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PROPRIETARY DRUG NAME® / GENERIC DRUG NAME: Eraxis™ / Ecalta® / Anidulafungin

PROTOCOL NO.: A8851021

PROTOCOL TITLE: Efficacy and Safety of Eraxis™/Ecalta® (Anidulafungin) Compared to Cancidas® (Caspofungin) in Neutropenic Patients With Invasive Candida Infection

Study Centers: A total of 10 centers in 6 countries took part in the study and randomized subjects; 3 centers in Poland, 2 centers each in France and Italy, 1 center each in Bosnia and Herzegovina, the Russian Federation, and Slovakia.

Study Initiation and Final Completion Dates: 12 August 2009 to 17 October 2011; this study was terminated prematurely on 18 May 2012 due to slow enrollment.

Phase of Development: Phase 3b

Study Objectives:

Primary Objective

- To assess the efficacy of anidulafungin and caspofungin with respect to the overall global response (clinical and microbiological success) at the end of intravenous treatment (EOIVT) in neutropenic subjects with a confirmed diagnosis of invasive infection due to *Candida* species.

Secondary Objectives:

- To evaluate the safety profile of anidulafungin and of caspofungin in this population.
- To evaluate the clinical and microbiological efficacy of anidulafungin and of caspofungin at various time points.

METHODS

Study Design: This was a Phase 3b, comparative, double-blind (third-party unblinded), double-dummy, randomized, multicenter, multinational, descriptive study of anidulafungin versus caspofungin for the treatment of culture-confirmed invasive candidiasis due to *Candida* species in neutropenic subjects ≥16 years of age.

Eligible subjects with a high suspicion of *Candida* infection were enrolled and had study treatment initiated, pending culture confirmation. Subjects in whom culture confirmation

was not obtained within 96 hours after enrollment, were to be discontinued from study treatment (but were to remain in the study for safety assessment only), and were then treated according to local standard practice. These subjects did not count toward the sample size of evaluable subjects.

Study treatment consisted of intravenous (IV) therapy with either anidulafungin or caspofungin (administered in a blinded fashion), with an option to switch to oral therapy with either fluconazole or voriconazole after at least 10 days of IV therapy, provided signs and symptoms of *Candida* infection were resolved and 2 consecutive cultures of blood and/or other specimens (as applicable) were negative. Oral drug therapy, if given, was administered in an unblinded, open-label fashion.

Study treatment, given either entirely as IV therapy or as sequential IV/oral therapy, was to be administered for at least 14 days following resolution of clinical signs and symptoms and after the last positive culture for *Candida* species. A maximum of 42 days of IV therapy and a maximum of 14 days of oral therapy was allowed. Thus, subjects may have received up to a maximum of 56 days of study therapy. Duration of trial was a minimum of 8 weeks and up to a maximum of 14 weeks, depending on subject response to therapy and the duration of each subjects' study drug administration.

The schedule of activities presented in Table 1.

Table 1. Schedule of Activities

	Screen[a]	Treatment Initiation (Day 1)	Daily Through EOT	Every 3 Days Through EOT	Day 10	End of IV Treatment (EOIVT)	End of Treatment (EOT)[b]	Follow-Up Visits at Week 2 (± 2 Days) and Week 6 (± 1 Week)[c]
Informed consent	X	-	-	-	-	-	-	-
Confirm eligibility, assign study number	X	-	X[d]	-	-	-	-	-
Randomization		X	-	-	-	-	-	-
Medical, surgical, and medication history	X	-	-	-	-	-	-	-
APACHE II[e]	X[e]	-	X[e]	-	-	X[e]	X[e]	-
Complete physical examination	X[f]	-	-	-	-	-	-	-
Brief physical examination[g]	-	X[h]	-	-	-	X	X	X
Temperature	X	X	X[i]	-	-	X	X	X
Signs and symptoms of Candida infection	X	X	-	X[i]	X	X	X	X
Fundoscopic examination[j]	X[k]	-	-	X[l]	-	X[l]	X[l]	X[l]
Serum or urine pregnancy test[m]	X[m]	-	-	-	-	X[m]	X[m]	X[m]
Blood cultures	X[n]	-	X[o]	-	-	X	X	X
Specimen cultures	X[p]	-	-	X[q]	-	X[q]	X[q]	X[q]
Hematology[r]	X	-	X[s]	-	-	X	X	X
Chemistry panel[t,s]	X	-	-	X[i]	-	X	X	X
Child-Pugh score	X	-	X[t]		-	-	-	-
(1,3)-βD-glucan[u]	X	-	-	X[u]	-	X	X	-
Study drug	-	X	X	-	-	X	X	-
Concomitant medications	X	X	X	-	-	X	X	X[v]
Assessment of clinical response	-	-	-	-	X[w]	-	-	-
Assessment of clinical and microbiologic success	-	-	-	-	-	X	X	X
Adverse events	-	X	X	-	-	X	X	X

AE = adverse event; ALT = alanine aminotransferase; APACHE = Acute Physiology and Chronic Health Evaluation; AST = aspartate aminotransferase; BUN = blood urea nitrogen; β-D-glucan = beta-D-glucan; IEC = Independent Ethics Committee; EOIVT = end of intravenous treatment; EOT = end of treatment; IRB = Institutional Review Board; IV = intravenous; RBC = red blood cells; Screen = screening; WBC = white blood cells.

a. Screening procedures/assessments were to be completed before the first dose of study drug.
b. EOT procedures were to be completed for all subjects who discontinued from the study, regardless of the reason.
c. For subjects who were withdrawn from study treatment (for any reason), only the following activities at the 2 week and 6 week Follow-up visits were to be performed: brief physical examination, assessment of temperature, blood sample for hematology and chemistry panel, adverse events since the last study visit recorded, and the use of systemic antifungal medications since the last study visit recorded. If the subject experienced an adverse event during the follow-up period, all concomitant medications the subject was receiving at the time of the adverse event were to be recorded.
d. Confirmation of positive culture results for *Candida* species within 96 hours after enrollment was required.
e. The APACHE II score, if performed for clinical reasons, was to be recorded.
f. A complete physical examination was to be performed within 72 hours before the first dose of study drug.

