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ORIGINAL ARTICLE

Pharmacoeconomic evaluation of micafungin versus caspofungin as definitive therapy for candidaemia and invasive candidiasis (IC) in Turkey

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Abstract

Micafungin was shown to be as efficacious as caspofungin in treating patients with candidaemia and invasive candidiasis (IC). However, it remains unknown if micafungin or caspofungin is a cost-effective definitive therapy for candidaemia and IC in Turkey. The present study aimed to determine the economic impact of using micafungin versus caspofungin for treatment of candidaemia and IC in the Turkish setting. A decision analytic model was constructed and was populated with data (i.e. transition probabilities, duration of initial antifungal treatment, reasons for treatment failure, percentage of patients who stepped down to oral fluconazole, and duration on oral fluconazole) obtained from a published randomised clinical trial. Cost inputs were derived from the latest Turkish resources while data that were not readily available in the literature were estimated by expert panels. One-way sensitivity analyses, threshold analyses, scenario analyses and probabilistic sensitivity analyses were conducted. Caspofungin (€2693) incurred a lower total cost than micafungin (€4422), with a net cost saving of €1729 per treated patient. Drug acquisition cost was the main cost driver for both study arms. The model outcome was robust over wide variations (of ±100.0% from the base case value) for all input parameters except for micafungin drug cost and the duration of initial treatment with micafungin. Caspofungin appears to be a cost-saving option in treating candidaemia and IC from the Turkish hospital perspective.

Keywords Antifungals · *Candida* spp. · Modelling

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Introduction

Candidaemia and invasive candidiasis (IC) have been associated with substantial morbidity and high mortality among critically ill and immunocompromised patients [1, 2]. In recent years, there has been a shift towards non-*albicans* species in global fungal epidemiology, including the Turkish setting [3–5] in which echinocandins exhibit excellent antifungal activity [6]. Therefore, an echinocandin (i.e. caspofungin, micafungin or anidulafungin) has been recommended by the latest Infectious Disease Society of America guideline as initial definitive therapy for treatment of candidaemia and IC in both non-neutropenic and neutropenic patients [2].

Micafungin was reported to be non-inferior to caspofungin in a double-blind, randomised clinical trial (RCT) by Pappas et al. [7]. To date, the cost-effectiveness data were mainly comparing an echinocandin with a triazole [8–12], or with a polyene [13–15]; limited economic studies compared the different echinocandins (i.e. micafungin versus caspofungin)

[16]. Previous studies have revealed that micafungin was cost-effective or cost-saving when compared to caspofungin for treatment of candidaemia and IC in the United Kingdom [17] and Australia [18], respectively. However, economic data from a developing country's perspective (e.g. Turkey) [19] remain scant. The present economic analysis, for the first time, aimed to determine the economic impact of using micafungin or caspofungin in treating patients with candidaemia and IC from the Turkish hospital perspective.

Materials and methods

Model structure

The current economic model (Fig. 1) was adopted from Neoh et al. [18] and was mainly constructed based on the pivotal double-blinded RCT by Pappas et al. [7]. In this non-inferiority trial [7], all patients with candidaemia and IC were randomly assigned to receive either intravenous (IV) micafungin 100 mg/day, IV micafungin 150 mg/day or IV caspofungin (70 mg on day 1 and 50 mg daily thereafter). This model only depicted the downstream economic consequences of using either micafungin 100 mg or caspofungin as primary definitive therapy for candidaemia and IC, as both treatment with micafungin 100 mg daily and 150 mg daily were shown to be equally effective in the RCT [7]. The primary outcome was determined at the end of IV antifungal therapy.

Five treatment pathways (i.e. treatment success, death, mycological persistence, emergent infection and clinical failure despite microbiological success) were outlined in the current model depending on whether or not the initial antifungal treatment failed, and if so, for what reason. Treatment success was defined as both clinical and microbiological success [7]. Emergent infection was defined as invasive fungal infection, caused by a different fungal species from the baseline *Candida* species, that developed during the treatment or follow-up period. If the patients failed the initial therapy for any reason other than death or clinical failure despite microbiological success, they were switched to an alternative antifungal therapy. This is due to the fact that treatment failure despite microbiological success was likely to be associated with the patients' underlying condition rather than the efficacy of antifungal agents [9]. The alternative antifungal therapy was chosen according to the reason for which the initial therapy failed (i.e. the types of *Candida* species which contributed to treatment failure and the site of the last positive fungal culture). All patients in the modified intention-to-treat population (MITTP) were followed until treatment succeeded or death. The MITTP, who received at least a single dose of study medication and had confirmed candidaemia or IC, was chosen for analysis as this population would best represent those encountered in daily clinical practice [14]. All patients were permitted to step down to oral fluconazole (400 mg daily) after at least ten days of IV antifungal therapy if they had improvement or resolution in signs and symptoms, had negative cultures for *Candida* species, *C. glabrata* or *C. krusei* was not the causative pathogen for baseline *Candida* infection, or had a

