KRAZATI (adagrasib) in Combination with Cetuximab Demonstrates Clinically Meaningful Activity as a Targeted Treatment Option for Patients with Previously Treated KRAS G12C-Mutated Locally Advanced or Metastatic Colorectal Cancer (CRC)

2024年 4月 8日

Late-breaking data to be featured in an oral presentation at the American Association for Cancer Research (AACR) annual meeting on Monday, April 8 and highlighted as part of the official meeting press program

PRINCETON, N.J.--(BUSINESS WIRE)-- Bristol Myers Squibb (NYSE: BMY) today announced data from the cohorts of the Phase 1/ 2 KRYSTAL-1 study evaluating KRAZATI® (adagrasib) in combination with cetuximab for the treatment of patients with previously treated KRAS^{G12C}-mutated locally advanced or metastatic colorectal cancer (CRC).

These late breaking data (abstract #CT013) will be featured in an oral presentation at the 2024 American Association for Cancer Research (AACR) annual meeting on Monday, April 8 at 11:10 a.m. Pacific Time and will be highlighted as part of the meeting's official press program. The data will also be published simultaneously in *Cancer Discovery* .

With a median follow up of 11.9 months in 94 patients, KRAZATI plus cetuximab demonstrated an objective response rate, the primary endpoint, of 34%, median progression-free survival of 6.9 months (95% CI, 5.7-7.4), and median overall survival of 15.9 months (95% CI, 11.8-18.8) in pre-treated patients with KRAS^{G12C}-mutated locally advanced or metastatic CRC. The median duration of response was 5.8 months. Disease control was observed in 85% of patients. The safety profile for KRAZATI plus cetuximab was manageable and consistent with previous reports, and with the known safety profile of each drug individually.

KRAS^{G12C} mutations act as oncogenic drivers and occur in approximately 3-4% of colorectal cancers. In previous studies, treatment with cetuximab as a single agent did not offer a clinical benefit in patients with KRAS-mutated colorectal cancer.

"Patients with KRAS ^{G12C}-mutated colorectal cancer have historically faced poor prognoses and remain in need of additional treatment options," said Scott Kopetz, M.D., Ph.D, FACP, associate vice president for translational research, and Professor, Department of Gastrointestinal Medical Oncology at The University of Texas MD Anderson Cancer Center. "Although KRAS had previously been considered 'undruggable,' these data from KRYSTAL-1 reinforce the potential benefit of adagrasib for these specific patients."

"While there has been progress in the treatment of colorectal cancer, there remain groups of patients, such as those with KRAS-mutated cancers, who continue to need new, targeted treatment options," said Anne Kerber, senior vice president, head of late clinical development, Hematology, Oncology, Cell Therapy (HOCT) at Bristol Myers Squibb. "These data highlight the significance of testing and identification of KRAS ^{G12C} mutations in patients with CRC."

The company announced in February 2024 that the FDA had accepted a supplemental new drug application for KRAZATI in combination with cetuximab as a targeted treatment option for patients with previously treated KRAS^{G12C}-mutated locally advanced or metastatic CRC for priority review and assigned a Prescription Drug User Fee Act (PDUFA) goal date of June 21, 2024.

Bristol Myers Squibb thanks the patients and investigators involved in the KRYSTAL-1 clinical trial.

This study was funded by Mirati Therapeutics, Inc., a Bristol Myers Squibb company.

ABOUT KRAZATI® (adagrasib)

KRAZATI (adagrasib) is highly selective and potent oral small-molecule inhibitor of KRAS^{G12C} that is optimized to sustain target inhibition, an attribute that could be important to treat KRAS^{G12C}-mutated cancers, as the KRAS^{G12C} protein regenerates every 24-48 hours. KRAS^{G12C} mutations act as oncogenic drivers and occur in approximately 14% of NSCLC (adenocarcinoma), 3-4% of colorectal cancers, and 1-2% of several other cancers.

In 2022, KRAZATI was granted accelerated approval for treatment of adult patients with KRAS^{G12C}-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy. This indication is approved under accelerated approval based on objective response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of a clinical benefit in a confirmatory trial(s). In 2024, the European Commission (EC) granted conditional marketing authorization for KRAZATI as a targeted treatment option for adult patients with KRAS^{G12C}-mutated advanced NSCLC and disease progression after at least one prior systemic therapy.

KRAZATI continues to be evaluated as monotherapy and in combination with other anti-cancer therapies in patients with advanced KRAS^{G12C}-mutated solid tumors, including NSCLC and colorectal cancer.

In 2022, the FDA granted breakthrough therapy designation for KRAZATI in combination with cetuximab in patients with KRAS^{G12C}-mutated

advanced colorectal cancer (CRC) whose cancer has progressed following prior treatment with chemotherapy and an anti-VEGF therapy.

For Prescribing Information, visit https://mirati.com/KRAZATI_USPI/.

ABOUT KRYSTAL-1

KRYSTAL-1 is an open-label, multicenter, multiple expansion cohort Phase 1/2 trial to determine the safety and efficacy of KRAZATI in patients with advanced solid tumors that harbor a $KRAS^{G12C}$ mutation. The primary endpoint for the Phase 2 cohort of the KRYSTAL-1 study was objective response rate. Secondary endpoints included duration of response, progression-free survival, overall survival and safety.

INDICATION

KRAZATI is indicated for the treatment of adult patients with $KRAS^{G12C}$-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy.

