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World Conference on Lung Cancer (WCLC)	
Lung Cancer	
RYBREVANT® (amivantamab-vmjw)	
Oral Session	
Abstract #1318	Lazertinib vs Osimertinib in 1L *EGFR*-Mutant Advanced NSCLC: A Randomized, Double-Blind, Exploratory Analysis From **MARIPOSA**
Abstract #3305	Subcutaneous vs Intravenous Amivantamab: Patient Satisfaction and Resource Utilization Results from the **PALOMA-3** Study
Abstract #1146	Amivantamab Plus Lazertinib vs Osimertinib in First-Line *EGFR*-Mutant Advanced NSCLC: Longer Follow-Up of the **MARIPOSA** Study
Mini Oral Session	
Abstract #2429	Amivantamab Plus Lazertinib vs Osimertinib in First-Line, *EGFR*-Mutant Advanced NSCLC: Patient-Relevant Outcomes From **MARIPOSA**
Abstract #1785	Preventing Infusion-Related Reactions With Intravenous Amivantamab: Primary Results From **SKIPPirr**, a Phase 2 Study
Abstract #1779	**PAPILLON**: *TP53* Co-Mutations, Sites of Insertion, and ctDNA Clearance Among Patients With *EGFR* Ex20ins-Mutated Advanced NSCLC
Poster Session	
Abstract #1773	Enhanced vs Standard Dermatologic Management With Amivantamab-Lazertinib in Advanced NSCLC: Phase 2 **COCOON** Study (TiP)
Abstract #1799	Development of a Patient-Friendly Lung Cancer Lexicon

European Society for Medical Oncology (ESMO)	
Lung Cancer	
RYBREVANT® (amivantamab-vmjw)	
Proffered Paper Session	
Abstract #LBA54	Overall Survival Among Patients Receiving Amivantamab Plus Chemotherapy vs Chemotherapy in *EGFR*-Mutated, Advanced Non-

	Small Cell Lung Cancer After Disease Progression on Osimertinib **(MARIPOSA-2)**
Mini Oral Session	
Abstract #LBA55	Mechanisms of Acquired Resistance to First-Line Amivantamab Plus Lazertinib Versus Osimertinib in Patients With *EGFR*-Mutant Advanced Non-Small Cell Lung Cancer: An Analysis From the Phase 3 **MARIPOSA** Study
Poster Session	
Abstract #5546	Preventing Infusion-Related Reactions With Intravenous Amivantamab: Updated Results From **SKIPPirr**, a Phase 2 Study
Colorectal Cancer	
RYBREVANT® (amivantamab-vmjw)	
Oral Session	
Abstract #2915	Amivantamab Plus FOLFOX or FOLFIRI in Metastatic Colorectal Cancer: Results From **OrigAMI-1**, an Open-Label, Phase 1b/2 Study
Abstract #1202P	A Deep Learning Approach Using Routine Pathology Images to Guide Precision Medicine in Metastatic CRC
Bladder Cancer	
TAR-200	
Proffered Paper Session	
Abstract #LBA84	TAR-200 Plus Cetrelimab or Cetrelimab Alone as Neoadjuvant Therapy in Patients With Muscle-Invasive Bladder Cancer Who Are Ineligible for or Refuse Neoadjuvant Platinum-Based Chemotherapy: Interim Analysis of **SunRISe-4**
Mini Oral Session	
Abstract #LBA85	TAR-200 in Combination With Cetrelimab (CET), TAR-200 Alone, or CET Alone in Patients With Bacillus Calmette–Guérin (BCG)-Unresponsive High-Risk Non–Muscle-Invasive Bladder Cancer (HR NMIBC): Results From **SunRISe-1**
Poster Session	
Abstract #1980P	Association of *PD-L1* Expression With Clinical Response to TAR-200 in the Phase 2b **SunRISe-1** Trial
TAR-210	
Poster Session	
Abstract #1973P	Urine-Based Molecular Testing Identifies *FGFR* Alteration-Positive Patients for Treatment With TAR-210
Prostate Cancer	
Abiraterone	
Oral Session	

