U.S. Food and Drug Administration Approves Empliciti® (elotuzumab) Plus Pomalidomide and Dexamethasone, a New Immunotherapy Combination for Certain Patients with Relapsed or Refractory Multiple Myeloma

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Terms:
#BristolMyers #cancer #carcinoma #CheckMate #doctor #FDA #HeadandNeck #ImmunoOncology #nivolumab #nurse #oncology #Opdivo #recurrent #Regulatory #SCCHN #squamous #Squibb $BMY

Dateline City:
PRINCETON, N.J.

- In the ELOQUENT-3 trial, treatment with Empliciti plus pomalidomide and dexamethasone (EPd) doubled median progression-free survival and overall response rate versus pomalidomide and dexamethasone (Pd) 1
- Low discontinuation rates due to adverse reactions were observed with both EPd and Pd alone 1
- Empliciti, when used in combination with pomalidomide and dexamethasone, can be administered once monthly after first two cycles 1

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) today announced that the U.S. Food and Drug Administration (FDA) approved Empliciti (elotuzumab) injection for intravenous use in combination with pomalidomide and dexamethasone (EPd) for the treatment of adult patients with multiple myeloma who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor. 1 In ELOQUENT-3, a randomized, open-label, Phase 2 trial, EPd demonstrated benefit in patients with relapsed or refractory multiple myeloma, doubling both median progression-free survival (PFS) and overall response rate (ORR) versus pomalidomide and dexamethasone (Pd). 1

"Empliciti plus pomalidomide and dexamethasone has been proven to extend the time that certain patients live without disease progression, giving health care professionals an effective new tool to tackle this relentless cancer," 1,2 said Joseph E. Eid, M.D., senior vice president and head of Medical, Bristol-Myers Squibb. "Today’s approval reinforces the importance of Immuno-Oncology in blood cancers and expands the role of Empliciti to address the needs of relapsed or refractory multiple myeloma patients."

Empliciti with pomalidomide and dexamethasone is associated with Warnings and Precautions related to: infusion reactions, infections, secondary primary malignancies, hepatotoxicity, interference with determination of complete response, pregnancy/females and males of reproductive potential and adverse reactions. 1 Please see the detailed important safety information below.

Following priority review by the FDA, EPd is the first triplet combination to be approved based on a randomized clinical trial using Pd as a comparator. 3,4 Results from the trial include:

- Progression-free survival (primary endpoint, investigator-assessed): 1,3 EPd reduced the risk of disease progression by 46% (hazard ratio [HR]: 0.54; 95% confidence interval [CI]: 0.34 to 0.86, p=0.0078), demonstrating a median PFS of 10.25 months (95% CI: 5.59 to non-estimable [NE]) vs. 4.67 months (95% CI: 2.83 to 7.16) for Pd alone after a minimum follow-up of 9.1 months. 1
- Overall response rate (secondary endpoint, investigator-assessed): 1,3 Response rates doubled in patients receiving EPd (53.3%; n=32/60 [95% CI: 40.0 to 66.3]) compared with patients receiving Pd alone (26.3%; n=15/57
Infusion Reactions

**IMPORTANT SAFETY INFORMATION**

EMPLICITI is available for injection for intravenous use in 300 mg and 400 mg vials.

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

EMPLICITI is indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

EMPLICITI is available for injection for intravenous use in 300 mg and 400 mg vials.

**INDICATIONS**

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

EMPLICITI is indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

**INFUSION SAFETY INFORMATION**

**Infusion Reactions**

- **Safety**: Serious adverse reactions were reported in 22% of patients treated with EPd and in 15% of patients treated with Pd. Discontinuation of any component of the treatment regimen due to adverse reactions occurred in 5.0% of patients in the EPd arm, compared to 1.8% of patients in the control arm.

“Despite remarkable recent innovations with novel therapies for the treatment of multiple myeloma, many patients still face poor outcomes, and particularly in the relapsed and relapsed, refractory setting,” said Paul Richardson, M.D., clinical program leader and director of clinical research of the Jerome Lipper Multiple Myeloma Center at Dana-Farber Cancer Institute. “This new regimen of elotuzumab combined with pomalidomide and dexamethasone not only extended the time to disease progression versus a standard of care but also doubled the response rate in some patients whose prior treatments had failed them. Thus to be able to offer an alternative with a meaningful clinical benefit is an important and significant milestone for our patients.”

Approximately 31,000 people in the United States will be diagnosed with multiple myeloma this year. A common characteristic for many patients is that they experience multiple relapses, which means that the cancer returns after a period of remission.

