

European Science Foundation
Standing Committee for the European Medical Research Councils (EMRC)

ESF EMRC EXPLORATORY WORKSHOP

**Network on primary HIV infection in
Europe: when and how**



Scientific Report

Cesano Maderno, Italy, 5-6 October 2006

**Convened by:
Giuseppe Tambussi**

Clinic of Infectious Diseases, Milano, IT



INTRODUCTION

Primary or acute HIV infection refers to the specific time of HIV viral infection or viral inoculation, while early HIV infection refers to the period of time when people have recently become infected. In the vast majority of adult cases (85%) early HIV infection is associated with an acute viral syndrome. Clinically, these symptoms are similar to those of any other acute viral illness – fever, sore throat, fatigue, weight loss, and myalgia. The clinical signs of HIV infection include skin rash, lymphadenopathy, splenomegaly, arthritis, and less frequently, aseptic meningitis. In infants, clinical signs and symptoms of HIV infections occur less frequently.

From a public health perspective, the identification of individuals with acute or early infection is extremely important. People need to be informed about their medical treatment options and how they can prevent the further spread of infection. HIV viral load, the amount of HIV circulating in the blood, can be very high in the first few weeks of infection. Some studies suggest that early treatment to suppress viral replication may affect the future course of disease. In addition, in order to prevent transmission, counselling and education about high-risk behaviours are essential during this stage of HIV disease. Viral load can be very high in genital secretions during early HIV infection, yet because people feel healthy, they may engage in behaviours that continue to spread infection.

In order to better understand the events occurring during acute and early infection, we want to explore the possibility to establish an European network, focused on the mechanisms of HIV infection and will use interventions in the acute and early phases of HIV infection to gain more information about the pathogenesis and treatment of HIV disease.

PURPOSE

The goal of this initiative is to build an European network of HIV Acute Infection and Early Disease Research Units through scientific collaboration agreements. Each awarded unit will perform innovative, integrated, investigator-initiated pathogenesis and clinical research on acute (i.e, within one month post initial infection) and early (i.e., up to 12 months post initial infection) HIV-1 infection. The multi-unit format (Network) is required to enrol sufficient numbers of these hard-to-identify patients for study.

SCIENTIFIC CONTENTS OF THE WORKSHOP

G. Tambussi welcomed the attendees and gave a brief introduction underlining the main objectives of the meeting.

Subsequently, Dr. C. Moquin-Patthey clearly illustrated the research tools available through ESF, and suggested different ways to approach such tools and how to properly meet the Foundation requirements for the applications.

Since Prof. Weber was not able to participate in the meeting, his lecture was divided into two distinct parts. Prof Phillips gave an outstanding introductory speech on the relevance of conducting controlled clinical trials. Then Prof. Babiker exhaustively explained the model of the SPARTC trial, showing the possibility to establish a large international network on primary HIV infection, involving a large number of investigators worldwide.

The convenor chaired the first session (Prof. Clumeck was absent). The session was focused on two large collaborative international networks that have been set up in order to study different aspects of primary HIV infection. Dr. Porter illustrated the CASCADE project, funded by the European Community, focused on the epidemiological surveillance of early-acute infections in Europe. Dr. Kinlock-de Loes, showed the result of a clinical trial, the QUEST study, that has been carried out worldwide and that has involved several investigators present at the meeting. Prof Emilie, presented the preliminary data of INTERPRIM study, a randomized study carried out in France and aimed at understanding whether or not Interferon alfa can be used to purge the latently infected cells reservoirs. Finally, Dr. D'Offizzi presented the final results of a study conducted in Italy, and stressed the challenge of performing clear diagnosis of primary infection and then to recruit these patients in clinical trials.

After the coffee break, Prof Phillips gave a very comprehensive lecture on laboratory tests available for the study of the immune response, particularly focused on the assays that can be utilized to understand the dynamics of the interaction between the host and the virus during the early phases of the HIV infection.

Dr. Yerly chaired the second session. Dr. Marchetti gave an interesting talk on immune surrogate markers that can be used to monitor antiviral therapy, while Dr. Gori showed the results of two studies that were carried out on patients with primary HIV infection. Prof Chiodi speech was focused on the results of studies on both B and NK cells dynamics during primary HIV Infection.

