Investigational Compound Ipilimumab Demonstrates Improved Overall Survival in Phase 3 Trial of Previously-Treated Patients with Metastatic Melanoma

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Study Meets Primary Endpoint of Overall Survival for Patients Treated with Ipilimumab (Hazard Ratio = 0.66 - 0.68)

Forty-four to 46 Percent of Patients Treated with Ipilimumab Alive at One Year and 22 to 24 Percent Alive at Two Years

Median Overall Survival Extended by 3.6 to 3.7 Months for Ipilimumab Patients

Results Published in New England Journal of Medicine and Presented at 46th Annual Meeting of the American Society of Clinical Oncology

Data Advance Understanding of the Potential Role of Immuno-Oncology in Patient Care

PRINCETON, N.J.--(BUSINESS WIRE)-- Bristol-Myers Squibb Company (NYSE: BMY) today announced positive results from a Phase 3 randomized, double blind study of ipilimumab which demonstrated that overall survival (OS) was significantly extended in patients with previously-treated metastatic melanoma who received ipilimumab. The results were statistically significant for patients receiving ipilimumab alone (hazard ratio 0.66, p=0.0026) or ipilimumab in combination with a gp100 peptide vaccine (hazard ratio 0.68, p=0.0004) when compared to those patients who received the control therapy of gp100 alone. Forty-four to 46 percent of patients treated with ipilimumab were alive at one year compared to 25 percent of patients treated with the control arm. At two years, 22 to 24 percent of patients treated with ipilimumab were alive compared to 14 percent of patients treated with the control arm.

As in other studies of ipilimumab, the most common side effects reported in the study were immune-related and based on the mechanism of action. These immune-related adverse events were sometimes severe and life-threatening, and most often affected the gastrointestinal, skin, liver, or endocrine systems.

The data were published today in the New England Journal of Medicine and presented at the 46th Annual Meeting of the American Society of Clinical Oncology. (Abstract # 4)

"Metastatic melanoma is one of the deadliest forms of cancer with no approved options for pre-treated patients," said Steven J. O'Day, M.D., Chief of Research and Director of the Melanoma Program at The Angeles Clinic and Research Institute, California, and presenter of the study results. "For the first time, a significant improvement in overall survival has been demonstrated in previously-treated advanced melanoma patients in a large, randomized Phase 3 study."

"Results from this ipilimumab study are exciting and show the potential of harnessing the immune system to treat cancers like metastatic melanoma," said F. Stephen Hodi, M.D., Department of Medicine, Harvard Medical School, Dana-Farber Cancer Institute and lead author on the New England Journal of Medicine paper.

Ipilimumab is a novel T-cell potentiator that specifically blocks the inhibitory signal of CTLA-4 (cytotoxic T lymphocyte-associated antigen 4), a molecule on T-cells that plays a critical role in regulating natural immune responses. Suppression of CTLA-4 can augment the immune system's T-cell response in fighting disease.
Study Results

In this study, median OS was 10, 10.1 and 6.4 months for the ipilimumab + gp100, ipilimumab alone and gp100 alone groups, respectively. The hazard ratios of the ipilimumab + gp100 group and the ipilimumab alone group relative to gp100 monotherapy are 0.68 and 0.66 with corresponding p-values of 0.0004 and 0.0026, respectively. At one year, 44-46% of patients treated with ipilimumab were alive compared to 25% of patients treated with gp100 alone. At two years, 22-24% of patients treated with ipilimumab were alive compared to 14% of patients treated with gp100 alone.

Grade 3/4 drug-related adverse events (AEs) were observed in 17%, 23% and 11% of the ipilimumab + gp100, ipilimumab and gp100 arms, respectively. Grade 3/4 immune-related AEs (irAEs) were seen in 10-15% of the ipilimumab treatment arms and 3% in the gp100 alone arm. Fourteen drug-related deaths (2.1%, 3.1% and 1.5% of the ipilimumab + gp100, ipilimumab and gp100 arms, respectively) occurred in the study, with seven (1.3%, 1.5% and 0%, of the ipilimumab + gp100, ipilimumab and gp100 arms, respectively) attributed to an irAE. Immune-related adverse events were treated with the use of supportive care and systemic steroids using established protocol-specific treatment guidelines.

About the Study

Study 020 is a randomized, double-blind global Phase 3 study of patients with unresectable Stage III or IV metastatic melanoma who have received prior therapies and were HLA-A2+. HLA-A2+ is a group of proteins that play a role in the body's immune system and the gp100 vaccine used as the comparator in study 020 is specific for patients who are HLA-A2+.

Eligible patients were randomized to receive ipilimumab + gp100 (3 mg/kg and 1mg/kg every three weeks for four doses; n=403), ipilimumab (3 mg/kg every three weeks for four doses) + placebo (n=137), or gp100 + placebo (n=136). There was no maintenance dosing phase. The primary endpoint was comparison of OS between patients who received ipilimumab + gp100 vs. gp100 alone. The secondary endpoints were an OS comparison of ipilimumab alone vs. gp100, progression free survival (PFS), best objective response rate (BORR) at Week 24, disease control rate (DCR) and safety. Re-induction was allowed within 28 days of documented progression, provided the patient had not experienced any dose limiting toxicities and response to the initial cycle of therapy was stable disease lasting ≥3 months from the first tumor assessment at Week 12, or complete response, or partial response. Patients in the study were re-induced with 1 to 3 additional courses of the originally assigned regimen in 7.2%, 6.5% and 1% of ipilimumab + gp100, ipilimumab and gp100 arms, respectively.

About Advanced Melanoma

Melanoma is a form of skin cancer characterized by the uncontrolled growth of pigment-producing cells (melanocytes) located in the skin. As with many cancers, it is more difficult to treat once the disease has spread beyond the skin to other parts of the body by way of the bloodstream or the lymphatic system (metastatic disease). Melanoma accounts for about three percent of skin cancer cases, but it causes most skin cancer deaths.

According to the World Health Organization, approximately 132,000 new cases of melanoma are diagnosed each year globally. The incidence of melanoma has increased ten-fold over the past 50 years, and has steadily increased since the 1970s. The American Cancer Society estimates that in 2009, there were 68,720 new cases of melanoma in the U.S.

About Bristol-Myers Squibb

For more information about Bristol-Myers Squibb, visit http://www.bms.com or follow us on Twitter at http://twitter.com/bmsnews.

This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding product development. 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. Among other risks, there can be no guarantee that ipilimumab will receive regulatory approval or, if approved, that it will become a commercially successful product. 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, 2009, 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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