



Quarterly Newsletter

Winter 2014

Welcome to the *Mycoses Study Group Quarterly Newsletter, Winter 2014*. This newsletter is intended to keep our investigators and supporters informed of the developments within the **MSG ERC** and to encourage support and involvement in our ongoing activities.

I. Meetings

MSG 2013 Annual Meeting and CME Symposium

On Tuesday, September 10th, the 2013 MSG Annual Meeting was held in Denver, CO. There were 52 investigators and 31 industry representatives present at the meeting. Updates were presented from the Education Committee, study chairs, and representatives from pharmaceutical and diagnostic companies. Following the updates, attendees met in breakout sessions to discuss and present new potential research concepts for *Candidiasis*, *Aspergillosis/other molds* and *Cryptococcosis/Endemic Fungi sections*.

On Wednesday, September 11th, the MSG hosted a Reception, followed by a CME Symposium entitled *Invasive Mycoses: Consider the Source, Consider the Host*. The symposium was a case-based live event. In total, 319 people attended the event! We want to thank our educational partner, Terranova Medica, and our CME provider, University of Nebraska for a successful program. We also want to thank the CME commercial supporters, Astellas, Merck, Gilead, T2 Biosystems, MiraVista, Viracor and IMMY Diagnostics. Program development is already underway for 2014 activities. We hope to have an even larger turnout next year at the Annual Meeting and symposium during ICAAC 2014 in Washington DC. Please be looking for our announcement of the date of the 2014 Annual Meeting and CME Symposium.

II. Clinical Trials Update

MSG-01: A randomized, double-blind, placebo controlled trial of caspofungin prophylaxis followed by preemptive therapy for invasive candidiasis in high risk adults in the critical care setting.

PI: Luis Ostrosky-Zeichner
Corporate Sponsor: Merck

This study was completed with 222 subjects enrolled. The data analysis is complete; the data were presented at SHEA 2011 in March. A revised manuscript has been accepted to CID (November 2013).

MSG-02: Candidemia Meta-analysis

PIs: Baddley, Andes, Safdar, Playford, Kullberg

Analysis and the manuscript are complete. The manuscript was published by *Clinical Infectious Diseases* – 2012;54(8):1110-22. doi:10.1093/cid/cis021

MSG-03: Invasive Aspergillosis Combination Study

PI: Kieren Marr

Corporate Sponsor: Pfizer

This trial was completed on February 22, 2011 with a total of 459 patients enrolled and 454 patients dosed. A poster was presented at ECCMID in London in April 2012. The manuscript has been submitted to *Annals of Internal Medicine* (October 2013).

MSG-04: Empirical Antifungal Therapy in the ICU

PI: Luis Ostrosky-Zeichner

Corporate Sponsor: Merck

This pilot study began enrollment in late December 2010. Due to slow enrollment, the Data Monitoring Committee recommended closing enrollment. The study's steering committee also felt that it was unlikely that study endpoints would be met due to slow enrollment and therefore closed the study on May 9, 2012 with 15 out of 114 patients enrolled. No safety issues were found with the study.

MSG-05: A re-analysis of the voriconazole versus amphotericin B followed by other licensed antifungal therapy for invasive aspergillosis trial (Herbrecht et al. NEJM 2002; 347: 408-15)

PI: Raoul Herbrecht

Corporate sponsor: Pfizer

The purpose of this project was to reanalyze the existing database from the pivotal study comparing voriconazole to amphotericin B followed by OLAT for primary treatment of invasive aspergillosis. The analysis was presented at ICAAC). This study is completed and a final version of the manuscript is being prepared.

MSG 06: The Phaeohyphomycosis Registry

PIs: Sanjay Revanker, John Baddley, Sharon Chen

Corporate sponsors: Merck, Gilead, Astellas

Enrollment began on October 31, 2012. 37 cases have been entered to this point. The registry will include cases diagnosed from January 1, 2011 to present. Eleven sites are active, two are in the IRB approval and contract phase, and site selection continues. Sites included are from South America (1), Australia (2), and North America (13). This project will prospectively identify 150 patients from these sites and collect all relevant

clinical, diagnostic, mycological and treatment/outcome information relating to this uncommon mycosis. These data will ultimately be merged with relevant data from the ongoing *Fungiscope* project led by Oliver Cornelly in FRG. An important component of this study is that CDC has agreed to serve as specimen repository for the project, providing access to these clinical specimens by all MSG investigators.

MSG 07: Cryptococcosis Combined Analyses

PI: Peter Pappas, John Baddley, Sharon Chen, Emilio DeBess, Eleni Galanis, Julie Harris, Nicola Marsden-Haug, John Perfect, Peter Phillips
Corporate Sponsor: Merck

This retrospective study proposes to evaluate archived cases of *C neoformans* and *C gattii* from UAB, Duke, Australia, BC Canada, Washington, and Oregon. Up to 1200 well defines cases are anticipated. UAB has signed data use agreements with DUMC (John Perfect) and Westmead Hospital, Sydney, AU (Sharon Chen). The agreements for other participating sites are still in review. UAB has received data from DUMC and Westmead. Data merger has begun. Analysis is planned to begin by early spring and to be completed by summer 2014.

MSG 08: Epidemic Mold Infections in U.S.

PI: Carol Kauffman, John Bennett, Dimitrios Kontoyiannis, Kieren Marr, Tom Patterson, John Perfect, Sanjay Revankar, Tom Walsh, Tom Chiller, Peter Pappas
Corporate Sponsor: CDC, Gilead, Merck

MSG has received funding from Merck and Gilead to support a project based on capturing the detailed long term clinical and therapeutic features of this outbreak. The MSG will also be receiving funds from CDC in support of this project. Data points are to include diagnostic, clinical, radiologic, treatment and outcomes data, and these data will be reviewed in a real-time fashion in order to help define disease management. MSG's role will consist of site selection, electronic case report form development, data management and analysis, and to create a Clinical Advisory Panel. Initially, investigators at sites with at least 10 cases will be invited to participate. Once these sites are operational, then the group will consider including sites with lower case burdens. 10 sites have received IRB approval, and enrollment has begun at 7 sites. Current enrollment is at 98.