Abstract #2786	Phenotypic and Genomic Characterization of De Novo Metastatic Prostate Cancer: An Ancillary Study of the **PEACE-1** Phase 3 Trial
AKEEGA®	
Poster Session	
Abstract #6604	Clinical Validity of FoundationOne® Liquid CDx Assay to Identify *BRCA*-mutated (*BRCA*+) Patients in the **MAGNITUDE** Study
Abstract #6631	Impact of *FANCA, ATM, CDK12* Alterations on Survival in Metastatic Castration-Resistant Prostate Cancer (mCRPC)
Early Assets	
Poster Session	
Abstract #1214	A Phase 1, First-in-Human, Open-Label, Multicenter, Trial-in-Progress of the Safety, Tolerability, and Preliminary Efficacy of JNJ-87189401 (PSMA-CD28 Bispecific Antibody) Combined With JNJ-78278343 (KLK2-CD3 Bispecific Antibody) for Advanced Prostate Cancer

About RYBREVANT®

RYBREVANT® (amivantamab-vmjw), a fully-human bispecific antibody targeting *EGFR* and MET with immune cell-directing activity, is approved in the **U.S.**, **Europe**, and in other markets around the world as monotherapy for the treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.[i] It is also approved in the U.S. in combination with chemotherapy (carboplatin and pemetrexed) for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations, as detected by an FDA-approved test. Additional supplemental reviews in multiple regions around the world for additional indications are ongoing.

For more information, visit: https://www.RYBREVANT.com.

About LAZCLUZE™

LAZCLUZE™ (lazertinib) is an oral, third-generation, brain-penetrant *EGFR* tyrosine kinase inhibitor (TKI) that targets both the T790M mutation and activating *EGFR* mutations while sparing wild type-*EGFR*. An analysis of the efficacy and safety of LAZCLUZE from the Phase 3 study was published in The Journal of Clinical Oncology in 2023. In 2018, Janssen Biotech, Inc., entered into a license and collaboration agreement with Yuhan Corporation for the development of LAZCLUZE.

About AKEEGA®

AKEEGA® is a combination, in the form of a dual-action tablet (DAT), of niraparib, a highly selective poly (ADP-ribose) polymerase (PARP) inhibitor, and abiraterone acetate, a CYP17 inhibitor. AKEEGA® together with prednisone or prednisolone was approved in April 2023 by the European Medicines Agency, and in August 2023 by the US FDA, for the treatment of patients with BRCA-mutated metastatic castration-resistant prostate cancer (mCRPC). Additional marketing authorization applications are under review across a number of countries globally.

Additional ongoing studies include the Phase 3 AMPLITUDE study, evaluating AKEEGA™ with prednisone or prednisolone in a biomarker-selected patient population with metastatic castration-sensitive prostate cancer (mCSPC).

About TAR-200

TAR-200 is an investigational targeted releasing system enabling controlled release of gemcitabine into the bladder, providing sustained local drug exposure over several weeks. The safety and efficacy of TAR-200, as monotherapy or in combination with cetrelimab, are being evaluated in Phase 2 and Phase 3 studies in patients with muscle-invasive bladder cancer in SunRISe-2 and SunRISe-4and with non-muscle invasive bladder cancer in SunRISe-1, SunRISe-3, and SunRISe-5.

About Cetrelimab

Administered intravenously, cetrelimab is an investigational programmed cell death receptor-1 (PD-1) monoclonal antibody being studied for the treatment of bladder cancer, prostate cancer, melanoma, and multiple myeloma as part of a combination treatment. Cetrelimab is also being evaluated in multiple other combination regimens across the Janssen Oncology portfolio.

