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# Efficacy of anidulafungin in 539 patients with invasive candidiasis: a patient-level pooled analysis of six clinical trials

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**Objectives:** To evaluate the efficacy of anidulafungin for the treatment of candidaemia and invasive candidiasis in a large dataset, including patients with deep-seated tissue candidiasis, neutropenia and infection due to non-*albicans Candida* species.

**Methods:** Data were pooled from six prospective, multicentre, multinational studies: four open-label, non-comparative studies of anidulafungin and two double-blind, double-dummy, randomized studies of anidulafungin versus caspofungin (clinical trial registrations: NCT00496197, NCT00548262, NCT00537329, NCT00689338, NCT00806351 and NCT00805740; ClinicalTrials.gov). In all studies, patients with culture-confirmed invasive candidiasis received a single intravenous (iv) loading dose of anidulafungin 200 mg on day 1, followed by 100 mg once-daily. Switch to oral fluconazole or voriconazole was permitted after 5–10 days of iv treatment in all studies except one. Antifungal treatment (iv plus oral therapy if applicable) was maintained for ≥14 days after the last positive *Candida* culture. The primary endpoint was successful global response at end of iv therapy (EOivT) in the modified ITT (mITT) population.

**Results:** In total, 539 patients were included (mITT population). The most common baseline *Candida* species were *Candida albicans* (47.9%), *Candida glabrata* (21.0%), *Candida tropicalis* (13.7%), *Candida parapsilosis* (13.2%) and *Candida krusei* (3.5%). Median duration of anidulafungin iv treatment was 10.0 days. The global response success rate at EOivT was 76.4% (95% CI 72.9%–80.0%). All-cause mortality was 13.0% on day 14 and 19.1% on day 28. Adverse events (AEs) were consistent with the known AE profile for anidulafungin.

**Conclusions:** These data demonstrate that anidulafungin is effective for treatment of candidaemia and invasive candidiasis in a broad patient population.

## Introduction

*Candida* species are among the leading causes of invasive fungal disease worldwide and one of the most common causes of hospital-acquired bloodstream infections, particularly in patients with cancer, receiving transplants or in ICUs.[1] Invasive candidiasis is associated with high mortality, ranging from 15% to 25% in adult patients.[2] High mortality is related to several factors, such as lack of adequate diagnostic assays, associated comorbidities, disease severity and the *Candida* species involved.[3–8] Although *Candida albicans* is the leading cause of invasive candidiasis in most clinical settings, approximately 50% of patients are now infected with

non-*albicans Candida* species.[9] The changing epidemiology has been partly attributed to the selection of less-susceptible *Candida* species/strains due to widespread and long-term use of fluconazole as a prophylactic and therapeutic agent.[10]

ESCMID recommends echinocandins as first-line treatment for patients with systemic candidiasis.[11] The 2016 Infectious Diseases Society of America guidelines also recommend echinocandins as first-line treatment for candidaemia in both non-neutropenic and neutropenic patients. Furthermore, echinocandins are recommended as an empirical therapy for suspected invasive candidiasis in non-neutropenic ICU patients, and for intra-abdominal candidiasis.[7] Echinocandins are highly active against a range of *Candida* species, resistance to them is rare and they are well tolerated, with similar safety profiles and few drug–drug interactions.[12]

Anidulafungin is an echinocandin that is approved for candidaemia/invasive candidiasis.[13,14] However, efficacy data for its use in patients with deep-seated tissue infections, neutropenia and infections due to *Candida krusei* and other non-*albicans Candida* species are limited. The registration trial of anidulafungin versus fluconazole enrolled too few patients in these groups to generate meaningful data regarding efficacy and excluded patients with *C. krusei* infections[15] (which are intrinsically resistant to fluconazole), thus highlighting the need for additional studies in these patients.

In this analysis, patient-level data from six studies were pooled to assess the efficacy of anidulafungin in a large dataset, including patients with deep-seated tissue candidiasis, neutropenia and infections due to *C. krusei* and other non-*albicans Candida* species.

## Patients and methods

### Ethics

All studies are registered with ClinicalTrials.gov and were conducted in compliance with the Declaration of Helsinki and International Conference on Harmonisation Good Clinical Practice Guidelines. The final protocols, amendments and informed consent documentation were reviewed and approved by the Institutional Review Boards and Independent Ethics Committees of the investigational centres. Patients provided written, informed consent.

### Study design and treatment

Data were pooled from six prospective, multicentre, multinational studies of patients with culture-proven candidaemia or invasive candidiasis (NCT00496197, NCT00548262, NCT00537329, NCT00689338, NCT00806351, NCT00805740):[16–19] four open-label, non-comparative studies, and two double-blind, double-dummy, randomized studies. The studies had similar study protocols and endpoints (Table S1, available as Supplementary data at *JAC* Online). Patients received intravenous (iv) anidulafungin 200 mg on day 1 followed by 100 mg once-daily. In all studies except one, treatment could be switched to oral fluconazole or voriconazole after ≥5 or ≥10 days of iv treatment. Antifungal treatment (iv plus oral if used) was maintained for ≥14 days after the last positive *Candida* culture.