Table 1. Schedule of Activities

g. A brief physical examination was a focused physical examination relevant to the subject's condition and progress, as determined by the Investigator, and included an assessment of vital signs. Other examinations may also have been performed at the discretion of the Investigator.
h. A brief physical examination was to be performed on the first day of administration of study drug. However, if a complete physical examination was performed within 24 hours before the first dose of study drug, then a brief physical examination was not required.
i. This assessment may have been obtained less frequently in subjects who had been discharged from the hospital and was receiving study drug treatment in the outpatient setting.
j. Fundoscopic examinations for determination of the presence or absence of endophthalmitis were to be performed by an ophthalmologist, unless it was not possible for practical reasons, in which case they may have been performed by a non-ophthalmologist physician. For subjects who developed a visual related adverse effect considered to be related to voriconazole, the fundoscopic examination (including follow-up examinations) was to be performed by an ophthalmologist.
k. For a subject enrolling on the basis of *Candida* endophthalmitis, the results of a fundoscopic examination performed within 96 hours prior to enrollment may have been used in place of the screening fundoscopic examination. If the subject was not being enrolled on the basis of *Candida* endophthalmitis, then a baseline fundoscopic examination was to be performed before the first dose of study drug. However, if, for practical reasons, a baseline fundoscopic examination could not be obtained before Day 1, the examination may have been performed within 48 hours after the first dose of study drug.
l. To be completed if the baseline fundoscopic examination was positive for findings consistent with *Candida* endophthalmitis.
m. In women of childbearing potential, a serum or urine pregnancy test was to be performed at Screening (before the first dose of study drug), at the EOIVT (in subjects who were not switched to oral antifungal therapy) visit or at the EOT (in subjects who were switched to oral antifungal therapy) visit, and at the 6 week Follow-up visit. Additional testing may have been performed as requested by the IRB/IEC or as required by local regulations.
n. Screening blood cultures were to be obtained on all subjects.
o. Blood cultures were to be repeated daily until negative twice consecutively, and then repeated at least once weekly thereafter while on study drug. Blood cultures collected while on study medication were to be obtained prior to administration of the dose.
p. For a subject enrolled on the basis of a documented or suspected non-blood tissue culture for *Candida* species obtained within 96 hours of enrollment, a specimen collected at screening was not required. If a subject enrolled on the basis of a blood culture only, then a specimen culture at screening may have been collected only if clinically indicated.
q. Specimen cultures were to be obtained as clinically indicated.
r. Hematology panel: RBC, hemoglobin, hematocrit, WBC (including differential: neutrophils, lymphocytes, monocytes, eosinophils, basophils), and platelets.
s. Chemistry panel: AST, ALT, alkaline phosphatase, bilirubin, BUN, creatinine, sodium, potassium, bicarbonate, chloride, albumin, and nonfasting glucose.
t. During the study treatment period, calculation of Child-Pugh score was to be repeated, as frequently as clinically indicated, in subjects who experienced a significant change in liver function (as judged by the investigator). The newly calculated score was to be communicated to the unblinded pharmacist for the purpose of adjusting the dose of caspofungin (according to the caspofungin product label), if necessary.
u. A blood sample for (1,3) β-D-glucan assay was to be obtained at screening, then repeated every 3 days until 2 successive negative fungal cultures from monitored samples (blood or other sites) were obtained. A blood sample for (1,3) β-D-glucan assay was also to be obtained at EOIVT and EOT.
v. Only antifungal medications and their indication for use (eg, for prophylaxis or treatment) were required to be reported during the follow-up period unless the subject experienced an adverse event during this time, in which case all concomitant medications the subject was receiving at the time of the adverse event were to be recorded.
w. In the event Day 10 and EOIVT occurred on the same day, both the Day 10 and EOIVT case report forms were required to be completed.

Number of Subjects (Planned and Analyzed): The sample size of 45 subjects was based on feasibility to confirm prior data regarding the efficacy and safety of anidulafungin in this small population. Therefore, this trial was not powered to stand alone and provide conclusive evidence of efficacy and/or safety (analyses were descriptive in nature). A total of 21 subjects were enrolled and randomized (15 to anidulafungin, 6 to caspofungin).

Diagnosis and Main Criteria for Inclusion: Male or female subjects, ≥16 years of age, with reduced neutrophils (defined as absolute neutrophil count of ≤500 cells/μL), and with a confirmed diagnosis of *Candida* infection (culture-confirmed within 96 hours after enrollment, based on at least 1 of the following: a) Candidemia, positive blood culture; b) evidence of invasive candidiasis, in addition to at least 1 of the following: fever (tympanic temperature of ≥38°C [100.4°F]), hyothermia (temperature <36°C [96.8°F]), low blood pressure, signs and/or symptoms of Candida infection, or radiologic findings consistent with *Candida* infection. Positive yeast or *Candida* cultures from urine (without signs and symptoms of pyelonephritis), sputum, bronchoalveolar lavage, endotracheal aspirate, and gastric drainage or aspiration did not qualify as positive cultures for study entry.

Excluded were female subjects who were pregnant or breast feeding or planning to become pregnant during the study, subjects with recent treatment (within 30 days prior to enrollment) with 1 of the study drugs, allergy to either study drug or this class of drugs, significant liver dysfunction, or suspected *Candida* osteomyelitis, endocarditis, meningitis, or any other infections of the central nervous system.

Study Treatment: Subjects were randomized (2:1 ratio) to receive active anidulafungin or active caspofungin by IV infusion. Due to differences in the duration of infusion for anidulafungin and caspofungin, administration of these drugs in a straightforward double-blind fashion would have resulted in treatment unmasking. In order to maintain blinding, this study employed a double-dummy design in which both an active drug and a placebo were administered to all subjects. Thus, and as outlined below in the 4 treatment groups 1 to 4: subjects randomized to anidulafungin treatment received active anidulafungin and placebo caspofungin in 2 different orders (Groups 1 and 2 below); and subjects randomized to caspofungin treatment received active caspofungin and placebo anidulafungin in 2 different randomized orders (Groups 3 and 4 below).

Treatment Groups:

- Group 1: Active anidulafungin followed by placebo caspofungin.
- Group 2: Placebo caspofungin followed by active anidulafungin.
- Group 3: Active caspofungin followed by placebo anidulafungin.
- Group 4: Placebo anidulafungin followed by active caspofungin.

On Day 1, subjects randomized to active anidulafungin received a loading dose of 200 mg; beginning on Day 2, subjects received a daily maintenance dose of 100 mg. Subjects randomized to caspofungin received a loading dose of 70 mg; beginning on Day 2, subjects

received a maintenance dose of 50 mg if they were <80 kg, did not have severe liver dysfunction, and were not receiving interacting drugs. For subjects weighing >80 kg, with severe liver impairment, or receiving concomitant therapy with rifampin, nevirapine, efavirenz, carbamazepine, dexamethasone, or phenytoin, the daily maintenance dose of caspofungin administered was to be according to the approved product labeling.