About TAR-210

TAR-210 is an investigational targeted releasing system designed to provide controlled release of erdafitinib into the bladder. The safety and efficacy of TAR-210 is being evaluated in a Phase 1 study in patients with MIBC and NMIBC (NCT05316155).

IMPORTANT SAFETY INFORMATION FOR RYBREVANT® & LAZCLUZE™
WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

RYBREVANT® can cause infusion-related reactions (IRR); signs and symptoms of IRR include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting. The median time to IRR onset is approximately 1 hour.

RYBREVANT® with LAZCLUZE™

RYBREVANT® in combination with LAZCLUZE™ can cause infusion-related reactions. In MARIPOSA (n=421), IRRs occurred in 63% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 5% and Grade 4 in 1% of patients. The incidence of infusion modifications due to IRR was 54% of patients, and IRRs leading to dose reduction of RYBREVANT® occurred in 0.7% of patients. Infusion-related reactions leading to permanent discontinuation of RYBREVANT® occurred in 4.5% of patients receiving RYBREVANT® in combination with LAZCLUZE™.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON (n=151), infusion-related reactions occurred in 42% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (1.3%) adverse reactions. The incidence of infusion modifications due to IRR was 40%, and 0.7% of patients permanently discontinued RYBREVANT®.

RYBREVANT® as a Single Agent

In CHRYSALIS (n=129), IRR occurred in 66% of patients treated with RYBREVANT®. Among patients receiving treatment on Week 1 Day 1, 65% experienced an IRR, while the incidence of IRR was 3.4% with the Day 2 infusion, 0.4% with the Week 2 infusion, and cumulatively 1.1% with subsequent infusions. Of the reported IRRs, 97% were Grade 1-2, 2.2% were Grade 3, and 0.4% were Grade 4. The median time to onset was 1 hour (range 0.1 to 18 hours) after start of infusion. The incidence of infusion modifications due to IRR was 62% and 1.3% of patients permanently discontinued RYBREVANT® due to IRR.

Premedicate with antihistamines, antipyretics, and glucocorticoids and infuse RYBREVANT® as recommended. Administer RYBREVANT® via a peripheral line on Week 1 and Week 2 to reduce the risk of infusion-related reactions. Monitor patients for signs and symptoms of infusion reactions during RYBREVANT® infusion in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity.

Interstitial Lung Disease/Pneumonitis

RYBREVANT® can cause severe and fatal interstitial lung disease (ILD)/pneumonitis.

RYBREVANT® with LAZCLUZE™

In MARIPOSA, ILD/pneumonitis occurred in 3.1% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 1.0% and Grade 4 in 0.2% of patients. There was one fatal case (0.2)% of ILD/pneumonitis and 2.9% of patients permanently discontinued RYBREVANT® and LAZCLUZE™ due to ILD/pneumonitis.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON, Grade 3 ILD/pneumonitis occurred in 2.6% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, all patients required permanent discontinuation.

RYBREVANT® as a Single Agent

In CHRYSALIS, ILD/pneumonitis occurred in 3.3% of patients treated with RYBREVANT®, with 0.7% of patients experiencing Grade 3 ILD/pneumonitis. Three patients (1%) discontinued RYBREVANT® due to ILD/pneumonitis.

Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). For patients receiving RYBREVANT® in combination with LAZCLUZE™, immediately withhold both drugs in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed. For patients receiving RYBREVANT® as a single agent or in combination with carboplatin and pemetrexed, immediately withhold RYBREVANT® in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Venous Thromboembolic (VTE) Events with Concomitant Use of RYBREVANT® and LAZCLUZE™

RYBREVANT® in combination with LAZCLUZE™ can cause serious and fatal venous thromboembolic (VTEs) events, including deep vein thrombosis and pulmonary embolism. The majority of these events occurred during the first four months of therapy.