“Relapse can be overwhelming and extremely challenging for multiple myeloma patients, particularly after they have already tried several therapies,” said Paul Giusti, president and chief executive officer of the Multiple Myeloma Research Foundation. “EMPLICITI, in combination with pomalidomide and dexamethasone, is an exciting new option for patients with relapsed or refractory myeloma.”

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

**About ELOQUENT-3**

ELOQUENT-3 was a randomized, open-label Phase 2 study evaluating the addition of Empliciti to pomalidomide and dexamethasone versus pomalidomide and dexamethasone in 117 patients with multiple myeloma who received two or more prior therapies and were either refractory or relapsed and refractory to lenalidomide and a proteasome inhibitor. Patients were randomized 1:1 to receive either EPd (n=60) or Pd (n=57) in 28-day cycles until disease progression or unacceptable toxicity. The approved dose of Empliciti, when used in combination with pomalidomide and dexamethasone, is 10 mg/kg administered intravenously every week for the first two 28-day cycles, followed by 20 mg/kg every four weeks until disease progression or unacceptable toxicity.

The primary efficacy outcome measure of the trial was PFS as determined by the investigator. The secondary efficacy outcome measure of ORR included complete, stringent-complete, very good partial responses or better based on the International Myeloma Working Group criteria. Data from the ELOQUENT-3 trial were presented at the 23rd Congress of the European Hematology Association in June 2018.

**Select Safety Profile for the ELOQUENT-3 Trial**

The most frequent serious adverse reactions in the population evaluated for safety (n=60 in the EPd arm and n=55 in the Pd arm) were pneumonia (13% vs. 11%) and respiratory tract infection (7% vs. 3.6%). Infusion reactions were reported in 3.3% of patients treated with EPd. Adverse reactions that occurred with a >/=10% incidence for Empliciti plus pomalidomide and dexamethasone-treated patients and >/=5% incidence than pomalidomide and dexamethasone-treated patients were constipation (22% vs. 11%), hyperglycemia (20% vs. 15%), pneumonia (18% vs. 13%), diarrhea (18% vs. 9%), respiratory tract infection (17% vs. 9%), bone pain (15% vs. 9%), dyspnea (15% vs. 7%), muscle spasms (13% vs. 5%), edema peripheral (13% vs. 7%) and lymphopenia (10% vs. 1.8%).

**INDICATIONS**

EMPLICITI is indicated in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received on or three prior therapies.

EMPLICITI is indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

EMPLICITI is available for injection for intravenous use in 300 mg and 400 mg vials.

**INFUSION SAFETY INFORMATION**

**Infusion Reactions**

- Infusion reactions were reported in 10% of patients treated with EMPLICITI in the ELOQUENT-2 trial [EMPLICITI + lenalidomide + dexamethasone (ERd) vs lenalidomide + dexamethasone (Rd)] and 3.3% in the ELOQUENT-3 trial [EMPLICITI + pomalidomide + dexamethasone (EPd) vs pomalidomide + dexamethasone (Pd)].

- In the ELOQUENT-2 trial, all infusion reactions were Grade 3 or lower, with Grade 3 infusion reactions occurring in 1% of patients. The most common symptoms included 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.
In the ELOQUENT-3 trial, the only infusion reaction symptom was chest discomfort (2%), which was Grade 1. All the patients who experienced an infusion reaction had them during the first treatment cycle.

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 EMPLICITI infusion.

Infections

In the ELOQUENT-2 trial (N=635), infections were reported in 81% of patients in the ERd arm and 74% in the Rd arm. Grade 3-4 infections were 28% (ERd) and 24% (Rd). Discontinuations due to infections were 3.5% (ERd) and 4.1% (Rd). Fatal infections were 2.5% (ERd) and 2.2% (Rd). Opportunistic infections were reported in 22% (ERd) and 13% (Rd). Fungal infections were 10% (ERd) and 5% (Rd). Herpes zoster was 14% (ERd) and 7% (Rd).

In the ELOQUENT-3 trial (N=115), infections were reported in 65% of patients in both the EPd arm and the Pd arm. Grade 3-4 infections were reported in 13% (EPd) and 22% (Pd). Discontinuations due to infections were 7% (EPd) and 5% (Pd). Fatal infections were 5% (EPd) and 3.6% (Pd). Opportunistic infections were reported in 10% (EPd) and 9% (Pd). Herpes zoster was reported in 5% (EPd) and 1.8% (Pd).

Monitor patients for development of infections and treat promptly.