Efficacy Endpoints:

Primary Endpoint

- The primary efficacy endpoint was the global response at EOIVT in the modified intent-to-treat (mITT) evaluable population.

Global response was based on the following definitions:

- Success: clinical and microbiological success
- Failure: clinical or microbiological failure
- Indeterminate: A subject was categorized as indeterminate if there was a clinical response of indeterminate and/or microbiologic response of indeterminate and there was neither clinical response of failure nor unsuccessful microbiologic response (persistence or new infection or relapse)

Secondary Endpoints

- Global response at EOT, and at 2-week and 6-week Follow-up (FU) Visits in the mITT population.
- Response based on clinical cure and microbiological success at EOIVT, EOT, 2-week, and 6-week FU Visits in the mITT population.
- Clinical response at Day 10.
- Rates of relapse (microbiologic response of recurrence) at the 2-week and 6-week FU Visits.
- Rates of new infection with an organism not identified at baseline and the 2-week and 6-week FU Visits.
- Time to first negative blood culture (if subject had a positive blood culture at Baseline).
- Safety.
- Time to death.
- All-cause mortality during study therapy and at FU Visits.

Safety Evaluations: Safety evaluations, including adverse events (AEs), physical examination (including height, weight, vital signs), clinical laboratory measurements, electrocardiograms, potential cases of drug-induced liver injury, visual safety monitoring (for voriconazole), microbiologic determinations, signs and symptoms of *Candida* infection, and fundoscopic examinations, were assessed throughout the study.

Statistical Methods:

Three data sets were analyzed:

- The safety population consisted of randomized subjects who received at least 1 dose of study drug. Subjects were analyzed according to treatment received, ie, as treated.

- The mITT population consisted of all subjects who received at least 1 dose of study drug and who had a positive culture for *Candida* species isolated from cultures obtained within 96 hours before study entry or at Screening. Due to logistical issues at the local level and the timing of screening activities/treatment initiation, subjects whose qualifying culture for study entry was collected outside the 96 hour window (ie, within 5 additional days) were included in the mITT population. The mITT population was the primary efficacy analysis population.

- The per protocol (PP) analysis set consisted of the subjects in the mITT population who, in addition:

    - Had completed a minimum of 10 days of treatment with IV anidulafungin, unless declared a clinical and/or microbiologic failure;

    - Received total antifungal treatment for a minimum duration of 14 days, unless declared a clinical and/or microbiologic failure;

    - Had not received more than 48 hours of systemic antifungal therapy (for treatment of current Candida infection) prior to the first dose of study drug;

    - Did not have a prosthetic device and/or vascular catheter (including central venous catheter or an implantable port) at a suspected site of infection, unless the device was removed at study entry or soon after first dose of study drug;

    - Had not taken more than 1 day of protocol prohibited antifungal therapy concomitant with study therapy, unless declared a clinical and/or microbiologic failure;

    - Had reached the 6-week FU Visit, unless the subject died or withdrew consent prior to 6-week FU; and

    - Did not have any protocol violations that could have had an impact on the efficacy endpoints.

Global response (ie, primary endpoint) was based on the assessment of clinical and microbiologic response provided by the investigator at this time point, and was programmatically determined as follows:

- Success: A subject was categorized as having successful response if there was a clinical response of cure or improvement and microbiologic eradication or presumed eradication

- Failure: A subject was categorized as having an unsuccessful response if there was a clinical response of failure and/or unsuccessful microbiologic response (persistence or new infection at FU or relapse at FU)or

- Indeterminate: A subject was categorized as indeterminate if there was a clinical response of indeterminate and/or microbiologic response of indeterminate and there was neither clinical response of failure nor unsuccessful microbiologic response (persistence or new infection or relapse)

Global response rate was estimated, and differences and confidence intervals (CIs) were calculated. Subjects with indeterminate or missing values were considered as treatment failures. The summary included the number of non-missing observations and estimated rates. A global response determination of failure at any time point was carried forward programmatically to all subsequent visits. A supportive analysis was repeated for global response at EOIVT in the PP population.

In order to investigate the robustness of the results, a sensitivity analysis was carried out. This analysis investigated the effect of 'indeterminate' and 'missing' global response on the analysis by excluding these subjects from the analysis of global response. For binary endpoints such as this, the descriptive comparison of observed response rates (anidulafungin minus caspofungin) was based on the difference in response rates at the specified time point. The CI for the comparison was also reported using the method of exact unconditional confidence limits for the difference.

Analyses of global response success rates at EOT, the 2-week FU Visit, and the 6-week FU Visit were produced using the same analysis methods as for the primary analysis.

Summaries of global response, clinical response, and microbiologic response by treatment group at EOIVT and EOT and at the 2 week and 6 week FU visits were produced for the mITT population. For clinical response, this gave a count and percentage of the number of subjects in each of the following categories: cure, improvement, failure, indeterminate, and missing. For microbiologic response, this gave a count and percentage of the number of subjects in each of the following categories: eradication, presumed eradication, persistence, indeterminate, and missing. Clinical responses at Day 10 were also summarized and analyzed.

Rates of relapse (recurrence) and new infection at the 2-week and 6-week FU Visits were summarized using the same methods as for the primary endpoint.

The analyses of time to death and time to first negative blood culture endpoints were summarized graphically using the Kaplan-Meier product limit estimator, by treatment.

Analysis of relapse rate was produced using the same analysis methods as for the primary analysis. This analysis was done in the mITT population for the 2-week and 6-week FU Visits.

Analysis of the rate of new infection was produced using the same analysis methods as for the primary analysis. This analysis was done in the mITT population for the 2-week and 6-week FU Visits.

All-cause mortality during study therapy and at the FU Visits was performed in the mITT and safety populations. Time to death was measured from the first dose of study drug, in days. Subjects who did not die during the study period had their observations censored at the latest date on the database or date of withdrawal.

Analysis of time to first negative blood culture during study therapy and the FU Visits was performed in the mITT population for subjects who had a positive blood culture in the period 48 hours before the first dose of study drug. Time to first negative blood culture was analyzed in the mITT population. Time to first negative blood culture was measured from the first dose of study drug, in days. Subjects who did not have a negative blood culture had their observations censored at the latest date on the database or at the date of withdrawal.

No formal statistical analyses were planned for safety data. The safety and other endpoints were listed and summarized in accordance with the Sponsor's reporting standards. All safety parameters were presented for the safety population.