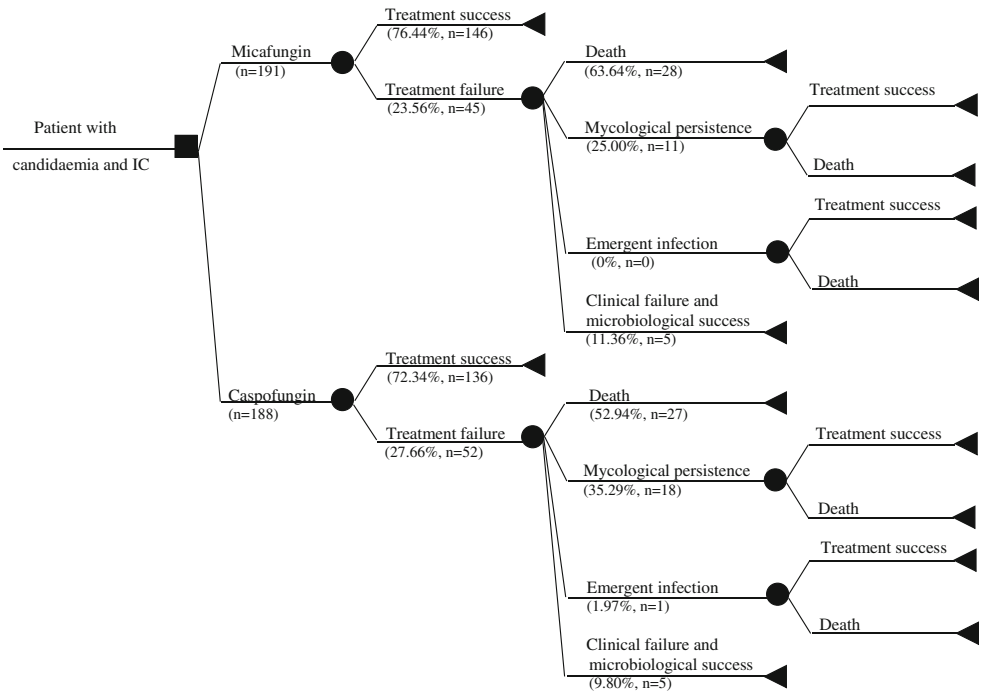

Fig. 1 Decision analytical model for treatment of candidaemia and IC

Candida isolate that was susceptible to fluconazole or absence of neutropenia.

Model perspective

The present analysis was performed from the Turkish hospital perspective. Accordingly, only direct medical costs incurred upon treatment of candidaemia and IC were included in this model. The included costs were as follows: (i) initial and alternative antifungal treatment, (ii) screening tests [i.e. chest X-ray, abdominal computed tomography (CT) scan, echocardiography, fundoscopy, non-blood cultures, blood cultures], (iii) monitoring tests [i.e. full blood count, renal function test, liver function test, electrolyte test], (iv) hospitalisation and (v) additional procedures performed in intensive care unit (ICU) setting [i.e. mechanical ventilation, dialysis, urine catheterisation, procalcitonin test, C-reactive protein (CRP) test].

Model inputs

Data from Pappas et al. [7] were used to populate the model including the transition probabilities, the dose and duration of initial antifungal treatment, the reasons for failing treatment, the percentage of patients who stepped down to oral fluconazole, and the duration on oral fluconazole. As per Pappas et al. [7], the median duration for micafungin and caspofungin therapy were the same (i.e. 14.0 days) while the median duration on oral fluconazole were 7.5 days (for micafungin arm) and 4.0 days (for caspofungin arm), respectively. Duration of ICU stays as well as the duration of hospitalisation for both micafungin and caspofungin arms were derived from a previous economic study [17].