MSG 09: Prospective study of cryptococcosis among non-HIV infected patients

PI: Kieren Marr, MD
Sponsor: NIAID

The newest MSG study was proposed by Kieren Marr to prospectively identify patients with cryptococcosis who are HIV negative. This study is observational, and will capture all relevant epidemiology, clinical and therapeutic data. In addition, immunologic and genetic studies will be performed on each study participant to explore host response to infection and genetic predispositions to disease expression. Enrollment begins at several US sites in March 2014.

The study was originally proposed as an international study, but is limited to US sites due to NIAID budget limitations. A parallel international study, MSG 09a, is being

proposed and would potentially involve sites in Canada, Australia, France and Brazil. Gilead and Astellas have been approached for support of this proposal, their decisions are pending.

EORTC/MSG Update Treatment Definitions Project

The EORTC and MSG are partnering again to update the definitions of invasive fungal infections. At least 10 working groups constituted of investigators from EORTC and MSG have been formed and will begin work soon to revisit these definitions which were last updated in 2008. Several of the groups have started the process of updating these definitions, and work will continue through much of 2014.

III. Other Activities

MSG Non-Profit Organization (NPO) Status

MSG has taken steps in becoming a NPO. Papers have been filed with the state of Alabama and the U.S. Internal Revenue Service (IRS). We expect IRS approval in the near future, but we are currently legally able to operate as a NPO while waiting for approval. The MSG's official name is now the [MSG Education and Research Consortium \(MSG ERC\)](#). A new MSG ERC website will be launched early 2014. Keep an eye open for our press release that is planned at the time the new website is launched. We will keep you posted via email for the launch and press release.

The Mycoses Study Group is adapting to a changing clinical research and continuing medical education environment by establishing a non-profit organization that is external to the UAB institution called the Mycoses Study Group Education and Research Consortium (MSGERC). The MSG Central Unit will remain at the UAB Division of Infectious Diseases for the purpose of conducting clinical trials at the UAB site and managing those trials at multi-center sites. However, other functions of the MSG would be handled by the MSG non-profit organization. Former MSG Administrator, Carolynn Thomas Jones, DNP, MSPH, RN has been brought in as a consultant Executive Director for the MSGERC to assist in the transition and to help the group vision and execute its new purpose. The purposes for this charitable, non-profit corporation are to provide:

- (a) robust and innovative continuing medical education;
- (b) a medical/scientific think tank for evidence-based medicine in the diagnoses, prevention, treatment and maintenance of patients at risk for or afflicted with invasive fungal infections;
- (c) a resource that supports patients and caregivers who are affected by these serious rare disease.

Educational Initiatives for 2014

The University of Nebraska Medical Center for Continuing Education, in conjunction with the Mycoses Study Group Educational & Research Consortium (MSG ERC) and Terranova Medica, LLC, are submitting grant requests for:

- An internet-based CME initiative with 4- and 8-month updates entitled, *The New Antifungal Toolkit: The Pharmacopeia and Beyond*.
- ICAAC-affiliated live CME symposium and companion web-based enduring materials initiative entitled, *Clinical Decision Making in Mycology: Working Through Difficult Clinical Scenarios*
- Web-based “Case of the Month”
- Web-based “Top 10 in Invasive Mycoses”

The first two grant proposals, *The New Antifungal Toolkit: The Pharmacopeia and Beyond* and the ICAAC-affiliated live CME symposium and companion web-based enduring materials initiative have been submitted for funding. We are working on the grant proposals for the Top 10 and Case of the Month submissions.

IV. MSG Administration

Administrative Structure

MSG Central Unit:

Peter G. Pappas, MD, PI
Beth Deerman, RN, MSN, Administrator, MSG Central Research Unit
Vicki Noles, Administrative Assistant
Joy Fleisher, Financial Associate
Lesa Resato Burson, CCRP, Regulatory Specialist, MSG Central Research Unit
Carolynn Thomas Jones, DNP, MSPH, RN, MSG ERC Consultant Executive Director

MSG Steering Committee (SC):

Peter G. Pappas, Chair (US)
Helen Boucher (US) Peter Donnelly (NETH) Raoul Herbrecht (FR)
Carol Kauffman (US) Bart-Jan Kullberg (NETH) Kieren Marr (US)
Marcio Nucci (BRA) Tom Patterson (US) John Perfect (US)
Jack Sobel (US) Tania Sorrell (AU) Thomas Walsh (US)
John Wingard (US)

John Bennett, Jack Edwards, Emilio Bouza, Eric Bow and Thierry Calandra will serve as non-voting advisors.

MSG Education Committee (EC):

US: George R. Thompson (Chair) John Baddley (Co-chair)
Barbara Alexander David Andes John Bennett
Helen Boucher Graeme Forrest Alison Freifeld
Susan Hadley Carolynn Jones Dimitrios Kontoyiannis
L.Ostrosky-Zeichner Peter Pappas Tom Patterson

Europe: Olivier Lortholary (FR)
Bart-Jan Kullberg (NETH)

Oliver Cornely (FRG)

Latin America: Luis Thompson (CHI)

Marcio Nucci (BRA)

Australia: Monica Slavin (AUS)

Educational Partners: Lisa Tushla, Tom Davis (TerraNova Medica, LLC)
Lois Colburn (University of Nebraska, CME)