RESULTS

Subject Disposition and Demography: At the time of study termination (18 May 2012), 21 subjects were randomized and treated with at least 1 dose of study drug, 14 (66.7%) subjects comprised the mITT population (ie, had microbiologically confirmed *Candida* infection), and 13 (61.9%) subjects comprised the PP population, as summarized in Table 2. All treated subjects in the anidulafungin and caspofungin treatment groups were analyzed for safety.

A total of 13 subjects discontinued treatment during the study: 5 subjects due to lack of microbiologic confirmation of *Candida* infection within 96 hours of study entry (see 'other' in Table 2), 3 subjects died, 3 subjects discontinued due to AEs that were considered related to study drug by the Investigator, and 2 subjects due to 'lack of efficacy' (Table 2).

Table 2. Subject Disposition and Discontinuations From Study Treatment

No. of Subjects	Anidulafungin N=15	Caspofungin N=6	Total
Screened: N=23			
Assigned to study treatment	15	6	21
Treated	15	6	21
Completed study	10	2	12
Discontinued study	9	4	13
Reason for discontinuation:			-
Subject died (during the study)[a]	2	1	-
Related to study drug	3	2	-
Adverse event	1	2	-
Lack of efficacy	2	0	-
Not related to study drug	4	1	-
Other[b]	4	1	-
Analyzed for safety			
Adverse events	15	6	21
Laboratory data	15	6	21

N = number of subjects; No. = number.

a. During the post-study period, 3 subjects each in the anidulafungin and caspofungin groups died.

b. Withdrawal reason of 'Other' refers to withdrawn from treatment due to lack of confirmation of *Candida* infection.

A summary of baseline and demographic characteristics is presented in Table 3 for the safety population. The mean ages of subjects for the anidulafungin and caspofungin treatment groups were 54.5 years and 50.7 years, respectively. The majority of subjects overall were White (20/21 subjects; 95%).

Table 3. Demographic and Baseline Characteristics; Safety Population

	Anidulafungin N=15	Caspofungin N=6
Gender, n		
Male	9	3
Female	6	3
Age (years), n		
18-44	2	2
45-64	9	2
≥65	4	2
Mean	54.5	50.7
SD	14.2	18.9
Range	18-78	21-72
Race, n		
White	14	6
Other	1	0
Weight (kg)		
Mean	74.5	69.9
SD	13.8	16.0
Range	53.0-100.0	51.9-93.0
APACHE II score by category[a], n (%)		
≤20	9 (81.8)	2 (66.7)
>20	2 (18.2)	1 (33.3)
APACHE II score[a]		
Mean	14.0	17.7
SD	5.31	6.11
Minimum, maximum	8, 24	11, 23
Median	13.0	19.0

APACHE = Acute Physiology and Chronic Health Evaluation; N = number of subjects; n = number of subjects meeting prespecified conditions; SD = standard deviation.

a. APACHE II score was available only if performed for clinical reasons; otherwise it was not required by the protocol to be calculated. Eleven (11) subjects in the anidulafungin treatment group and 3 subjects in the caspofungin treatment group had APACHE II scores available at Baseline.

Efficacy Results: A decision was made by the Sponsor to terminate study prematurely due to slow enrollment; the study was terminated on 18 May 2012. Termination of this study was not associated with safety issues.

Primary Endpoint Results:

For the mITT population, the global responses (rates of success [primary endpoint]) for anidulafungin and caspofungin at EOIVT were 8 (72.7%) of 11 subjects and 3 (100%) of 3 subjects, respectively. The estimated treatment difference (anidulafungin minus caspofungin) at EOIVT was -27.3% (95% CI: -80.9%, 40.3%; Table 4).

Table 4. Global Response Rates at End of IV Treatment; Modified Intent-to-Treat Population

Global Response	Anidulafungin N=11 n (%)	Caspofungin N=3 n (%)	Percent Difference (95% CI)[a]
Success[b]	8 (72.7)	3 (100.0)	-27.3 (-80.9, 40.3)
Failure[c]	3 (27.3)	0	-
Indeterminate	0	0	-
Missing	0	0	-

CI = confidence interval; IV = intravenous; N = number of subjects; n = number of subjects meeting prespecified criteria.

a. 95% CI is the exact unconditional limits for the difference in global success.
b. Global response of success was defined as clinical cure or improvement and microbiologic eradication or presumed eradication.
c. Global response of failure at any time point was carried forward to all subsequent visits.

Secondary Endpoint Results:

Global Response (Rates of Success) at End of Treatment and 2-Week and 6-Week Follow-Up Visits: The global responses (rates of success) at EOT and at the 2-week and 6-week FU Visits based on mITT population were consistent with that observed at EOIVT. The clinical responses (rates of cure or improvement) at EOT were 72.7% (8 of 11 subjects) for the anidulafungin treatment group and 100% (3 of 3 subjects) for the caspofungin treatment group (Table 5). According to the clinical protocol, clinical and microbiologic assessments at the 2-week and 6-week FU Visits were not required for subjects who discontinued from treatment for any reason therefore, only subjects who successfully completed therapy were included in these groups.

Table 5. Global Response Rates – Modified Intent-to-Treat Population

Visit	Global Response	Anidulafungin n/N (%)	Caspofungin n/N (%)	Percent Difference (95% CI)[a]
EOT	Success	8/11 (72.7)	3/3 (100.0)	-27.3 (-80.9, 40.3)
	Failure	3/11 (27.3)	0	-
	Indeterminate	0	0	-
	Missing	0	0	-
Week 2 FU	Success	6/10 (60.0)	1/1 (100.0)	-40.0 (-97.5, 63.9)
	Failure	3/10 (30.0)	0	-
	Indeterminate	0	0	-
	Missing	1/10 (10.0)	0	-
Week 6 FU	Success	5/10 (50.0)	1/1 (100.0)	-50.0 (-97.5, 55.0)
	Failure	4/10 (40.0)	0	-
	Indeterminate	0	0	-
	Missing	1/10 (10.0)	0	-

Global response of success was defined as clinical cure or improvement and microbiologic eradication or presumed eradication.
Global response of failure at any time point was carried forward to all subsequent visits.
Only subjects who completed treatment and subjects with global response of failure at EOIVT or EOT were included in the 2-week and 6-week FU group.
Three subjects were excluded from the 2-week and 6-week FU visits since study treatment was discontinued by the investigator. Per protocol, clinical and microbiologic assessments at the 2-week and 6-week FU visits were not required for subjects who discontinued from treatment.
CI = confidence interval; EOIVT = end of intravenous treatment; EOT = end of treatment; FU = follow-up; N = number of subjects; n = number of subjects meeting pre-specified criteria.
a. 95% CI is the exact unconditional limits for the difference.