For inputs that were not available from Pappas et al. [7], the data were obtained either from other published studies or expert opinion. For instance, the percentage of patients treated in the intensive care unit (ICU; 53.5%) was obtained from a Turkish candidaemia study [3]. An expert panel of six infectious diseases clinicians from Turkey (including E.S., O.U., A.A., N.B., O.G.T., and M.D.) was used to provide local data on the use of screening tests for the diagnosis of candidaemia or IC, the use of tests monitoring the treatment response or side effects of the antifungals prescribed, and the type of alternative antifungal agents used when initial treatment failed (Table 1). The details on expert panel's consensus have been described [20]. The panel validated the economic model and determined if clinical data obtained from the study by Pappas et al. [7] were generalisable to the Turkish setting. For antifungal agents that were dosed by body weight, an average of 70.0 kg was estimated by the expert panel. The panel also estimated that 3.0–5.0% of the patients in the casponfungin arm had liver insufficiency (Child-Pugh score of 7–9) and anidulafungin was the preferred alternative treatment option.

Other model assumptions

The present model assumed that:

a) Patients would experience only one treatment failure resulting in a switch to an alternative antifungal agent. The switch to alternative therapy would result in successful outcome.
b) Mean duration to death or failure in both study arms was 14.0 days.
c) Mean duration for alternative antifungal therapy was 14.0 days from the last positive culture, except for

Table 1 Alternative antifungal agents for treatment failure with micafungin and caspofungin

Types of initial antifungal therapy	Types of treatment failure	Types of fungal species	Site of last positive culture found	Alternative(s)	Dosing regimen
Micafungin	Mycological persistence	*Candida albicans*, other *Candida* spp.	Blood	IV Fluconazole	Standard[a]
		C. albicans, other *Candida* spp.	Peritoneum	IV Fluconazole	Standard[a]
		Candida parapsilosis	Blood or peritoneum	IV Voriconazole	Standard[b]
		Candida krusei	Blood or peritoneum	LAmB	3 mg/kg/day
Caspofungin	Mycological persistence	*C. albicans*, other *Candida* spp.	Blood	IV Fluconazole	Standard[a]
		C. albicans, other *Candida* spp.	Peritoneum	IV Fluconazole	Standard[a]
		C. parapsilosis	Blood or peritoneum	IV Voriconazole	Standard[b]
		Candida glabrata	Blood or peritoneum	LAmB	3 mg/kg/day
	Emergent infection	*C. albicans and C. glabrata*	Blood	IV Voriconazole or LAmB	Standard[b] or 5 mg/kg/day

[a] 800 mg daily for day 1 (loading dose) and then 400 mg daily (maintenance dose)

[b] 6 mg/kg twice daily for day 1 (loading dose) and then 4 mg/kg twice daily (maintenance dose)

abdominal infections (28.0 days), endocarditis (6 weeks) and endophthalmitis (6 weeks).

d) All *Candida albicans* attributed to treatment failures was susceptible to fluconazole.

e) Patients were hospitalised throughout the study period.

Cost calculations

Costs of resource utilisation were based on the Sosyal Güvenlik Kurumu (SGK) [21] (Table 2). SGK is the only authorised governmental reimbursement department which declares the prices of drugs and medical procedures used in the Turkish setting. All costs were converted from Turkish Lira (TL) to 2017 Euro (€) [TL1 = €0.2218]. The cost per treatment success was calculated as the cost of a full course of IV micafungin or caspofungin (± oral fluconazole), the cost of screening and monitoring tests and the hospitalisation costs. The cost of each treatment failure that resulted in a switch to an alternative antifungal was calculated by adding the cost of initial antifungal therapy and the cost of an alternative antifungal therapy. The cost per deceased patient was calculated as the cost of the initial antifungal treatment before death. The costs associated with adverse events that led to discontinuation were not calculated in the current model given the similar rates of these adverse events in both micafungin and caspofungin arms [7].

Table 2 Costs of resource utilisation [21]

Item	Unit	Cost (€)
Caspofungin	70 mg/vial	116.45
	50 mg/vial	92.49
Micafungin	100 mg/vial	184.77
Anidulafungin	100 mg/vial	128.33
Fluconazole	200 mg/vial	1.77
	200 mg/tablet	1.33
Voriconazole	200 mg/vial	46.01
	200 mg/tablet	10.17
Posaconazole	105 mL/vial	146.33
LAmB	50 mg/vial	65.43
Feniramine	Dose	0.15
Chest X-ray	1 test	3.13
CT scan (upper abdomen)	1 test	13.42
Echocardiography	1 test	5.81
Fundoscopy	1 test	3.77
Non-blood culture	1 test	4.15
Blood culture	1 test	4.15
Full blood count	1 test	0.73
Renal function test[a]	1 test	0.27
Liver function test	1 test	0.27
Electrolytes test[b]	1 test	0.27
Procalcitonin	1 test	0.85
C-reactive protein	1 test	0.61
Mechanical ventilation	1 day	9.87
Dialysis	1	21.58
Central vein catheterisation	1	14.49
Urine catheterisation	1	1.97
Hospitalisation	General ward per day	9.98
	ICU per day	42.14

