June 1, 2018

Results of Phase III OPTIMISMM Study Presented at ASCO 2018 Showed the PVd Triplet Improved PFS in Early Lines of Relapsed or Refractory Multiple Myeloma

The OPTIMISMM study is the first Phase 3 Study to report findings for a triplet combination regimen in which 100% of patients have received prior lenalidomide therapy

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ:CELG) today announced results from the OPTIMISMM study, a phase III, randomized, open-label, international clinical study of the investigational combination regimen of POMALYST® (pomalidomide), bortezomib and dexamethasone in patients with relapsed or refractory multiple myeloma (RRMM) who had received at least one prior treatment including lenalidomide. The results were presented at the 54th Annual American Society of Clinical Oncology Scientific Sessions (ASCO) in Chicago, Illinois on June 1-5, 2018.

OPTIMISMM evaluated the efficacy and safety of POMALYST/IMNOVID (pomalidomide) plus bortezomib and low-dose dexamethasone (PVd) versus bortezomib and low-dose dexamethasone (Vd) in patients with early RRMM (1-3 prior lines of therapy). It is the only phase III trial to report results with a triplet combination in patients who have all received prior lenalidomide therapy. With lenalidomide becoming a standard of care, this represents a patient population for which there is a growing unmet medical need.

An analysis of the results found that the treatment with PVd resulted in significantly improved progression-free survival (PFS) and an earlier, deeper, more durable response in these patients compared to Vd treatment. The study, which included a high percentage of patients refractory to lenalidomide (71% in the PVd arm, 69% in the Vd arm), met its primary endpoint of PFS. Those receiving PVd achieved a statistically significant longer PFS than those in the Vd treatment arm (11.20 months vs. 7.10 months, respectively [P= < .0001, HR 0.61; 95% CI: (0.49-0.77)]), reducing the risk of disease progression or death by 39% in the PVd arm. The PFS benefit was observed in the following subgroups of patients: LEN-refractory, LEN-nonrefractory, prior PI exposure or high-risk cytogenetics. Overall response rate (ORR), one of the study's secondary endpoints, was also significantly higher in the PVd treatment arm, compared to those receiving Vd (82.2% vs. 50.0%, $p < 0.001$). Additionally, time to treatment response was shorter in the PVd arm (0.9 months PVd vs. 1.4 months Vd), complete response was higher in the PVd arm (15.7% PVd vs. 4.0% Vd) and those receiving PVd experienced a longer duration of response than those in the Vd arm (13.7 months PVd vs. 10.9 months Vd.)

In an exploratory sub-group analysis, patients who had received one prior line of therapy reported longer PFS (20.73 months in PVd arm (n=40) vs. 11.63 months in Vd arm (n=41)) and ORR (90.1% in PVd arm vs. 54.8% in Vd arm) with a 46% reduction in the risk of disease progression or death in the PVd treatment arm compared with Vd. Other secondary endpoints included overall survival and safety.

"In the early relapse setting, there remains a need for a deeper understanding of potential treatment options, and in particular for patients who have received prior lenalidomide-based therapy. These are the first phase III clinical findings to report a significant and clinically meaningful progression-free survival improvement in patients who have previously received lenalidomide, a majority of whom are lenalidomide refractory," said Paul Richardson, MD, Clinical Program Leader and Director of Clinical Research, Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology, Dana-Farber Cancer Institute.

The most common Grade 3/4 treatment-emergent adverse events (TEAE) were neutropenia (PVd: 42% vs. Vd: 9%), infections (PVd: 31% vs. Vd: 18%) and thrombocytopenia (PVd: 27% vs. Vd: 29%.) Rates of grade 3 or 4 deep vein thrombosis in the PVd vs. Vd arms were 0.7% vs. 0.4% and rates of grade 3 or 4 pulmonary embolism in PVd vs. Vd were 4.0% vs. 0.4%. No events were fatal. SPMs occurred in 3.2% (2.7 per 100 person years) of patients treated with PVd and 1.5% (1.2 per 100 person years) of patients treated with Vd. The most common reason for treatment discontinuation was progressive disease.