Response (Investigator's assessment) based on clinical cure and microbiologic success (eradication or presumed eradication) at EOIVT, EOT, and at the 2-week and 6-week FU visits in the mITT population is presented in Table 6. Among subjects with global response at EOIVT, 7 (87.5%) of 8 subjects in the anidulafungin treatment group and 2 (66.7%) of 3 subjects in the caspofungin treatment group were reported as having a clinical cure and microbiologic success.

Table 6. Summary of Response (Clinical Cure and Microbiologic Success) by Visit; Modified Intent-to-Treat Population

Response Category	Anidulafungin N=11	Caspofungin N=3
Summary of response at EOIVT		
Total[a]	8	3
Clinical cure and microbiologic success[b], n (%)	7 (87.5)	2 (66.7)
Summary of response at EOT		
Total[a]	8	3
Clinical cure and microbiologic success[b], n (%)	6 (75.0)	3 (100.0)
Summary of response at 2-week follow-up[c]		
Total[a]	6	1
Clinical cure and microbiologic success[b], n (%)	4 (66.7)	1 (100.0)
Summary of response at 6-week follow-up[d]		
Total[a]	6	1
Clinical cure and microbiologic success[b], n (%)	6 (100.0)	1 (100.0)

EOIVT = end of intravenous treatment; EOT = end of treatment; N = number of subjects; n = number of subjects meeting prespecified criteria.
a. Total = subjects with clinical cure or improvement and microbiologic eradication or presumed eradication.
b. Microbiologic success = microbiologic eradication or presumed eradication.
c. 2-week follow-up included only subjects who successfully completed treatment and were alive at the EOT.
d. 6-week follow-up included only subjects who were at alive at the 2-week Follow-up Visit.

For the mITT population, the clinical responses (clinical cure or improvement) for anidulafungin and caspofungin at Day 10 were 7 (63.6%) of 11 subjects and 3 (100%) of 3 subjects, respectively. The estimated treatment difference (anidulafungin minus caspofungin) at Day 10 was -36.4 (95% CI: -90.6, 31.9; Table 7).

Table 7. Clinical Response at Day 10; Modified Intent-to-Treat Population

	Anidulafungin N=11 n (%)	Caspofungin N=3 n (%)
Clinical response		
No. of successes[a]	7 (63.6)	3 (100.0)
No. of failures	0	0
No. of indeterminates	2 (18.2)	0
No. of missing[b]	2 (18.2)	0
Analysis		
Success rate (%)	63.6	100.0
95% CI for treatment groups[c]	(30.8, 89.1)	(29.2, 100.0)
Estimated treatment difference (%)	-36.4	
95% CI for the difference[d]	(-90.6, 31.9)	

CI = confidence interval; N = number of subjects; n = number of subjects meeting prespecified criteria; No. = number.
a. Successful response was defined as clinical cure or improvement.
b. Missing denoted that the subject had died or the visit was not performed.
c. 95% CI for individual treatment groups was calculated by using the methods of Clopper and Pearson.
d. 95% CI is the exact unconditional limits for the difference.

There were no reported relapses (ie, microbiologic response of recurrence) at the 2-week or 6-week FU Visit for subjects in the mITT population for either treatment group.

There were no reported new infections (ie, microbiologic response of new infection) with an organism not identified at Baseline at the 2-week or 6-week FU Visit for subjects in the mITT population for either treatment group.

A summary of time to first negative blood culture for subjects who had a positive blood culture for *Candida* species on Day 1 of treatment (mITT population) is presented in Table 8. Of the 5 subjects in the anidulafungin treatment group who achieved a negative blood culture (defined as the first of consecutive negative blood cultures separated by at least 24 hours), the median time was 2.0 days (range: 2 to 5 days).

Table 8. Summary of Time to First Negative Blood Culture; Modified Intent-to-Treat Population

	Anidulafungin N=6	Caspofungin N=0
Number of subjects with negative blood cultures	5	0
Median (days)	2.0	NA
Range (days)	2-5	NA

Analysis included only subjects with a positive culture for *Candida* species on Day 1 of study treatment. Negative blood culture was defined as the first of 2 consecutive negative blood cultures separated by at least 24 hours.
N = number of subjects; NA = not applicable.

Safety Results: A total of 20 subjects reported 172 all-causality treatment-emergent adverse events (TEAEs), of which 26 were considered treatment related (Table 9). A majority of the TEAEs were considered mild or moderate in severity. Nine subjects experienced at least 1 or more treatment-emergent serious adverse event (SAEs) during the study, with 1 subject experiencing a treatment-related SAE.

Table 9. Treatment-Emergent Adverse Events; Safety Population

No. of Subjects	Anidulafungin N=15		Caspofungin N=6	
	All Causality	Treatment-Related	All Causality	Treatment-Related
Subjects evaluable for AEs	15	15	6	6
No. of AEs[a]	129	14	43	12
Subjects with AEs[a]	14	5	6	2
Subjects with serious AEs	5	1	4	0
Subjects with severe AEs[a]	7	2	5	0
Subjects discontinued due to AEs [a]	4	1	2	0
Subjects with dose reduced or temporary discontinuation due to AEs[a]	1	0	0	0

Included data up to 30 days after last dose of study drug. Except for the number of AEs, subjects were counted only once per treatment in each row. Serious AEs were according to the Investigator's assessment.
AEs = adverse events; N = number of subjects; No. = number.
a. SAEs and AEs were not separated in this table.

Treatment emergent non SAEs in ≥5% of subjects TEAEs (all causality) according to Medical Dictionary for Regulatory Activities (version 15.0) system organ class and preferred term by treatment group are displayed in Table 10. The most frequently reported TEAEs (all causality) were nausea and pyrexia for anidulafungin group and increased gamma-glutamyltransferase in caspofungin group.

