VELCADE® Data At EHA 2014 Highlight Efficacy In Newly-Diagnosed Mantle Cell Lymphoma And Reinforce Its Role As A Backbone Of Multiple Myeloma Therapy

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Note: This press release corresponds to EHA abstracts S1345 and P958

BEERSE, BELGIUM, 15 JUNE, 2014 - Janssen-Cilag International NV today announced Phase III study data demonstrating that the investigational use of a VELCADE® (bortezomib)-based combination in the treatment of patients with Mantle Cell Lymphoma (MCL) who were newly-diagnosed and unsuitable, or not considered, for a stem-cell transplant, resulted in a significant increase in progression-free survival (PFS) versus standard of care.[1] The increase in PFS seen was 96 percent as assessed by investigators and 56 percent as assessed by an independent review committee.[1] These data have been presented as part of the official programme of events at the 19th Annual Congress of the European Hematology Association (EHA), taking place on 12-15 June, 2014 in Milan, Italy.

In addition to the VELCADE® (bortezomib)-based data in the treatment of patients with MCL, studies on VELCADE in Multiple Myeloma (MM) have continued to reinforce its position as a backbone of therapy. As part of a study looking at the benefits of subcutaneous (under the skin) vs. intravenous (direct into the vein) administration of VELCADE in patients with relapsed MM, investigators reported on a subgroup of patients with renal function impairment. Data looked at overall response rates, speed of response and the likelihood of patients who had received subcutaneous VELCADE to reverse their renal impairment.[2]

Data on VELCADE-based combination therapy in Mantle Cell Lymphoma (abstract S1345)

Analysis of the randomised, open-label, active-controlled, multicentre, international prospective Phase III LYM-3002 study, reported on 15 June, 2014, highlighted that, compared to the treatment combination R-CHOP[1] , the VELCADE-based regimen, VR-CAP[2] increased progression-free survival (PFS) (the time patients live without their disease progressing) by 96 percent (30.7 vs. 16.1 months; HR 0.51; p<0.001) in previously-untreated patients with MCL, as assessed by investigators. Analysis performed by an independent review committee (IRC) also found a significant, 56 percent increase in PFS (24.7 vs. 14.4 months; HR 0.63; p<0.001).[1]

"Mantle Cell Lymphoma is an aggressive blood cancer and treatment options for newly diagnosed patients are limited," said Tadeusz Robak, Professor of Hematology at the Medical University of Lodz, Poland and principal investigator on the trial. "This study clearly demonstrates a range of potential benefits in using a bortezomib-based frontline therapy in those patients. It is encouraging that a relatively short treatment duration with the bortezomib-based regimen results in a longer time until the next chemotherapy is needed."

The study includes 487 patients with newly-diagnosed MCL who were ineligible, or not considered, for bone marrow transplantation. Its objective is to compare the efficacy and safety of the combination of VR-CAP with a current standard of care in frontline MCL, R-CHOP. The primary endpoint is progression-free survival. At a median follow-up of 40 months, median PFS was 30.7 months (VR-CAP) vs. 16.1 months (R-CHOP) (HR=0.51, P<0.001) as assessed by investigators. Analysis performed by an independent review committee also found a significant, 56 percent increase in PFS (24.7 vs. 14.4 months; HR 0.63; p<0.001). Median overall survival (OS), a key secondary endpoint, had not been reached for patients who received VR-CAP, although a median OS of 56 months was observed in patients treated with R-CHOP (HR 0.80; P=0.17). Though not a pre-specified endpoint, the four-year survival rate showed a trend towards prolonged survival with VR-CAP. At four years, survival was reported as 64.4 percent in the experimental arm vs. 53.9 percent in the control arm.[1] The overall response rate (ORR) was 92 percent in the VR-CAP arm compared to 90 percent in the control arm (OR=1.4; P=0.275]. The complete response rate (CR+CRu) was 53 percent in the VR-CAP arm compared to 42 percent in the control arm (OR=1.7; P=0.007].[1]

Overall, among patients receiving VR-CAP compared to R-CHOP, serious adverse events (AE) were reported in 38 percent vs. 30 percent of patients and grade ≥ 3 AEs were reported in 93 percent vs. 85 percent. Discontinuations of treatment due to AEs were nine percent (VR-CAP) vs. seven percent (R-CHOP) and on-treatment drug-related deaths were two percent vs. three percent.[1]

