The novel oral glucan synthase inhibitor SCY-078 shows in vitro activity against Candida spp. biofilms

L.J. Marcos- Zambrano1,4, Marta Gómez-Perosanz1,2, P. Escribano1,2,3, E. Bouza1,2,3,4, J. Guinea1,2,3,4

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INTRODUCTION AND PURPOSE

SCY-078 (formerly MK-3118) is a new semi-synthetic derivative of the terpenoid enufamafungin, a potent, but structurally different to echinocandins, inhibitor of 1,3-
D-glucan synthase. SCY-078 is available for iv/oral administration showing similar activity to caspofungin against Candida spp. and Aspergillus spp. isolates mostly collected in the USA.

Hypothetically the mechanism of action of SCY-078 predicts antifungal activity against Candida biofilms although its activity has been studied exclusively against planktonic forms.

We studied the antifungal activity of SCY-078 and micafungin against the sessile forms of C. albicans and non-Candida isolates causing fungemia in patients recently admitted to a large European hospital in Madrid, Spain.

METHODS

ISOLATES
C. albicans n= 55
C. parapsilosis n= 33
C. glabrata n= 31
C. tropicalis n= 8
C. krusei n= 12
Candida spp. n= 26
Non-Candida yeasts n= 23
Fluconazole resistant isolates n= 24
Echinocandin resistant isolates n= 9

Biofilm susceptibility to micafungin and SCY-078 by XTT
Determination of sessile MIC (SMIC078) as 80% reduction of metabolic activity in comparison with untreated control

Table 1. Antifungal susceptibility of biofilms to micafungin and SCY-078.

<table>
<thead>
<tr>
<th>Species</th>
<th>SMIC078 (Micafungin/SCY-078)</th>
<th>Percentile 90</th>
<th>Percentile 90</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. albicans</td>
<td>1.0/125</td>
<td>232</td>
<td>0.015 - 232</td>
<td></td>
</tr>
<tr>
<td>C. parapsilosis</td>
<td>16/125</td>
<td>232</td>
<td>0.015 - 232</td>
<td></td>
</tr>
<tr>
<td>C. glabrata</td>
<td>0.03/0.25</td>
<td>232</td>
<td>0.015 - 232</td>
<td></td>
</tr>
<tr>
<td>C. tropicalis</td>
<td>23/125</td>
<td>232</td>
<td>0.015 - 232</td>
<td></td>
</tr>
<tr>
<td>C. krusei</td>
<td>0.125/0.5</td>
<td>0.53/16</td>
<td>0.125/0.5 - 0.53/16</td>
<td></td>
</tr>
<tr>
<td>Candida spp.</td>
<td>28/23</td>
<td>0.3/10.6/23</td>
<td>0.150 - 232</td>
<td></td>
</tr>
<tr>
<td>Non-Candida</td>
<td>232</td>
<td>232</td>
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<tr>
<td>Fluconazole R</td>
<td>0.125/0.5</td>
<td>232</td>
<td>0.015/0.125 - 232</td>
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<td>C. mut. Candida</td>
<td>0.125/0.5</td>
<td>232</td>
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RESULTS

The anti-biofilm activity of the drugs tested is shown in Table 1. SMIC078 values for SCY-078 and micafungin were essentially the same against the biofilms generated by the different Candida spp. with the exception of C. glabrata in which micafungin had significantly lower SMIC values (P>0.001).

The impact of SCY-078 and micafungin exposure on the preformed biofilm structure was assessed by SEM (Figure 1).

C. albicans biofilms appeared with swollen blastospores and thin hyphae after exposure to micafungin (figure 2b) or SCY-078 (figure 2c).

The effect of micafungin against C. parapsilosis biofilms was slight and only a small reduction on the amount of yeast was observed (figure 2a), whereas the reduction in the amount of blastospores was more prominent after SCY-078 exposure (figure 2f).

C. tropicalis biofilm was very dense and thick (figure 3f) but micafungin (figure 2b) and SCY-078 (figure 2e) led to the presence of thin hyphae and swollen blastospores.

C. glabrata biofilm (figure 3j) was formed by a layer of clumped blastospores that became damaged after micafungin treatment (figure 3k) whereas SCY-078 treatment led to a lower effect (figure 3l).

CONCLUSIONS

Our study showed that SCY-078 has a high in vitro activity against Candida invasive isolates in sessile forms (biofilms) comparable to micafungin.

This study was supported by Scynexis and by FIII (Plan de I+D)

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