The last session "National programs on PHI", was chaired by Prof. D'Arminio. Dr. Meyer, Dr. Mirò-Meda and Dr. Stellbrink, presented the France, Spain and Germany programmes on

primary HIV infection, and clearly showed the capability to build efficient National programmes, but also they have underlined the need to join the efforts in order to reach a reasonable number of patients and to have the chance to design randomized clinical trials. Given the delay due to very interesting discussions after each session, Dr. Tambussi postponed his talk to the afternoon round table.

After lunch, the round table was chaired by the convenor. Unfortunately, a strike of the public ground transportation in Italy, forced to shorten the schedule of the round table. Just before leaving, Dr. Moquin-Pathey assured her full support to help the group to define the best tool within those available in the ESF research programmes to attain this end.

Dr. Tambussi skipped his talk and made an official proposal to set up a stable European collaborative research group. This proposal stimulated a very interesting discussion about the possible strategies to achieve this.

ASSESSMENT OF THE RESULTS, CONTRIBUTION TO FUTURE DIRECTIONS OF THE FIELD

All attendees agreed to support the main objective of the workshop, i.e. to build a network HIV primary HIV infection and early disease Research Units in Europe.

Unlike many other major cooperative research projects, the structure of the groups and funding should not be linked to a specific experiment or clinical trial. Thus this mechanism has the potential for considerable flexibility in resource allocation which will facilitate the rapid testing of hypotheses about the pathogenesis of HIV infection and early phase clinical trials of promising treatments of acute/early HIV infection.

The multi year nature of a program announcement provides additional and necessary flexibility to allow the support for the scientific capability to expand and keep pace, as warranted, with this emerging, rapidly developing and high priority area of HIV-related research.

The participants authorized the convenor to explore, on behalf of each of them, the grant opportunities in this specific field.

FINAL PROGRAMME

Thursday 5 October 2006

Evening Arrival

Friday 6 October 2006

08.30 Welcome - Giuseppe Tambussi

08.35 Presentation of the European Science Foundation (ESF)

C. Moquin-Patthey (Standing Committee for European Medical Research Councils)

08.45 Lecture: Should We Treat Acute HIV Infection? – Rodeny Phillips/Abdel Babiker

Session 1: Setting up networks for studies and trials in PHI

Chairman: Giuseppe Tambussi

09.05 The CASCADE project - Kholoud Porter

09.20 The QUEST trial - Sabine Kinloch-de Loes

09.35 Existing international networks: the SPARTAC model - Abdel Babiker

09.50 The management of PHI patients in clinical trials - Gianpiero D'Offizi

10.05 The ANRS Intreprim trial – Dominique Emilie

Discussion

10.30 Coffee break

10.30 Lecture: HIV specific cellular immune responses in PHI - Rodney Phillips

Session 2: Highly standardized research lab collaborations across Europe

Chairman: Sabine Yerly

10.50 Immune surrogate markers and disease progression – Giulia Marchetti

11.15 Model of research lab network in Italy - Andrea Gori

11.30 The Swedish-Italian collaboration - Francesca Chiodi

Discussion

Session 3: National programs on PHI

Chairman: Antonella d'Arminio Monforte

12.00 France: the PRIMO cohort – Laurence Meyer

12.15 Spain - Josè Maria Miro Meda

12.30 Germany - Hans-Jürgen Stellbrink

Discussion

13.30 Lunch

14.30 Round table: Are we paving the road to an European network on PHI?

Chairs: Giuseppe Tambussi ALL

Departure

STATISTICAL INFORMATION ON PARTICIPATION

Total number of attendees: 16

Total number of attendees per country: 6 Italy; 4 United Kingdom; 2 France; 1 Germany; 1 Spain; 1 Sweden; 1 Switzerland.

