

SHIONOGI INTEGRATED SYMPOSIUM AT TIMM 2023

Breaking the mould: challenging the status quo of clinical trial response definitions for invasive fungal disease - **a debate**

Sunday 22nd October 2023, Plenary room, 12:30–14:15 EEST
Megaron Athens International Conference Centre, Athens, Greece



Session aim

To critically assess the current EORTC/MSG clinical trial definitions for outcomes and responses to antifungal therapy via debate

Proposition

“This house believes that the EORTC/MSG definitions of responses to antifungal therapy are no longer fit for purpose”

Faculty

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| Chair | Prof. Cornelia Lass-Flörl, Medical University of Innsbruck, Austria |
| Moderator | Prof. Malcolm Richardson, Manchester University NHS Foundation Trust, UK |
| Proposers | Prof. Johan Maertens, University Hospitals Leuven, Belgium Prof. Martin Hoenigl, Medical University of Graz, Austria |
| Opposers | Prof. Monica Slavin, The Peter MacCallum Cancer Centre, Australia Prof. George Thompson, University of California, USA |

Agenda

Session times in EEST

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| 12:30–12:45 | Welcome and introduction to the proposition | Prof. Cornelia Lass-Flörl |
| 12:45–12:50 | The rules of engagement | Prof. Malcolm Richardson |
| 12:50–13:05 | Proposer of the proposition | Prof. Johan Maertens |
| 13:05–13:20 | Opposer to the proposition | Prof. Monica Slavin |
| 13:20–13:30 | Secunder for the proposition | Prof. Martin Hoenigl |
| 13:30–13:40 | Secunder against the proposition | Prof. George Thompson |
| 13:40–14:00 | Q&A | Prof. Cornelia Lass-Flörl |
| 14:00–14:05 | Proposer and opposer summaries | Prof. Johan Maertens and Prof. Monica Slavin |
| 14:05–14:15 | Debate summary and meeting close | Prof. Malcolm Richardson and Prof. Cornelia Lass-Flörl |

The importance of clinical trial response definitions for new antifungals

The field of invasive fungal disease (IFD) continues to evolve rapidly. The launch of a limited number of antifungals in the last few years and the clinical development of new agents with novel mechanisms of action signify an exciting time for mycology. Nevertheless, significant unmet medical needs continue to face us. For new antifungals to become available to patients, consensus definitions for assessing response in clinical trials are of foremost importance.

The current definitions of response and study outcomes in clinical trials of invasive fungal infection (IFI) were published in 2008 by the European Organization for Research and Treatment of Cancer and the Mycoses Study Group (EORTC/MSG).¹ Their objective was to establish consensus criteria for evaluating therapeutic responses to antifungal therapy in Phase 3 clinical trials of IFI.

Uses and challenges of the current clinical trial response definitions

In patients where all three sub-elements (clinical, mycological and radiological) of the current response definitions are congruent in indicating improvement, the assessment of therapeutic responses appears to be clear and straightforward. However, divergence among these signals is all too common, making the assessment of the therapeutic response more challenging.

In addition, the current definitions have not been objectively assessed for certain types of difficult to treat infections, such as extrapulmonary invasive aspergillosis (IA), nor infections caused by rarer moulds or the endemic mycoses. The time to assess response in clinical trials may not be appropriate for all moulds, as the natural course of different IFDs may not reflect the natural course of IA. Mortality is also a complex endpoint to use in clinical trials of patients with IFD, as this can be impacted by both the disease and underlying risk factors. Lastly, although there are associated limitations, the role of biomarkers and laboratory tests in assessing treatment responses has significantly increased.

In closing, the current EORTC/MSG definitions of response to antifungal therapy have now been used in many clinical trials and have been shown to be appropriate in first-line studies of some types of IFD to an extent, as well as in allowing comparison of clinical trial results. Nonetheless, challenges remain. It has been 15 years since the current definitions were published, and notable progress has been made in the field and in our overall understanding of IFD since then.

The purpose of this debate

This debate is a unique chance to assemble the world's leading IFD experts in one forum, to contest and explore the fundamental aspects of how we assess responses to antifungal therapy in clinical trials.

Should we keep the status quo of response definitions for IFD, modify the definitions, or restart the development of them de novo?

Reference:

1. Segal BH, et al. Defining responses to therapy and study outcomes in clinical trials of invasive fungal diseases: Mycoses Study Group and European Organization for Research and Treatment of Cancer consensus criteria. *Clinical Infectious Diseases* 2008;47:674–83.



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