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 MedImmune LLC, with the strong interest in understanding the PML disease and progress 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

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

| HIV+ | Multiple sclerosis patients treated with natalizumab |
|------|----------------------------------------------------|
|      | Hematological malignancies                         |
|      | Solid malignancies                                 |
|      | Transplant organ recipients                        |
|      | Sarcoidosis                                        |
|      | Rheumatoid autoimmune disease                     |
|      | • Systemic lupus erythematosus                     |
|      | • Rheumatoid arthritis                            |
|      | • Sjögren’s syndrome                               |
|      | • Psoriasis                                        |
|      | • Dermato- and poly-myositis                       |
|      | Primary immunodeficiency                           |
|      | • Hyper IgM syndrome                               |
|      | • Wiscott Aldrich syndrome                         |
|      | • Job’s syndrome                                   |
|      | • Purine nucleoside phosphorylase deficiency (SCID) |
|      | • ICF syndrome                                     |
|      | • Common variable immunodeficiency (CVID)          |
|      | Good’s syndrome                                   |
|      | Viral and alcoholic liver cirrhosis                |
|      | Idiopathic CD4+ T cell deficiency                  |

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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.

References

1. Aksamit AJ Jr (2012) Progressive multifocal leukoencephalopathy. Continuum (Minneap Minn) 18: 1374-1391.
2. Aschermann Z, Gomori E, Kovacs GG, Pal E, Simon G, et al. (2007) X-linked hyper-IgM syndrome associated with a rapid course of multifocal leukoencephalopathy. Arch Neurol 64: 273-276.
3. Delgado-Alvarado M, Sedano MJ, Gonzalez-Quintanilla V, de Lucas EM, Polo JM, et al. (2013) Progressive multifocal leukoencephalopathy and idiopathic CD4 lymphocytopenia. J Neurol Sci 327: 75-79.
4. Landry ML, Eid T, Bannykh S, Major E (2008) False negative PCR despite high levels of JC virus DNA in spinal fluid: Implications for diagnostic testing. J Clin Virol 43: 247-249.
5. Molloy ES, Calabrese LH (2012) Progressive multifocal leukoencephalopathy associated with immunosuppressive therapy in rheumatic diseases: evolving role of biologic therapies. Arthritis Rheum 64: 3043-3051.
6. Molloy ES, Calabrese LH (2009) Progressive multifocal leukoencephalopathy: a national estimate of frequency in systemic lupus erythematosus and other rheumatic diseases. Arthritis Rheum 60: 3761-3765.
7. Sorensen PS, Bertolotto A, Edan G, Giovannoni G, Gold R, et al. (2012) Risk stratification for progressive multifocal leukoencephalopathy in patients treated with natalizumab. Mult Scler 18: 143-152.
8. Neff RT, Hurst FP, Falta EM, Bohan EM, Lentine KL, et al. (2008) Progressive multifocal leukoencephalopathy and use of mycophenolate mofetil after kidney transplantation. Transplantation 86: 1474-1478.
9. Jamilloux Y, Nèd A, Lecouffe-Despres M, Fèvre A, Kerever S, et al. (2014) Progressive multifocal leukoencephalopathy in patients with sarcoidosis. Neurology 82: 1307-1313.
10. Clifford DB, Ances B, Costello C, Rosen-Schmidt S, Andersson M, et al. (2011) Rituximab-associated progressive multifocal leukoencephalopathy in rheumatoid arthritis. Arch Neurol 68: 1156-1164.
11. Sveinsson O, Matell H, Herrman L. (2013) Progressive multifocal leukoencephalopathy in a patient with Good’s syndrome. BMJ Case Rep 2013.
12. Haider S, Nafziger D, Gutierrez JA, Brar I, Mateo N, et al. (2000) Progressive multifocal leukoencephalopathy and idiopathic CD4+ lymphocytopenia: a case report and review of reported cases. Clin Infect Dis 31: E20-22.
13. Colucci M, Cocito L, Capello E, Mancardi GL, Serrati C, et al. (2004) Progressive multifocal leukoencephalopathy in an adult patient with ICF syndrome. J Neurol Sci 217: 107-110.
14. Narula S, LaRosa DF, Kamoun M, Dalmau J, Levinson AI (2007) Progressive multifocal leukoencephalopathy in a patient with common variable immunodeficiency and abnormal CD8+ T-cell subset distribution. Ann Allergy Asthma Immunol 98: 483-489.
15. Kothyary N, Diak IL, Brinker A, Bezabeh S, Avigan M, et al. (2011) Progressive multifocal leukoencephalopathy associated with efalizumab use in psoriasis patients. J Am Acad Dermatol 65: 546-551.
16. Gheuens S, Pierone G, Peeters P, Koralnik IJ (2010) Progressive multifocal leukoencephalopathy in individuals with minimal or occult immunosuppression. J Neurol Neurosurg Psychiatry 81: 247-254.
17. Marie L, Guegan-Massier E, Levesque H (2011) Progressive multifocal leukoencephalopathy in refractory polymyositis treated with rituximab. Eur J Intern Med 22: e13-14.
18. Suzuki H, Takakashi Y, Miyajima H (2006) Progressive multifocal leukoencephalopathy complicating X-linked hyper-IgM syndrome in an adult. Intern Med 45: 1187-1188.
19. Angelini L, Pietrogrande MC, Delle Piane MR, Zibordi F, Cinque P, Maccagnano C, et al. (2001) Progressive multifocal leukoencephalopathy in a child with hyperimmunoglobulin E recurrent infection syndrome and review of the literature. Neuropediatrics 32: 250–255.
20. Katz DA, Berger JR, Hamilton B, Major EO, Post MJ (1994) Progressive multifocal leukoencephalopathy complicating Wiskott-Aldrich syndrome. Report of a case and review of the literature of progressive multifocal leukoencephalopathy with other inherited immunodeficiency states. Arch Neurol 51: 422-426.
21. Parvaneh N, Ashrafi MR, Yeganeh M, Pouladi N, Sayarifar F, et al. (2007) Progressive multifocal leukoencephalopathy in purine nucleoside phosphorylase deficiency. Brain Dev 29: 124-126.
22. Matsuda H, Hayashi K, Meguro M, Saruta T (2006) A Case Report of Progressive Multifocal Leukoencephalopathy in a Human T-Cell Lymphotropic Virus Type 1-Infected Hemodialytic Patient. Therapeutic Apheresis and Dialysis 10: 291–295.
23. Acket B, Guillaume M, Tardy J, Dumas H, Sattler V, et al. (2010) Progressive multifocal leukoencephalopathy in a patient with alcoholic cirrhosis. Gastroenterol Clin Biol 34: 336-338.