Primary Endpoints Met in Phase 3 of Imbruvica with Rituximab in Waldenstom's Macroglobulinemia

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A Phase 3 of Imbruvica (ibrutinib) in combination with Rituxan (rituximab) in relapsed/refractory and treatment-naïve patients with Waldenstrom's macroglobulinemia (WM) has successfully met its primary endpoint by demonstrating improvement of progression-free survival (PFS) compared to rituximab alone.

Janssen Research & Development, LLC (Janssen) and Pharmacyclics LLC, an AbbVie company, announced the news this morning, and intend to share and discuss the data from the iNNOVATE (PCYC-1127) study in a future publication or medical congress.

Additionally, results from the study showed early positive results at the interim analysis stage, which will support future discussions with regulatory authorities.

Imbruvica was one of the first therapies to receive approval from the U.S. Food and Drug Administration (FDA) after also receiving Breakthrough Therapy Designation. As of January 2015, alone, it has been indicated to treat adults with WM, a type of non-Hodgkin lymphoma (NHL) in which the cancer cells make large amounts of the abnormal macroglobulin protein. An estimated 1,000-1,500 people are diagnosed with WM annually.

The therapy is also currently indicated to treat 5 other patient populations, including: chronic lymphocytic leukemia (CLL), small lymhocytic lymphoma (SLL), mantle cell lymphoma (MCL) in patients who have received at least one prior therapy, marginal zone lymphoma (MZL) in patients who require systemic therapy and have received at least one prior anti-CD20-based therapy, and chronic graft-versus-host disease (cGVHD) in patients who failed one or more lines of systemic therapy.

Imbruvica is a once-daily oral therapy that operates as an inhibitor of the Bruton's tyrosine kinase (BTK) protein. BTK is a key signaling molecule in the B-cell receptor signaling complex that plays a fundamental part in the survival and spreading of malignant B-cells, and could lead to other serious and life-threatening conditions.

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"It is gratifying to see that patients with Waldenström's macroglobulinemia – a rare, difficult-to-treat form of blood cancer – have achieved this magnitude of benefit with the IMBRUVICA combination with rituximab as compared to rituximab alone in either the relapsed/refractory or newly diagnosed setting," said Craig Tendler, M.D., Vice President, Late-Stage Development and Global Medical Affairs, Janssen Oncology in a press release. "Since the approval of IMBRUVICA in 2013 for Waldenström's, we have added to the body of evidence and patient experience, by conducting this randomized Phase 3 trial and confirming IMBRUVICA's clinical benefit first seen in the relapsed/refractory setting and now demonstrated with earlier use in the treatment journey for the WM patient."

The iNNOVATE study enrolled 150 patients with relapsed/refractory and treatment-naïve WM, and in the study, patients were randomized to receive intravenous rituximab 375/mg/m^2 for 4 consecutive weeks, followed by a second 4-week rituximab course after a 3-month interval. All patients received either ibrutinib 420 mg or placebo once daily continuously until criteria for permanent discontinuation were met.

"This is a first-of-its-kind prospective randomized trial in Waldenström's macroglobulinemia," said Meletios A. Dimopoulos, M.D., Professor and Chairman of the Department of Clinical Therapeutics at the National and Kapodistrian University of Athens School of Medicine. "The full report of this study will be of important clinical significance regarding the benefits of the combination of ibrutinib with rituximab in patients with WM."

To date, Imbruvica has been used to treat more than 90,000 patients.

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