

# The MSG

## *Mycoses Study Group*

### *Quarterly Newsletter Summer 2009*



Welcome to the ***Mycoses Study Group Quarterly Newsletter, Summer 2009***. This newsletter is intended to keep our investigators and supporters apprised of the developments within the **MSG** and to encourage support and involvement in our ongoing activities.

#### *I. Meetings*

*MSG Reception at ICAAC: San Francisco, CA  
September 12-15, 2009*

There will be a **MSG 2009 Reception and Business Meeting** on **September 13, 2009** from **5:30-7:30 PM** in the **Conference Theater** at the **Grand Hyatt San Francisco Hotel** located at 345 Stockton Street San Francisco, CA 94108. Light snacks and beverages will be offered, followed by a short business meeting and update of current and future MSG projects.

The MSG is also co-sponsoring several symposia at ICAAC this fall. These include two symposia entitled '**Innovative Therapeutics for Invasive Fungal Infections**' and '**Identification and Clinical Significance of New Fungal Species**'. Both of these symposia will take place on Monday, September 14.

#### *MSG 2010 Annual Meeting*

The **MSG 2010 Annual Meeting** will be held on **April 7- 8, 2010** at the Courtyard Marriott in Downtown Philadelphia. More information will be provided at a later date. Please make plans to join us in Philly!

## *Advances Against Aspergillosis*

The MSG is a supporter of the AAA. During their next meeting, AAA4, which is scheduled for February 4-6, 2010 in Rome, Italy, a MSG lecturer (to be named) will be presenting. Be sure to visit their website to stay apprised ([WWW.AAA2010.org](http://WWW.AAA2010.org)).

### *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 & Co.

All 16 selected sites necessary for this study have been opened for enrollment. Currently, enrollment is at 74% completion with **165** subjects enrolled. The study is registered on Clinicaltrials.gov website.

#### **MSG-02: Candidemia meta-analysis**

PIs: Baddley, Andes, Safdar, Playford, Kullberg

Although not formally a “clinical trial”, this concept was presented and approved by the **MSG Steering Committee** and will examine the randomized candidemia treatment trials that have been completed to date. The ‘**working group**’ consists of junior investigators (John Baddley, David Andes, Nasia Safdar,) and a senior advisory group. Bart-Jan Kullberg serves as the primary senior advisor to this group, helping formulate an analysis plan, assigning responsibilities, establishing a timetable, etc. An update will be provided at the **MSG Reception at ICAAC**, and a full presentation is expected at the **2010 MSG annual meeting**.

#### **MSG-03: Invasive Aspergillosis Combination Study**

PI: Kieren Marr

Corporate Sponsor: Pfizer

At this time, 175 total sites, domestic and international, have been selected to participate in this pivotal trial. To date, 49 domestic sites and 109 international sites have been opened for enrollment. 199 patients have been enrolled, 22 from the U.S. and 177 from international sites. We are continuing to recruit additional centers for participation and welcome all suggestions. Please contact our administrator, Beth Deerman, RN, BSN ([jbeth@uab.edu](mailto:jbeth@uab.edu)) with suggestions regarding additional sites.

## **MSG-04: Empirical Antifungal Therapy in the ICU**

PI: Luis Ostrosky-Zeichner

Corporate Sponsor: Merck & Co.

The MSG Steering Committee has approved a new clinical trial entitled “*A pilot randomized, double-blind, placebo-controlled trial of caspofungin empirical therapy for invasive candidiasis in high-risk adults in the critical care setting*“. This is a feasibility study that will assess the utility of a clinical scoring system to select ICU patients to be included in a study comparing caspofungin vs. placebo for empiric therapy for patients at high risk for invasive candidiasis. The trial will be conducted at selected international sites, and will have a target enrollment of approximately 120 patients. There will be a working meeting of the protocol committee at ICAAC (TBD) to provide further input into the development of the protocol.