[a] Consists of creatinine and urea levels in blood or urine sample

[b] Consists of sodium, potassium, magnesium, calcium, chloride and phosphate levels

Sensitivity analyses

A series of sensitivity analyses was performed to determine the robustness of the model outcome. These included sequential modifications of the value of key variables (±100.0% from the base case value) or until the model outcome was inverted (threshold analysis) (Table 3). Key variables involved in the sensitivity analyses were drug acquisition costs, duration of initial antifungal treatment, cost and duration of hospitalisation and ICU stays, and mean duration to failure or death. Scenario analyses were performed to assess the (i) impact of expert panel's estimation, (ii) variation in the percentage of patients in the caspofungin arm who had liver insufficiency, and (iii) not stepping down to oral fluconazole. A two-way exchange of outcome probabilities between micafungin and caspofungin arms was performed to investigate if the model was robust to the changes in probability of patient distribution in each arm.

Probabilistic sensitivity analysis was performed to determine the input variable that had the most influence on the model outcome using @Risk 7.5® (Palisade Corporation, NY, US) [22]. A Monte Carlo simulation of 10,000 patients was run. Transition probabilities were allowed to vary simultaneously with an uncertainty of ±10.0% according to beta distribution (Table 4). The cost-saving acceptability curve (Fig. 2) was employed to estimate the probability of caspofungin being a cost-saving option in treating patients with candidaemia and IC.

Results

Base case analysis

Micafungin (€4422) was associated with an incremental cost of €1729 per treatment success when compared to caspofungin (€2693) (Table 5). Treatment success contributed the most to the overall costs in both comparators. The major cost driver was the drug acquisition cost (€3605 and €1793), contributing 81.5% and 66.6% of the total cost per patient

Table 3 Variation range for variables in sensitivity analysis

Variable	Base case	Variation range	
		Low	High
Micafungin 100 mg cost/vial	€184.77	€96.15	€369.54
Caspofungin 70 mg cost/vial	€116.00	€0.00	€232.89
Caspofungin 50 mg cost/vial	€92.49	€0.00	€184.98
Hospitalisation (general ward) cost/day	€9.98	€0.00	€19.96
ICU cost/day	€42.14	€0.00	€84.28
Duration of initial treatment (micafungin)	14.0 days	1.0 day	28.0 days
Duration of initial treatment (caspofungin)	14.0 days	0.0 day	28.0 days
Total duration of hospitalisation (micafungin)	45.2 days	0.0 day	90.4 days
Total duration of hospitalisation (caspofungin)	43.6 days	0.0 day	87.2 days
Duration of ICU stay (micafungin)	11.0 days	0.0 day	22.0 days
Duration of ICU stay (caspofungin)	11.9 days	0.0 day	23.8 days
Mean duration to death or failure (micafungin or caspofungin)	14.0 days	0.0 day	28.0 days
Counting the cost of screening and monitoring test	Yes	No	Yes
Percentage of patients with liver insufficiency	3.0%	0.0%	5.0%
Step down to oral fluconazole	Yes	No	Yes

treated with micafungin and caspofungin, respectively. This was followed by the hospitalisation costs (€600 and €602), 13.6% and 22.4% of the total cost per patient treated with micafungin and caspofungin, respectively. Cost pertaining to the utilisation of monitoring tests during the initial and alternative antifungal therapies was the lowest, accounting for only 0.61% and 1.05% of total cost incurred for treatment with micafungin and caspofungin, respectively.

Probabilistic analysis

The mean cost of micafungin therapy was €4422 (95% CI: €4361–4489) while caspofungin therapy afforded a lower mean cost of €2693 (95% CI: €2649–2745). Accordingly, caspofungin therapy was associated with a mean cost-saving of €1729 per treatment success (95% CI: €1649–1813). As shown in Fig. 2, the chance of caspofungin being a cost-saving option as definitive therapy for treatment of candidaemia and IC was above 50.0%. The model outcome was most sensitive to the probability of patients who died in the micafungin arm (Fig. 3).