### Patients

#### Key inclusion criteria

The pooled analysis included data from adult patients with culture-confirmed candidaemia (positive blood culture) or invasive candidiasis (positive culture for *Candida* species from a normally sterile site, or newly placed drain in a normally sterile site, with or without a positive blood culture for *Candida* species) obtained within 96 h prior to the initiation of treatment. Patients could enter studies based on microbiological evidence suggestive of *Candida* infection (e.g. positive blood or tissue specimen culture positive for yeast); however, confirmation of *Candida* species was required within 96 h to remain in the study. Patients were required to have clinical signs and symptoms of systemic *Candida* infection, such as: fever, hypothermia or hypotension within 48 h before starting treatment; localized signs and symptoms of inflammation at a site infected with *Candida* species; or radiological findings suggestive of invasive candidiasis.

In the pooled database, patients were identified as neutropenic if they had a baseline absolute neutrophil count (ANC) of ≤500 cells/μL or a total white blood cell (WBC) count of ≤500 cells/μL, or if they had been classified as neutropenic at baseline by the investigators.

#### Key exclusion criteria

Patients were excluded if they: received >48 h of prior antifungal therapy; had at infection sites prosthetic devices or vascular catheters (including central venous catheters) that could not be removed prior to or within 24–48 h of study entry; or had previously failed treatment for the current episode of candidaemia or invasive candidiasis.

### Objectives/study endpoints

The purpose of the analysis was to determine the efficacy of anidulafungin for the treatment of candidaemia and invasive candidiasis in a large dataset, including patients with deep-seated tissue candidiasis, neutropenia and infections due to *C. krusei* and other non-*albicans Candida* species.

The ITT population comprised all patients who received ≥1 dose of anidulafungin and was used for the safety analysis. The modified ITT (mITT) population comprised all patients in the ITT population with candidaemia/culture-confirmed invasive candidiasis who received ≥1 dose of anidulafungin, and was used for the efficacy analysis.

### Efficacy endpoints

The primary efficacy endpoint was global response at end of iv therapy (EOivT) in the mITT population. A global response was considered successful if there was both clinical success (resolution of signs and symptoms of candidaemia/invasive candidiasis and no need for additional systemic antifungal therapy for *Candida* infection) and microbiological success (eradication of *Candida* species present at baseline, as determined on follow-up culture, or presumed eradication where follow-up culture samples could not be obtained for a patient with a successful clinical response). Global response at end of treatment (EOT) in the mITT population and all-cause mortality on days 14 and 28 after the first administration of study drug (ITT and mITT populations) were secondary endpoints.

### Safety and tolerability endpoints

Safety was a secondary endpoint. Adverse events (AEs; occurring during active treatment or within 30 days of the last dose of treatment) and serious AEs (SAEs) were collected from all studies and summarized by Medical Dictionary for Regulatory Activities (MedDRA)-preferred term. Treatment-related AEs were based on the investigators' judgement.

### Statistical analysis

No hypotheses for efficacy endpoints were tested. Success rates for global response were estimated with 95% CIs for binomial proportion using the Clopper–Pearson method. In the efficacy analysis, indeterminate or missing data were considered failures.

Multivariate logistic regression was used to identify independent predictors significantly related to failures. The following continuous variables were included in the model: age, weight and baseline APACHE II score. Dichotomous variables were: neutropenia; sex; broad-spectrum antibiotic use; central venous catheter use; ICU stay ≥4 days; total parenteral

