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Novel Chemotherapy Agent Bendamustine Significantly More Effective First-Line Therapy than Chlorambucil in CLL

- Blood marrow normalised in 31% (versus 2%) of patients, with manageable side-effects

Cambridge (United Kingdom), 4th August 2009: Nearly a third (31%) of all bendamustine-treated patients saw all clinical evidence of their advanced chronic lymphocytic leukaemia (CLL) disappear when used as a first-line treatment option, according to the results of a large new multicentre phase III study published online by the Journal of Clinical Oncology today. Only 2% of patients treated with chlorambucil (the standard treatment) in the study achieved the same results.¹

Professor Wolfgang U. Knauf of the Onkologische Gemeinschaftspraxis, Frankfurter Diakonie Kliniken, Frankfurt, Germany, who led the study, said: "CLL is the most common form of adult leukaemia in the Western world. It is also incurable, and so the goal of treatment is to stabilise the cancer over the long-term by extending periods of remission, during which patients can lead practically normal lives, symptom-free. Existing treatment options are limited for those with advanced CLL, but our new study shows that bendamustine couples significantly better efficacy with a manageable toxicity profile, so offering patients the hope of a better quality of life, for longer than traditional treatments."

CLL is a slowly progressing blood and bone marrow form of the disease presenting mostly in the elderly (average age of diagnosis is 68)². Blood cells that are normally produced in a controlled way lose this control and an increasing number of abnormal leukaemic lymphocytes circulate in the blood, eventually replacing the normal white cells, red cells and platelets in the bone marrow. Bendamustine has a unique mode of action compared with other cytotoxic agents. This means that it is able to kill cancer cells that have become resistant to previous chemotherapies³ and may return the blood marrow to normal, resulting in a complete response and thus a disappearance of all signs and symptoms of the disease.

In the study, patients treated with the chemotherapy agent bendamustine (162 of the total 319 patients) achieved a median progression-free survival of 21.6 months, compared to only 8.3

months for chlorambucil ($p < 0.0001$), enabling them to live without worsening CLL for over a year longer.¹

An improvement in the duration of remission was also shown (median 21.8 months in the bendamustine group, versus 8.0 months in the chlorambucil group), and complete or partial responses were achieved in 68% of bendamustine-treated, and 31% of chlorambucil-treated patients ($p < 0.0001$).¹

Haematological adverse events (grades III-IV Common Toxicity Criteria (CTC)) were more common with bendamustine than with chlorambucil (occurring in 40% versus 19% of patients). Severe infections (grades III-IV) occurred in 7% of bendamustine-treated patients and 3% of chlorambucil-treated patients. The side effects experienced by patients treated with bendamustine, were manageable and of short duration.

About the study

The study was a randomised, open-label, parallel-group, phase III trial conducted at 45 centres in Austria, Bulgaria, France, Germany, Italy, Spain, Sweden and the UK. 319 previously untreated patients (≤ 75 years of age) with Binet stage B* or Binet stage C** were randomised to receive either bendamustine 100mg/m²/day intravenously on days 1–2 ($n=162$), or chlorambucil 0.8mg/kg (Broca's normal weight)*** orally on days 1 and 15 ($n=157$). Treatment cycles were repeated every four weeks for a maximum of six cycles, and response was assessed according to National Cancer Institute Working Group criteria. Safety endpoints included infection rates and adverse events.

About Bendamustine

Bendamustine has marketing authorisations in Germany (RIBOMUSTIN) and Switzerland and will be marketed by the Mundipharma independent associated companies in Europe with indications as a single-agent or in combination with other anti-cancer agents for diseases such as indolent non-Hodgkin's lymphomas (NHL), multiple myeloma (MM) and chronic lymphocytic leukaemia (CLL). RIBOMUSTIN is licensed from Astellas Deutschland GmbH. In the United States, bendamustine (TREANDA[®]) is marketed by Cephalon Inc 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. SymBio Pharmaceuticals Ltd holds exclusive rights to develop and market bendamustine HCL in Japan (sublicensed to Eisai Co Ltd) and selected Asian countries.

Bendamustine is currently undergoing regulatory review in 12 countries across Europe. Significantly, the American Society of Clinical Oncology (ASCO) included bendamustine for the treatment of CLL in its 2008 shortlist of major clinical advancements in the treatment of cancer, with the greatest potential impact on patient care.⁴

About CLL

CLL can lead to bone marrow failure, infection and eventually, a spreading of the cancer to other areas of the body. These patients often have more than two co-morbidities, making them less suitable for fludarabine based regimens, thereby limiting treatment options. Such patients also have a lower overall survival rate.⁵

About Mundipharma

The Mundipharma independent associated companies, including Mundipharma International, Purdue Pharma and Napp Pharmaceuticals are privately owned companies and joint ventures covering the world's pharmaceutical markets. The companies worldwide are dedicated to bringing to patients with severe and debilitating diseases the benefit of novel treatment options in fields such as severe pain, haemato-oncology, rheumatoid arthritis and respiratory disease. For more information: www.mundipharma.co.uk

** ≥ 3 lymph node regions involved including hepatomegaly and splenomegaly*

*** Anaemia and/or thrombocytopenia regardless of the number of lymph node regions*

**** Broca's normal weight in kg: the body weight for the dose being the height of the patient in cm minus 100)*

-Ends-

References

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For further information, please contact:

Nicole Moores
Cohn & Wolfe
020 7331 5337
nicole.moores@cohnwolfe.com

Alison Wright
Cohn & Wolfe
020 7331 5386
alison.wright@cohnwolfe.com