26 July 2011
EMA/287852/2011 FINAL
Patient Health Protection

Programme - Transatlantic workshop: Drug-related Progressive Multifocal Leukoencephalopathy (PML)

25-26 July 2011: European Medicines Agency, 7 Westferry Circus, Canary Wharf, London, UK, meeting room 2A

Workshop's general objectives

During this workshop we expect to bring together the experts and the stakeholders on PML to a common purpose of reducing the burden of PML, thereby improving public health protection, through the following objectives:

1. Finding common understanding of the priorities for research in the area;

2. Mapping the ongoing research and identify gaps in the area;

3. Fostering funding and partnerships to conduct research to fill knowledge and research gaps in the field that will impact in health care protection;

4. Agreeing on a mechanism to ensure information sharing and regular stocktaking of research results, knowledge, knowledge gaps.

Scope

Progressive Multifocal Leukoencephalopathy (PML) is a severe demyelinating disease of the central nervous system (CNS) caused by JC virus (JCV). PML has been reported in many different conditions that affect immune response. PML is also established as an adverse reaction of several medicinal products that affect immunological functions. Over the last 5-10 years it has been more frequently reported as an adverse event of some therapeutic monoclonal

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antibodies (MAbs) with immunosuppressive action. There is no generally agreed specific and effective therapy targeting JCV and PML. Different medicines have been tested for treating JCV and PML, but none have yet demonstrated efficacy.

MAbs play a central role in the treatment of diseases in different areas including oncology, haematology, neurology and rheumatology. Many MAbs have important benefits in some illnesses, and some of them represent the most effective or even the only effective option to treat some diseases. Drug-induced PML is of major public health importance and therefore medicines regulators should have a leading role and apply a proactive approach to research and knowledge management in this field. Through focussed research to fill knowledge gaps, the PML Research Agenda Project will contribute to better public health protection, including through medicines regulation.

Who will attend?

The presentations and discussions will include experts and impacted stakeholders in the following areas:

- Regulatory field: FDA, EMA, and EU national regulatory agencies
- Public funding bodies from EU and US
- Academic researchers- in the area of JC virus and PML
- Clinical Researchers- in the area of JC virus and PML
- Patients representatives
- Healthcare professional representatives
- Pharmaceutical industry representatives

Programme coordinator:

Monica Vinhas de Souza (EMA)

EU Coordination:

Monica Vinhas de Souza (EMA), Peter Arlett (EMA), Henry Fitt (EMA)

U.S. Coordination:

Gerald Dal Pan (FDA), Janice Soreth (FDA)

EU programme committee (in alphabetical order):

Eric Abadie (CHMP), Peter Arlett (EMA), Michael Berntgen (EMA), Hilde Boone (EMA), Henry Fitt (EMA), Manuel Haas (EMA), Brigitte Keller-Stanislawski (PhVWP), Bert Leufkens (CHMP), Luca Pani (CHMP), Christian Schneider (CHMP) Rafe Suvarna (CHMP), Monica Vinhas de Souza (EMA),

	Draft programme	Presenter
	25 July 2011 Day 1	
8.30-9.00	Welcome to the participants	Hans-Georg Eichler– Senior Medical Officer, EMA Gerald Dal Pan- Director of the Office of Surveillance and Epidemiology, Centre for Drug Evaluation and Research, FDA
9.00-9.30	Opening the workshop	
	PML - Balancing risks and benefits - the patients' view	Christoph Thalheim - European Multiple Sclerosis Platform
9.30-11.00	**Session 1:** **Overview of PML as an adverse event of immunobiologicals (MABs)** This session aims to present a characterization of the (past and current) scenario of the cases of drug-induced PML, discussing the mechanisms, the more important implicated drugs and the established risks.	Session Co-chairperson: June Raine (CHMP-PhVWP) and Christoph Thalheim (European Multiple Sclerosis Platform)
	The possible mechanisms of the disease	Eugene Major(NIH)
	The outcomes of patients' drug induced PML	Joseph Berger (Kentucky University)
	Natalizumab (Tysabri) and PML- the current figures, the risks and the particularities	Brigitte Keller-Stanislawski (PEI)
	The relationship between PML-Rituximab and other immunobiologicals- an overview	Renaud du Pasquier (University of Lausanne)
	The risk in transplanted patients	Marco Tuccori (University Hospital of Pisa)
	Questions/discussion	
11.00-11.15	***Coffee break***	
11.15-13.00	**Session 2:** **The regulatory role- a collaborative approach** This session aims to discuss the role of the regulatory bodies regarding drug-related PML- specially the recent cases with MAbs. The measures adopted by regulatory agencies: the need for a collaborative approach and evidence to drive risk minimization	Session Co-chairperson: Alice Hughes (FDA) and Eric Abadie (EMA-CHMP)
	Activities in USA, the experience of FDA Neurology Division (FDA)	Russel Katz (FDA)
	Risk communication in EU	Rafe Suvarna (MHRA)