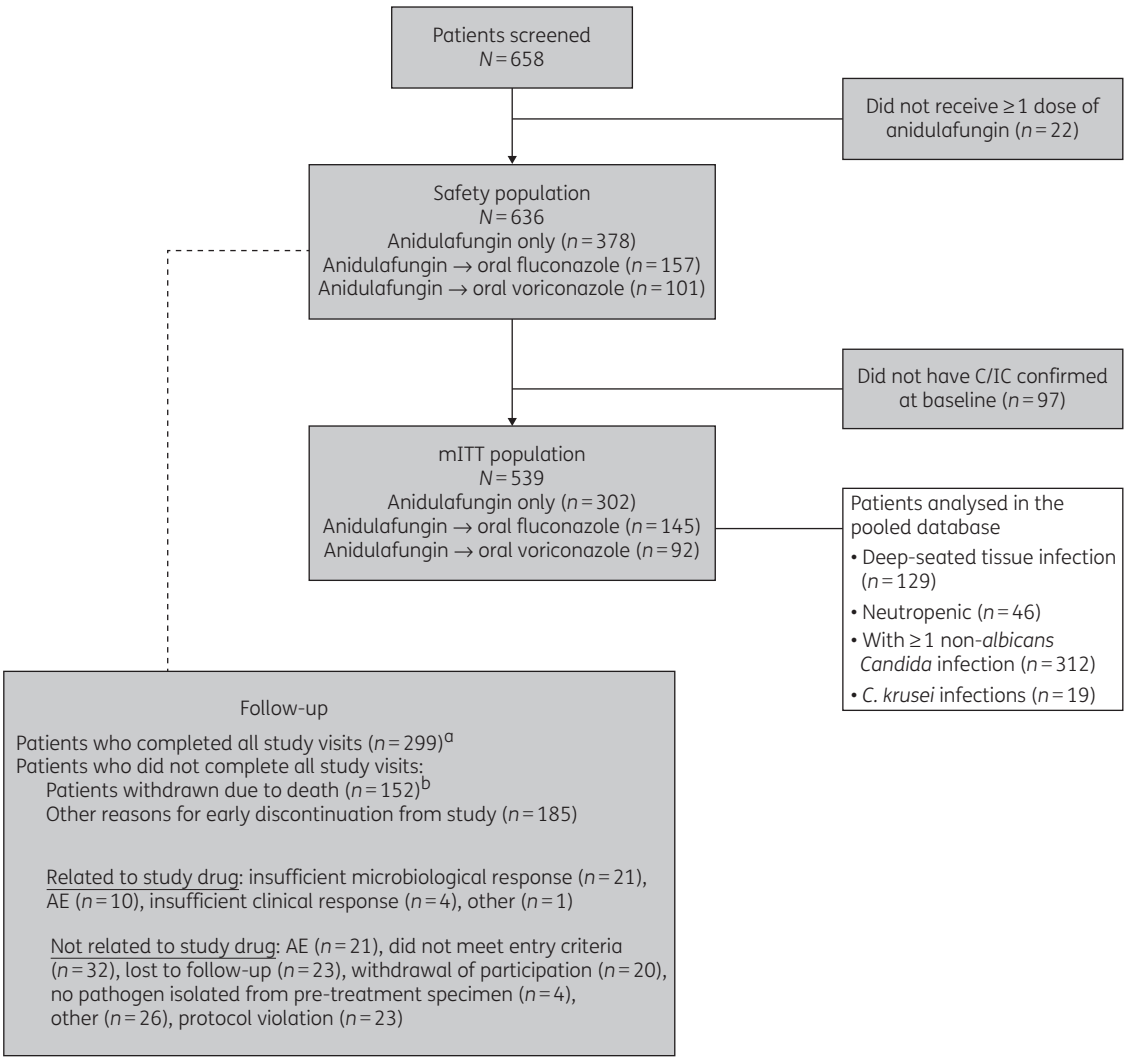


**Figure 1.** Patient disposition. AE, adverse event; C/IC, candidaemia or invasive candidiasis; mITT, modified ITT. [a]Patients who completed all visits as described in the respective protocols. [b]In the period from the first dose of study medication until the end of study follow-up visit.

nutrition; surgery or abdominal surgery; mechanical ventilation; renal insufficiency/failure/dialysis; use of systemic steroids or other immunosuppressive agents; chemotherapy; and presence of multiple baseline pathogens.

## Results

### *Patients*

Across the six studies, 636 patients received ≥1 dose of anidulafungin (ITT population; Figure 1). Among these, 539 patients had culture-confirmed candidaemia or invasive candidiasis at baseline or within 96 h of treatment initiation (mITT population).

Patient demographics and baseline characteristics in the mITT population are presented in Table 1. Most patients were male, with a mean age of 57.5 years, and had a median (range) APACHE II score of 15.0 (2–44). The most frequently isolated *Candida* species at baseline was *C. albicans* (47.9%), followed by *Candida glabrata* (21.0%), *Candida tropicalis* (13.7%), *Candida parapsilosis* (13.2%) and *C. krusei* (3.5%). Overall, 496 (92.0%) patients had one *Candida* species recovered at baseline and 43 (8.0%) patients had >1 *Candida* species recovered at baseline.

The median (range) duration of anidulafungin iv treatment was 10.0 (1–42) days, with a median (range) duration of overall therapy (iv and oral) of 15.0 (1–67) days. Details on switching to oral therapy are given in Table 2.

### *Efficacy*

The global response success rate at EOivT was 76.4% (95% CI 72.9%–80.0%), with a clinical success rate of 80.3% (95% CI 77.0%–83.7%) and a microbiological success rate of 82.4% (95% CI 79.2%–85.6%) (Figure 2a).

Global response success rates at EOivT varied by pathogen and are shown in Figure 3(a). Similar findings were observed for global response success rates at EOT (Table S2). All-cause mortality in the