### *III. MSG / FDA / EMEA Galactomannan Project*

The proposal for the use of galactomannan as a qualified biomarker in the context of a clinical trial for treatment of invasive aspergillosis was judged by the FDA Biomarker Qualification Review Team and the EMEA to have a potentially important impact on drug development and regulatory review. Johan Maertens, Paul Verweij, Barb Alexander, Kieren Marr, and Joe Wheat have spearheaded this effort in the US and Europe. Their leadership and the **MSG's** supporting role in bringing this effort together culminated in the submission of this document to the FDA/EMEA in March 2008. Our response to the FDA's queries was submitted in June, 2009. We are awaiting their response.

### *IV. The MSG Education Committee*

The EC is actively working on setting the 2009 educational agenda. We continue to work closely with the University of Wisconsin as the CME provider and Debra Joyce of Fallon Medica as we develop this agenda and approach potential sponsors for financial support of these activities. These programs will be developed for a variety of venues including, but not limited to, support for the MSG Annual Meeting CME Program, traditional grand rounds, regional seminars, national/international meetings, support of Dr. Fungus, and Web-based educational programs.

### *V. Ongoing discussions*

We are having ongoing discussions with the following companies concerning the **MSG's** involvement in the clinical development of these compounds:

**SPRI:** We await the development/availability of the I.V. formulation of posaconazole for evaluation in clinical trials of aspergillosis and zygomycosis.

**Novartis:** These discussions remain on hold at this time pending further assessment by Novartis regarding the future of efungimab (Mycograb). If the development of this product moves forward, the MSG remains interested in the clinical development of efungimab in the context of a large international candidemia trial.

We are also in very preliminary discussions over the further development of deferasirox (Exjade) as adjunctive therapy for zygomycosis. More in the coming months.

**Merck :** The impact of the Merck/Schering-Plough merger, planned for later this year, is unclear, but as this moves forward we will provide any useful insights that pertain to the research environment.

**Basilea:** Many of our members are participating in studies involving isavuconazole for the treatment of candidemia and aspergillosis. These studies are on hold, pending further notice, but likely to be resumed in the next 6 months or so. The MSG has not entered into any formal discussion with Basilea concerning further development of isavuconazole, but we remain very interested in this compound.

## *VI. MSG Administration*

### **Authorship Guidelines**

MSG authorship guidelines were presented at the annual meeting and were previously approved by the MSG Steering Committee. These guidelines will take effect immediately. A synopsis of these guidelines is provided below:

#### **1. Composition of the writing committee for papers**

A writing committee, which will oversee authority of the primary results from each official MSG study, will be appointed by the protocol chair and the principal investigator of the MSG. The chair of the writing committee will be the protocol chair, and the committee will typically consist of:

- a) The protocol chair
- b) The principal investigator of the MSG
- c) The study statistician(s)
- d) Other individuals who have substantially contributed to this study as determined by the protocol chair and MSG PI including investigators, an employee of the sponsoring company, central unit staff or study coordinators;
- e) All authors must meet the International Committee of Medical Journal Editors (ICMJE) guidelines for authorship. These criteria are based on 1) substantial contributions to concept and design or acquisition of data or analysis and interpretation of data; 2) drafting or revising the manuscript for important intellectual content; and 3) approval of the final version of the manuscript to be published.
- f) For joint studies involving other study groups (eg, ACTG, EORTC), the writing committee will be merged with a similarly constituted writing committee from the collaborative group.

g) If additional manuscripts result from any official MSG study, then additional writing committees will be constituted for each of these manuscripts. The same general guidelines will apply.

## **2. Authorship**

Authorship and the order in which authors are listed for a given manuscript should reflect workload, intellectual contribution, and patient enrollment. The composition of authorship would differ depending on the number of institutions involved, the number of patients accrued, and the nature of any special assessments such as laboratory studies.

The masthead for authorship of a manuscript will be determined by journal guidelines. For example, the number of authors may vary from few (3-7) to many (15-25). The writing committee chair will determine the ultimate order of names of the masthead. If there is any appeal about the order of authors, the MSG principal investigator will make the final decision.

