EUCAST technical note on anidulafungin

M. C. Arendrup, J.-L. Rodriguez-Tudela, C. Lass-Flörl, M. Cuenca-Estrella, J. P. Donnelly, W. Hope and The European committee on antimicrobial susceptibility testing - subcommittee on antifungal susceptibility testing (EUCAST-AFST)*

1) Unit of Mycology, Department of Microbiological Surveillance and Research, Statens Serum Institute, Copenhagen, Denmark, 2) Mycology Reference Laboratory, National Center for Microbiology, Instituto de Salud Carlos III, Majadahonda, Spain, 3) Division of Hygiene and Microbiology, Innsbruck Medical University, Innsbruck, Austria, 4) Department of Haemotology, Radboud University Nijmegen Medical Centre & Nijmegen University Centre for Infectious Diseases, Radboud University, Nijmegen, the Netherlands and 5) The University of Manchester, Manchester, UK

Abstract

The European Committee on Antimicrobial Susceptibility Testing-Subcommittee on Antifungal Susceptibility Testing has determined breakpoints for anidulafungin for Candida spp. This Technical Note is based on the EUCAST anidulafungin rationale document (available at: http://www.eucast.org). Species-specific breakpoints for C. albicans are $S \leq 0.03 \text{ mg/L}$ and $R > 0.03 \text{ mg/L}$ and for C. glabrata, C. tropicalis and C. krusei $S \leq 0.06 \text{ mg/L}$ and $R > 0.06 \text{ mg/L}$. C. parapsilosis was not regarded a good target for anidulafungin. There are insufficient data to set breakpoints for other species. The breakpoints are based upon pharmacokinetic data, epidemiological cut-off values and clinical experience. Breakpoints will be reviewed regularly.

Keywords: Anidulafungin, breakpoints, EUCAST Technical Note, susceptibility testing

Original Submission: 31 May 2011; Revised Submission: 28 July 2011; Accepted: 8 August 2011

Editor: E. Roilides

Article published online: 17 August 2011

Anidulafungin is an echinocandin antifungal agent active against most Candida species. Anidulafungin is predominantly used for the treatment of disseminated candidiasis in non-neutropenic adult patients. Most data regarding anidulafungin in vitro susceptibility are derived from patients with candidemia and a smaller number of patients with deep-seated organ infection.

The European Committee on Antimicrobial Susceptibility Testing-Subcommittee on Antifungal Susceptibility Testing (EUCAST-AFST) has determined breakpoints for anidulafungin for Candida spp. This Technical Note is based on the EUCAST anidulafungin rationale document (available on the EUCAST website: http://www.eucast.org). The rationale document includes more detail and published references related to the selection of EUCAST-AFST breakpoints (http://www.srga.org/eucastwt/MICTAB/EUCAST%20clinical%20MIC%20breakpoints%20-%20antimicrobials%20for%20Candida%20infections.htm).

The breakpoints are based on dosages of 200 mg/kg on day 1, then 100 mg/kg/day, and were established using MIC values from many sources. Wild-type isolates exhibit MICs of C. albicans $\leq 0.03 \text{ mg/L}$, C. glabrata, C. krusei and C. tropicalis $\leq 0.06 \text{ mg/L}$ and C. parapsilosis $\leq 4 \text{ mg/L}$. Isolates with mutations in the hot spot regions of the target gene have been associated with clinical failures or breakthrough infections during echinocandin treatment [1–3]. The anidulafungin MICs of such mutant isolates are as follows: $C. albicans > 0.03 \text{ mg/L}$, $C. glabrata > 0.06 \text{ mg/L}$, $C. tropicalis > 0.06 \text{ mg/L}$ and $C. krusei > 0.03 \text{ mg/L}$ [4]. However, it should be noted that most of the data on breakthrough infections derive from studies with caspofungin as caspofungin has been in use the longest (approved in Europe in 2001, whereas anidulafungin was approved in 2007). The clinical data from three clinical trials were used [5–7]. These studies did not include MICs by the EUCAST method so a correlation of in vitro MICs with clinical outcome is not possible.

The EUCAST breakpoints (Table 1) are based on pharmacokinetic and microbiological data and clinical experience.
Breakpoints for anidulafungin will be reviewed regularly. A number of in vitro studies on susceptibility of the fungus, of the target enzyme itself or in animal models have demonstrated cross-resistance between the three currently available echinocandins (anidulafungin, caspofungin and micafungin) for isolates with hot spot mutations in the target gene [3,10–15]. Hence, isolates categorized as anidulafungin susceptible can be regarded as susceptible to caspofungin and micafungin until drug-specific breakpoints are available for these two compounds.

Acknowledgements

None.

Transparency Declaration

The authors do not have any potential conflicts of interests related particularly to this paper. MCA has received research grants and acted as speaker for Astellas, Gilead, MSD and Pfizer, and been a consultant for Gilead, MSD and Pcovery. JLRT has received grant support from Astellas Pharma, Gilead Sciences, Merck Sharp and Dohme, Pfizer, Schering Plough, Soria Melguizo SA, the European Union, the ALBAN programme, the Spanish Agency for International Cooperation, the Spanish Ministry of Culture and Education, The Spanish Health Research Fund, The Instituto de Salud Carlos III, The Ramon Areces Foundation and The Mutua Madrileña Foundation. He has been an advisor/consultant to the Panamerican Health Organization, Gilead Sciences, Merck Sharp and Dohme, Pfizer and Schering Plough. He has been paid for talks on behalf of Gilead Sciences, Merck Sharp and Dohme, Pfizer and Schering Plough. JPD has been a consultant for Astellas, Gilead, Merck and Pfizer, received research grants from Pfizer and is on the speakers bureau for Gilead, Merck and Pfizer. WWH has research grants, consultant and/or speakers bureau, for Pfizer, Astellas, Gilead, Merck, Vectura and F2G.

References