In MARIPOSA, VTEs occurred in 36% of patients receiving RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 10% and Grade 4 in 0.5% of patients. On-study VTEs occurred in 1.2% of patients (n=5) while receiving anticoagulation therapy. There were two fatal cases of VTE (0.5%), 9% of patients had VTE leading to dose interruptions of RYBREVANT®, and 7% of patients had VTE leading to dose interruptions of LAZCLUZE™; 1% of patients had VTE leading to dose reductions of RYBREVANT®, and 0.5% of patients had VTE leading to dose reductions of LAZCLUZE™; 3.1% of patients had VTE leading to permanent discontinuation of RYBREVANT® and 1.9% of patients had VTE leading to permanent discontinuation of LAZCLUZE™. The median time to onset of VTEs was 84 days (range: 6 to 777).

Administer prophylactic anticoagulation for the first four months of treatment. The use of Vitamin K antagonists is not recommended. Monitor for signs and symptoms of VTE events and treat as medically appropriate.

Withhold RYBREVANT® and LAZCLUZE™ based on severity. Once anticoagulant treatment has been initiated, resume RYBREVANT® and LAZCLUZE™ at the same dose level at the discretion of the healthcare provider. In the event of VTE recurrence despite therapeutic anticoagulation, permanently discontinue RYBREVANT® and continue treatment with LAZCLUZE™ at the same dose level at the discretion of the healthcare provider.

Dermatologic Adverse Reactions

RYBREVANT® can cause severe rash including toxic epidermal necrolysis (TEN), dermatitis acneiform, pruritus, and dry skin.

RYBREVANT® with LAZCLUZE™

In MARIPOSA, rash occurred in 86% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 26% of patients. The median time to onset of rash was 14 days (range: 1 to 556 days). Rash leading to dose interruptions occurred in 37% of patients for RYBREVANT® and 30% for LAZCLUZE™, rash leading to dose reductions occurred in 23% of patients for RYBREVANT® and 19% for LAZCLUZE™, and rash leading to permanent discontinuation occurred in 5% of patients for RYBREVANT® and 1.7% for LAZCLUZE™.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON, rash occurred in 89% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (19%) adverse reactions. Rash leading to dose reductions occurred in 19% of patients, and 2% permanently discontinued RYBREVANT® and 1.3% discontinued pemetrexed.

RYBREVANT® as a Single Agent

In CHRYSALIS, rash occurred in 74% of patients treated with RYBREVANT® as a single agent, including Grade 3 rash in 3.3% of patients. The median time to onset of rash was 14 days (range: 1 to 276 days). Rash leading to dose reduction occurred in 5% of patients, and RYBREVANT® was permanently discontinued due to rash in 0.7% of patients.

Toxic epidermal necrolysis occurred in one patient (0.3%) treated with RYBREVANT® as a single agent.

Instruct patients to limit sun exposure during and for 2 months after treatment with RYBREVANT®. Advise patients to wear protective clothing and use broad-spectrum UVA/UVB sunscreen. Alcohol-free (e.g., isopropanol-free, ethanol-free) emollient cream is recommended for dry skin.

When initiating RYBREVANT® treatment with or without LAZCLUZE™, administer alcohol-free emollient cream to reduce the risk of dermatologic adverse reactions. Consider prophylactic measures (e.g. use of oral antibiotics) to reduce the risk of dermatologic reactions. If skin reactions develop, start topical corticosteroids and topical and/or oral antibiotics. For Grade 3 reactions, add oral steroids and consider dermatologic consultation. Promptly refer patients presenting with severe rash, atypical appearance or distribution, or lack of improvement within 2 weeks to a dermatologist. For patients receiving RYBREVANT® in combination with

LAZCLUZE™, withhold, dose reduce or permanently discontinue both drugs based on severity. For patients receiving RYBREVANT® as a single agent or in combination with carboplatin and pemetrexed, withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Ocular Toxicity

RYBREVANT® can cause ocular toxicity including keratitis, blepharitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, eye pruritus, and uveitis.