This indication is approved under accelerated approval based on objective response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of a clinical benefit in a confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

GASTROINTESTINAL ADVERSE REACTIONS

- In the pooled safety population, serious gastrointestinal adverse reactions observed were gastrointestinal obstruction in 1.6%, including 1.4% grade 3 or 4, gastrointestinal bleeding in 0.5% of patients, including 0.5% grade 3, and colitis in 0.3%, including 0.3% grade 3. In addition, nausea, diarrhea, or vomiting occurred in 89% of 366 patients, including 9% grade 3. Nausea, diarrhea, or vomiting led to dosage interruption or dose reduction in 29% of patients and permanent discontinuation of KRAZATI in 0.3%
- Monitor and manage patients using supportive care, including antidiarrheals, antiemetics, or fluid replacement, as indicated. Withhold, reduce the dose, or permanently discontinue KRAZATI based on severity

QTC INTERVAL PROLONGATION

- KRAZATI can cause QTc interval prolongation, which can increase the risk for ventricular tachyarrhythmias (e.g., torsades de pointes) or sudden death
- In the pooled safety population, 6% of 366 patients with at least one post-baseline electrocardiogram (ECG) assessment had an average QTc ≥501 ms, and 11% of patients had an increase from baseline of QTc >60 msec. KRAZATI causes concentration-dependent increases in the QTc interval
- Avoid concomitant use of KRAZATI with other products with a known potential to prolong the QTc interval. Avoid use of KRAZATI in patients with congenital long QT syndrome and in patients with concurrent QTc prolongation
- Monitor ECGs and electrolytes prior to starting KRAZATI, during concomitant use, and as clinically indicated in patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities, and in patients who are taking medications that are known to prolong the QT interval. Withhold, reduce the dose, or permanently discontinue KRAZATI, depending on severity

HEPATOTOXICITY

- KRAZATI can cause hepatotoxicity
- In the pooled safety population, hepatotoxicity occurred in 37%, and 7% were grade 3 or 4. A total of 32% of patients who received KRAZATI had increased alanine aminotransferase (ALT)/increased aspartate aminotransferase (AST); 5% were grade 3 and 0.5% were grade 4. Increased ALT/AST leading to dose interruption or reduction occurred in 11% of patients. KRAZATI was discontinued due to increased ALT/AST in 0.5% of patients
- Monitor liver laboratory tests (AST, ALT, alkaline phosphatase, and total bilirubin) prior to the start of KRAZATI, and monthly for 3 months or as clinically indicated, with more frequent testing in patients who develop transaminase elevations. Reduce the dose, withhold, or permanently discontinue KRAZATI based on severity

INTERSTITIAL LUNG DISEASE /PNEUMONITIS

- KRAZATI can cause interstitial lung disease (ILD)/pneumonitis, which can be fatal. In the pooled safety population, ILD/pneumonitis occurred in 4.1% of patients, 1.4% were grade 3 or 4, and 1 case was fatal. The median time to first onset for ILD/pneumonitis was 12 weeks (range: 5 to 31 weeks). KRAZATI was discontinued due to ILD/pneumonitis in 0.8% of patients
- Monitor patients for new or worsening respiratory symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever). Withhold KRAZATI in patients with suspected ILD/pneumonitis and permanently discontinue KRAZATI if no other potential causes of ILD/pneumonitis are identified

ADVERSE REACTIONS

- The most common adverse reactions (≥25%) are nausea, diarrhea, vomiting, fatigue, musculoskeletal pain, hepatotoxicity, renal impairment, edema, dyspnea, decreased appetite

FEMALES AND MALES OF REPRODUCTIVE POTENTIAL

- Infertility: Based on findings from animal studies, KRAZATI may impair fertility in females and males of reproductive potential

Please see U.S. Full Prescribing Information for KRAZATI at https://mirati.com/KRAZATI_USPI/.

About Colorectal Cancer

Colorectal cancer (CRC) is cancer that develops in the colon or the rectum, which are part of the body's digestive or gastrointestinal system. CRC is the third most commonly diagnosed cancer in the world. In 2020, it is estimated that there were approximately 1,931,000 new cases of the disease; it is the second leading cause of cancer-related deaths among men and women combined.

Bristol Myers Squibb: Creating a Better Future for People with Cancer

Bristol Myers Squibb is inspired by a single vision — transforming patients' lives through science. The goal of the company's cancer research is to deliver medicines that offer each patient a better, healthier life and to make cure a possibility. Building on a legacy across a broad range of cancers that have changed survival expectations for many, Bristol Myers Squibb researchers are exploring new frontiers in personalized medicine and, through innovative digital platforms, are turning data into insights that sharpen their focus. Deep understanding of causal human biology, cutting-edge capabilities and differentiated research platforms uniquely position the company to approach cancer from every angle.

Cancer can have a relentless grasp on many parts of a patient's life, and Bristol Myers Squibb is committed to taking actions to address all aspects of care, from diagnosis to survivorship. As a leader in cancer care, Bristol Myers Squibb is working to empower all people with cancer to have a better future.

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 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 future study results may not be consistent with the results to date, and that KRAZATI (adagrasib) in combination with cetuximab may not achieve its primary study endpoint or KRAZATI (adagrasib) *in combination with cetuximab may not achieve its primary study endpoint or receive regulatory approval for the additional indication described in this release in the currently anticipated timeline or at all, any marketing approvals, if granted, may have significant limitations on their use, and, if approved, whether such combination treatment for such additional 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, 2023, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. The forward-looking statements included in this document are made only as of the date of this document and except as otherwise required by applicable law, Bristol Myers Squibb undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.*

corporatefinancial-news

Bristol Myers Squibb

Media Inquiries:

media@bms.com

Investors:

investor.relations@bms.com

Source: Bristol Myers Squibb

Multimedia Files:

Download:
Download original jpg 99 KB 1497 x 206
Download thumbnail png 5 KB 200 x 28
Download lowres png 15 KB 480 x 66
Download square png 8 KB 250 x 250