M/F ratio: 10/6

Age: 25-35 (1); 36-45 (2); 46-55 (9); 56-65 (4);

FINAL LIST OF PARTICIPANTS

Convenor:

Giuseppe TAMBUSI Clinic of Infectious Diseases, San Raffaele Scientific Institute
Via Stamira d'Ancona, 20
20127 Milano Italy
Tel: +39 02 26467960
Fax: +39 02 26437030
Email: g.tambussi@hsr.it

ESF Representative:

Carole MOQUIN-PATTEY European Science Foundation, EMRC Unit
1 quay Lezay-Marnésia
67080 Strasbourg France
Tel: +33 388 76 71 00
Fax: +33 388 35 07 32
Email: cmoquin-patthey@esf.org

Participants:

Abdel BABIKER Medical Research Council HIV and Infectious, Diseases Group, Clinical Trials Unit
222 Euston Road
London NW1 2DA United Kingdom
Tel: +44 20 76704732
Fax: +44 20 76704815
Email: Abdel.Babiker@ctu.mrc.ac.uk

Francesca CHIODI, Microbiology and Tumorbiology Center, Karolinska Institute
Nobels väg 16
17177 Stockholm Sweden
Tel: +46 8 524 863 15
Email: Francesca.Chiodi@mtc.ki.se

Antonella D'ARMINIO MONFORTE Istituto di Malattie Infettive e Tropicali, Ospedale L. Sacco Università di Milano
Via G.B. Grassi, 74
20157 Milano Italy
Tel: +39 02 3560010
Fax: +39 02 3560805
Email: antonella.darminio@unimi.it

Gianpiero D'OFFIZI National Institute for Infectious Diseases Lazzaro Spallanzani (I.R.C.C.S), Clinical Department
Via Portuense, 292
00149 Roma Italy
Tel: +39 06 55170360
Fax: +39 06 55170407
Email: gdoffizi@inmi.it

Dominique EMILIE INSERM U131
32 rue des Carnets
92140 Clamart France
Tel: +33 1 41 28 000
Fax: +33 1 46 32 793
Email: emilie@ipsc.u-psud.fr

Andrea GORI Istituto di Malattie Infettive e Tropicali Ospedale L. Sacco Università di Milano
Via G. B. Grassi, 74
20157 Milano Italy
Tel: +39 02 39043350
Fax: +39 02 3560805
Email: andrea.gori@unimi.it

Sabine KINLOCH-DE LOES

Royal Free Centre for HIV Medicine Royal
Free University College Medical School
23 Pond St.
London NW3 2QG United Kingdom
Email: sabine@kinloch.u-net.com

Adriano LAZZARIN Clinic of Infectious
Diseases, San Raffaele Scientific Institute
Via Stamira d'Ancona, 20
20127 Milano Italy
Tel: +39 02 26437939
Email: a.lazzarin@hsr.it

Giulia MARCHETTI Istituto di Malattie
Infettive e Tropicali, Ospedale L. Sacco
Università di Milano
Via G.B. Grassi, 74
20157 Milano Italy
Tel: +39 02 39043350
Fax: +39 02 3560805
Email: giulia.marchetti@unimi.it

Laurence MEYER Service d'Epidémiologie et
de Santé Publique, INSERM U569/ INED /
Paris XI, Hôpital de Bicêtre
82 rue du Général Leclerc
94276 Le Kremlin-Bicêtre cedex - France
Tel: 33 1 45 21 23 34
Fax: 33 1 45 21 20 75
Email: meyer@vjf.inserm.fr

Jose Maria MIRO' MEDA Hospital Clinic
Universitari
Helios-Villarroel Building-Desk no. 26
Villarroel, 170
08036 Barcelona Spain
Tel: +34 93 2275586/5400
Email: miro97@fundsoriano.es

Rodney PHILLIPS The Peter Medawar
Building for Pathogen Research, University
of Oxford
Oxford United Kingdom
Tel: +44 1865 281230 Secretary
Fax: +44 1865 281890
Email: rodney.phillips@ndm.ox.ac.uk

Kholoud PORTER Medical Research Council,
HIV and Infectious Diseases Group, Clinical
Trials Unit
222 Euston Road
London NW1 2DA United Kingdom
Tel: +44 20 76704732
Fax: +44 20 76704815
Email: kp@ctu.mrc.ac.uk

Hans-Jurgen STELLBRINK
Universitätskrankenhaus Eppendorf,
Medizinische Kernklinik und Poliklinik
Martinistr. 52
20246 Hamburg Germany
Tel: +49 42803 2831
Fax: +49 42803 5187
Email: stellbri@uke.uni-
hamburg.destellbri@uk

Sabine YERLY Laboratoire de Virologie,
Hopitaux Universitaires de Genève
Rue Micheli-du-Crest 24
Genève Switzerland
Email: Sabine.Yerly@hcuge.ch