RYBREVANT® with LAZCLUZE™

In MARIPOSA, ocular toxicity occurred in 16% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 or 4 ocular toxicity in 0.7% of patients. Withhold, reduce the dose, or permanently discontinue RYBREVANT® and continue LAZCLUZE™ based on severity.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON, ocular toxicity including blepharitis, dry eye, conjunctival redness, blurred vision, and eye pruritus occurred in 9%. All events were Grade 1-2.

RYBREVANT® as a Single Agent

In CHRYSALIS, keratitis occurred in 0.7% and uveitis occurred in 0.3% of patients treated with RYBREVANT®. All events were Grade 1-2.

Promptly refer patients with new or worsening eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity. Continue LAZCLUZE™ based on severity.

Embryo-Fetal Toxicity

Based on its mechanism of action and findings from animal models, RYBREVANT® and LAZCLUZE™ can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential of the potential risk to the fetus.

Advise female patients of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of RYBREVANT®.

Advise females of reproductive potential to use effective contraception during treatment with LAZCLUZE™ and for 3 weeks after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with LAZCLUZE™ and for 3 weeks after the last dose.

Adverse Reactions

RYBREVANT® with LAZCLUZE™

For the 421 patients in the MARIPOSA clinical trial who received RYBREVANT® in combination with LAZCLUZE™, the most common adverse reactions (≥20%) were rash (86%), nail toxicity (71%), infusion-related reactions (RYBREVANT®, 63%), musculoskeletal pain (47%), stomatitis (43%), edema (43%), VTE (36%), paresthesia (35%), fatigue (32%), diarrhea (31%), constipation (29%), COVID-19 (26%), hemorrhage (25%), dry skin (25%), decreased appetite (24%), pruritus (24%), nausea (21%), and ocular toxicity (16%). The most common Grade 3 or 4 laboratory abnormalities (≥ 2%) were decreased albumin (8%), decreased sodium (7%), increased ALT (7%), decreased potassium (5%), decreased hemoglobin (3.8%), increased AST (3.8%), increased GGT (2.6%) and increased magnesium (2.6%).

Serious adverse reactions occurred in 49% of patients who received RYBREVANT® in combination with LAZCLUZE™. Serious adverse reactions occurring in ≥2% of patients included VTE (11%), pneumonia (4.3%), ILD/pneumonitis and rash (2.9% each), COVID-19 (2.4%), pleural effusion, and infusion-related reaction (RYBREVANT®) (2.1% each). Fatal adverse reactions occurred in 7% of patients who received RYBREVANT® in combination with LAZCLUZE™ due to death not otherwise specified (1.2%); sepsis and respiratory failure (1% each); pneumonia, myocardial infarction, and sudden death (0.7% each); cerebral infarction, pulmonary embolism (PE), and COVID-19 infection (0.5% each); and ILD/pneumonitis, acute respiratory distress syndrome (ARDS), and cardiopulmonary arrest (0.2% each).

RYBREVANT® with Carboplatin and Pemetrexed

For the 151 patients in the PAPILLON clinical trial who received RYBREVANT® in combination with carboplatin and pemetrexed, the most common adverse reactions (≥ 20%) were rash (90%), nail toxicity (62%), stomatitis (43%), infusion-related reaction (42%), fatigue (42%), edema (40%), constipation (40%), decreased appetite (36%), nausea (36%), COVID-19 (24%), diarrhea (21%), and

vomiting (21%). The most common Grade 3 to 4 laboratory abnormalities (≥ 2%) were decreased albumin (7%), increased alanine aminotransferase (4%), increased gamma-glutamyl transferase (4%), decreased sodium (7%), decreased potassium (11%), decreased magnesium (2%), and decreases in white blood cells (17%), hemoglobin (11%), neutrophils (36%), platelets (10%), and lymphocytes (11%).

Serious adverse reactions occurred in 37% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed. Serious adverse reactions in ≥2% of patients included rash, pneumonia, ILD, pulmonary embolism, vomiting, and COVID-19. Fatal adverse reactions occurred in 7 patients (4.6%) due to pneumonia, cerebrovascular accident, cardio-respiratory arrest, COVID-19, sepsis, and death not otherwise specified.

