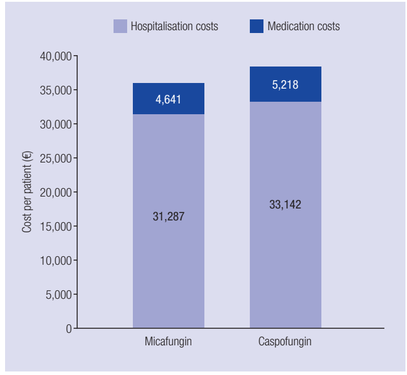
- Based upon clinical or mycological cure rates, it was estimated that the NNT with micafungin to achieve an additional clinical or mycological cure was 12 and 6 patients, respectively (Figure 3).

Figure 3. The number needed to treat to achieve additional clinical or mycological cure.



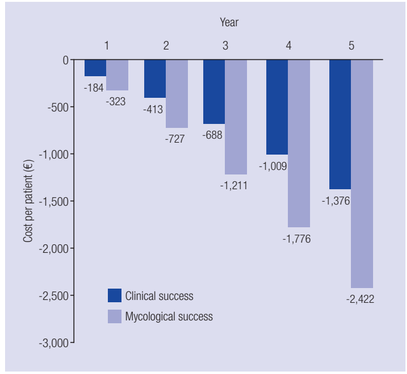
- The average costs per patient treated with micafungin and with caspofungin were estimated to be €35,928 and €38,360, respectively (Figure 4). Micafungin reduced the cost of hospitalisation as a result of fewer people requiring a treatment switch to L-AmB (assumed to be given solely in the ICU).

Figure 4. Average cost per patient.



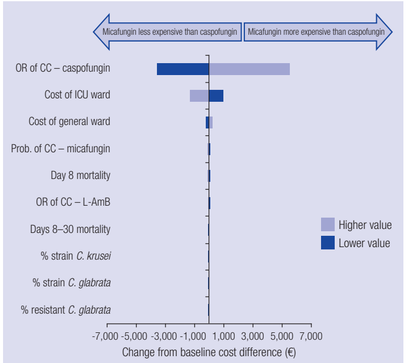
- The 5-year cumulative budget impact of switching to micafungin treatment (using either clinical or mycological success to determine treatment switch) is shown in Figure 5.

Figure 5. Cumulative budget impact of switching to micafungin treatment (using clinical success or mycological success to determine treatment switch).



- The cumulative budget impact of increasing micafungin use by 4% in year 1 and 1% for 4 years thereafter was -€1,376 when clinical success was used to determine treatment switch or -€2,422 when mycological success was used to determine treatment switch.
- *Sensitivity analyses*: the impact of the top 10 most influential parameters on the estimated cost difference is displayed in Figure 6.

Figure 6. Impact of the top 10 most influential parameters on the cost difference between micafungin and caspofungin.



CC = clinical cure; OR = odds ratio; Prob. = probability

Conclusions

- Micafungin represents a potentially cost-saving treatment for adult ICU patients with confirmed invasive candidiasis/candidaemia in France.
- Reduced costs associated with micafungin use are due to lower hospital costs (shorter stay) due to decreased ICU costs associated with subsequent treatment.

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Acknowledgements

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