Source: *Janssen EMEA*

February 24, 2023 07:04 ET

Janssen Receives Positive CHMP Opinion for AKEEGA® (Niraparib and Abiraterone Acetate Dual Action Tablet) Plus Prednisone or Prednisolone for the Treatment of Adult Patients with BRCA1/2 Gene-Mutated Metastatic Castration Resistant Prostate Cancer

If approved, niraparib in combination with abiraterone acetate (AA), will be the first dual action tablet (DAT) available in the European Union for first-line treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) with BRCA1/2 mutations, when given with prednisone (P) or prednisolone. [1]

The positive CHMP opinion is based on results from the Phase 3 MAGNITUDE study where the addition of niraparib to AA plus P significantly improved radiographic progression-free survival (rPFS) compared to standard of care in untreated mCRPC patients with BRCA1/2 mutations.[2]

BEERSE, Belgium, Feb. 24, 2023 (GLOBE NEWSWIRE) -- The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended marketing authorisation for AKEEGA® (niraparib and AA), in the form of a DAT, given with P or prednisolone, for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) and BRCA1/2 mutations (germline and/or somatic) in whom chemotherapy is not clinically indicated.[1]

Niraparib is a highly selective poly adenosine diphosphate-ribose polymerase (PARP) inhibitor.[2] Together with AA, a cytochrome P450 17α-hydroxylase (CYP17) inhibitor,[3] the combination DAT regimen targets two oncogenic drivers (mutations responsible for both the development and maintenance of prostate cancer) in patients with mCRPC, namely androgen receptor axis (AR-axis) and BRCA1/2 gene mutations.[4,5]

Prostate cancer is the most common cancer in men in Europe.[6] Despite treatment advances, for those whose cancer has progressed to mCRPC, the impact can be devastating with an average overall survival ranging from 13-36 months.[7,8,9] Patients with mCRPC and BRCA gene mutations are more likely to have aggressive disease, poor outcomes and a shorter survival time.[10,11,12,13] BRCA1/2 gene mutations have been identified in approximately 10-15 percent of patients with mCRPC.[14,15]

“Metastatic castration-resistant prostate cancer remains a lethal disease, with high unmet needs in terms of treatment options, particularly for patients with BRCA1/2 gene mutations,” said Elena Castro*, Consultant Oncologist, Hospital Universitario 12 de Octubre, Instituto de Investigación Sanitaria Hospital 12 de Octubre, Madrid, Spain. “We’ve seen that in these patients, niraparib combined with abiraterone acetate and prednisone significantly reduces the risk of disease progression or death compared to AAP. This niraparib-based regimen is a welcomed targeted treatment option and, if approved, has the potential to impact the standard of care for men with mCRPC BRCA who are treated with first-line therapy.”

“In recent years, we’ve focused on precision medicine in prostate cancer because we know patients with gene mutations, such as BRCA1/2, face a worse prognosis than those without,” said Martin Vogel, EMEA Therapeutic Area Lead Oncology, Janssen-Cilag GmbH. “The positive CHMP opinion reinforces the benefit of this niraparib combination and marks an important milestone in addressing BRCA1/2 mutations as we continue to drive progress towards changing the outlook for patients with mCRPC.”

The positive CHMP opinion is based on results of the randomised, double-blind, placebo controlled, Phase 3 MAGNITUDE study (NCT03748641) which assessed whether the addition of niraparib to AAP improved outcomes in those with first-line mCRPC, with or without alterations in homologous recombination repair (HRR) associated genes.[1,16] Patients with HRR gene alterations were randomised to receive niraparib 200 mg once daily plus AAP [n=212], or placebo and AAP [n=211]. In MAGNITUDE, a total of 423 patients with HRR gene alterations were enrolled, 225 (53.2 percent) of whom had BRCA mutations.[14] This is the largest cohort of BRCA1/2-positive patients with mCRPC.[16] First results, presented at the American Society of Clinical Oncology – Genitourinary Cancers Symposium (ASCO GU) 2022 Annual Meeting,[2] showed niraparib plus AAP significantly improved rPFS (as analysed by blinded independent central review) in all HRR-positive patients. This improvement was most pronounced in patients with BRCA1/2 gene mutations, where a statistically significant 47 percent risk reduction was observed for rPFS (HR 0.53; p=0.001).[2] Updated results from the second interim analysis (IA2) of MAGNITUDE were presented at the recent ASCO GU 2023 Annual Meeting.[16] In the IA2, at 24.8 months of median follow-up in the BRCA subgroup, rPFS by central review demonstrated a consistent and clinically meaningful treatment effect favouring niraparib plus AAP, with a median rPFS of 19.5 months compared with 10.9 months for placebo plus AAP. Additionally, in the BRCA subgroup, there was a trend towards improved overall survival (OS) with niraparib plus AAP, strong improvement in time to symptomatic progression (TSP) and continued consistent improvement of time-to-initiation of cytotoxic chemotherapy (TCC).[16]