"The results of the OPTIMISMM trial continue to bolster the growing body of research into combination regimens based on

the foundation of our IMiD® therapies," said Nadim Ahmed, President of Hematology and Oncology for Celgene. "We are excited by the findings, as they illustrate the potential for a pomalidomide-based triplet regimen to be used earlier in the treatment course. The study also included patients who received PVd immediately following progression after lenalidomide treatment, a growing and clinically relevant patient population for which no phase III data were available until now."

Pomalyst plus dexamethasone in combination with bortezomib is not approved in any country for any use.

ABOUT OPTIMISMM

OPTIMISMM is the first phase III trial to compare the efficacy and safety of PVd vs. Vd as an early line of therapy in patients with RRMM (with 1-3 prior lines of therapy) and prior lenalidomide (LEN) exposure, including LEN-refractory patients. The study was a multi-center, international, open-label, randomized phase III clinical trial to compare the efficacy and safety of a POMALYST (lenalidomide), bortezomib and low-dose dexamethasone (PVd) treatment regimen to a bortezomib and low-dose dexamethasone (Vd) treatment regimen in patients with relapsed or refractory multiple myeloma.

This global study evaluated 559 patients with relapsed or refractory multiple myeloma who had received up to three prior lines of therapy, including two or more cycles of lenalidomide treatment, who had an ECOG score of PS ≤ 2. Prior treatment with bortezomib was allowed, except for patients whose disease progressed while on a regimen containing bortezomib 1.3 mg/m^2 twice weekly dosing. Patients were stratified based on age (≤ 75 years old vs > 75 years old), number of prior antimyeloma regimens (1 vs. > 1), and β2-microglobulin levels (< 3.5 mg/L vs ≥ 3.5 to ≤ 5.5 mg/L vs > 5.5 mg/L) at screening. The median age of the patients was 67 years in the PVd group and 68 years in the Vd group.

Patients were randomized 1:1 to receive PVd or Vd. In 21-day cycles, patients received POMALYST 4 mg/d on days 1-14 (PVd arm only); bortezomib 1.3 mg/m^2 on days 1, 4, 8 and 11 of cycles 1-8 and on days 1 and 8 of cycles 9 and beyond; and dexamethasone 20 mg/d (10 mg if aged > 75 years) on the days of and after receiving bortezomib treatment.

About POMALYST

Indication

POMALYST® (pomalidomide) is a thalidomide analogue indicated, in combination with dexamethasone, for patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy.

Important Safety Information

WARNING: EMBRYO-FETAL TOXICITY and VENOUS AND ARTERIAL THROMBOEMBOLISM

Embryo-Fetal Toxicity

- **POMALYST is contraindicated in pregnancy. POMALYST is a thalidomide analogue. Thalidomide is a known human teratogen that causes severe birth defects or embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting POMALYST treatment.**
- **Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after stopping POMALYST treatment.**

POMALYST is only available through a restricted distribution program called POMALYST REMS®.

Venous and Arterial Thromboembolism

- **Deep venous thrombosis (DVT), pulmonary embolism (PE), myocardial infarction, and stroke occur in patients with multiple myeloma treated with POMALYST. Prophylactic antithrombotic measures were employed in clinical trials. Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.**

CONTRAINDICATIONS

- **Pregnancy:** POMALYST can cause fetal harm and is contraindicated in females who are pregnant. If POMALYST is

used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential risk to a fetus.