Sensitivity and scenario analyses

As shown in Table 3, the model outcome favouring caspofungin was insensitive to changes (of ±100.0% from the base case value) for all input variables except micafungin drug cost and the duration of initial treatment with micafungin. Threshold analysis revealed that when the cost of micafungin was reduced to less than €96.15 per vial (i.e. -48.0% from the base case value), the model outcome would favour the micafungin arm. Also, micafungin would be a preferred alternative when the mean duration of initial treatment with micafungin reduced to one day. The overall costs of

Table 4 Uncertainty distribution for input variables in probabilistic sensitivity analysis

Input variables	Uncertainty distribution	
	Micafungin	Caspofungin
Treatment success	68.80–76.44-84.08%	65.11–72.34-79.58%
Treatment failure	21.20–23.56-25.92%	24.89–27.66-30.43%
Death	57.28–63.64-70.00%	47.65–52.94-58.23%
Mycological persistence	22.50–25.00-27.50%	31.76–35.29-38.82%
Emergent infection	0.00–0.00-10.0%	1.76–1.96-2.16%
Clinical failure and microbiological success	10.22–11.36-12.50%	8.82–9.80-10.78%

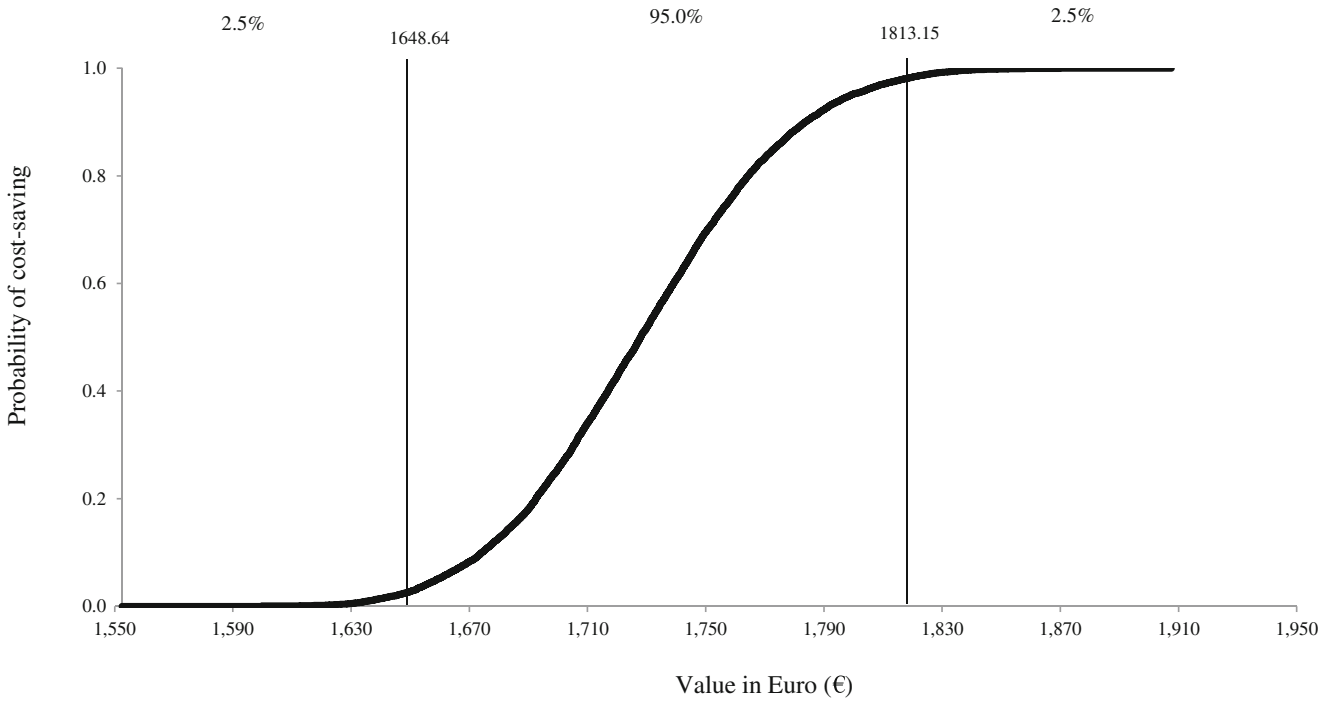

Fig. 2 Cost-saving probability curve of caspofungin

micafungin and caspofungin reduced to €3821 and €2090, respectively, when hospitalisation costs including general ward and ICU costs were eliminated.