The observed safety profile of the combination of niraparib and AAP was consistent with the known safety profile of each agent.[2] Of the patients with HRR gene alterations, 67 percent experienced Grade 3/4 adverse events (AEs) in the combination arm versus 46.4 percent in the control arm. Discontinuation rates due to AEs for the combination arm and control arm were 10.8 percent and 4.7 percent, respectively. The combination of niraparib and AAP also maintained overall quality of life in comparison with placebo and AAP as measured on the Functional Assessment of Cancer Therapy–Prostate (FACT-P) scale.[2]

“Prostate cancer is a heterogeneous disease made up of many biologically distinct subpopulations. The data from MAGNITUDE supports the significant value of biomarker testing to identify the subgroup of patients most likely to derive a clinical benefit from a targeted treatment, and overcome the poor prognosis of mCRPC with BRCA mutations,” said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Janssen Research & Development, LLC. “At Janssen, we are dedicated to continued innovation in prostate cancer and now look forward to working with health authorities to bring this niraparib-based treatment option to patients as soon as possible.”

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About Niraparib

Niraparib is an orally administered, highly selective poly (ADP ribose) polymerase (PARP) inhibitor, that is currently being studied by Janssen for the treatment of patients with prostate cancer.[4] Additional ongoing studies include the Phase 3 AMPLITUDE study (NCT04497844) evaluating the combination of niraparib and AAP in a HRR biomarker-selected patient population with metastatic hormone-sensitive prostate cancer (mHSPC).[17]

In April 2016, Janssen Biotech, Inc. entered into a worldwide (except Japan) collaboration and license agreement with TESARO, Inc. (acquired by GSK in 2019), for exclusive rights to niraparib in prostate cancer.[18]

In the EU, niraparib is indicated as monotherapy for the maintenance treatment of adult patients with advanced epithelial high-grade ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response following completion of first-line platinum-based chemotherapy; and as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high grade serious epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy.[5] Niraparib is currently marketed by GSK as ZEJULA®.[5]

About abiraterone acetate

Abiraterone acetate is an orally administered androgen biosynthesis inhibitor. In the European Union, abiraterone acetate is indicated with prednisone or prednisolone for the treatment of newly diagnosed high risk mHSPC in adult men in combination with androgen deprivation therapy (ADT); the treatment of mCRPC in adult men who are asymptomatic or mildly symptomatic after failure of ADT in whom chemotherapy is not yet clinically indicated; and the treatment of mCRPC in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen.[3]

Abiraterone acetate is currently marketed by Janssen-Cilag International NV as ZYTIGA®.[3]

About Metastatic Castration-Resistant Prostate Cancer
Metastatic castration-resistant prostate cancer (mCRPC) characterises cancer that no longer responds to ADT and has spread to other parts of the body.[19] The most common metastatic sites are bones, followed by the lymph nodes, liver and lungs.[20] Prostate cancer is the most common cancer in men in Europe.[6] In 2020, more than one million men around the world were diagnosed with prostate cancer.[21] Patients with mCRPC and HRR gene alterations, of which BRCA mutations are the most common, are more likely to have aggressive disease, poor outcomes and a shorter survival time.[10,11,12,13]

About MAGNITUDE
MAGNITUDE (NCT03748641) is a Phase 3 randomised, double-blind, placebo-controlled, multicentre clinical study evaluating the safety and efficacy of the combination of niraparib and AAP for patients with mCRPC, with or without certain HRR gene alterations and who have not received prior therapy for mCRPC except for standard of care, next-generation androgen receptor inhibitors and up to 4 months of AAP.[4] The study includes patients with (HRR biomarker [BM] positive; ATM, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, HDAC2, PALB2) and without specified gene alterations (HRR BM negative), who were randomised 1:1 to receive niraparib 200 mg once daily plus AAP or placebo plus AAP.[4] Additionally in an open-label cohort of HRR-positive patients, all patients received the DAT formulation of niraparib and abiraterone acetate plus prednisone. The primary endpoint of the MAGNITUDE trial is rPFS assessed by blinded independent central review. Secondary endpoints include time-to-initiation of cytotoxic chemotherapy, time to symptomatic progression and overall survival.[4]

About the Janssen Pharmaceutical Companies of Johnson & Johnson
At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular, Metabolism & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

Learn more at www.janssen.com/emea/. Follow us at www.twitter.com/JanssenEMEA for our latest news. Janssen Pharmaceutica NV, Janssen-Cilag GmBH and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

*Dr. Castro has served as a consultant to Janssen; she has not been paid for any media work.

Cautions Concerning Forward-Looking Statements
This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of niraparib. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialise, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen-Cilag GmBH, Janssen Research & Development, LLC, any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behaviour and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 1, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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CP-373718
February 2023