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ORAL ABSTRACT 526

Emerging data from CLL10 presented at ASH suggests *Levact*® (bendamustine) and rituximab as new treatment option for fit elderly CLL patients

New Orleans, USA, 9 December 2013 - New interim analysis study findings presented for the first time today at the 55th American Society of Hematology (ASH) Annual Meeting in New Orleans suggest bendamustine and rituximab (BR) as a new treatment option for fit elderly patients with advanced Chronic Lymphocytic Leukaemia (CLL)[1].

The CLL10 Phase III trial of 564 patients with previously untreated CLL was designed to prove the non-inferiority of BR compared to FCR, the current gold standard first-line treatment regimen for patients classified as medically fit (CIRS score ≤6) with advanced CLL. According to these interim results the non-inferiority of BR versus FCR in the full study population cannot yet be proven as progression-free survival (PFS) was 85.0% at 2 years in the FCR arm compared to 78.2% in the BR arm (p=0.041). No difference in overall survival (OS) was observed across both arms after two years, 95.8% of the patients in the BR arm were still alive versus 94.2% of the FCR arm (p=0.593).

However, PFS was also assessed in a prespecified sub-group analysis in younger (under 65) and older patients (65 and older). Whilst in patients under 65 the study demonstrated a significant difference in PFS between both treatment arms in favour of FCR (median PFS for BR 36.5 mo vs not reached for FCR; p=0.016) there was shown to be no difference in efficacy in patients 65 and older (not reached vs. 45.6 mo; p=0.757). This sub-group analysis is highly relevant to real life as almost 70% of patients presenting with advanced CLL are over 65[3]. In the CLL10 study population, over a third (FCR: 34% vs BR: 41%) of patients were over the age of 65[2]. These interim findings suggest that the efficacy of BR is comparable to FCR in fit elderly patients. Notably no treatment regimen has previously been proven to have comparable efficacy to FCR, the well established gold standard.

This study also demonstrated that patients treated with FCR experienced significantly more frequent severe adverse events than those treated with BR. More specifically, severe hematotoxicity (temporary depletion of blood cells in the bone marrow) was observed in a

third more patients treated with FCR (90.0% vs 66.9%, p<0.001). Additionally severe neutropenia (low neutrophil count) which leaves a patient more susceptible to infections affected 81.7% of patients treated with FCR, compared to 56.8% of those treated with BR (p<0.001). Among the fit elderly patients nearly twice as many treated with FCR suffered severe infections (FCR: 47.4% vs BR: 26.5%; p=0.002). Furthermore, there were more treatment-related deaths among patients in the FCR arm than those in the BR arm (3.9% in the FCR arm and 2.1% in the BR arm).

Importantly, patients on the BR arm were more likely to complete all six cycles of treatment (80% in the BR arm vs 71% in the FCR arm). This difference was further pronounced in elderly patients (75% of patients over 65 receiving BR completed all six cycles vs. 61% receiving FCR)[2].

Chronic lymphocytic leukaemia is the most common type of leukaemia in the Western world with an incidence of 4.2 cases per 100,000 people annually, increasing to around 30 cases per 100,000 in the over-80s. Nearly 70% of patients are diagnosed at age 65 or older[3]. However, many of the milestone studies leading to recent advances in CLL treatment were conducted in populations considerably younger than the average age of the CLL population and the current challenge is improving the management of elderly patients. In elderly populations, the outcome of treatment is often compromised by comorbidities and poor performance status.

“These interim data suggest that bendamustine and rituximab is an alternative treatment option to FCR which appears to have an improved safety profile. Furthermore, in medically fit elderly patients bendamustine and rituximab appears as effective as FCR,” said the study’s primary investigator, Dr Barbara Eichhorst of the Department of Internal Medicine, Center of Integrated Oncology Köln Bonn, University of Cologne.

Bendamustine is currently licensed as monotherapy in CLL for first-line treatment (Binet stage B or C) of patients for whom fludarabine combination chemotherapy is not appropriate.

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Notes to Editors:

About Mundipharma
The Mundipharma network of independent associated companies consists of privately owned companies and joint ventures covering the world’s pharmaceutical markets. These companies are committed to bringing to patients the benefits of pioneering treatment options

in the core therapy areas of oncology, pain, respiratory and rheumatoid arthritis. They are also committed to independent thinking and ground breaking solutions. Through innovation, design and acquisition, the Mundipharma network of independent associated companies delivers cutting-edge treatments to meet the most pressing needs of healthcare professionals and patients. For further information please visit: www.mundipharma.com

About Bendamustine
Bendamustine was first discovered in Germany 50 years ago in what was then the German Democratic Republic (East Germany). In 2008 the US Food and Drug Administration (FDA) approved bendamustine for the treatment of iNHL and chronic lymphocytic leukaemia (CLL), and it subsequently received European approval in 2010 for certain types of indolent Non-Hodgkins Lymphoma (iNHL), multiple myeloma and chronic lymphocyctic leukaemia (CLL).

Bendamustine has marketing authorisations in Germany, France, UK, Italy, Spain, Austria, Switzerland, Sweden, Norway, Finland, Denmark, Poland, Slovakia, Ireland, Cyprus, Iceland, Belgium, The Netherlands, Greece, Slovenia, Portugal, Czech Republic, Romania and Bulgaria where it is marketed by the Mundipharma network of independent associated companies.

Bendamustine is licensed (Levact®, Ribomustin®, Ribovact®) from Astellas Deutschland GmbH. In the United States, bendamustine (TREANDA®) is marketed by Teva Pharmaceutical Industries Ltd. (NYSE: TEVA) and indicated for the treatment of patients with CLL, and indolent B-cell NHL that progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.

About Chronic Lymphocytic Leukaemia (CLL)[4]
CLL is the most common type of chronic leukaemia and occurs when a type of white blood cell called a lymphocyte becomes cancerous. It mostly occurs in people over the age of 60 and is very rare in people under 40. Men are twice as likely to develop CLL as women.

CLL is a slow developing disease and people can live for many years without symptoms or treatment. CLL is very hard to spot and around 50% of cases are diagnosed through a routine blood test for something else.

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References

1.Eichhorst B, Wendtner C-M, et al. *(FCR) versus Bendamustine and Rituximab (BR) in previously untreated and physically fit patients (pts) with advanced chronic lymphocytic leukemia (CLL).* (Oral presentation at the 55th American Society of Hematology (ASH) Annual Meeting in New Orleans - abstract number 526)
2.MINT data on file 014, November 2013
3.*SEER Stat Fact Sheets: Chronic Lymphocytic Leukemia* (accessed 29/10/2010)
4.*Chronic Lymphocytic Leukaemia (CLL): A Quick Guide*, Cancer Research UK http://www.cancerresearchuk.org/prod_consump/groups/cr_common/@cah/@gen/documents/generalcontent/about-cll.pdf.pdf (accessed 01/11/2013)