Per ICMJE and these guidelines, acquisition of funding, collection of data or general supervision of their research, membership on a data review committee (DRC) or data safety and monitoring board (DSMB) alone *do not* necessarily qualify for authorship. For persons who do not meet the criteria for authorship, but have contributed to the manuscript, these individuals should be listed in the acknowledgements section.

## **3. Data analysis for proposed publications**

Data analysis for proposed publications will generally be performed by the independent statistician for the individual MSG study. In cases where the study statistician does not perform the analysis, the study statistician must validate the analyses prior to submission of the manuscript to any journal. Authors will have independent access to the data set in accordance with the current guidelines of the ICMJE, taking into account regulatory requirements for subject confidentiality.

## **4. Approval of draft manuscripts**

The writing committee will prepare drafts of the manuscript. Before a submission of the final paper to a peer-reviewed journal, the draft will be circulated to all investigators participating in the particular study, the MSG central unit, the MSG principal investigator, the study statistician, and representatives of industry, where appropriate, for suggestions and comments.

## **5. Journal submission and editorial changes**

Selection of the journal will be at the discretion of the chair of the writing committee. After a journal review of a manuscript has been completed, the dialogue between editors, reviewers and the writing committee will be handled at the writing committee level.

## **6. Acknowledgements**

In addition to authorship, an MSG manuscript will acknowledge all participating and institutions that have enrolled patients. The listing of institutions will be in order of the

number of valuable patients. The listing may include up to four persons per participating institution, participating MSG central unit staff and biostatistical staff.

#### **7. Publication of sub-study results**

Primary manuscripts for sub-studies will follow the above procedure with the exception that publication of data from a sub-study should not interfere with the completion of the parent manuscript, the parent study (eg, reveal the randomization code) or publication of the primary manuscript.

#### **8. Publishing individual site results**

Rarely, the site investigators may create manuscripts detailing the study at their sites. However, these manuscripts must be submitted for review to the MSG central unit and the biostatistical unit prior to submission for publication. The maximum length of time a manuscript or abstract can be held by the MSG central unit, industry co-sponsor and the fiscal unit before review prior to publication will be defined in the CTA in the site list of responsibilities. The submission of manuscripts restricted to individual site data will not interfere with the completion of the parent study (eg, reveal the randomization code) or publication of the primary manuscript.

#### **9. Policy on abstracts**

- a) Guidelines for manuscript writing listed above apply where appropriate to abstracts. Timelines as outlined in the signed CTA will be observed.
- b) No presentation of primary results from any MSG study will be made without the approval of the MSG PI, the biostatistician, or the industry co-sponsor.
- c) A copy of all abstracts based on MSG studies must be submitted to the MSG investigator and the study biostatistician simultaneously before submission for consideration for presentation.

### **Administrative Structure**

#### **MSG Central Unit:**

Peter G. Pappas, MD, PI  
Beth Deerman, RN, Administrator  
Peggy Cornelius, Financial Associate  
Joyce Kanute, Administrative Assistant

#### **MSG Steering Committee (SC):**

Peter G. Pappas, Chair (US)  
Carol Kauffman (US)    Tania Sorrell (AUS)  
John Wingard (US)    Jack Sobel (US)    Eric Bow (CAN)  
Tom Patterson (US)    John Perfect (US)    Marcio Nucci (BRA)  
Raoul Herbrecht (FR)    Emilio Bouza (SPA)    Thierry Calandra (SU)  
John Bennett and Jack Edwards will serve as non-voting advisors.

**MSG Education Committee (EC):**

**US:** Susan Hadley (Chair)

David Andes (Co-chair)

John Bennett

Alison Freifeld

Peter Pappas

Barbara Alexander

Helen Boucher

Dimitrios Kontoyiannis

Tom Patterson

John Baddley

Graeme Forest

L. Ostrosky-Zeichner

Kieren Marr

**Europe:** Olivier Lortholary (FR)    Oliver Cornely (FRG)

Bart-Jan Kullberg (NETH)

**Latin America:** Luis Thompson (CHI)    Marcio Nucci (BRA)

**Australia:** David Ellis (AUS)