**Table 1.** Patient demographics and baseline characteristics (mITT population)

| Characteristic | Total ($N = 539$) |
|---|---|
| Sex, *n* (%) | |
| male | 297 (55.1) |
| Age, years | |
| mean (SD) | 57.5 (16.3) |
| range | 18–91 |
| White/Black/Asian/other/not specified, % | 69.0/10.9/12.4/6.1/1.5 |
| Weight, kg | |
| mean (SD) | 74.4 (21.6) |
| range | 32.0–240.0 |
| Baseline APACHE II score ($N = 536$) | |
| mean (SD) | 14.9 (6.2) |
| median | 15.0 |
| range | 2–44 |
| APACHE II score $\leq$20, *n* (%) | 435 (80.7) |
| APACHE II score >20, *n* (%) | 101 (18.7) |
| Risk factors for invasive candidiasis, *n* (%)[a] | |
| broad-spectrum antibiotics | 421 (88.4) |
| central venous catheter | 377 (79.2) |
| length of ICU stay $\geq$4 days | 236 (49.6) |
| total parenteral nutrition | 215 (45.2) |
| surgery | 213 (44.7) |
| mechanical ventilation | 197 (41.4) |
| abdominal surgery | 192 (40.3) |
| renal failure | 151 (31.7) |
| other[b] | 125 (26.3) |
| use of systemic steroids or other immunosuppressants | 120 (25.2) |
| anticancer chemotherapy | 67 (14.1) |
| neutropenia[c] | 43 (9.0) |
| solid organ transplant | 28 (5.9) |
| Baseline pathogen, *n* (%)[a] | |
| *Candida albicans* | 258 (47.9) |
| *Candida glabrata* | 113 (21.0) |
| *Candida tropicalis* | 74 (13.7) |
| *Candida parapsilosis* | 71 (13.2) |
| *Candida krusei* | 19 (3.5) |
| *Candida kefyr* | 6 (1.1) |
| *Candida dubliniensis* | 5 (0.9) |
| *Candida guilliermondii* | 4 (0.7) |
| *Candida famata* | 3 (0.6) |
| *Candida lusitaniae* | 3 (0.6) |
| *Candida pelliculosa* | 3 (0.6) |
| *Candida norvegensis* | 2 (0.4) |
| *Candida rugosa* | 1 (0.2) |
| Baseline site of infection, *n* (%) | |
| blood only | 408 (75.7) |
| non-blood sterile site only | 111 (20.6) |
| blood and non-blood sterile site | 20 (3.7) |

mITT, modified ITT.
[a]Patients may be counted in >1 category.
[b]'Other' risk factors included: mucosal colonization ($n = 52$); immunosuppressive therapy ($n = 23$); diabetes ($n = 8$); and other recorded risk factors ($n = 49$).
[c]Forty-three patients had neutropenia as a risk factor at baseline as reported by the investigator in the case report form, and did not necessarily correspond to the 46 patients identified as neutropenic in the pooled database as per the definition in the inclusion criteria.

mITT population was 13.0% ($n = 70/539$) on day 14 and 19.1% ($n = 103/539$) on day 28.

### *Patients with deep-seated tissue candidiasis*

A total of 129 patients with microbiologically confirmed deep-seated tissue candidiasis of $\geq$1 organs, with or without concomitant candidaemia, were analysed. Patients had a mean (SD) age of 60.2 (16.6) years and a median (range) APACHE II score of 15.0 (2–44).

The most frequently isolated *Candida* species at baseline were *C. albicans* (64.3%), *C. glabrata* (31.0%), *C. tropicalis* (11.6%) and *C. krusei* (5.4%). Sixteen (12.4%) patients had multiple *Candida* species recovered at baseline. The sites of infection were intra-abdominal ($n = 107$; 82.9%), pleural cavity ($n = 7$; 5.4%), kidney ($n = 5$; 3.9%), lung ($n = 4$; 3.1%), bone ($n = 2$; 1.6%), eye ($n = 2$; 1.6%), skin/soft tissue ($n = 2$; 1.6%) and other sites ($n = 5$; 3.9%). Of these 129 patients, 21 (16.3%) had concomitant candidaemia.

The median (range) duration of iv anidulafungin treatment was 14.0 (1–42) days and the median (range) duration of overall therapy (iv and oral) was 16.0 (1–56) days. The global response success rate at EOivT was 79.1% (95% CI 72.0%–86.1%) (Figure 2b). Global response success rates at EOivT varied by pathogen, with the highest response rates observed in patients with infections due to *C. glabrata* (80.0%; 95% CI 67.6%–92.4%) and *C. albicans* (79.5%; 95% CI 70.8%–88.2%) (Figure 3b). All-cause mortality in the mITT population was 14.7% ($n = 19/129$) on day 14 and 20.2% ($n = 26/129$) on day 28.

### *Patients with neutropenia*

Overall, 46 neutropenic patients were identified (mITT population) based on an ANC of $\leq$500 cells/μL or a WBC of $\leq$500 cells/μL, or if they had been classified as neutropenic by the investigators at baseline.

Most patients were white ($n = 33$; 71.7%) and male ($n = 28$; 60.9%), with a mean age of 56.0 years. Among patients with ANC or WBC available at baseline and throughout the treatment period ($n = 28$), median (range) duration of neutropenia was 16.0 (1–43) days. Coexisting conditions in 46 neutropenic patients included leukaemia ($n = 21$; 45.7%), lymphoma ($n = 11$; 23.9%), plasma cell disorder [plasma cell myeloma or plasmacytoma ($n = 6$; 13.0%)], solid tumour ($n = 7$; 15.2%) and bone marrow transplant ($n = 4$; 8.7%). There were 58 *Candida* strains isolated at baseline in the 46 neutropenic patients (16 *C. tropicalis*; 9 *C. krusei*; 8 *C. parapsilosis*; 7 *C. albicans*; 7 *C. glabrata*; 4 *Candida keyfr*; 2 *Candida ciferrii*; 2 *Candida famata*; 1 *Candida dubliniensis*; 1 *Candida guilliermondii* and 1 *Candida norvegensis*).

Nine (19.6%) patients had multiple *Candida* species recovered at baseline.