Second Primary Malignancies

In the ELOQUENT-2 trial (N=635), invasive second primary malignancies (SPM) were 9% (ERd) and 6% (Rd). The rate of hematologic malignancies was 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).

In the ELOQUENT-3 trial (N=115), invasive SPMs were 0% (EPd) and 1.8% (Pd).

Monitor patients for the development of SPMs.

Hepatotoxicity

In the ELOQUENT-2 trial (N=635), AST/ALT >3X the upper limit, total bilirubin >2X the upper limit, and alkaline phosphatase <2X the upper limit were 2.5% (ERd) vs 0.6% (Rd). Of 8 patients experiencing hepatotoxicity, 2 patients discontinued treatment while 6 patients had resolution and continued. Monitor liver enzymes periodically. Stop EMPLICITI upon ≥Grade 3 elevation of liver enzymes. Continuation of treatment may be considered after return to baseline values.

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 available data on EMPLICITI use in pregnant women to inform a drug-associated risk of major birth defects and miscarriage.

There is a risk of fetal harm, including severe life-threatening human birth defects, associated with lenalidomide and pomalidomide, and they are contraindicated for use in pregnancy. Refer to the respective product 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

ELOQUENT-2 trial:

- Serious adverse reactions were 65% (ERd) and 57% (Rd). The most frequent serious adverse reactions in the ERd arm compared to the Rd arm were: pneumonia (15%, 11%), pyrexia (7%, 5%), 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 (62%, 52%), diarrhea (47%, 36%), pyrexia (37%, 25%), constipation (36%, 27%), cough (34%, 19%), peripheral neuropathy (27%, 21%), nasopharyngitis (25%, 19%), upper respiratory tract infection (23%, 17%), decreased appetite (21%, 13%), and pneumonia (20%, 14%).

ELOQUENT-3 trial:

- Serious adverse reactions were 22% (EPd) and 15% (Pd). The most frequent serious adverse reactions in the EPd arm compared to the Pd arm were: pneumonia (13%, 11%) and respiratory tract infection (7%, 3.6%).

- The most common adverse reactions in EPd arm (≥20% EPd) and Pd, respectively, were constipation (22%, 11%) and hyperglycemia (20%, 15%).

Please see the full Prescribing Information.

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.

Empliciti was initially approved by the FDA in 2015 in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies.

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 medicines, including Immuno-Oncology (I-O) therapeutic approaches, for hard-to-treat cancers that could potentially improve outcomes for these patients.

We are leading the integrated scientific understanding of both tumor cell and immune system pathways, 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 24 clinical-stage molecules designed to target different immune system pathways. Our deep expertise and innovative clinical trial designs position us to advance the 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 a deeper understanding of the role of immune biomarkers and how a patient’s tumor biology can be used as a guide for treatment decisions throughout their journey.

We understand making the promise of transformational medicines like I-O therapies 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 Bristol-Myers Squibb’s Patient Access Support

Bristol-Myers Squibb remains committed to providing assistance so that cancer patients who need our medicines can access them and expedite time to therapy.

BMS Access Support®, the Bristol-Myers Squibb patient access and reimbursement program, is designed to help appropriate patients initiate and maintain access to BMS medicines during their treatment journey. BMS Access Support offers benefit investigation, prior authorization assistance, as well as co-pay assistance for eligible, commercially insured patients. More information about our access and reimbursement support can be obtained by calling BMS Access Support at 1-800-861-0048 or by visiting www.bmsaccesssupport.com.

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 or follow us on LinkedIn, Twitter, YouTube and Facebook.

About AbbVie in Oncology

At AbbVie, we strive to discover and develop medicines that deliver transformational improvements in cancer treatment by uniquely combining our deep knowledge in core areas of biology with cutting-edge technologies, and by working together with our partners - scientists, clinical experts, industry peers, advocates, and patients. We remain focused on delivering these transformative advances in treatment across some of the most debilitating and widespread cancers. We are also committed to exploring solutions to help patients obtain access to our cancer medicines. With the acquisitions of Pharmacyclics in 2015 and Stemcentrx in 2016, our research and development efforts, and through collaborations, AbbVie’s oncology portfolio now consists of marketed medicines and a pipeline containing multiple new molecules being evaluated worldwide in more than 200 clinical trials and more than 20 different tumor types. For more information, please visit https://www.abbvie.com/our-science/therapeutic-focus-areas/oncology.html.

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, 2017 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.

References


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English

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#FDA approves $BMY therapy for certain previously treated patients with #MultipleMyeloma.