The model outcome was robust in all scenario analyses (i.e. estimations made by expert panel, the percentage of patients with liver insufficiency, not stepping down to oral fluconazole), while the total cost per treated patient for micafungin and caspofungin arms remained at the range of €4277–4422 and €2544–2734, respectively. The two-way exchange in the outcome probabilities between micafungin and caspofungin arms did not change the model outcome, with a net cost-saving favouring caspofungin by €2042.

Discussion

Unlike Sidhu et al. [17], the present study performed a cost-minimisation analysis instead of a cost-effectiveness analysis as micafungin was shown to be as effective as caspofungin in treating patients with candidaemia and IC [7]. Accordingly, the difference in total cost between the comparators was reported as the model outcome. The present economic analysis, for the first time, demonstrated that caspofungin is a cost-saving option for the treatment of candidaemia and IC in Turkey; a developing country [19]. The present findings are different from earlier studies in which micafungin was

Table 5 Proportional cost of micafungin and caspofungin as definitive therapy for candidaemia and IC

Therapy outcome	Micafungin			Caspofungin		
	Proportion (%)	Cost (€)/ patient[a]	Proportional cost[b] (€)	Proportion (%)	Cost (€)/ patient[a]	Proportional cost[b] (€)
Treatment success	76.44	4362	3335	72.34	2566	1856
Treatment failure	23.56	4614	1087	27.66	3026	837
Death	14.99	4193	629	14.64	2328	341
Mycological persistence	5.89	5801	342	9.76	4284	396
Emergent infection	0.00	0	0	0.55	5147	29
Clinical failure and microbiological success	2.68	4358	117	2.71	2622	71
Total cost per patient[b]			4422			2693

[a] All shown cost values were rounded to the nearest no decimal point

[b] Calculations involving cost values took two decimal points into consideration (data not shown) associated with each cost value

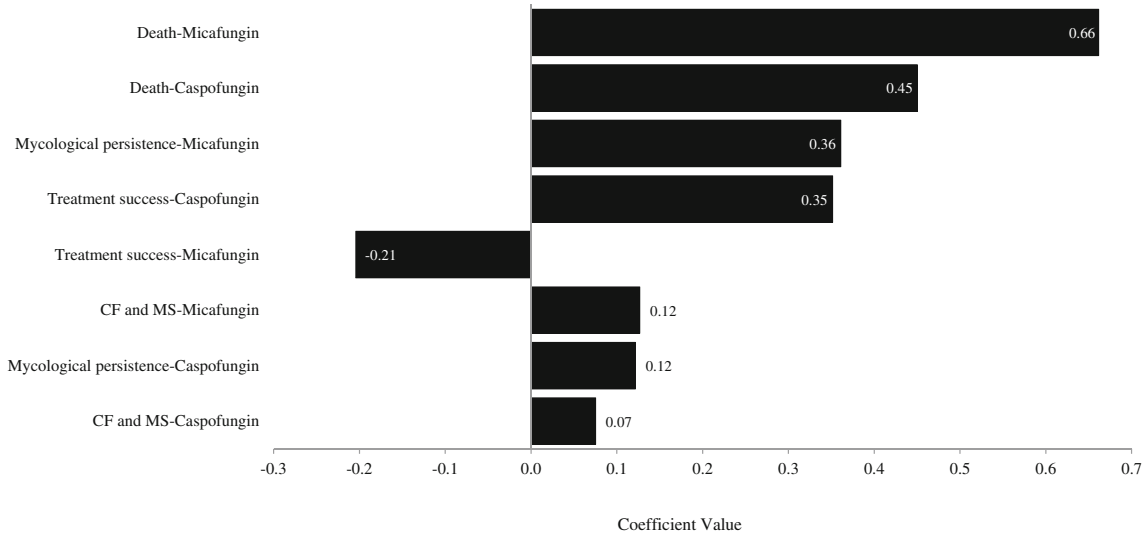

Fig. 3 Tornado diagram of the regression coefficients of input variables

reported to be more cost-effective from the United Kingdom's healthcare perspective [17] or cost-saving [18] from the Australian healthcare perspective when compared to caspofungin. This could be due to the drug acquisition cost being the main cost driver to the total cost in both study arms. The higher drug acquisition cost of micafungin in the Turkish healthcare setting led to higher total cost per patient treated with micafungin. In order to achieve a 100% probability of micafungin being a more cost-saving option than caspofungin (Fig. 2), the cost of micafungin would need to be reduced to less than €96.15/vial, which is about €20.29 cheaper than caspofungin 70 mg.

