

## A Collaborative Approach to Addressing PML: The PML Consortium

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### Introduction

Progressive multifocal leukoencephalopathy (PML) is a rare but severe and often fatal disease of the central nervous system most commonly associated with severe immunodeficiency. PML occurs in many clinical conditions as shown in the table below (Table 1) [1-23]. The greatest number of PML cases occurs as a sequel to HIV infection. This was especially prominent in the early days of AIDS, prior to combined antiretroviral therapy, but continues in developing countries where current therapies are not readily available, or patient compliance is not optimal. In the past decade there was a notable increase in number of PML cases associated with several novel therapeutic products, and this is the major reason why PML Consortium has a strong interest in understanding this disease. The PML Consortium was founded in 2009 by Biogen Idec, Elan, and Roche with a vision of finding methods to better predict, prevent, and treat PML.

<b>HIV+</b>
<b>Multiple sclerosis patients treated with natalizumab</b>
<b>Hematological malignancies</b>
<b>Solid malignancies</b>
<b>Transplant organ recipients</b>
<b>Sarcoidosis</b>
<b>Rheumatoid autoimmune disease</b>
<ul style="list-style-type: none"> <li>• Systemic lupus erythematosus</li> <li>• Rheumatoid arthritis</li> <li>• Sjögren's syndrome</li> <li>• Psoriasis</li> <li>• Dermato- and poly-myositis</li> </ul>
<b>Primary immunodeficiency</b>
<ul style="list-style-type: none"> <li>• Hyper IgM syndrome</li> <li>• Wiscott Aldrich syndrome</li> <li>• Job's syndrome</li> <li>• Purine nucleoside phosphorylase deficiency (SCID)</li> <li>• ICF syndrome</li> <li>• Common variable immunodeficiency (CVID)</li> </ul>
<b>Good's syndrome</b>
<b>Viral and alcoholic liver cirrhosis</b>
<b>Idiopathic CD4+ T cell deficiency</b>

**Table 1:** PML risk populations identified from literature reports (1994-2013).

The mission of the Consortium is to perform research to understand the pathogenesis of and to reduce occurrence, morbidity and mortality of PML through a multi-company, not-for-profit, collaborative approach with shared strategy, investment, data acquisition and analysis and communication within a pre-defined scope and duration. Our current members include Biogen Idec, MedImmune, Pfizer, and Roche. Through our work, we hope to help define how PML develops and progresses so that we may provide better protection for patients.

### Consortium Activities

#### Research Support

Support of research into PML and its causative virus, JC polyomavirus (JCV), is a cornerstone of the PML Consortium. Joint funding of research distributes costs among our companies, allowing us to fund more projects than any of our individual companies could fund alone; it also provides the benefit of a peer review process that includes many different perspectives, including those of company experts and members of the Consortium's Scientific Advisory Board, a group of key opinion leaders in scientific and medical communities. To date, we have funded 13 grants and will fund more this year. The research we support is addressing some of the most fundamental questions about JCV and how it causes PML, and includes basic virology research, immune responses to JCV, PML pathogenesis, as well as the establishment of potential animal models to enable future research. Though exploring these fundamental questions, we hope to provide better ways to protect patients from developing PML.

In addition to funding research, we foster active scientific discussion. We hold annual symposia where Consortium members and grantees discuss the grantees' pre-publication results. We also hold mini-symposia to explore insights that may be gained from broader research fields such as virology, immunology and genetics. Grantees are also encouraged to communicate their results to the broader scientific community, through external conference presentations and publications.

#### Engaging scientists, clinicians, and regulatory authorities

In addition to supporting research and clinical activities, the Consortium believes strongly in engaging the broader scientific, medical, and regulatory communities. We organized our first biannual conference in 2013 to bring researchers, clinicians and regulators together to discuss PML, and are currently organizing a second research conference, to be held in Sweden in the fall of 2015. We also built a comprehensive website on PML which serves as a central

source of information about PML for health care professionals, patients and their families.

## Looking Ahead

Sharing the results of laboratory research and analyses of clinical data will be critical to ensuring future progress in this area, as well as engaging research, clinical, regulatory, and patient communities in continued exchanges about PML. Although the Consortium is a relatively young organization, we hope that our work will have a significant impact on our understanding of PML. As our companies develop new therapies, we are hopeful that the information we acquire through the Consortium's work will help us to limit the risks of drug therapies.

More information about the PML Consortium, including information about the Consortium's grant program and upcoming research conference, is available on the Consortium's website, [www.pmlconsortium.org](http://www.pmlconsortium.org).

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