Invasive candidiasis in patients with solid tumours treated with anidulafungin: efficacy analysis from six pooled studies

Francesco Giuseppe De Rosa,1 Maria Rita Capparella,2 Jean Li Yan,3 Jalal Alam1

1Department of Medical Sciences, University of Turin, Turin, Italy; 2Pfizer PFE, Paris, France; 3Pfizer Inc, New York, USA

INTRODUCTION
– Candida species are the most frequent cause of invasive fungal infection in patients with cancer1 and patients with solid tumours are at increased risk of invasive candidiasis (IC).2–4
– An underlying pathology of solid tumours is the third-most common factor associated with IC, after surgery and medical care in the intensive care unit.5
– The Infectious Diseases Society of America guidelines recommend echinocandins as empiric treatment for suspected candidaemia in adult patients in intensive care and in haemato-oncological settings.6
– Echinocandins are effective against a range of Candida species7 and the class includes anidulafungin, which is approved in the United States and Europe for treatment of candidaemia and IC.

METHODS

Setting
– Patient-level efficacy data were analysed from four anidulafungin open-label, non-comparative studies6–9 and two double-blind, double-dummy, randomised studies that evaluated anidulafungin and caspofungin in patients with IC. (Pfizer data on file) (Table 1). All studies had similar study protocols and endpoints, which permitted pooling of data.

Patients
– Male or female patients were included if they were aged ≥18 years with culture-confirmed candidiasis (from blood, other sterile site or newly placed drain) within 48 h of study entry. Patients were also required to have clinical signs and symptoms of systemic Candida infection.
– Patients were excluded if they had received ≥48 h of prior antifungal therapy, had prosthetic devices or vascular catheters at infection sites that could not be removed prior to or within 48 h of study entry, or had previously failed treatment for the current episode of candidaemia or IC.
– For the purpose of this analysis, patients were selected from the pooled database if they had a past ≥6-month interval or present ≥6-month history of solid tumours, prior to study entry.

- Solid tumour status was obtained by examining patient medical histories using the following search criteria: tumour, neoplasm (proliferative, neoplastic, neoplasm, mass, cancer, malig–ne, malignant), malignancy, growth, onco* (oncology, oncological), gastrointestinal, hepatic, haematological, retinocarcinoma and hepatitis.

Treatments
– In all six studies, patients received a single intravenous (IV) loading dose of 200 mg anidulafungin on Day 1, followed by 100 mg daily once.
– Patients could be switched to oral azole therapy after 5–10 days (Table 1) based on pre-specified criteria or, in the respective studies, IV anidulafungin and oral azole (if required) were maintained for >14 days after the last IV dose of anidulafungin.9
– Out of 539 patients in the pooled database of six studies, 139 patients had confirmed IC and had a past or present medical history of solid tumours (26%); Baseline characteristics are shown in Table 2.

RESULTS

Table 1: Pre-specified endpoints included in the analysis

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Region</th>
<th>Type of study</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety</td>
<td>USA, Asia</td>
<td>Open-label</td>
<td>Candidaemia and IC</td>
</tr>
<tr>
<td>Efficacy</td>
<td>USA, Asia</td>
<td>Open-label</td>
<td>Candidaemia and IC</td>
</tr>
<tr>
<td>USA, Latin America</td>
<td>Open-label</td>
<td>Candidaemia and IC</td>
<td></td>
</tr>
<tr>
<td>USA, China, Russia</td>
<td>Open-label</td>
<td>Candidaemia, Caspofungin Comparator</td>
<td></td>
</tr>
<tr>
<td>USA, China, Russia</td>
<td>Double-blind, double-dummy</td>
<td>Candidaemia, Caspofungin Comparator</td>
<td></td>
</tr>
<tr>
<td>USA, China, Russia</td>
<td>Double-blind, double-dummy</td>
<td>Candidaemia, Caspofungin Comparator</td>
<td></td>
</tr>
</tbody>
</table>

Endpoints
– The primary endpoint of the pooled analysis was global response success rate at the end of IV therapy (EDVT) in the modified intent-to-treat (mITT) population, and included clinical and microbiological success.
– The mITT population included those who received ≥1 dose of anidulafungin (ITT population) and had a confirmed diagnosis of candidaemia or IC, and were successfully treated with anidulafungin for ≥14 days.
– Global response success rate by baseline pathogen and site of infection were also evaluated.

Secondary endpoints were global response success rate at end of all therapy (EOIVT), and all-cause mortality at Days 74 and 28. All studies also assessed safety.

Statistical analysis
– Analyses were for descriptive purposes. No hypothesis was tested.
– The top five risk factors for IC included use of broad-spectrum antibiotics (88.5%), central venous catheter (80.3%), total parenteral nutrition (54.1%), abdominal surgery (52.5%) and surgery (50.8%) (Figure 1).

Overall, 54 patients switched from IV to oral therapy (b incumbent or voriconazole) after a median 8.0 days (range 4–34).

CONCLUSIONS
– In this population of patients with candidaemia/IC and solid tumours, anidulafungin had a global response success rate at EDVT (73.4%) similar to that observed in the registrational study (75.6%).
– The response rate was also high in patients infected with C. parapsilosis.
– Anidulafungin is effective for the treatment of candidaemia/IC in patients with solid tumours.

ACKNOWLEDGEMENTS

This study was supported by Pfizer Medical writing support was provided by Neil Cockburn at Complete Medical Communications, and was funded by Pfizer.

DISCLOSURES

MRC: AJ and AM have received honoraria from Pfizer. ACG has received advisory board or speaker fees from Pfizer and MSD.

REFERENCES