Four-Year Follow-up with Empliciti (elotuzumab) Plus Lenalidomide/Dexamethasone (ELd) in Patients with Advanced Multiple Myeloma Shows Long-term Efficacy in ELOQUENT-2 Trial

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Combination therapy demonstrated a sustained reduction in risk of progression/death of 29% and relative improvement of 50% in progression-free survival rate of ELd (21%) compared to Ld alone (14%)

The extended follow-up data is the longest of an Immuno-Oncology agent in relapsed/refractory multiple myeloma

The data showed a safety profile consistent with prior findings

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE:BMY) presented four-year follow-up data from the Phase 3 ELOQUENT-2 study in which Empliciti (elotuzumab) plus lenalidomide/dexamethasone (ELd) continued to demonstrate efficacy in patients with relapsed/refractory multiple myeloma (RRMM), compared to patients treated with lenalidomide/dexamethasone (Ld) alone.

The data also showed a safety profile consistent with prior findings. The results were presented in an oral session today during the 22nd Congress of the European Hematology Association in Madrid, Spain and offer the longest follow-up efficacy and safety data of an Immuno-Oncology agent.

ELd therapy maintained a reduction in the risk of disease progression or death of 29% (HR 0.71; 95% CI: 0.59 to 0.86). At four-years, ELd therapy continued to demonstrate a clinically meaningful and sustained
relative improvement of 50% in progression-free survival (PFS) rate, 21% (95% CI: 16.6, 22.3), compared to Ld therapy, 14% (95% CI: 12.1, 17.3). PFS benefits seen in patients receiving ELd therapy were consistent across certain patient subsets and sustained through two-year, three-year and four-year follow-up. Patients with high risk* (n=60 ELd, n=66 Ld) showed relative risk reduction of 36% (HR=0.64; 95% CI: 0.43 to 0.97) and more than doubling of median PFS (15.2 ELd vs 7.4 Ld) with ELd in comparison to Ld.

Patients receiving ELd therapy demonstrated an overall response rate (ORR) of 79% (253/321 patients, 95% CI: 73.9 to 83.2), compared to 66% (214/325 patients, 95% CI: 60.4 to 71.0) among patients receiving Ld therapy alone. While OS was not pre-specified for the four-year follow-up, Empliciti in combination with Ld data also demonstrated a median overall survival (OS) benefit of 48 months (95% CI: 40.3 to 54.4) in favor of ELd versus a median OS of 40 months for Ld (95% CI: 33.3 to 45.4), a difference of 22% (HR 0.78; 95% CI: 0.63 to 0.96). Early separation of OS Kaplan Meier survival curves was maintained over time in favor of ELd versus Ld.

“These extended four-year follow-up data demonstrated that adding Empliciti to Ld yielded clinically relevant improvements and reductions in the risk of disease progression or death for patients with relapsed/refractory multiple myeloma, compared to Ld alone,” Meletios A. Dimopoulos, M.D., ELOQUENT-2 investigator and professor and chairman of the Department of Clinical Therapeutics at the National and Kapodistrian University of Athens School of Medicine. “This data at four-year follow-up is particularly notable as it suggests the ability of this Immuno-Oncology agent to build a sustainable immune response in some patients with advanced multiple myeloma.”

The rates of adverse events (AE) were similar between patients receiving ELd or Ld therapy and consistent with those reported at two- and three-year follow-up. The most common AEs (all grades) in ELd and Ld, respectively, were diarrhea (49%, 38%), fatigue (48%, 41%), anemia (43%, 38%), pyrexia (40%, 25%), constipation (36%, 28%), neutropenia (35%, 43%), cough (34%, 19%), back pain (31%, 29%), and muscle spasm (31%, 26%).

“The long-term efficacy data for Empliciti in patients with advanced multiple myeloma shows the combination of this Immuno-Oncology agent with standard lenalidomide/dexamethasone treatment can improve patient outcomes,” said Jonathan Leith, Ph.D., hematology development lead, Bristol-Myers Squibb. “These findings illustrate Bristol-Myers Squibb’s commitment to exploring how Immuno-Oncology agents might best help appropriate patients.”