WARNINGS AND PRECAUTIONS

- **Embryo-Fetal Toxicity & Females of Reproductive Potential: See Boxed WARNINGS**
  - Males: Pomalidomide is present in the semen of patients receiving the drug. Males must always use a latex or synthetic condom during any sexual contact with females of reproductive potential while taking POMALYST and for up to 4 weeks after discontinuing POMALYST, even if they have undergone a successful vasectomy. Males must not donate sperm.
  - Blood Donation: Patients must not donate blood during treatment with POMALYST and for 4 weeks following discontinuation of POMALYST therapy because the blood might be given to a pregnant female patient whose fetus must not be exposed to POMALYST.
- **POMALYST REMS® Program: See Boxed WARNINGS**
  - Prescribers and pharmacies must be certified with the **POMALYST REMS** program by enrolling and complying with the REMS requirements; pharmacies must only dispense to patients who are authorized to receive POMALYST. Patients must sign a Patient-Physician Agreement Form and comply with REMS requirements; female patients of reproductive potential who are not pregnant must comply with the pregnancy testing and contraception requirements and males must comply with contraception requirements.
  - Further information about the **POMALYST REMS** program is available at **www.CelgeneRiskManagement.com** or by telephone at 1-888-423-5436.
- **Venous and Arterial Thromboembolism: See Boxed WARNINGS.** Patients with known risk factors, including prior thrombosis, may be at greater risk, and actions should be taken to try to minimize all modifiable factors (e.g., hyperlipidemia, hypertension, smoking). Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.
- **Increased Mortality with Pembrolizumab:** In clinical trials in patients with multiple myeloma, the addition of pembrolizumab to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.
- **Hematologic Toxicity:** Neutropenia (46%) was the most frequently reported Grade 3/4 adverse reaction in patients taking POMALYST in clinical trials, followed by anemia and thrombocytopenia. Monitor complete blood counts weekly for the first 8 weeks and monthly thereafter. Patients may require dose interruption and/or modification.
- **Hepatotoxicity:** Hepatic failure, including fatal cases, has occurred in patients treated with POMALYST. Elevated levels of alanine aminotransferase and bilirubin have also been observed in patients treated with POMALYST. Monitor liver function tests monthly. Stop POMALYST upon elevation of liver enzymes. After return to baseline values, treatment at a lower dose may be considered.
- **Severe Cutaneous Reactions Including Hypersensitivity Reactions:** Angioedema and severe cutaneous reactions including Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported. DRESS may present with a cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, fever, and/or lymphadenopathy with systemic complications such as hepatitis, nephritis, pneumonitis, myocarditis, and/or pericarditis. Discontinue POMALYST for angioedema, skin exfoliation, bullae, or any other severe cutaneous reactions such as SJS, TEN or DRESS, and do not resume therapy.
- **Dizziness and Confusional State:** In patients taking POMALYST in clinical trials, 14% experienced dizziness (1% Grade 3 or 4) and 7% a confusional state (3% Grade 3 or 4). Instruct patients to avoid situations where dizziness or confusional state may be a problem and not to take other medications that may cause dizziness or confusional state without adequate medical advice.
- **Neuropathy:** In patients taking POMALYST in clinical trials, 18% experienced neuropathy (2% Grade 3 in one trial) and 12% peripheral neuropathy.
- **Second Primary Malignancies:** Cases of acute myelogenous leukemia have been reported in patients receiving POMALYST as an investigational therapy outside of multiple myeloma.
- **Tumor Lysis Syndrome (TLS):** TLS may occur in patients treated with POMALYST. Patients at risk are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.

ADVERSE REACTIONS

The most common adverse reactions for POMALYST (≥30%) included fatigue and asthenia, neutropenia, anemia, constipation, nausea, diarrhea, dyspnea, upper-respiratory tract infections, back pain, and pyrexia.

In the phase III trial, nearly all patients treated with POMALYST + low-dose dex experienced at least one adverse reaction (99%). Adverse reactions (≥15% in the POMALYST + low-dose dex arm and ≥2% higher than control) included neutropenia (51.3%), fatigue and asthenia (46.7%), upper respiratory tract infection (31%), thrombocytopenia (29.7%), pyrexia (26.7%), dyspnea (25.3%), diarrhea (22%), constipation (21.7%), back pain (19.7%), cough (20%), pneumonia (19.3%), bone pain (18%), edema peripheral (17.3%), peripheral neuropathy (17.3%), muscle spasms (15.3%), and nausea (15%). Grade 3 or 4 adverse reactions (≥15% in the POMALYST + low-dose dex arm and ≥1% higher than control) included neutropenia (48.3%), thrombocytopenia (22%), and pneumonia (15.7%).