Other secondary endpoint results for patients receiving VR-CAP vs. R-CHOP included:[1]

- 30.5 vs. 16.1 months median time to progression (HR 0.58; P<0.001)
- 44.5 vs. 24.8 months median time to subsequent anti-lymphoma treatment (HR 0.50; P<0.001)
- 40.6 vs. 20.5 months median treatment-free interval (HR 0.50; P<0.001)

Subcutaneous (under the skin) vs. intravenous (direct to vein) administration of VELCADE (abstract P958)

Results of a sub-analysis of the pivotal MMY-3021 study, reported on 14 June 2014, showed that subcutaneous (SC) administration of VELCADE in patients with Multiple Myeloma (MM) who had renal impairment appeared to provide a more rapid time-to-response (TTR) and higher response rates (ORR) than with intravenous (IV) administration. This was accompanied by higher rates of renal impairment reversal.[2]

In MM patients with moderate-to-severe renal impairment:[2]

- The overall response rate (ORR) was 53 percent in the SC arm and 31% in the IV arm (RR 1.73, CR 6% vs. 0%).
- Median TTR was 2.3 months for SC patients and 3.3 months in IV patients (HR 1.205).
- Renal impairment was reversed in 30 percent (10/33) of SC patients vs. 15 percent (2/13) of those treated with IV.
- Grade ≥3 adverse events were seen in 70 percent of SC patients vs. 77 percent of patients on IV.

About VELCADE (bortezomib)[3]
VELCADE (bortezomib) is a medicine currently licensed in the EU to treat the blood-based cancer, Multiple Myeloma. It contains an active substance called bortezomib and is the first in a specific class of medicines known as proteasome inhibitors. Proteasomes are present in all cells and play an important role in controlling cell function, growth and also how cells interact with the other cells around them. Bortezomib reversibly interrupts the normal working of cell proteasomes causing myeloma cancer cells to stop growing and die.

VELCADE has a predictable safety profile and a favourable benefit-risk ratio. The most common side effects reported with VELCADE (bortezomib) include fatigue, gastrointestinal adverse events, transient thrombocytopenia and neuropathy.[3]

VELCADE is the market leader in the treatment of frontline non-transplant eligible Multiple Myeloma. It is co-developed by Millennium: the Takeda oncology company and Janssen Pharmaceutical Companies. Millennium: the Takeda oncology company is responsible for commercialisation of VELCADE in the U.S.; Janssen Pharmaceutical Companies are responsible for commercialisation in Europe and the rest of the world. Takeda Pharmaceutical Company Limited and Janssen Pharmaceutical K.K. co-promote VELCADE in Japan. VELCADE is approved in more than 90 countries and has been used to treat more than 550,000 patients worldwide.

VELCADE (bortezomib) in Mantle Cell Lymphoma
In Europe, VELCADE is not currently licensed to treat Mantle Cell Lymphoma (MCL). VELCADE's approved indications can be viewed online at:[3]
http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000539/human_med_001130.jsp&mid=WC0b01ac058001d124

In 2006, the United States approved VELCADE for the treatment of patients with MCL who have received at least one prior therapy. VELCADE has subsequently been approved for the treatment of relapsed MCL in 53 additional countries, including Canada and Switzerland.

About Mantle Cell Lymphoma
MCL is a rare and aggressive blood cancer that usually occurs in older adults, with the median age at diagnosis being 65 years. The disease typically begins in the lymph nodes, but can spread to other tissues such as bone marrow, liver and spleen. The incidence rates among men and women in Europe are approximately 0.64 and 0.27 cases per 100,000 persons per year, respectively. MCL patients generally have a poor prognosis. Median overall survival is typically three to four years, and only one to two years in patients following the first relapse.[4,5,6,7]

About Multiple Myeloma
Multiple Myeloma is an incurable blood cancer that starts in the bone marrow and is characterised by an excess proliferation of abnormal plasma cells.[8] It is the second most frequent form of malignant bone marrow diseases and is a relatively rare form of cancer that accounts for roughly one percent of all cancers and roughly two percent of all deaths from cancer. In Europe, around 60,000 people are living with the disease and there are 21,420 new cases and 15,000 deaths every year.[9]