Bristol-Myers Squibb

YERVOY® (ipilimumab) Receives Marketing Authorisation for First-Line Treatment of Adult Patients with Advanced Melanoma in Europe

Yervoy, an innovative immuno-oncology therapy that has demonstrated durable long-term survival in some patients,[1,2] is now approved for use in previously-untreated patients

(PARIS, FRANCE, November 8, 2013) – Bristol-Myers Squibb today announced that the European Commission (EC) has approved YERVOY® (ipilimumab) for the first-line treatment of adult patients with advanced (unresectable or metastatic) melanoma.[3] When initially approved in Europe in July 2011 for the treatment of adult patients with previously-treated advanced melanoma, ipilimumab represented the first major treatment advance in this disease in more than 30 years, providing the first overall survival benefit ever seen in the treatment of metastatic melanoma in a phase III study.[1]

"This first-line approval of ipilimumab is important news for the many people with advanced melanoma across Europe who have not received prior treatment. Despite some advances in the first-line treatment of advanced melanoma, for many patients there remains a high unmet need for improved survival outcomes," commented Ron Cooper, President, Bristol-Myers Squibb Europe. "The granting of this licence extension underscores the belief in the therapeutic potential of treatments like ipilimumab, which is the first approved therapy from our immuno-oncology pipeline. At Bristol-Myers Squibb, we are committed to the research and development of immuno-oncology, a rapidly evolving and innovative treatment modality that harnesses the natural capabilities of a patient's own immune system to fight cancer."

Historically, the median life expectancy for patients with metastatic melanoma, one of the most aggressive forms of skin cancer, was just 6 to 9 months.[4]

"Ipilimumab is currently the only treatment for advanced melanoma that has demonstrated durable long-term survival in pretreated melanoma, in a randomised phase III trial.[1,2] With today's approval, we may now be able to offer this innovative immuno-oncology therapy to our advanced melanoma patients earlier in the course of their treatment," said Professor Dirk Schadendorf, University Hospital Essen, Germany.

The recommended treatment regimen of YERVOY is 3 mg/kg administered intravenously over a 90-minute period every 3 weeks for a total of 4 doses.[5] The types of adverse events attributed to

ipilimumab are generally mechanism (immune-) based and are managed using protocol-specific guidelines.[2,5,6] Immune-related adverse reactions, which can be severe or life-threatening, may involve the gastrointestinal, liver, skin, nervous, endocrine, or other organ systems.[2,5] The safety profile of ipilimumab 3 mg/kg in chemotherapy-naive patients pooled across phase II/III clinical trials (N= 75) and in treatment naïve patients in a retrospective observational study (N= 120) was similar to that in previously-treated advanced melanoma.[5,7]

The extension of the Marketing Authorisation was supported by data derived from phase 2 and 3 studies conducted in advanced melanoma patients, as well as from two retrospective observational studies in first-line advanced melanoma patients who were treated with ipilimumab 3mg/kg monotherapy.[3,7,8] These observational data were presented at the European Cancer Congress (27 September – 1 October 2013). Overall survival (OS) of ipilimumab 3 mg/kg monotherapy in chemotherapy-naive patients pooled across phase 2 and 3 clinical trials (N= 78; randomised) and in treatment-naive patients in two retrospective observational studies (N= 120 and N= 61) were generally consistent.[3,7,8] The estimated 1-year survival rates were 59.5% (95% CI: 50.1 - 67.8) and 49.3% (95% CI: 35.6 - 61.6) in the two retrospective observational studies.[3,7,8] The estimated 1-year and 2-year survival rates for chemotherapy-naive patients (N= 78) pooled across phase 2 and 3 clinical trials were 54.1% (95% CI: 42.5 - 65.6) and 32% (95% CI: 20.7 - 42.9), respectively.[3,7,8]

This extension of the indication for ipilimumab is applicable to all 28 European Union member states as well as Iceland and Norway. Bristol-Myers Squibb will now work closely with local health authorities in these countries to expedite the availability of ipilimumab for the first-line treatment of adult patients with advanced melanoma, with the aim of addressing the significant unmet need in treating this devastating disease.

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About Metastatic Melanoma

Melanoma is a form of skin cancer characterised by the uncontrolled growth of pigment-producing cells (melanocytes) located in the skin.[9] Metastatic melanoma is one of the most aggressive forms of the disease, and occurs when cancer spreads beyond the surface of the skin to other organs, such as the lymph nodes, lungs, brain or other areas of the body.[9,10,11] Some cancer cells can actively evade surveillance by the immune system, allowing tumours to survive. Historically, the median life expectancy for metastatic melanoma patients was just 6 to 9 months.4

The incidence of melanoma in Europe has more than doubled over the past 30 years.[12] Unlike most other solid tumours, melanoma affects younger, middle aged people.[13] The median age at diagnosis for melanoma is 57 and the median age at death from this disease is 67.[13] Melanoma is mostly curable when treated in its early stages.[14]

About YERVOY® (ipilimumab)

Ipilimumab which is a recombinant, human monoclonal antibody, blocks the cytotoxic T-lymphocyte antigen-4 (CTLA-4). CTLA-4 is a negative regulator of T-cell activation. Ipilimumab binds to CTLA-4 and blocks the interaction of CTLA-4 with its ligands, CD80/CD86. Blockade of CTLA-4 has been shown to augment T-cell activation and proliferation. The mechanism of action of ipilimumab's effect in patients with melanoma is indirect, possibly through T-cell mediated anti-tumour immune responses.

In July 2011, the EU approved ipilimumab 3 mg/kg for the treatment of adult patients with previously-treated unresectable or metastatic melanoma. On 25 March 2011, the U.S. Food and Drug Administration (FDA) approved ipilimumab 3 mg/kg for the treatment of patients with unresectable (inoperable) or metastatic melanoma in the U.S, regardless of line of therapy.

The value of ipilimumab as a second-line treatment in adults with advanced (unresectable or metastatic) melanoma, has already been recognised by many countries across Europe and has been made accessible by local authorities to patients in Austria, Belgium, Denmark, England, Finland, France, Germany, Ireland, Italy, Luxembourg, Netherlands, Norway, Scotland, Spain, Sweden, Switzerland and Wales.

For full Prescribing Information, please refer to the Yervoy Summary of Product Characteristics.[5] For information on European Commission decisions and annexes relating to ipilimumab, in all EU languages, please visit http://ec.europa.eu/health/documents/community-register/html/alfregister.htm.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases.

Bristol-Myers Squibb Forward-Looking Statement

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding the research, development and commercialization of pharmaceutical products. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2012, in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

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