DRUG INTERACTIONS

Avoid concomitant use of POMALYST with strong inhibitors of CYP1A2. Consider alternative treatments. If a strong CYP1A2 inhibitor must be used, reduce POMALYST dose by 50%.

USE IN SPECIFIC POPULATIONS

- **Pregnancy: See Boxed WARNINGS.** If pregnancy does occur during treatment, immediately discontinue the drug and refer patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. There is a POMALYST pregnancy exposure registry that monitors pregnancy outcomes in females exposed to POMALYST during pregnancy as well as female partners of male patients who are exposed to POMALYST. This registry is also used to understand the root cause for the pregnancy. Report any suspected fetal exposure to POMALYST to the FDA via the MedWatch program at 1-800-FDA-1088 and also to Celgene Corporation at 1-888-423-5436.
- **Lactation:** There is no information regarding the presence of pomalidomide in human milk, the effects of POMALYST on the breastfed child, or the effects of POMALYST on milk production. Pomalidomide was excreted in the milk of lactating rats. Because many drugs are excreted in human milk and because of the potential for adverse reactions in a breastfed child from POMALYST, advise women not to breastfeed during treatment with POMALYST.
- **Pediatric Use:** Safety and effectiveness have not been established in pediatric patients.
- **Geriatric Use:** No dosage adjustment is required for POMALYST based on age. Patients > 65 years of age were more likely than patients ≤65 years of age to experience pneumonia.
- **Renal Impairment:** Reduce POMALYST dose by 25% in patients with severe renal impairment requiring dialysis. Take dose of POMALYST following hemodialysis on hemodialysis days.
- **Hepatic Impairment:** Reduce POMALYST dose by 25% in patients with mild to moderate hepatic impairment and 50% in patients with severe hepatic impairment.
- **Smoking Tobacco:** Advise patients that smoking may reduce the efficacy of POMALYST. Cigarette smoking reduces the AUC of pomalidomide by 32% by CYP1A2 induction.

Please see full Prescribing Information, including Boxed WARNINGS.

About Celgene's Immunomodulatory Drugs

Immunomodulatory Drugs (IMiDs®) are Celgene's proprietary small molecule, orally available compounds for the treatment of some blood cancers. IMiD agents are hypothesized to have multiple mechanisms of action. They have been found to increase activation and proliferation of T cells, and proliferation of the IL-2 protein and activity of CD8+ effector T cells. IMiD agents have also been found to affect the stimulation and expression of natural killer (NK) cells, working within the environment of the cell to stimulate the immune system to attack the cancer cells, as well as attack the cancer cells directly. In addition to immunomodulatory properties, IMiD agents are hypothesized to have tumoricidal and antiangiogenic activity. Celgene's portfolio of IMiD agents have become a foundation of multiple myeloma research, with a growing number of studies exploring these compounds as combination partners across a range of settings of the disease.

About Celgene

Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global biopharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through next-generation solutions in protein homeostasis, immuno-oncology, epigenetics, immunology and neuro-inflammation. For more information, please visit www.celgene.com. Follow Celgene on Social Media: @Celgene, Pinterest, LinkedIn, Facebook and YouTube.

Forward-Looking Statements

This press release contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" and similar expressions. Forward-looking statements are based on management's current plans, estimates, assumptions and projections, and speak only as of the date they are made. We undertake no obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond our control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a number of factors, many of which are discussed in more detail in our Annual Report on Form 10-K and our other reports filed with the Securities and Exchange Commission.

Hyperlinks are provided as a convenience and for informational purposes only. Celgene bears no responsibility for the security or content of external websites.

View source version on businesswire.com: https://www.businesswire.com/news/home/20180601005584/en/

Celgene Corporation
Investors:
+1-908-673-9628
ir@celgene.com
or
Media:
+1-908-673-2275
media@celgene.com

Source: Celgene Corporation