The median (range) duration of anidulafungin iv treatment was 11.5 (1–42) days and the median duration of overall therapy (iv and oral) was 16.0 (1–67) days. Overall, 16 patients (34.8%) switched from iv to oral therapy (7 patients to fluconazole and 9 to voriconazole). The median (range) duration of oral therapy was 11.5 (6–38) days.

The global response success rate at EOivT was 56.5% (95% CI 42.2%–70.8%) (Figure 2b). Among patients with ANC or WBC available at baseline visit, throughout the study treatment period and

**Table 2.** Duration and time to switch to oral therapy for all patients (modified ITT population)

| | All patients with switch permitted[a] (*N* = 515) | |
|---|---|---|
| | switch permitted after ≥5 days[b] (*N* = 334) | switch permitted after ≥10 days[c] (*N* = 181) |
| Patients switching to oral therapy, *n* (%) | 173 (51.8) | 63 (34.8) |
| Duration of oral therapy, days | | |
| median | 6.0 | 14.0 |
| mean | 8.0 | 16.6 |
| range | 5–28 | 11–38 |
| Time to switch to oral therapy, days | | |
| median | 5.0 | 13.0 |
| mean | 7.0 | 15.5 |
| range | 4–27 | 7–37 |
| Patients switching to voriconazole therapy, *n* (%) | 76 (22.8) | 16 (8.8) |
| Duration of voriconazole therapy, days | | |
| median | 7.0 | 13.5 |
| mean | 8.6 | 17.1 |
| range | 5–28 | 11–38 |
| Time to switch to voriconazole therapy, days | | |
| median | 6.0 | 12.0 |
| mean | 7.5 | 16.0 |
| range | 4–27 | 10–37 |
| Patients switching to fluconazole therapy, *n* (%) | 97 (29.0) | 47 (26.0) |
| Duration of fluconazole therapy, days | | |
| median | 6.0 | 14.0 |
| mean | 7.6 | 16.4 |
| range | 5–25 | 11–35 |
| Time to switch to fluconazole therapy, days | | |
| median | 5.0 | 13.0 |
| mean | 6.5 | 15.3 |
| range | 4–24 | 7–34 |

[a]In study A8851022, switch to oral therapy was not permitted and 24 patients were not included in this table.
[b]Studies A8851011, A8851015 and A8851016.
[c]Studies A8851019 and A8851021.

at EOT visit, the global response success rate at EOivT in patients with persistent neutropenia was 53.8% (*n* = 7/13; 95% CI 26.7%–80.9%) versus 80.0% (*n* = 12/15; 95% CI 59.8%–100.0%) among patients who had resolved neutropenia. Global response success rates at EOivT by pathogen are shown in Figure 3(c).

All-cause mortality in the mITT population was 19.6% (*n* = 9/46) on day 14 and 23.9% (*n* = 11/46) on day 28.

### *Patients with infections due to non-albicans Candida species*

A total of 312 patients had infection due to ≥1 non-*albicans Candida* species, of whom 269 were infected by a single non-*albicans Candida* strain. Patient demographics and baseline characteristics for the most commonly isolated baseline *Candida* species are presented in Table S3. Of infections due to non-*albicans Candida* species, most were due to *C. glabrata* (*n* = 113/312; 36.2%), followed by *C. tropicalis* (*n* = 74/312; 23.7%) and *C. parapsilosis* (*n* = 71/312; 22.8%). *In vitro* susceptibility to anidulafungin was 100% for all *Candida* species except *C. parapsilosis* (86.7%) (Table S4). MICs of anidulafungin were higher for *C. parapsilosis* compared with other *Candida species*.

Among patients infected by non-*albicans Candida* species, global response success rates at EOivT by main pathogen are shown in Figure 3(a). The global response success rate at EOivT was 75.8% (*n* = 204/269) in patients infected by a single non-*albicans Candida* species versus 74.2% (*n* = 23/31) in patients with mixed *C. albicans* and non-*albicans Candida* species. In patients with infection due to ≥2 non-*albicans Candida* species, the global response success rate at EOivT was 66.7% (*n* = 8/12) (Table 3).

All-cause mortality in the monomicrobial and polymicrobial mITT population is presented in Table 3.

### *Patients with infection due to C. krusei*

In total, 19 patients with *C. krusei* infection were identified. At baseline, 57.9% of patients (*n* = 11/19) were candidaemic while 42.1% (*n* = 8/19) were neutropenic (<500 cells/μL). Median (range) APACHE II score was 16.0 (5–24). Patient demographics and baseline characteristics are presented in Table S3. All *C. krusei* isolates were susceptible to anidulafungin *in vitro*. The global