Table 10. Treatment-Emergent Nonserious Adverse Events in ≥5% of Subjects by System Organ Class and Preferred Term (All Causalities); Safety Population

MedDRA System Organ Class Preferred Term	Anidulafungin n (%)	Caspofungin n (%)
Number (%) of subjects: evaluable for AEs	15	6
Number (%) of subjects: with AEs	14 (93.3)	5 (83.3)
Blood and lymphatic system disorders	3 (20.0)	1 (16.7)
Anaemia	1 (6.7)	1 (16.7)
Lymphadenopathy	1 (6.7)	0
Lymphopenia	1 (6.7)	0
Neutropenia	1 (6.7)	0
Thrombocytopenia	1 (6.7)	0
Cardiac disorders	3 (20.0)	0
Atrial fibrillation	1 (6.7)	0
Bradycardia	1 (6.7)	0
Supraventricular tachycardia	1 (6.7)	0
Tachycardia	1 (6.7)	0
Eye disorders	2 (13.3)	1 (16.7)
Colour blindness acquired	0	1 (16.7)
Conjunctivitis	1 (6.7)	0
Phosphenes	0	1 (16.7)
Retinal exudates	1 (6.7)	0
Retinal haemorrhage	1 (6.7)	0
Visual brightness	0	1 (16.7)
Gastrointestinal disorders	10 (66.7)	2 (33.3)
Abdominal distension	0	1 (16.7)
Abdominal pain	3 (20.0)	0
Constipation	1 (6.7)	0
Diarrhoea	2 (13.3)	1 (16.7)
Dry mouth	1 (6.7)	0
Dyspepsia	0	1 (16.7)
Gingival disorder	1 (6.7)	0
Melaena	2 (13.3)	1 (16.7)
Mouth haemorrhage	0	1 (16.7)
Nausea	5 (33.3)	1 (16.7)
Palatal disorder	1 (6.7)	0
Stomatitis	1 (6.7)	0
Vomiting	0	1 (16.7)
General disorders and administration site conditions	7 (46.7)	2 (33.3)
Asthenia	1 (6.7)	0
Catheter site inflammation	1 (6.7)	0
Chills	1 (6.7)	0
General physical health deterioration	1 (6.7)	0
Generalised oedema	0	1 (16.7)
Malaise	1 (6.7)	0
Mucosal inflammation	1 (6.7)	1 (16.7)
Oedema peripheral	2 (13.3)	0
Pain	0	1 (16.7)
Pyrexia	6 (40.0)	1 (16.7)
Hepatobiliary disorders	1 (6.7)	0
Hyperbilirubinaemia	1 (6.7)	0

Table 10. Treatment-Emergent Nonserious Adverse Events in ≥5% of Subjects by System Organ Class and Preferred Term (All Causalities); Safety Population

MedDRA System Organ Class Preferred Term	Anidulafungin n (%)	Caspofungin n (%)
Infections and infestations	6 (40.0)	3 (50.0)
Aspergillosis	2 (13.3)	0
Bronchopneumonia	1 (6.7)	0
Enterococcal bacteraemia	1 (6.7)	1 (16.7)
Enterococcal infection	1 (6.7)	0
Escherichia bacteraemia	2 (13.3)	0
Furuncle	1 (6.7)	0
Klebsiella bacteraemia	1 (6.7)	0
Oral fungal infection	1 (6.7)	0
Oral herpes	1 (6.7)	0
Postoperative wound infection	0	1 (16.7)
Pseudomonas infection	1 (6.7)	0
Sepsis	1 (6.7)	0
Staphylococcal bacteraemia	1 (6.7)	0
Streptococcal bacteraemia	1 (6.7)	0
Urinary tract infection enterococcal	0	1 (16.7)
Injury, poisoning and procedural complications	1 (6.7)	0
Eschar	1 (6.7)	0
Investigations	7 (46.7)	3 (50.0)
Alanine aminotransferase increased	1 (6.7)	1 (16.7)
Aspartate aminotransferase increased	1 (6.7)	1 (16.7)
Bacterial test positive	1 (6.7)	0
Blood alkaline phosphatase increased	3 (20.0)	1 (16.7)
Blood bilirubin increased	1 (6.7)	1 (16.7)
Blood creatine increased	1 (6.7)	0
Blood creatinine increased	1 (6.7)	1 (16.7)
Blood lactate dehydrogenase increased	1 (6.7)	0
Blood urea increased	1 (6.7)	0
Breath sounds abnormal	1 (6.7)	0
Fungal test positive	2 (13.3)	0
Gamma-glutamyltransferase increased	1 (6.7)	2 (33.3)
Weight increased	1 (6.7)	0
Metabolism and nutrition disorders	4 (26.7)	1 (16.7)
Feeding disorder	1 (6.7)	0
Hyperkalaemia	1 (6.7)	0
Hypoalbuminaemia	2 (13.3)	0
Hypocalcaemia	1 (6.7)	0
Hypokalaemia	2 (13.3)	1 (16.7)
Hyponatraemia	1 (6.7)	0
Musculoskeletal and connective tissue disorders	2 (13.3)	0
Pain in extremity	1 (6.7)	0
Soft tissue necrosis	1 (6.7)	0
Nervous system disorders	3 (20.0)	1 (16.7)
Coma	0	1 (16.7)
Headache	2 (13.3)	0
Somnolence	1 (6.7)	1 (16.7)
Tremor	1 (6.7)	0
Psychiatric disorders	2 (13.3)	1 (16.7)
Agitation	0	1 (16.7)
Anxiety	1 (6.7)	0
Confusional state	2 (13.3)	0
Insomnia	1 (6.7)	0

Table 10. Treatment-Emergent Nonserious Adverse Events in ≥5% of Subjects by System Organ Class and Preferred Term (All Causalities); Safety Population

MedDRA System Organ Class Preferred Term	Anidulafungin n (%)	Caspofungin n (%)
Renal and urinary disorders	4 (26.7)	1 (16.7)
Anuria	0	1 (16.7)
Costovertebral angle tenderness	1 (6.7)	0
Haematuria	1 (6.7)	0
Renal failure	1 (6.7)	0
Urinary retention	1 (6.7)	0
Respiratory, thoracic and mediastinal disorders	6 (40.0)	1 (16.7)
Acute pulmonary oedema	1 (6.7)	0
Cough	2 (13.3)	0
Dyspnoea	3 (20.0)	0
Hypoventilation	1 (6.7)	0
Hypoxia	1 (6.7)	0
Pleural effusion	3 (20.0)	0
Pulmonary congestion	0	1 (16.7)
Rales	3 (20.0)	1 (16.7)
Skin and subcutaneous tissue disorders	5 (33.3)	2 (33.3)
Decubitus ulcer	1 (6.7)	0
Generalised erythema	0	1 (16.7)
Papule	0	1 (16.7)
Pruritus	0	1 (16.7)
Purpura	1 (6.7)	0
Rash	2 (13.3)	0
Rash generalised	1 (6.7)	0
Rash maculo-papular	1 (6.7)	0
Toxic skin eruption	1 (6.7)	0
Vascular disorders	2 (13.3)	1 (16.7)
Haematoma	1 (6.7)	0
Hyperaemia	1 (6.7)	0
Hypotension	1 (6.7)	1 (16.7)

Subjects were only counted once per treatment for each row. Includes data up to 30 days after last dose of study drug.
MedDRA (version 15.0) coding dictionary applied.
AE = adverse events; MedDRA = Medical Dictionary for Regulatory Activities.