RYBREVANT® as a Single Agent

For the 129 patients in the CHRYSALIS clinical trial who received RYBREVANT® as a single agent, the most common adverse reactions (≥20%) were rash (84%), IRR (64%), paronychia (50%), musculoskeletal pain (47%), dyspnea (37%), nausea (36%), fatigue (33%), edema (27%), stomatitis (26%), cough (25%), constipation (23%), and vomiting (22%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased lymphocytes (8%), decreased albumin (8%), decreased phosphate (8%), decreased potassium (6%), increased alkaline phosphatase (4.8%), increased glucose (4%), increased gamma-glutamyl transferase (4%), and decreased sodium (4%).

Serious adverse reactions occurred in 30% of patients who received RYBREVANT®. Serious adverse reactions in ≥2% of patients included pulmonary embolism, pneumonitis/ILD, dyspnea, musculoskeletal pain, pneumonia, and muscular weakness. Fatal adverse reactions occurred in 2 patients (1.5%) due to pneumonia and 1 patient (0.8%) due to sudden death.

LAZCLUZE™ Drug Interactions

Avoid concomitant use of LAZCLUZE™ with strong and moderate CYP3A4 inducers. Consider an alternate concomitant medication with no potential to induce CYP3A4.

Monitor for adverse reactions associated with a CYP3A4 or BCRP substrate where minimal concentration changes may lead to serious adverse reactions, as recommended in the approved product labeling for the CYP3A4 or BCRP substrate.

Please read full Prescribing Information for RYBREVANT®.

Please read full Prescribing Information for LAZCLUZE™.

IMPORTANT SAFETY INFORMATION FOR AKEEGA™

WARNINGS AND PRECAUTIONS
The safety population described in the WARNINGS and PRECAUTIONS reflect exposure to AKEEGA™ in combination with prednisone in BRCAm patients in Cohort 1 (N=113) of MAGNITUDE.

Myelodysplastic Syndrome/Acute Myeloid Leukemia
AKEEGA™ may cause myelodysplastic syndrome/acute myeloid leukemia (MDS/AML).

MDS/AML, including cases with fatal outcome, has been observed in patients treated with niraparib, a component of AKEEGA™.

All patients treated with niraparib who developed secondary MDS/cancer-therapy-related AML had received previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

For suspected MDS/AML or prolonged hematological toxicities, refer the patient to a hematologist for further evaluation. Discontinue AKEEGA™ if MDS/AML is confirmed.

Myelosuppression

AKEEGA™ may cause myelosuppression (anemia, thrombocytopenia, or neutropenia).

In MAGNITUDE Cohort 1, Grade 3-4 anemia, thrombocytopenia, and neutropenia were reported, respectively in 28%, 8%, and 7% of patients receiving AKEEGA™. Overall, 27% of patients required a red blood cell transfusion, including 11% who required multiple transfusions. Discontinuation due to anemia occurred in 3% of patients.

Monitor complete blood counts weekly during the first month of AKEEGA™ treatment, every two weeks for the next two months, monthly for the remainder of the first year and then every other month, and as clinically indicated. Do not start AKEEGA™ until patients have adequately recovered from hematologic toxicity caused by previous therapy. If hematologic toxicities do not resolve

within 28 days following interruption, discontinue AKEEGA™ and refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics.

Hypokalemia, Fluid Retention, and Cardiovascular Adverse Reactions

AKEEGA™ may cause hypokalemia and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition [see Clinical Pharmacology (12.1)]. In post-marketing experience, QT prolongation and Torsades de Pointes have been observed in patients who develop hypokalemia while taking abiraterone acetate, a component of AKEEGA™. Hypertension and hypertensive crisis have also been reported in patients treated with niraparib, a component of AKEEGA™.