It is important to note that hospitalisation was not the major cost driver in the present economic study, in contrast to most published literature [16, 17, 23]. The model outcome was robust to changes in the total duration of hospitalisation, length of ICU stay as well as daily costs of hospitalisation and ICU. Unlike the developed countries, the cost of hospitalisation or ICU is relatively low in Turkey when compared to the drug acquisition costs for innovators [24].

In the present model, the costs of managing adverse events that led to treatment discontinuation were not incorporated given that similar incidences were observed in both arms and that most of the adverse events were signs and symptoms associated with worsening patient condition [7]. Furthermore, the costs of managing common side effects were not included as they were often self-limiting and did not lead to treatment discontinuation or further management. Hence, incorporating the secondary costs associated with these side effects would have negligible impact on the total cost difference between both comparators.

In contrast, it is important to include secondary costs related to treatment failure [25], providing an accurate estimation of the total costs involved in managing patients with invasive fungal diseases [16, 26]. Inappropriate selection of antifungal treatment has been identified as a major independent cost driver in treating patients with candidaemia and IC [27]. Indeed, the present model considered all possible treatment pathways as reported in the RCT [7] and their downstream economic consequences. Our model also reflected the latest clinical practice and caseload of candidaemia and IC in Turkey given that the type and the duration of alternative therapy following initial treatment failure were validated by the expert panel. The clinical variables that greatly impacted the model outcome was death in the micafungin arm, followed by death in the caspofungin arm as these variables had one of the highest proportions of patient distribution as seen in the RCT.

Several limitations were noted in the present study. First, extrapolating the findings from the current model to neutropenic patients would be difficult as the majority of the patients in the Pappas et al. trial [7] were non-neutropenic. The present model which allowed only a single switch to the alternative therapy upon treatment failure may not reflect the real-life setting that would have multiple switches to antifungal agents. Nevertheless, the present model took into account the secondary costs related to treatment failure where alternative antifungal agents were prescribed based on the causative pathogen and the site of last positive culture. The expert opinions, which may be subject to bias, are commonly used in the absence of published literatures [28, 29]. In addition, as demonstrated in the scenario analysis, our model was insensitive to the expert panel's estimations.

In conclusion, the present study has shown that caspofungin is a cost-saving option of €1729 per successfully-treated patient with candidaemia and IC in Turkey, as opposed to the previous economic findings.

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Compliance with ethical standards

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Ethical approval Not required.