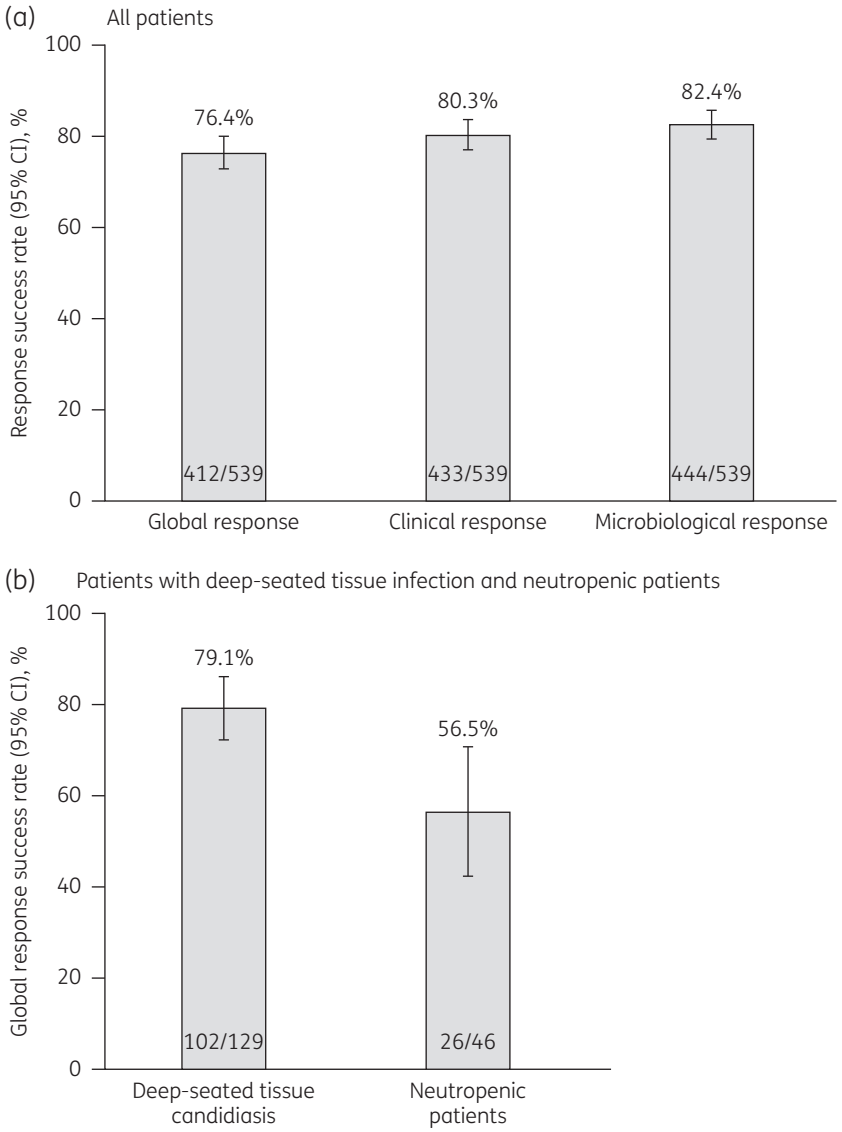


**Figure 2.** (a) Global, clinical and microbiological response success rates in all patients at end of intravenous therapy (EOivT); and (b) global response success rates at EOivT in patients with deep-seated tissue infection and neutropenic patients (mITT population).

response success rate at EOivT was 73.7% (95% CI 53.9%–93.5%) (Figure 3a).

All-cause mortality in the mITT population was 5.3% ($n = 1/19$) on both days 14 and 28.

### *Multivariate logistic regression*

In the multivariate logistic regression analysis of the global population, neutropenia [odds ratio (OR) 2.6; 95% CI 1.1–6.2], and higher APACHE II scores (OR 1.1; 95% CI 1.0–1.1) were identified as factors associated with global response of failure (Table S5).

### *Safety*

A total of 636 patients received treatment with anidulafungin. At least one AE was reported in 554 patients (87.1%). The most frequently reported AEs were in the categories of infections (40.6%), gastrointestinal disorders (34.0%), and respiratory, thoracic and mediastinal disorders (28.6%). The most common (≥5%) AEs by MedDRA-preferred term were diarrhoea (10.2%), hypokalaemia (9.0%), pyrexia (8.6%), hypotension (8.0%), septic shock (7.1%), nausea (6.9%), vomiting (6.4%), anaemia (6.1%) and hypertension (5.8%). Most AEs were mild or moderate in severity. There were 192 reported treatment-related AEs in 99 (15.6%) patients and most were mild or moderate. Ten (1.6%) patients discontinued therapy due to treatment-related AEs.

A total of 527 SAEs occurred in 301 patients. The most common categories were infections and infestations (18.7%), respiratory, thoracic and mediastinal disorders (9.4%), cardiac disorders (8.6%), general disorders and administration-site conditions (7.5%), and gastrointestinal disorders (6.9%).