	Draft programme	Presenter
	Changes in the incidence, how to best communicate to patients and physicians? The FDA perspective	Alice Hughes (FDA)
	A common case definition for PML	Dirk Mentzer (PEI)
	National registry in Italy	Gioacchino Tedeschi (Seconda Università di Napoli)
	The TYSEDMUS Study	Christian Confavreux (European database for Multiple Sclerosis-FR)
	Industry experience with PML	Carmen Bozic (PML-Consortium/Biogen)
	Questions/discussion	
13.00-14.30	***Lunch break***	
14.30-16.00	**Session 3:** **Treatment of drug-induced PML** This session aims to present a critical appraisal of the current scenario of the treatment of (drug-related) PML, the difficulties of the development of therapies for the treatment of PML, and the need for progress in this area.	Session Co-chairperson: Eugene Major (NIH) and Victoria Palmi Reig (EMA)
	Development of models for testing possible treatments	Igor Koralnik (Harvard University)
	New drugs to treat JCV and PML: the current stage and the perspectives for the future	Teresa Compton (Biogen Elan)
	Plasma exchange: What is the evidence about plasma exchange in natalizumab related PML: is plasma exchange beneficial?	Ralf Gold (Ruhr University Bochum)
	IRIS, can the risk for developing IRIS be mitigated? How should IRIS be treated?	Joseph Berger (Kentucky University)
	Questions/discussion	
16.00-16.15	***Coffee break***	
16.15-17.45	**Session 4:** **Ongoing research in PML** This session aims to provide overview of the ongoing research in the field and the possible directions to be followed in the area.	Session Co-chairperson: Gerald Dal Pan (FDA) and Brigitte Keller-Stanislawski (PEI)
	PML development: risk factors and predictive biomarkers- limitations and perspective	Heinz Wiendl (University of Münster)
	Diagnosis of PML: Available methodologies and improvements of the tools	Joseph Berger (Kentucky University)
	Viral subtypes and the development of the disease, what is the evidence in the area	Igor Koralnik (Harvard University)
	The research in the field: where to progress (TRANSLATIONAL MEDICINE)	Eugene Major (NIH)

	Draft programme	Presenter
	Questions/discussion	
17.45	End of first day	
	26 July 2011 - Day 2	
9.00-10.20	**Session 5:** **Research agendas** This session aims to present how drug induced PML has led to important initiatives started in different settings (regulatory bodies, industry…). The session also aims to ensure that the key research questions are identified.	Session Co-chairperson: Igor Koralnik (Harvard University) and Richard Bergström (EFPIA)
	Regulators initiative, the PML research agenda	Ana Hidalgo-Simon (EMA)
	Academia	Eugene Major (NIH)
	Interface Academia-Clinical Practice	Joseph Berger (Kentucky University)
	PML consortium - industry	Susan Goelz (PML-Consortium/Biogen-ELAN)
	Questions/discussion	
10.20-10.30	***Coffee break***	
10.30-12.00	**Session 6:** **Building collaboration** This session aims to discuss the possible ways to build partnerships for research in the area	Session Co-chairperson: Henry Fitt (EMA), Janice Soreth (FDA)
	Challenges and opportunities from public private partnerships as a way to build collaboration in research	Richard Bergström (EFPIA)
	The importance of clarity in relationships and transparency: The role of ENCePP	Henry Fitt (EMA)
	Drug Safety Surveillance Initiatives	Gerald dal Pan (FDA)
	How to facilitate the communications/data exchange?	Janice Soreth (FDA)
	Questions/discussion	
12.00-13.15	***Lunch break***	

	Draft programme	Presenter
13.15-14.35	**Session 7:** **Funding of research** This session aims to explore some of the key existing funding mechanisms for health researchers.	Session Co-chairperson: Peter Arlett (EMA) and Eugene Major as NIH funder representative
	Public funding of research – EU perspective	Stefanie Prilla (EMA)
	Public funding of research – US perspective	Eugene Major as NIH funder representative
	The role of the pharmaceutical industry funding research in this area	Sophie Banzet (PML Consortium/Roche)
	Public Private Partnerships as funders	Hugh Laverty - IMI JU
	Questions/discussion	
14.35-14.50	***Coffee break***	
14.50-16.30	**Session 8** **Keeping abreast of progress for the benefits of public health** This session aims to brainstorm and identify mechanisms to ensure information sharing and regular stocktaking of research results, knowledge, knowledge gaps. To ensure optimal medicines regulation and patient health protection.	Session Co-chairperson: Joseph Berger (Kentucky University) and Manuel Haas (EMA)
	EU Regulator's perspective	Peter Arlett (EMA)
	US Regulators perspective	Russel Katz (FDA)
	Industry PML consortium view	Sophie Banzet (PML Consortium/Roche)
	Clinical Researchers	Igor Koralnik (Harvard University)
	Researchers	Eugene Major (NIH)
	Physicians view	Ralf Gold (Ruhr University Bochum)
	Patient view	Christoph Thalheim (European Multiple Sclerosis Plataform)
	Questions/discussion	
16.30-17.00	**Workshop conclusions and next steps**	Peter Arlett for EMA and Gerald Dal Pan for FDA
	Questions/discussion	
17.00	End of workshop	