In MAGNITUDE Cohort 1, which used prednisone 10 mg daily in combination with AKEEGA™, Grades 3-4 hypokalemia was detected in 2.7% of patients on the AKEEGA™ arm and Grades 3-4 hypertension were observed in 14% of patients on the AKEEGA™ arm.

The safety of AKEEGA™ in patients with New York Heart Association (NYHA) Class II to IV heart failure has not been established because these patients were excluded from MAGNITUDE.

Monitor patients for hypertension, hypokalemia, and fluid retention at least weekly for the first two months, then once a month. Closely monitor patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalemia, or fluid retention, such as those with heart failure, recent myocardial infarction, cardiovascular disease, or ventricular arrhythmia. Control hypertension and correct hypokalemia before and during treatment with AKEEGA™.

Discontinue AKEEGA™ in patients who develop hypertensive crisis or other severe cardiovascular adverse reactions.

Hepatotoxicity

AKEEGA™ may cause hepatotoxicity.

Hepatotoxicity in patients receiving abiraterone acetate, a component of AKEEGA™, has been reported in clinical trials. In post-marketing experience, there have been abiraterone acetate-associated severe hepatic toxicity, including fulminant hepatitis, acute liver failure, and deaths.

In MAGNITUDE Cohort 1, Grade 3-4 ALT or AST increases (at least 5 x ULN) were reported in 1.8% of patients. The safety of AKEEGA™ in patients with moderate or severe hepatic impairment has not been established as these patients were excluded from MAGNITUDE.

Measure serum transaminases (ALT and AST) and bilirubin levels prior to starting treatment with AKEEGA™, every two weeks for the first three months of treatment and monthly thereafter. Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT, or bilirubin from the patient's baseline should prompt more frequent monitoring and may require dosage modifications.

Permanently discontinue AKEEGA™ for patients who develop a concurrent elevation of ALT greater than 3 x ULN and total bilirubin greater than 2 x ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation, or in patients who develop ALT or AST ≥20 x ULN at any time after receiving AKEEGA™.

Adrenocortical Insufficiency

AKEEGA™ may cause adrenal insufficiency.

Adrenocortical insufficiency has been reported in clinical trials in patients receiving abiraterone acetate, a component of AKEEGA™, in combination with prednisone, following interruption of daily steroids and/or with concurrent infection or stress. Monitor patients for symptoms and signs of adrenocortical insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions, or experience unusual stress. Symptoms and signs of adrenocortical insufficiency may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with abiraterone acetate. If clinically indicated, perform appropriate tests to confirm the diagnosis of adrenocortical insufficiency. Increased doses of corticosteroids may be indicated before, during, and after stressful situations.

Hypoglycemia

AKEEGA™ may cause hypoglycemia in patients being treated with other medications for diabetes.

Severe hypoglycemia has been reported when abiraterone acetate, a component of AKEEGA™, was administered to patients receiving medications containing thiazolidinediones (including pioglitazone) or repaglinide.
Monitor blood glucose in patients with diabetes during and after discontinuation of treatment with AKEEGA™. Assess if antidiabetic drug dosage needs to be adjusted to minimize the risk of hypoglycemia.

Increased Fractures and Mortality in Combination with Radium 223 Dichloride

AKEEGA™ with prednisone is not recommended for use in combination with Ra-223 dichloride outside of clinical trials.

The clinical efficacy and safety of concurrent initiation of abiraterone acetate plus prednisone/prednisolone and radium Ra 223 dichloride was assessed in a randomized, placebo-controlled multicenter study (ERA-223 trial) in 806 patients with asymptomatic or mildly symptomatic castration-resistant prostate cancer with bone metastases. The study was unblinded early based on an Independent Data Monitoring Committee recommendation.