TEAEs (treatment-related) by treatment group are displayed in Table 11.

Table 11. Treatment-Emergent Adverse Events by (Treatment Related) Safety Population

System Organ Class Preferred Term	Anidulafungin n	Caspofungin n
Number of subjects: evaluable for AEs	15	6
Number of subjects: with AEs	5	2
Discontinued due to AEs	1	0
Eye disorders	0	1
Vision disorders	0	1
Colour blindness acquired	0	1
Phosphenes	0	1
Visual brightness	0	1
Gastrointestinal disorders	2	1
Gastrointestinal motility and defaecation conditions	0	1
Diarrhoea	0	1
Gastrointestinal signs and symptoms	2	1
Dyspepsia	0	1
Nausea	2	1
General disorders and administration site conditions	1	0
General system disorders NEC	1	0
Malaise	1	0
Oedema peripheral	1	0
Infections and infestations	1	0
Fungal infectious disorders	1	0
Candidiasis	1	0
Investigations	2	1
Enzyme investigations NEC	1	1
Blood alkaline phosphatase increased	1	1
Hepatobiliary investigations	2	1
Alanine aminotransferase increased	1	0
Aspartate aminotransferase increased	1	0
Gamma-glutamyltransferase increased	1	1
Metabolism and nutrition disorders	1	0
Bone, calcium, magnesium and phosphorus metabolism disorders	1	0
Hypocalcaemia	1	0
Nervous system disorders	1	0
Headaches	1	0
Psychiatric disorders	0	1
Anxiety disorders and symptoms	0	1
Agitation	0	1
Respiratory, thoracic and mediastinal disorders	1	1
Respiratory disorders NEC	1	1
Cough	1	0
Rales	0	1
Skin and subcutaneous tissue disorders	2	1
Epidermal and dermal conditions	2	1
Generalised erythema	0	1
Pruritus	0	1
Rash	1	0
Rash generalised	1	0

Subjects were only counted once per treatment for each row.
Included data up to 30 days after last dose of study drug.
MedDRA (version 15.0) coding dictionary applied.
AEs and SAEs are not separated out in this table.
AE = adverse events; MedDRA = Medical Dictionary for Regulatory Activities; SAEs = serious adverse events.

A summary of SAEs (all causalities) by treatment group for the safety population is presented in Table 12.

Table 12. Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term (All Causalities) Safety Population

MedDRA System Organ Class Preferred Term	Anidulafungin n (%)	Caspofungin n (%)
Number (%) of subjects: evaluable for AEs	15	6
Number (%) of subjects: with AEs	5 (33.3)	4 (66.7)
General disorders and administration site conditions	1 (6.7)	1 (16.7)
Drug ineffective	1 (6.7)	0
Multi-organ failure	0	1 (16.7)
Hepatobiliary disorders	0	1 (16.7)
Hepatotoxicity	0	1 (16.7)
Infections and infestations	2 (13.3)	2 (33.3)
Candidiasis	1 (6.7)	0
Pneumonia	1 (6.7)	0
Sepsis	0	2 (33.3)
Septic shock	0	1 (16.7)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	2 (13.3)	2 (33.3)
Acute leukaemia	1 (6.7)	0
Acute lymphocytic leukaemia	0	1 (16.7)
Leukaemia	1 (6.7)	0
Lymphoma	0	1 (16.7)
Respiratory, thoracic and mediastinal disorders	2 (13.3)	0
Respiratory distress	1 (6.7)	0
Respiratory failure	1 (6.7)	0

Subjects were only counted once per treatment for each row. Includes data up to 30 days after last dose of study drug.
MedDRA (version 15.0) coding dictionary applied.
AE = adverse events; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects with SAEs; SAEs = serious adverse events.

SAEs for the safety population are presented in Table 13. One SAE was considered by the Investigator as related to treatment with anidulafungin. Of the 5 subjects in the anidulafungin treatment group and 4 subjects in the caspofungin treatment group with SAEs with a fatal outcome, none of the events were considered by the Investigator as related to study treatment.

Table 13. Serious Adverse Events; Safety Population

Serial No.	Study Drug (Dose)	Action Taken (Drug Level)[a]	Therapy Stop Day[b]	Event Onset Day[c]	Event Stop Day[d]	MedDRA Preferred Term[e]	Investigator Causality	Clinical Outcome/ Seriousness
1	Anidulafungin (100 mg)	Posttherapy	14	33	NA	Respiratory distress	Unrelated	Fatal
2	Anidulafungin (100 mg)	Permanently withdrawn	12	14	NA	Candidiasis	Related	Not recovered, not resolved/ hospitalization, life threatening
3	Anidulafungin (200 mg)	Posttherapy	12	27	NA	Acute leukaemia	Unrelated	Fatal/hospitalization
4	Anidulafungin (200 mg)	Dose not changed	4	1[f]	NA	Septic shock	Unrelated	Fatal/life-threatening
5	Anidulafungin (100 mg)	Posttherapy	4	9	NA	Respiratory failure	Unrelated	Fatal
6	Anidulafungin (100 mg)	NA	35	31	NA	Disease progression[g]	Unrelated	Fatal
7	Voriconazole (400 mg)	Permanently withdrawn	35	31	NA	Disease progression[g]	Unrelated	Fatal
8	Anidulafungin (100 mg)	Permanently withdrawn	8	8	NA	Pneumonia	Unrelated	Recovering, resolving/important medical event
			8	8	41	Drug ineffective	Unrelated	Recovered, resolved/important medical event
9	Caspofungin (140 mg)	Permanently withdrawn	25	9	NA	Lymphoma	Unrelated	Fatal
10	Caspofungin (70 mg)	Dose not changed	3	2	NA	Sepsis	Unrelated	Fatal
11	Caspofungin (70 mg)	Permanently withdrawn	3	4	NA	Hepatotoxicity	Unrelated	Not recovered, not resolved/ important medical event
			3	5	NA	Sepsis	Unrelated	Fatal
			3	5	NA	Multi-organ failure	Unrelated	Fatal
			3	5	NA	Septic shock	Unrelated	Fatal
12	Caspofungin (70 mg)	Posttherapy	33	32	NA	Acute lymphocytic leukaemia	Unrelated	Fatal/hospitalization
			33	32	NA	Disease progression	Unrelated	Fatal/hospitalization
13	Clofarabine (90 mg)	Unknown	33	32	NA	Acute lymphocytic leukemia	No data	Fatal/ hospitalization
			33	32	NA	Disease progression	No data	Fatal/hospitalization
14	Idarubicin HCl (20 mg)	Unknown	33	32	NA	Acute lymphocytic leukaemia	Related	Fatal/hospitalization
			33	32	NA	Disease progression	Related	Fatal/hospitalization

MedDRA = Medical Dictionary for Regulatory Activities; NA = not available, not applicable; No. = number; OC = Oracle Clinical (Sponsor's database); SAE = serious adverse event; SDW = safety data warehouse.

a. Dose for treatment was at the earliest onset date of the SAE.

b. Therapy stop date was calculated as OC last active therapy date minus OC first active therapy date plus 1.

