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First And Only Treatment for Multicentric Castleman's Disease, SYLVANT™, Now Approved in Canada

Approved with Priority Review designation, new therapy gives patients and physicians an important option in the treatment of this rare blood disorder

Toronto, ON – December 4, 2014 – Janssen Inc. announced today that Health Canada has approved SYLVANT™ (siltuximab) for the treatment of patients with multicentric Castleman's disease (MCD) who are human immunodeficiency virus (HIV)-negative and human herpes virus-8 (HHV-8)-negative. SYLVANT™ is the first clinically proven treatment approved in Canada for MCD. [1]

Multicentric Castleman's disease is a rare condition and therefore it is difficult to estimate prevalence. However, a recent study estimated the 10-year prevalence of MCD in North America to be 2.5 patients per million.[2] It is a serious blood disorder in which lymphocytes, a type of white blood cell, are overproduced, leading to enlarged lymph nodes.[3] Infections, multisystem organ failure and cancers like lymphoma are common causes of death in patients with MCD.[4,5]

"The approval of SYLVANT™ marks a breakthrough for patients who are living with Castleman's disease as there is an unmet medical need for treatments in this area," said Dr. John Kuruvilla, Hematologist at Princess Margaret Cancer Centre. "Since the disease is so rare, there has been little development in this area and clinicians struggle to manage the condition with available therapies. This new treatment option has proven efficacy in shrinking tumours and tangible improvements in disease related symptoms."

The approval of SYLVANT™ was based mainly on a pivotal, multi-national, randomized, double-blind, placebo-controlled study that evaluated the efficacy and safety of SYLVANT™ plus best supportive care (BSC) versus placebo plus BSC in 79 patients with MCD who are HIV-negative and HHV-8-negative. [6] Best supportive care currently is the treatment used to manage MCD-related symptoms (like fever or pain). The study data showed that more than one-third of patients in the SYLVANT™ arm met the primary endpoint of durable tumour and symptomatic response (a reduction in tumour size and disease symptoms) compared to none of the patients on placebo (34 per cent versus 0 per cent; 95 per cent confidence interval: 11.1, 54.8; p=0.0012).[7]

In the study, patients were randomized 2:1 to receive either SYLVANT™ plus BSC or placebo plus BSC until protocol-defined treatment failure, after which patients taking the placebo could cross over to the

SYLVANT™ arm. The median duration of follow-up in the study across both groups was 422 days. The median time to treatment failure was not reached for patients who received SYLVANT™, while patients who received placebo experienced treatment failure at a median of 134 days ($p<0.0084$).[8]

About SYLVANT™

SYLVANT™ is an anti-interleukin 6 (IL-6) monoclonal antibody that binds to human IL-6, which is a multifunctional cytokine produced by various cells such as T cells, B cells, monocytes, fibroblasts and endothelial cells.[9] Overproduction of IL-6 from activated B cells in affected lymph nodes has been implicated in the mechanism causing MCD.[10] SYLVANT™ is administered as an intravenous (IV) infusion once every three weeks.

The most frequent adverse reactions (greater than 10 per cent compared to placebo) during treatment with SYLVANT™ in the pivotal MCD clinical trial were rash (29 per cent), pruritus (itching) (36 per cent), upper respiratory tract infection (32 per cent), increased weight (17 per cent), renal impairment (11 per cent), hypertriglyceridemia (11per cent), and localized edema (18 per cent).[11]

About MCD

Cases of MCD that are HIV-negative and HHV8-negative are also referred to as idiopathic MCD or iMCD.[12] In MCD, the immune system is weakened making it harder to fight infections. Common symptoms of MCD include enlarged lymph nodes (appearing as lumps under the skin), fever, weakness, fatigue, night sweats, weight loss, loss of appetite, nausea, vomiting and nerve damage that leads to numbness and weakness.[13]

Unlike unicentric Castleman's disease, which is localized and affects only a single area or group of lymph nodes, patients with MCD have more than one group of lymph nodes in different anatomical areas that are affected. Unicentric disease can be treated by surgically removing the diseased lymph node, while multicentric disease is usually much more difficult to treat.[14,15]

About Janssen Inc.

Janssen Inc. is one of the Janssen Pharmaceutical Companies of Johnson & Johnson, which are dedicated to addressing and solving some of the most important unmet medical needs in oncology, immunology, neuroscience, infectious diseases and vaccines, and cardiovascular and metabolic diseases. Driven by our commitment to patients, we bring innovative products, services and solutions to people throughout the world. Please visit www.janssen.ca for more information.

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* Dr. Kuruvilla was not compensated for any media work. He has been a paid consultant to Janssen Inc.

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