At the primary analysis, increased incidences of fractures (29% vs 11%) and deaths (39% vs 36%) have been observed in patients who received abiraterone acetate plus prednisone/prednisolone in combination with radium Ra 223 dichloride compared to patients who received placebo in combination with abiraterone acetate plus prednisone.
It is recommended that subsequent treatment with Ra-223 not be initiated for at least five days after the last administration of AKEEGA™, in combination with prednisone.

Posterior Reversible Encephalopathy Syndrome

AKEEGA™ may cause Posterior Reversible Encephalopathy Syndrome (PRES).
PRES has been observed in patients treated with niraparib as a single agent at higher than the recommended dose of niraparib included in AKEEGA™.

Monitor all patients treated with AKEEGA™ for signs and symptoms of PRES. If PRES is suspected, promptly discontinue AKEEGA™ and administer appropriate treatment. The safety of reinitiating AKEEGA™ in patients previously experiencing PRES is not known.

Embryo-Fetal Toxicity

The safety and efficacy of AKEEGA™ have not been established in females. Based on animal reproductive studies and mechanism of action, AKEEGA™ can cause fetal harm and loss of pregnancy when administered to a pregnant female.
Niraparib has the potential to cause teratogenicity and/or embryo-fetal death since niraparib is genotoxic and targets actively dividing cells in animals and patients (e.g., bone marrow).

In animal reproduction studies, oral administration of abiraterone acetate to pregnant rats during organogenesis caused adverse developmental effects at maternal exposures approximately ≥0.03 times the human exposure (AUC) at the recommended dose.

Advise males with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of AKEEGA™. Females who are or may become pregnant should handle AKEEGA™ with protection, e.g., gloves.

Based on animal studies, AKEEGA™ may impair fertility in males of reproductive potential.

ADVERSE REACTIONS

The safety of AKEEGA™ in patients with BRCAm mCRPC was evaluated in Cohort 1 of MAGNITUDE.

The most common adverse reactions (≥10%), including laboratory abnormalities, are decreased hemoglobin, decreased lymphocytes, decreased white blood cells, musculoskeletal pain, fatigue, decreased platelets, increased alkaline phosphatase, constipation, hypertension, nausea, decreased neutrophils, increased creatinine, increased potassium, decreased potassium, increased AST, increased ALT, edema, dyspnea, decreased appetite, vomiting, dizziness, COVID-19, headache, abdominal pain, hemorrhage, urinary tract infection, cough, insomnia, increased bilirubin, weight decreased, arrhythmia, fall, and pyrexia.

Serious adverse reactions reported in >2% of patients included COVID-19 (7%), anemia (4.4%), pneumonia (3.5%), and hemorrhage (3.5%). Fatal adverse reactions occurred in 9% of patients who received AKEEGA™, including COVID-19 (5%), cardiopulmonary arrest (1%), dyspnea (1%), pneumonia (1%), and septic shock (1%).

DRUG INTERACTIONS

Effect of Other Drugs on AKEEGA™

Avoid coadministration with strong CYP3A4 inducers.

Abiraterone is a substrate of CYP3A4. Strong CYP3A4 inducers may decrease abiraterone concentrations, which may reduce the effectiveness of abiraterone.

Effects of AKEEGA™ on Other Drugs

Avoid coadministration unless otherwise recommended in the Prescribing Information for CYP2D6 substrates for which minimal changes in concentration may lead to serious toxicities. If alternative treatments cannot be used, consider a dose reduction of the concomitant CYP2D6 substrate drug.

Abiraterone is a CYP2D6 moderate inhibitor. AKEEGA™ increases the concentration of CYP2D6 substrates, which may increase the risk of adverse reactions related to these substrates.

Monitor patients for signs of toxicity related to a CYP2C8 substrate for which a minimal change in plasma concentration may lead to serious or life-threatening adverse reactions.

Abiraterone is a CYP2C8 inhibitor. AKEEGA™ increases the concentration of CYP2C8 substrates, which may increase the risk of adverse reactions related to these substrates.

Please see the full Prescribing Information for AKEEGA™.