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A protocol for an international, multicentre pharmacokinetic study for Screening Antifungal Exposure in Intensive Care Units: The SAFE-ICU study

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[a] University of Queensland Centre for Clinical Research, Faculty of Medicine, The University of Queensland, Brisbane, QLD, Australia
[b] Departments of Intensive Care Medicine and Pharmacy, Royal Brisbane & Women's Hospital, Brisbane, QLD, Australia
[c] Division of Anaesthesiology Critical Care Emergency and Pain Medicine, Nîmes University Hospital, University of Montpellier, Nîmes, France
[d] Jamieson Trauma Institute, Royal Brisbane & Women's Hospital, Brisbane, QLD, Australia
[e] Department of Intensive Care, Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, Portugal
[f] Department of Pharmacy and Radboudumc Institute of Health Sciences, And Radboudumc/CWZ Center of Expertise in Mycology, Radboud University Medical Center, Nijmegen, Netherlands
[g] Department of Critical Care, The University of Melbourne, Melbourne, VIC, Australia
[h] Department of Intensive Care, Royal Melbourne Hospital, Melbourne, VIC, Australia
[i] Department of Intensive Care Medicine, Ghent University Hospital, Ghent, Belgium
[j] Department of Internal Medicine and Pediatrics, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium
[k] 3rd Department of Critical Care, EVGENIDIO Hospital, Medical School, National and Kapodistrian University of Athens, Greece
[l] UR-UM103 IMAGINE, Univ Montpellier, Division of Anesthesia Critical Care, Pain and Emergency Medicine, Nîmes University Hospital, Montpellier, France
[m] Kulliyyah of Medicine, International Islamic University Malaysia, Kuantan Campus, Malaysia
[n] Clinical Research in Pneumonia & Sepsis, Vall D'Hebron Institute of Research, Barcelona, Spain
[o] Faculty of Medicine, The University of Queensland, New Orleans, LA, United States
[p] Intensive Care Unit, Ochsner Health System, New Orleans, LA, United States
[q] National Centre for Infections in Cancer and Department of Infectious Diseases, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia
[r] Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia
[s] Victorian Infectious Diseases Service, Royal Melbourne Hospital, Melbourne, VIC, Australia
[t] Intensive Care Medicine, Department of Perioperative, Intensive Care and Pain Medicine, University of Helsinki and Helsinki University Hospital, Finland
[u] Department of Public Health and Infectious Diseases, University “Sapienza” of Rome, Rome, Italy
[v] Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, Hong Kong
[w] Department of Clinical Pharmacology, Medical University of Vienna, Vienna, Austria

Abstract
Objective: To describe whether contemporary dosing of antifungal drugs achieves therapeutic exposures in critically ill patients that are associated with optimal outcomes. Adequate antifungal therapy is a key determinant of survival of critically ill patients with fungal infections. Critical illness can alter an antifungal agents’ pharmacokinetics, increasing the risk of inappropriate antifungal exposure that may lead to treatment failure and/or toxicity. Design, setting and participants: This international, multicentre, observational pharmacokinetic study will comprise adult critically ill patients prescribed antifungal agents including fluconazole, voriconazole, posaconazole, isavuconazole, caspofungin, micafungin, anidulafungin, and amphotericin B for the treatment or prophylaxis of invasive fungal disease. A minimum of 12 patients are targeted for enrolment for each antifungal agent, across 12 countries and 30 intensive care units to perform descriptive pharmacokinetics. Pharmacokinetic sampling will occur during two dosing intervals (occasions): firstly, between days 1 and 3, and secondly, between days 4 and 7 of the antifungal course, collecting three samples per occasion. Patients’ demographic and clinical data will be collected. Main outcome measures: The primary endpoint of the study is attainment of pharmacokinetic/pharmacodynamic target exposures that are associated with optimal efficacy. Thirty-day mortality will also be measured. Results and conclusions: This study will describe whether contemporary antifungal drug dosing achieves drug exposures associated with optimal outcomes. Data will also be used for the development of antifungal dosing algorithms for critically ill patients. Optimised drug dosing should be considered a priority for improving clinical outcomes for critically ill patients with fungal infections. © 2023

Author Keywords
Antifungal agents; Critically ill; Dosing; Intensive care unit; Pharmacokinetics

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Correspondence Address
Roberts J.A.; University of Queensland Centre for Clinical Research, Australia; email: j.roberts2@uq.edu.au

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