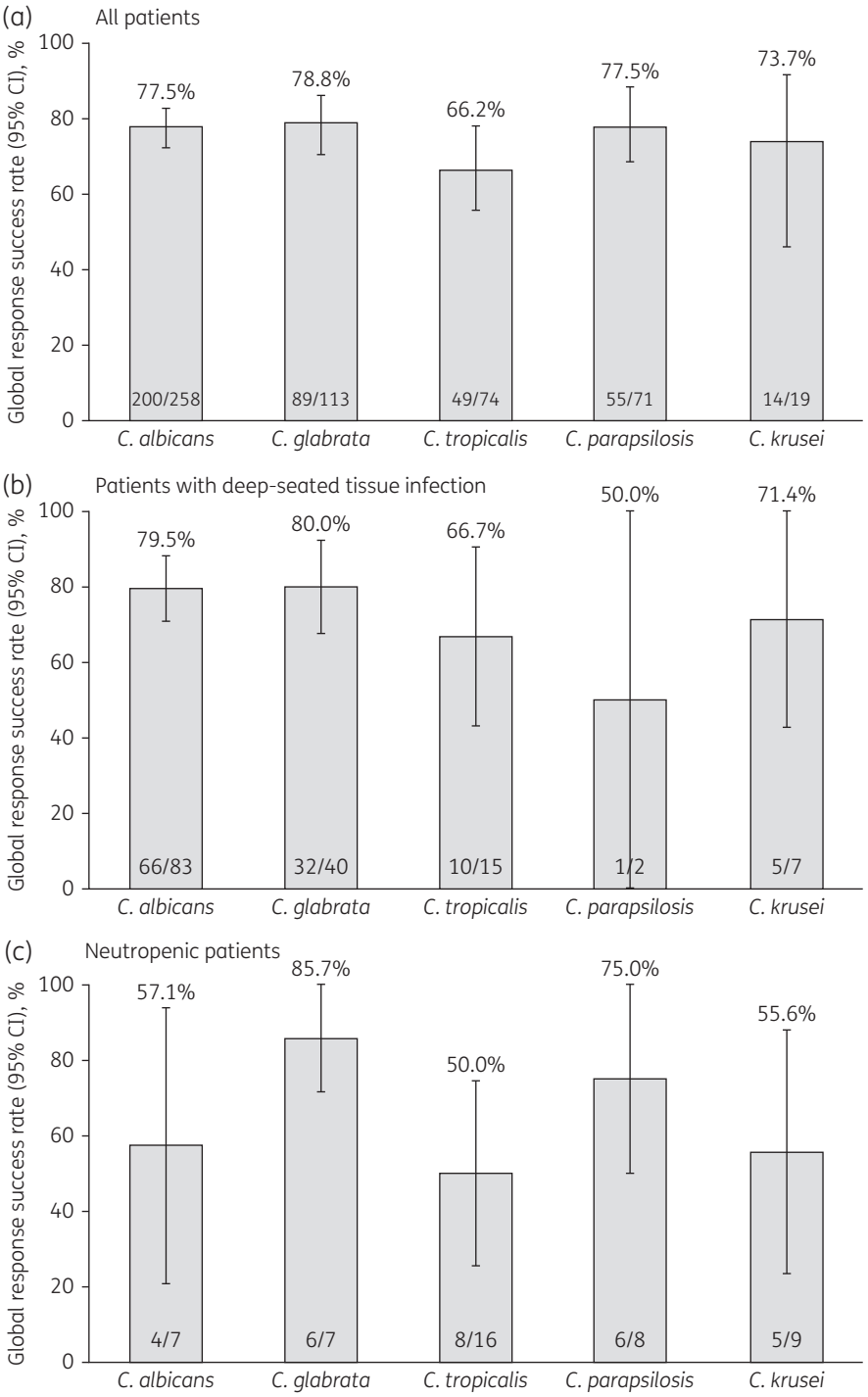


**Figure 3.** Global response success rates at end of intravenous therapy stratified by main baseline pathogen (patients could have more than one *Candida* species at baseline) in (a) all patients, (b) patients with deep-seated tissue candidiasis and (c) neutropenic patients.

No new safety concerns were identified in the overall pooled population or in any of the patient subgroups analysed.

All-cause mortality in the ITT population was 13.2% ($n = 84/636$) on day 14 and 19.3% ($n = 123/636$) on day 28.

## Discussion

This patient-level pooled analysis of six studies evaluated the efficacy of anidulafungin for the treatment of candidaemia and invasive candidiasis in all patients and in subgroups with deep-seated

**Table 3.** Distribution of patients with infections caused by a single or multiple *Candida* isolates, at baseline, global response at end of intravenous therapy (EOivT) and all-cause mortality (days 14 and 28) in the modified ITT (mITT) population ($N = 539$)

| Patients with *Candida* infection at baseline | | Global response at EOivT, *n* (%); 95% CI | All-cause mortality, *n* (%) | |
|---|---|---|---|---|
| | | | day 14 | day 28 |
| Patients with single *Candida* isolate, *n* (%) | 496 (92.0) | | | |
| *C. albicans*, *n* (%) | 227 (45.8) | 177 (78.0); 72.6%–83.4% | 32 (14.1) | 44 (19.4) |
| *C.* non-*albicans*, *n* (%) | 269 (54.2) | 204 (75.8); 70.7%–81.0% | 33 (12.3) | 51 (19.0) |
| Patients with multiple *Candida* isolates | 43 (8.0) | | | |
| *C. albicans* and ≥1 *C.* non-*albicans* | 31 (72.1) | 23 (74.2); 58.8%–89.6% | 3 (9.7) | 6 (19.4) |
| >1 *C.* non-*albicans* | 12 (27.9) | 8 (66.7); 40.0%–93.3% | 2 (16.7) | 2 (16.7) |

tissue infections, neutropenia and infections due to non-*albicans Candida* species, including *C. krusei*. We believe these data represent the largest collection of patients in special populations with *Candida* infection and treated with the same iv antifungal drug (anidulafungin) in a clinical trial setting.

