



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

## Regulators initiative: the PML research agenda

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Transatlantic workshop: Drug-related Progressive Multifocal  
Leukoencephalopathy (PML)  
25-26 July 2011: European Medicines Agency

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An agency of the European Union





# Agenda for this Presentation

- Why are regulators proposing a Research Agenda for PML
- How this Agenda was developed
- Proposed Research Agenda
- The way forward



# Background

- The advent of novel therapies for a variety of immune-mediated disorders has been accompanied by the emergence of PML as an important drug-induced adverse event.
- Because of the impact of PML on public health there is a need to focus research efforts onto key questions linked to public health protection.
- Novel collaborative approach may be transferable to other public health/regulatory challenges.



# Why are regulators proposing a Research Agenda for PML?

- Some issues identified on product-specific setting
- Common challenges and common needs across products and therapeutic areas
- Challenging circumstances surrounding PML

Demand new ways to allow the  
use of highly efficacious  
medicines to fulfil  
unmet medical needs

• Stimulation of PML  
research  
• Integration of PML research



• Effective risk minimisation steps  
• Optimisation of benefit risk balance  
• Better public health protection & promotion



# How this Agenda was developed ?

- Initiative of the European Medicines Agency (EMA) and the Food and Drug Administration (FDA)
- Through review of:
  - existing evidence-base,
  - product-based experience,
  - operational experience in both the EU and the U.S. of regulating medicines associated with PML.
- This research agenda embraces:
  - basic biology,
  - clinical aspects,
  - risk management issues to provide a framework for managing the risk of drug-induced PML.
- This research agenda identifies:
  - key questions, and
  - the accelerated delivery of answers.



# Research Agenda

The objective is to **improve public health** by accelerating the delivery of answers to JCV and PML knowledge gaps which will impact, either directly or indirectly, on the **prevention or treatment of drug induced PML**.



# Proposed Research Agenda

Key Research Questions regarding Drug-induced PML to support practical interventions:

1. What is the best approach to ascertain the number of drug-induced cases of PML?
2. Is it possible to identify populations at risk or patients not at risk prior to the treatment initiation with a drug associated with PML?
3. Are there early biomarkers of drug-induced PML that might be used in the mitigation of severity of the clinical manifestation of PML?
4. What is a suitable in vivo/animal model for PML?
5. What are the best drugs or combination of drugs with anti-JCV activity?
6. What are the best treatment strategies for both PML and IRIS?
7. What is the long-term safety and effectiveness of plasma exchange/immunoadsorption in patients with drug-induced PML?
8. What is the best tool for evaluation of effectiveness of risk minimisation activities in PML?



# Key Research Questions regarding Drug-induced PML to support practical interventions 1

- What is the best approach to ascertain the number of drug-induced cases of PML?
  - Case definition
  - Case capture



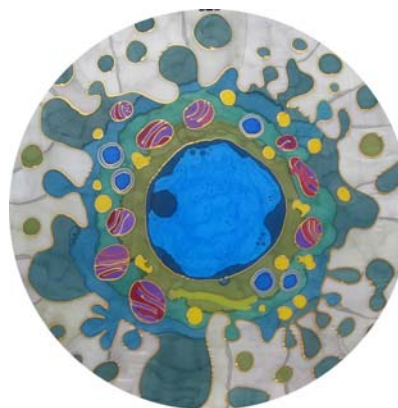




## Key Research Questions regarding Drug-induced PML to support practical interventions 2

- Is it possible to identify populations at risk or patients not at risk prior to the treatment initiation with a drug associated with PML?

- Such stratification would have a direct benefit on decisions involving risk for patients





## Key Research Questions regarding Drug-induced PML to support practical interventions 3

- Are there early biomarkers of drug-induced PML that might be used in the mitigation of severity of the clinical manifestation of PML?
  - Early diagnosis is associated with better outcome





# Key Research Questions regarding Drug-induced PML to support practical interventions 4

- What is a suitable in vivo/animal model for PML?
  - A model would be invaluable to test new treatments





## Key Research Questions regarding Drug-induced PML to support practical interventions 5



- What are the best drugs or combination of drugs with anti-JCV activity?

- Currently no specific treatment available



# Key Research Questions regarding Drug-induced PML to support practical interventions 6

- What are the best treatment strategies for both PML and IRIS?



- Can the benefits of proposed therapies be demonstrated?
- How can we best treat IRIS?



## Key Research Questions regarding Drug-induced PML to support practical interventions 7

- What is the long-term safety and effectiveness of plasma exchange/immunoadsorption in patients with drug-induced PML?



- How can we measure long-term harm and benefit in these patients?



# Key Research Questions regarding Drug-induced PML to support practical interventions 8

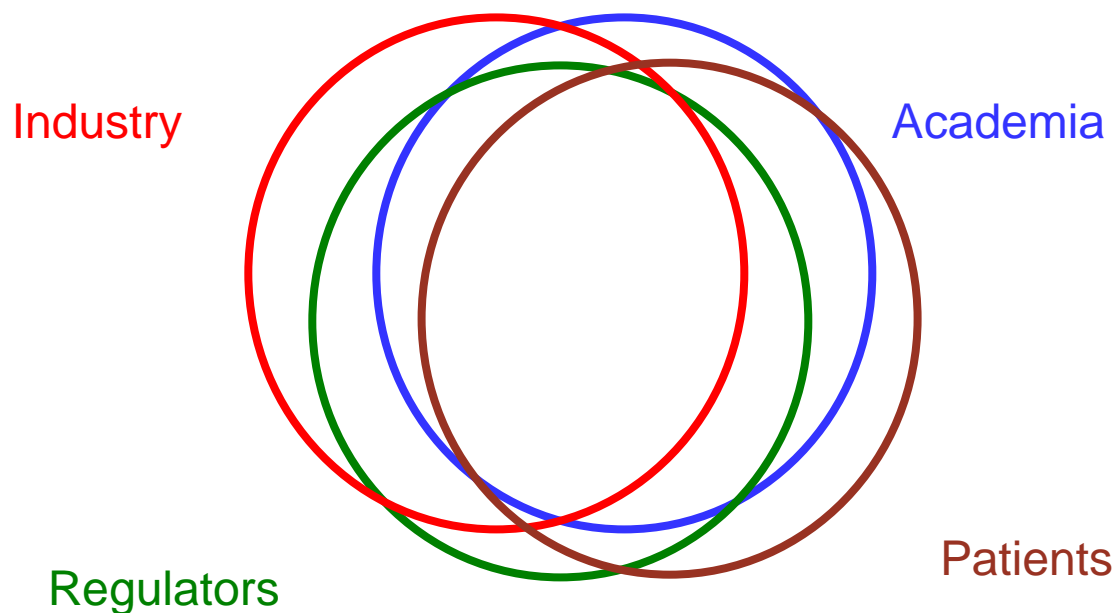
- What is the best tool for evaluation of effectiveness of risk minimisation activities in PML?

- How can we measure if our actions are effective?





# Research Agendas







# The way forward



# The way forward

- Funding.
- Fostering collaboration.
- Alignment of research agendas:
  - consensus; and
  - Priorities.
- Communication aspects.



# The way forward

- Funding.
- Fostering collaboration.
- Alignment of research agendas:
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Coming.....

Session 6 (collaboration), 7 (funding) and 8 (benefits for public health)



# Thank you

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