Bristol-Myers Squibb Presents Overall Survival and Safety Data From Pivotal CC-486 Study QUAZAR AML-001

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Maintenance treatment with CC-486 resulted in a significant improvement in overall survival compared with placebo for front-line AML patients

CC-486 had a manageable safety profile

Data presented at the 2019 American Society of Hematology (ASH) Annual Meeting

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) today announced clinical results from the QUAZAR AML-001 study, evaluating investigational agent CC-486 as maintenance therapy in a broad population of patients with front-line, newly diagnosed acute myeloid leukemia (AML) who have achieved remission with intensive induction chemotherapy. Data were presented during a late-breaker oral presentation at the 2019 ASH Annual Meeting in Orlando, Fla.

In the QUAZAR AML-001 study, treatment with CC-486 in the maintenance setting provided patients a statistically significant and clinically meaningful improvement in overall survival (OS) and relapse-free survival (RFS), as compared to those patients treated with placebo.

Patients in the phase 3, international, randomized, double-blind, placebo-controlled study QUAZAR AML-001 were at least 55 years old, had de novo or secondary AML with intermediate or poor-risk cytogenetics and had achieved their first complete remission (CR) or complete remission with incomplete count recovery (CRi) after intensive induction chemotherapy. Patients had received intensive induction chemotherapy, with or without consolidation chemotherapy per investigator's choice and were deemed not candidates for hematopoietic stem-cell transplant prior to study entry.

“Despite a number of recent advances in the treatment of AML, the prognosis remains poor, as most patients will relapse and ultimately die of their disease,” said Dr. Andrew Wei, MBBS, Ph.D., from Alfred Hospital and Monash University, Melbourne, Australia. “The role of maintenance therapy in AML has historically been a contentious issue. Based on the results of the QUAZAR study, we are excited about the clinical development of CC-486 and the potential to establish maintenance therapy as a new treatment paradigm for patients with AML in first remission.”

Following intensive induction chemotherapy, 81% of patients had achieved a CR and 19% of patients had achieved a CRi. Eighty percent of patients had received at least one cycle of consolidation therapy prior to enrollment in the study. Four hundred seventy-two patients were then randomized 1:1 to receive initially either investigational CC-486 300mg (n=238) or placebo (n=234) once daily for 14 days of each 28-day cycle. Patients remained on treatment until unacceptable toxicity or disease progression.

At a median follow-up of 41.2 months, the primary endpoint of OS was significantly improved for patients receiving CC-486 compared to placebo. Median OS from time of randomization was 24.7 months in the CC-486 arm compared to 14.8 months for placebo (p=0.0009; HR 0.69 [95% CI: 0.55, 0.86]). Median RFS, the key secondary endpoint, was 10.2 months for those receiving CC-486 compared to 4.8 months for those receiving placebo (p=0.0001; HR 0.65 [95% CI: 0.52, 0.81]).

Improvements in OS and RFS for those treated with CC-486 compared to placebo were demonstrated, regardless of cytogenetic risk category, prior consolidation or CR/CRi status at enrollment. Health-related quality of life (HRQoL) was preserved from baseline for patients receiving CC-486 compared to placebo during treatment.

The median duration of treatment was 12 cycles (1-80) for CC-486 and 6 cycles with placebo (1-73). The most commonly occurring adverse events (AEs) of all grades with CC-486 and placebo, respectively, were nausea (65% vs. 24%), vomiting (60% vs. 10%) and diarrhea (50% vs. 22%). The most common grade 3-4 AEs for CC-486 and placebo, respectively, were neutropenia (41% vs. 24%), thrombocytopenia (23% vs. 22%) and anemia (14% vs. 13%). Serious AEs were reported in 34% of CC-486 patients and 25% of placebo patients, and were mainly infections, which occurred in 17% and 8% of CC-486 and placebo patients, respectively. There were 13% of CC-486 patients and 4% of placebo patients who discontinued treatment.
due to AEs.