About ELOQUENT-2

The ELOQUENT-2 trial randomized 646 patients with RRMM who had one to three prior therapies to receive either ELd (321 patients) or Ld (325 patients) in 28-day cycles until their disease progressed, the occurrence of unacceptable toxicity or they withdrew consent. In the ELd arm, patients were administered 10 mg/kg by IV of elotuzumab for weeks one and two of the 28-day cycle and then every other week, along with 25 mg of lenalidomide by mouth for days 1-21 of the cycle and the weekly equivalent of 40 mg of dexamethasone by mouth. In the Ld arm, patients were given 25 mg of lenalidomide by mouth for days 1-21 of the cycle and the weekly equivalent of 40 mg of dexamethasone by mouth.

The occurrence of treatment-related Grade 3-4 AEs in 5% or more of patients were generally comparable between the ELd and Ld groups: vascular diseases (10% vs. 8%; mostly venous-related), second primary malignancies (9% vs. 6%), and cardiac disorders (5% vs. 8%). ELd therapy did have a slightly higher incidence of infection compared to Ld (33% vs. 26%). ELd treatment also had higher overall rates than Ld of any grade infection (84% vs. 75%) and second primary malignancies (17% vs. 11%). However, exposure to ELd was longer than to Ld, with a median treatment cycle of 19 months (9 to 42) compared to 14 months (6 to 25), respectively. While disease progression and infection were major causes of deaths in both groups, fewer were reported with ELd (165) than with Ld (186) treatment.

On November 30, 2015, the U.S. Food and Drug Administration (FDA) approved Empliciti in combination with lenalidomide and dexamethasone in patients with multiple myeloma who have received one to three prior therapies. On May 11, 2016, the European Commission approved Empliciti in combination with lenalidomide and dexamethasone in patients with multiple myeloma who have received at least one prior therapy.

Bristol-Myers Squibb & Immuno-Oncology: Advancing Oncology Research

At Bristol-Myers Squibb, patients are at the center of everything we do. Our vision for the future of cancer care is focused on researching and developing transformational Immuno-Oncology (I-O) medicines for hard-to-treat cancers that could potentially improve outcomes for these patients.

We are leading the scientific understanding of I-O through our extensive portfolio of investigational compounds and approved agents. Our differentiated clinical development program is studying broad patient populations across more than 50 types of cancers with 14 clinical-stage molecules designed to target different immune system pathways. Our deep expertise and innovative clinical trial designs...
position us to advance I-O/I-O, I-O/chemotherapy, I-O/targeted therapies and I-O/radiation therapies across multiple tumors and potentially deliver the next wave of therapies with a sense of urgency. We also continue to pioneer research that will help facilitate a deeper understanding of the role of immune biomarkers and how patients’ individual tumor biology can be used as a guide for treatment decisions throughout their journey.

We understand making the promise of I-O a reality for the many patients who may benefit from these therapies requires not only innovation on our part but also close collaboration with leading experts in the field. Our partnerships with academia, government, advocacy and biotech companies support our collective goal of providing new treatment options to advance the standards of clinical practice.

About Empliciti

Empliciti is an immunostimulatory antibody that specifically targets Signaling Lymphocyte Activation Molecule Family member 7 (SLAMF7), a cell-surface glycoprotein. SLAMF7 is expressed on myeloma cells independent of cytogenetic abnormalities. SLAMF7 also is expressed on Natural Killer cells, plasma cells and at lower levels on specific immune cell subsets of differentiated cells within the hematopoietic lineage.

Empliciti has a dual mechanism-of-action. It directly activates the immune system through Natural Killer cells via the SLAMF7 pathway. Empliciti also targets SLAMF7 on myeloma cells, tagging these malignant cells for Natural Killer cell-mediated destruction via antibody-dependent cellular toxicity.

Bristol-Myers Squibb and AbbVie are co-developing Empliciti, with Bristol-Myers Squibb solely responsible for commercial activities.

U.S. FDA-APPROVED INDICATION FOR EMPPLICITI™

EMPLICITI™ (elotuzumab) is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies.

IMPORTANT SAFETY INFORMATION

Infusion Reactions

- EMPLICITI can cause infusion reactions. Common symptoms include fever, chills, and hypertension. Bradycardia and hypotension also developed during infusions. In the trial, 5% of patients required interruption of the administration of EMPLICITI for a median of 25 minutes due to infusion reactions, and 1% of patients discontinued due to infusion reactions. Of the patients who experienced an infusion reaction, 70% (23/33) had them during the first dose. If a Grade 2 or higher infusion reaction occurs, interrupt the EMPLICITI infusion and institute appropriate medical and supportive measures. If the infusion reaction recurs, stop the EMPLICITI infusion and do not restart it on that day. Severe infusion reactions may require permanent discontinuation of EMPLICITI therapy and emergency treatment.
- Premedicate with dexamethasone, H1 Blocker, H2 Blocker, and acetaminophen prior to infusing with EMPLICITI.

