Marina Djordjevic, MD

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Dr. Djordjevic is currently starting work on her doctoral thesis "Fungal Infection," under the tutorship of Dr. Jorge Garbino and Prof. Dr. Daniel Lew at University Hospital of Geneva, Switzerland. She is finishing her master thesis "Clinical-Epidemiological Characteristics and the Significance of Immuno-Diagnostic Tests in Tularemia" in Serbia.

Swiss Society for Infectious Diseases (SSI)/ISID Infectious Diseases Research Fellowship Program Final Report

by Marina Djordjevic, MD • Infectious Diseases Clinic, University of Nis • Serbia

During my stay at the University Hospital of Geneva Switzerland in the Department of Infectious Diseases, for one year from October 2004 to October 2005, I participated as a co-investigator under tutorship of Dr. Jorge Garbino and Prof. Dr. Daniel Lew in the following five clinical studies:

- Azithromycin in prevention of pneumonia in ventilated patients colonized with *Pseudomonas aeruginosa.*
- Micafungin versus Caspofungin in the treatment of invasive candidiasis or candidemia.
- Swiss candidemia surveillance in University Hospital of Geneva
- Ceftobiprole versus Vancomycine in the treatment of complicated infections of the skin and soft tissue.
- Retrospective Survay of Aspergillosis in the non neutropenic host

1) Azithromycin in prevention of pneumonia in ventilated patients colonized with *Pseudomonas aeruginosa.*

The primary study objective was the study of the clinical efficacy of azithromycin 300mg i.v. 1/d used as quorum-sensing (QS) blocker, for prevention/delaying occurrence of *P. aeruginosa* pneumonia. The secondary objective was to demonstrate using in vitro and in vivo parameters if AZI can be used clinically as QS blocker against *P. aeruginosa*, to check if *P. aeruginosa* can develop resistance to the QS blocker effect of AZI, and further to check if prolonged use of AZI may induce resistance to any of 11 antipseudomonas antibiotics.

The study population was intubated patients with respiratory tract colonized by *Pseudomonas aeruginosa* (documented by tracheal aspirate). The study design was Multicente, 2-parallel group, double blind, randomized. Medication given was Azithromycin 300 mg i.v. daily vs. Placebo. The study duration was until extubation; or occurrence of pneumonia; or exitus; or a maximum of 20 days.

2) Micafungin versus Caspofungin in the treatment of invasive candidiasis or candidemia.

The objective was to determine the effectiveness and the safety of Micafungine vs. Caspofungine in the treatment of the invasive candidiasis and candidemia. The population group was adults with invasive candidiasis or candidemia. The study design was a Phase III, multicenter, double blind, randomized study. Medicaments used were a) Micafungine 100 mg/day; b) Micafungine 150 mg/day; c) Caspofungine 70 mg first day then 50 mg/day. All were given for at least 14 days. Inclusion criteria were patients with invasive candidiasis or documented candidemia.

3) Swiss candidemia surveillance in University Hospital of Geneva

The objective was to study prospectively epidemiology of candidemia and to centralize specimens of invasive Candida infections in a referent laboratory. The population was adults with candidemia (candida isolated from blood culture) and the study design was multicenter, prospective. Inclusion criteria were patients with documented candidemia.

4) Ceftobiprole versus Vancomycine in the treatment of complicated infections of the skin and soft tissue.

The objective of this study was to compare clinic results among patients with complicated infections of the skin and soft tissue. The population was adults with complicated infections of the skin and soft tissue and the study design was phase III, randomized, double-blinded, multicenter. Medicaments were given for a minimum of 7 days: a) Ceftobiprole 500 mg/12h, b) Vancomycine 1 g/12h. Criteria of inclusion were patients with diagnosis of complicated infections of the skin and soft tissue.

5) Retrospective Survey of Aspergillosis in the non neutropenic host

The objectives of this study were to collect retrospectively cases of aspergillosis in the non-neutropenic host. The primary objectives were to establish the frequency of Invasive aspergillosis and aspergilloma in the non-neutropenic patient population, and to establish the spectrum of other clinical manifestations and the potential association between certain disease manifestations, underlying condition(s)/disease(s) and clinical course. Secondary objectives were to identify the patients' comorbidities, to describe the different clinical presentations and their clinical course, to evaluate the contribution of the diagnostic procedures and diagnostic tools, to describe the response to antifungal treatment (duration, total dose) and the outcome, to evaluate our search strategies to identify patients in view of a future prospective study of aspergillosis in non-neutropenic patients. Study characteristics were retrospective observational study starting in 2004. The study duration was a 1-year period for the data collected in the year 2003. The study included patients with: signs and symptoms of disease; and evidence for mold infection by histology (confirmed aspergillus spp. by PCR) or culture from the site. A variety of approaches for identification of patients were used such as: clinical diagnosis (ICD code), direct exams, cultures, PCR, Galactomannan, autopsy, biopsy, radiological

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reports, surgical reports, administration of anti Aspergillus systemic antifungal agents.

The study population were the non-neutropenic, non-bone marrow patient population with signs and symptoms of disease and evidence for mold infection by histology (to be confirmed as aspergillus spp. by PCR) or culture from the site. This comprised the following groups of patient: Immunocompromised hosts, excluding the neutropenic and BMT patients; solid organ transplant recipients; surgical patients; ICU patients; intubated patients; patients with chronic lung diseases or cavities; patients under systemic corticotherapy or other immunosuppressive drugs; patients lacking recognized risk factors. Disease diagnostic criteria were signs or symptoms of disease and detection of aspergillus by culture or PCR. Patient inclusion criteria included the diagnosis of proven or probable: invasive aspergillosis (any organ or site); disseminated aspergillosis; sub-acute or chronic pulmonary aspergillosis; aspergilloma; aspergillus rhinosinusitis. And exclusion criteria included patients with allergic bronchopulmonary aspergillosis; patients with chronic fibrosing colonization; invasive aspergillosis in neutropenic patients; invasive aspergillosis in bone marrow transplant patients; invasive aspergillosis in leukemic patients. The sample size of the study was a minimum of 30–40 patients over a 1-year retrospective study period.

Apart from clinical research, I was involved in clinical consultations, clinical rounds and presentations, number of seminars and congresses. During the year I was accepted for a number of poster presentations and participated in several congresses. ❖

This Fellowship has been very important for my professional development. It has opened new areas of interest and scientific and clinical knowledge in the field of fungal infections and in the development of new drugs for their treatment.

I would like to thank ISID for supporting my research. I am also grateful to Dr. Jorge Garbino and Prof. Dr. Daniel Lew of the Infectious Diseases Department, Geneva for their support, great advice and vast experience.