Table 13. Serious Adverse Events; Safety Population

Serial No.	Study Drug (Dose)	Action Taken (Drug Level)[a]	Therapy Stop Day[b]	Event Onset Day[c]	Event Stop Day[d]	MedDRA Preferred Term[e]	Investigator Causality	Clinical Outcome/ Seriousness

c. Onset study day was calculated as SDW onset date minus OC first active therapy date plus 1.
d. Event stop day was calculated as SDW SAE stop date minus OC first active therapy date plus 1.
e. MedDRA (version 15.0) coding dictionary applied.
f. Onset of event was 3.5 hours prior to dose.
g. Onset of event was 3.5 hours prior to dose.

Six subjects were permanently discontinued due to AEs, of which 1 subject (anidulafungin treatment group) was discontinued due to study drug (candidiasis) (Table 14). One subject (anidulafungin treatment group) had a temporary discontinuation of treatment due to AEs (somnolence and confusional state); neither of the AEs was considered related to treatment with anidulafungin.

Table 14. Discontinuations Due to Adverse Events; Safety Population

Serial No.	System Organ Class[a]	Preferred Term[a]	Treatment Phase	Treatment at Onset	Adverse Event			Severity/ Outcome	Causality of AEs
					Study Start Day[b]/ Study Stop Day[b]	Time Postdose (Hours)	Duration (Hours)		
1	Infections and infestations	Aspergillosis	Active	Anidulafungin	14/(34)[c]	18	(488.0)[c]	Severe/still present	Other illness – chronic lymphatic leukemia
2	Infections and infestations	Candidiasis[d]	Active	Anidulafungin	14/(36)[c]	47	(541.5)[c]	Severe/still present	Anidulafungin
3	Neoplasms benign, malignant, and unspecified (including cysts and polyps)	Leukaemia[d]	Active	Anidulafungin	31/35	120	96.0	Severe/resolved	Other illness – acute myeloblastic leukemia
4	General disorders and administrative site conditions	Drug ineffective[d]	Active	Anidulafungin	8/41	(0)[c]	(737.52)[c]	Severe/resolved	Disease under study
	General disorders and administrative site conditions	Drug ineffective[d]	Post	Anidulafungin	8/41	(>720)[c]	(78.48)[c]	Severe/resolved	Disease under study
5	Neoplasms benign, malignant, and unspecified (including cysts and polyps)	Lymphoma[d]	Active	Caspofungin	9/26	1.67	425.92	Severe/resolved	Other illness – non-Hodgkin's lymphoma
6	Hepatobiliary disorders	Hepatotoxicity[d]	Active	Caspofungin	4/(5)[c]	15.5	(41.00)[c]	Severe/still present	Concomitant treatment - methotrexate

Age was from screening.
AEs = adverse events; MedDRA = Medical Dictionary for Regulatory Activities, SAE = serious adverse event.
a. MedDRA (version 15.0) coding dictionary applied.
b. Day relative to start of study treatment; first day of study treatment = Day 1.
c. Values in brackets were imputed from incomplete dates and times.
d. SAE according to Investigator's assessment.

A total of 9 deaths (safety population) were reported in this study. The numbers of subject deaths in each treatment group are shown in Table 15 for the safety and mITT populations.

Table 15. Deaths; All Causality

	Anidulafungin n (%)	Caspofungin n (%)	Total n (%)
Safety population; N	15	6	21
Death	5 (33.3)	4 (66.7)	9 (42.9)
mITT population; N	11	3	14
Death	4 (36.4)	2 (66.7)	6 (42.9)

mITT = modified intent-to-treat; N = number of subjects; n = number of subjects meeting prespecified criteria.

All-Cause-Mortality: A summary of all-cause mortality for the safety population is presented in Table 16. Of the 5 subject deaths in the anidulafungin treatment group, 1 death each was reported at the EOIVT, EOT, and 2-week FU Visit; 2 deaths were reported at the 6-week FU Visit.

Table 16. Summary of All-Cause Mortality; Safety Population

Total No. of Deaths	Anidulafungin N=15 n (%)	Caspofungin N=6 n (%)
Total No. of deaths	5 (33.3)	4 (66.7)
No. of deaths at EOIVT	1 (6.7)	1 (16.7)
No. of deaths at EOT-oral	1 (6.7)	0
No. of deaths at 2-week FU	1 (6.7)	3 (50.0)
No. of deaths at 6-week FU	2 (13.3)	0

EOIVT = end of intravenous treatment; EOT = end of treatment; FU = follow-up; N = number of subjects; n = number of subjects meeting prespecified criteria; No. = number.

Time-to-Death: Table 17 summarizes time to death for the safety population. Five of 15 subjects in the anidulafungin treatment group died during the study; the median time to death was 34.0 days (range: 5 to 36 days). Four (4) of 6 subjects in the caspofungin treatment group died during the study; the median time to death was 15.5 days (range: 3 to 41 days).

Table 17. Summary of Time to Death; Safety Population

	Anidulafungin N=15	Caspofungin N=6
Number died (n)	5	4
Median (days)	34.0	15.5
Range (days)	5-36	3-41

N = number of subjects; n = number of subjects meeting prespecified criteria.

CONCLUSIONS: The results of this descriptive study suggest that anidulafungin was effective for the treatment of invasive candidiasis in neutropenic subjects. The global response success rate at EOIVT (primary endpoint) was approximately 73% and was similar to the global response success rate at the same time point observed in non-neutropenic subjects in the anidulafungin registrational study and in currently published studies of neutropenic subjects treated with other echinocandin agents.

A meaningful interpretation and comparison of treatment outcomes with caspofungin was difficult due to the low number of subjects with microbiologically confirmed *Candida* infection in the caspofungin treatment group.

In this study, both anidulafungin and caspofungin were safe and well tolerated. Anidulafungin exhibited a safety profile similar to that observed in the anidulafungin registrational study and approved product labeling.