Infections

- In a clinical trial of patients with multiple myeloma (N=635), infections were reported in 81.4% of patients in the EMPLICITI with lenalidomide/dexamethasone arm (ERd) and 74.4% in the lenalidomide/dexamethasone arm (Rd). Grade 3-4 infections were 28% (ERd) and 24.3% (Rd). Opportunistic infections were reported in 22% (ERd) and 12.9% (Rd). Fungal infections were 9.7% (ERd) and 5.4% (Rd). Herpes zoster was 13.5% (ERd) and 6.9% (Rd). Discontinuations due to infections were 3.5% (ERd) and 4.1% (Rd). Fatal infections were 2.5% (ERd) and 2.2% (Rd). Monitor patients for the development of infections and treat promptly.

Second Primary Malignancies

- In a clinical trial of patients with multiple myeloma (N=635), invasive second primary malignancies (SPM) were 9.1% (ERd) and 5.7% (Rd). The rate of hematologic malignancies were the same between ERd and Rd treatment arms (1.6%). Solid tumors were reported in 3.5% (ERd) and 2.2% (Rd). Skin cancer was reported in 4.4% (ERd) and 2.8% (Rd). Monitor patients for the development of SPMs.

Hepatotoxicity

- Elevations in liver enzymes (AST/ALT greater than 3 times the upper limit, total bilirubin greater than 2 times the upper limit, and alkaline phosphatase less than 2 times the upper limit) consistent with hepatotoxicity were 2.5% (ERd) and 0.6% (Rd). Two patients experiencing hepatotoxicity discontinued treatment; however, 6 out of 8 patients had resolution and continued treatment. Monitor liver enzymes periodically. Stop EMPLICITI upon Grade 3 or higher elevation of liver enzymes.
enzymes. After return to baseline values, continuation of treatment may be considered.

**Interference with Determination of Complete Response**

- EMPLICITI is a humanized IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis and immunofixation assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and possibly relapse from complete response in patients with IgG kappa myeloma protein.

**Pregnancy/Females and Males of Reproductive Potential**

- There are no studies with EMPLICITI with pregnant women to inform any drug associated risks.
- There is a risk of fetal harm, including severe life-threatening human birth defects associated with lenalidomide and it is contraindicated for use in pregnancy. Refer to the lenalidomide full prescribing information for requirements regarding contraception and the prohibitions against blood and/or sperm donation due to presence and transmission in blood and/or semen and for additional information.

**Adverse Reactions**

- Infusion reactions were reported in approximately 10% of patients treated with EMPLICITI with lenalidomide and dexamethasone. All reports of infusion reaction were Grade 3 or lower. Grade 3 infusion reactions occurred in 1% of patients.
- Serious adverse reactions were 65.4% (ERd) and 56.5% (Rd). The most frequent serious adverse reactions in the ERd arm compared to the Rd arm were: pneumonia (15.4%, 11%), pyrexia (6.9%, 4.7%), respiratory tract infection (3.1%, 1.3%), anemia (2.8%, 1.9%), pulmonary embolism (3.1%, 2.5%), and acute renal failure (2.5%, 1.9%).
- The most common adverse reactions in ERd and Rd, respectively (>20%) were fatigue (61.6%, 51.7%), diarrhea (46.9%, 36.0%), pyrexia (37.4%, 24.6%), constipation (35.5%, 27.1%), cough (34.3%, 18.9%), peripheral neuropathy (26.7%, 20.8%), nasopharyngitis (24.5%, 19.2%), upper respiratory tract infection (22.6%, 17.4%), decreased appetite (20.8%, 12.6%), and pneumonia (20.1%, 14.2%).

Please see the full Prescribing Information for **EMPLICITI**.

**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. For more information about Bristol-Myers Squibb, visit us at [BMS.com](http://www.bms.com) or follow us on [LinkedIn](https://www.linkedin.com), [Twitter](https://twitter.com), [YouTube](https://www.youtube.com) and [Facebook](https://www.facebook.com).

**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, 2016 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.

*High risk = ISS stage II or III and t(4;14) or del(17p) abnormality

Standard risk = patients not meeting either the definition of high risk or low risk, which is defined as ISS stage I or II and absence of t(4;14), del(17p) and 1q21 abnormalities and age <55

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$BMY announces extended 4-yr data in patients with #MultipleMyeloma at #EHA17