References

1. McCarty TP, Pappas PG (2016) Invasive Candidiasis. Infect Dis Clin N Am 30:103–124
2. Pappas PG, Kauffman CA, Andes DR et al (2016) Clinical practice guideline for the management of Candidiasis: 2016 update by the Infectious Diseases Society of America. Clin Infect Dis 62:e1–50
3. Mirza Çiftçi A, Şenol E, Kalkancı A (2016) Epidemiology and risk factors of candidaemia among hospitalized patients in a Turkish tertiary care hospital. In: Abstracts of the 26th European Congress of Clinical Microbiology and Infectious Diseases, Amsterdam, Netherlands, 2016. Abstract EV0739. European Society of Clinical Microbiology and Infectious Diseases, Basel, Switzerland
4. Yapar N, Pullukcu H, Avkan-Oguz V et al (2011) Evaluation of species distribution and risk factors of candidaemia: a multicenter case-control study. Med Mycol 49:26–31
5. Ulu Kilic A, Alp E, Cevahir F, Ture Z, Yozgat N (2017) Epidemiology and cost implications of candidemia, a 6-year analysis from a developing country. Mycoses 60:198–203
6. Espinel-Ingroff A, Canton E (2011) *In vitro* activity of echinocandins against non-*Candida albicans*: is echinocandin antifungal activity the same? Enferm Infecc Microbiol Clin 29(Suppl 2):3–9
7. Pappas PG, Rotstein CMF, Betts RF et al (2007) Micafungin versus caspofungin for treatment of candidemia and other forms of invasive candidiasis. Clin Infect Dis 45:883–893
8. Reboli AC, Rotstein C, Kett DH et al (2011) Resource utilization and cost of treatment with anidulafungin or fluconazole for candidaemia and other forms of invasive candidiasis: focus on critically ill patients. PharmacoEconomics 29:705–717
9. Neoh CF, Liew D, Slavin M et al (2011) Cost-effectiveness analysis of anidulafungin versus fluconazole for the treatment of invasive candidiasis. J Antimicrob Chemother 66:1906–1915
10. Auzinger G, Playford EG, Graham CN et al (2015) Cost-effectiveness analysis of anidulafungin for the treatment of candidaemia and other forms of invasive candidiasis. BMC Infect Dis 15:463
11. Grau S, Salavert M, Carlos Pozo Laderas J, Garcia Vargas M, Barrueta JA, Mir N (2013) Cost-effectiveness of anidulafungin in confirmed candidaemia and other invasive *Candida* infections in Spain. J Mycol Med 23:155–163
12. Heimann SM, Cornely OA, Wisplinghoff H et al (2015) Candidemia in the intensive care unit: analysis of direct treatment costs and clinical outcome in patients treated with echinocandins or fluconazole. Eur J Clin Microbiol Infect Dis 34:331–338
13. Neoh CF, Liew D, Slavin MA et al (2013) Economic evaluation of micafungin vs. liposomal amphotericin B (LAmB) for the treatment of candidaemia and invasive candidiasis (IC). Mycoses 56:532–542
14. Cornely OA, Sidhu M, Odeyemi I, van Engen AK, van der Waal JM, Schoeman O (2008) Economic analysis of micafungin versus liposomal amphotericin B for treatment of candidaemia and invasive candidiasis in Germany. Curr Med Res Opin 24:1743–1753
15. Wingard JR, Wood CA, Sullivan E, Berger ML, Gerth WC, Mansley EC (2005) Caspofungin versus amphotericin B for candidemia: a pharmacoeconomic analysis. Clin Ther 27:960–969
16. Neoh CF, Slavin M, Chen SC, Stewart K, Kong DC (2014) Echinocandins in the treatment of candidaemia and invasive candidiasis: clinical and economic perspectives. Int J Antimicrob Agents 43:207–214
17. Sidhu MK, van Engen AK, Kleintjens J, Schoeman O, Palazzo M (2009) Cost-effectiveness analysis of micafungin versus caspofungin for treatment of systemic *Candida* infections in the United Kingdom. Curr Med Res Opin 25:2049–2059
18. Neoh CF, Liew D, Slavin MA et al (2013) Economic evaluation of micafungin versus caspofungin for the treatment of candidaemia and invasive candidiasis. Intern Med J 43:668–677
19. Ministry of Foreign Affairs, Republic of Turkey. Turkey's Development Cooperation: General Characteristics And The Least Developed Countries (LDC) Aspect. http://www.mfa.gov.tr/turkey_s-development-cooperation.en.mfa . Accessed 10th May 2017
20. Neoh CF, Senol E, Kara A, Dinleyici EC, Turner SJ, Kong DCM (2017 Nov) Cost-effectiveness analysis of anidulafungin vs fluconazole for the treatment of invasive candidiasis (IC) in Turkey. Mycoses 60(11):714–722
21. Republic of Turkey-Social Security Institution. http://www.sgk.gov.tr/wps/portal/en?CSRT=16458562213556365941 . Accessed 22 November 2016
22. O'Hagan A, Stevenson M, Madan J (2007) Monte Carlo probabilistic sensitivity analysis for patient level simulation models: efficient estimation of mean and variance using ANOVA. Health Econ 16:1009–1023
23. Rotstein C, Cragin L, Laverdiere M et al (2008) Economic evaluation of voriconazole for the treatment of candidemia in Canadian adults. Can J Infect Dis Med Microbiol 19:219–226
24. Turner SJ, Senol E, Kara A, Al-Badriyeh D, Dinleyici EC, Kong DC (2013) Pharmacoeconomic evaluation of voriconazole vs. liposomal amphotericin B in empiric treatment of invasive fungal infections in Turkey. BMC Infect Dis 13:560
25. Dixon S, McKeen E, Tabberer M, Paisley S (2004) Economic evaluations of treatments for systemic fungal infections: a systematic review of the literature. PharmacoEconomics 22:421–433
26. Johnson MD, Kleinberg M, Danziger L, Ostrosky-Zeichner L (2005) Pharmacoeconomics of antifungal pharmacotherapy: challenges and future directions. Expert Opin Pharmacother 6:2617–2632
27. Arnold HM, Micek ST, Shorr AF et al (2010) Hospital resource utilization and costs of inappropriate treatment of candidemia. Pharmacotherapy 30:361–368
28. Petitti DB (2000) Meta-analysis, decision analysis, and cost-effectiveness analysis. Oxford University Press, New York
29. Gold M, Siegel J, Russell L et al (1996) Cost-effectiveness in health and medicine. Oxford University Press, New York