Anidulafungin alone (iv), or followed by a switch to oral fluconazole/voriconazole, was effective for candidaemia and invasive candidiasis in all study populations. The overall global response rate at EOivT (76.4%) was similar to that reported in the anidulafungin registration study (75.6%),[15] despite the shorter duration of iv therapy and earlier transition to oral therapy in this pooled analysis. This was also similar to the EOivT success rate reported in the caspofungin registration trial (73.4%).[20] *C. albicans* and *C. glabrata* were still the most common baseline pathogens in the current analysis, similar to the epidemiological findings reported in the anidulafungin registration study.[15] In contrast, *C. tropicalis* was the most commonly recovered baseline pathogen in patients with neutropenia (34.8%).

In patients with deep-seated tissue candidiasis, the global response success rate at EOivT (79.1%) was high and consistent with the registration study (75.6%).[15]

The global response success rates of anidulafungin in patients with neutropenia were also comparable to those found in other studies.[20–22] Rates of successful global response at EOivT in patients with resolved neutropenia (80.0%) and persistent neutropenia (53.8%) were similar to those reported for micafungin in similar patients (75.0% and 50.0%, respectively).[21] These data, together with the multivariate analysis, support the well-known concept that outcomes in persistently neutropenic patients are typically worse than in patients without neutropenia.

The global response success rate in patients with *C. albicans* was 77.5%, consistent with the rate reported in the registration study (81.1%).[15] Previous studies have reported that anidulafungin may be less potent for the treatment of *C. glabrata*;[23–25] however, in this study, the global response rate was 78.8%. Response rates among patients with infection due to *C. tropicalis* and *C. krusei* were 66.2% and 73.7%, respectively.

Consistent with previous studies, MICs in this study were higher for *C. parapsilosis* versus other *Candida* species.[7,26–31] Data on the effectiveness of echinocandins against *C. parapsilosis* are limited.[15,20–22] Furthermore, *C. parapsilosis* has been associated with higher persistence and breakthrough rates among patients receiving an echinocandin.[1] The results of this analysis show that anidulafungin had a success rate of 77.5%, comparable with that observed in patients with infection due to *C. albicans*.

The efficacy of anidulafungin in patients with infections due to different non-*albicans Candida* species was similar to that of caspofungin in a pooled analysis.[32] *C. krusei* is intrinsically resistant to fluconazole, and echinocandins appear to be the most active against this important pathogen.[33,34] In the anidulafungin registration trial the patients infected with *C. krusei* had to be excluded because fluconazole was used as comparator.[15] The present dataset is the largest to provide prospectively collected information on the efficacy of anidulafungin against *C. krusei*.

We demonstrate for the first time that anidulafungin is effective for the treatment of patients with infection due to *C. krusei* with a success rate of 73.7% at EOivT and where 42.1% of patients were neutropenic. In addition, the present study reports on the largest prospectively collected set of patients with infection due to *C. glabrata*, which may exhibit resistance to both azoles and echinocandins.[35] We demonstrate a success rate of anidulafungin of 78.8%, which is not significantly different from that for *C. albicans* infections in the same pooled dataset.

AEs were mostly mild or moderate in severity, and consistent with the known safety profile of anidulafungin in adult patients with invasive candidiasis/candidaemia, with no new safety concerns identified.

Limitations to this analysis were that four studies were open label and conducted at various sites and centres, and at different times. In addition, the two double-blind, double-dummy, randomized studies of anidulafungin versus caspofungin included in the present analysis have not been peer-reviewed and published previously. Furthermore, this was a *post hoc* analysis.

In conclusion, response to anidulafungin in this large dataset of patients with invasive candidiasis/candidaemia was consistent with previously reported data, supporting registration trial findings. Anidulafungin is effective for the treatment of invasive candidiasis/candidaemia (including deep-seated tissue candidiasis), infections in patients with neutropenia and infections due to non-*albicans Candida* species.

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B. J. K. or his employer have received personal fees from Astellas, Amplyx, Cidara, Gilead and Pfizer. B. J. K. received remuneration from Pfizer for his services as a member of the Data Monitoring Committee for studies A8851021 and A8851022. M. N. has received research grant support from Merck and Pfizer, and personal fees from Astellas, Basilea, Gilead, Merck and Pfizer. R. H. has received research grant support from Pfizer, and has received personal fees from Astellas, Basilea, Gilead, Merck and Pfizer. During the conduct of the study, P. M. received research grant support from Pfizer. J. L. Y., J. A., U. C., and M. R. C. are employees of Pfizer. H. S. and R. S. were employees of Pfizer during the conduct of the study. All other authors have nothing to disclose.

### *Author contributions*

All authors were involved in the concept and design of this analysis. J. L. Y., J. A., M. R. C. and U. C. were involved in data collection for this analysis. All authors were involved in data analysis and interpretation, manuscript writing and approved the final manuscript. All authors are accountable for all aspects of the work.

## Supplementary data

Tables S1–S5 are available as Supplementary data at *JAC* Online (http://jac.oxfordjournals.org/).

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