“We are extremely encouraged by the results of the QUAZAR AML-001 study as a part of our continuing commitment to both epigenetic research and myeloid diseases,” said Samit Hirawat, M.D., Chief Medical Officer of Bristol-Myers Squibb. “We now look forward to taking the next steps to bring CC-486 to eligible AML patients in need.”

Based on the results of QUAZAR AML-001, Bristol-Myers Squibb is planning regulatory submissions in the first half of 2020. CC-486 is not approved for any use in any country.

About AML

Acute myeloid leukemia (AML) is the most common type of acute leukemia. AML starts in the bone marrow but moves quickly into the blood. Unlike in normal blood cell development, in AML the rapid build up of abnormal white blood cells in the bone marrow may interfere with the production of normal blood cells, resulting in decreased healthy white blood cells, red blood cells and platelets. AML is a complex, diverse disease associated with multiple genetic mutations and usually gets worse quickly if not treated. There will be an estimated 21,450 new cases of AML in the United States this year, accounting for 1.2% of all cancer cases, with an estimated 10,920 deaths resulting from the disease. There are an estimated 61,048 people living with AML in the United States.

About QUAZAR AML-001

QUAZAR AML-001 is a phase 3, international, randomized, double-blind, placebo-controlled study of CC-486 as AML maintenance therapy in patients who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy (with or without consolidation). The primary endpoint of the study was overall survival. Secondary endpoints included relapse-free survival (RFS), safety and tolerability, healthcare resource utilization and patient-reported outcomes per the FACIT-Fatigue Scale and EQ-5D questionnaire. The study enrolled 472 patients, randomized 1:1 to receive initially either oral CC-486 300mg or placebo once daily for 14 days of a 28-day cycle plus best supportive care. Patients remained on treatment until unacceptable toxicity or disease progression.

About CC-486

CC-486 is an oral hypomethylating agent that incorporates into DNA and RNA allowing for sustained epigenetic regulation due to prolonged exposure. The main mechanism of action is thought to be hypomethylation of DNA, as well as direct cytotoxicity to abnormal hematopoietic cells in the bone marrow. Hypomethylation may restore normal function to genes that are critical for differentiation and proliferation.

Bristol-Myers Squibb: Advancing Cancer Research

At Bristol-Myers Squibb, patients are at the center of everything we do. The goal of our cancer research is to increase quality, long-term survival and make cure a possibility. We harness our deep scientific experience, cutting-edge technologies and discovery platforms to discover, develop and deliver novel treatments for patients.

Building upon our transformative work and legacy in hematology and Immuno-Oncology that has changed survival expectations for many cancers, our researchers are advancing a deep and diverse pipeline across multiple modalities. In the field of immune cell therapy, this includes registrational chimeric antigen receptor (CAR) T-cell agents for numerous diseases, and a growing early-stage pipeline that expands cell and gene therapy targets, and technologies. We are developing cancer treatments directed at key biological pathways using our protein homeostasis platform, a research capability that has been the basis of our approved therapies for multiple myeloma and several promising compounds in early to mid-stage development. Our scientists are targeting different immune system pathways to address interactions between tumors, the microenvironment and the immune system to further expand upon the progress we have made and help more patients respond to treatment. Combining these approaches is key to delivering new options for the treatment of cancer and addressing the growing issue of resistance to immunotherapy. We source innovation internally, and in collaboration with academia, government, advocacy groups and biotechnology companies, to help make the promise of transformational medicines a reality for patients.

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, Facebook and Instagram.

Cautionary Statement Regarding Forward-Looking Statements

This press release contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 regarding, among other things, the research, development and commercialization of pharmaceutical products. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements are based on historical performance and current expectations and projections about our future financial results, goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be beyond our control and could cause our future financial results, goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. These risks, assumptions, uncertainties and other factors include, among others, that results from future studies involving CC-486 will be consistent with the results to date, that CC-486 may not receive regulatory approval for the indication described in this release in the currently anticipated timeline or at all and, if approved, whether such product candidate for such indication described in this release will be commercially successful. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many risks and uncertainties that affect Bristol-Myers Squibb's business and market, particularly those identified in the cautionary statement and risk factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2018, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on