RYBREVANT® (amivantamab-vmjw)
Injection for IV Use | 350 mg/7 mL (50 mg/mL)

+

LAZCLUZE™ (lazertinib)
Tablets | 240 mg/80 mg

Proactive Therapy Management Guide for Adverse Reactions

For all RYBREVANT®-based regimens

INDICATIONS

RYBREVANT® (amivantamab-vmjw) is indicated:

- in combination with LAZCLUZE™ (lazertinib) for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.
- in combination with carboplatin and pemetrexed for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor.
- in combination with 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.
- as a single agent 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.

SELECT IMPORTANT SAFETY INFORMATION

Warnings and Precautions for RYBREVANT® and LAZCLUZE™ include Infusion-Related Reactions, Interstitial Lung Disease/Pneumonitis, Venous Thromboembolic Events, Dermatologic Adverse Reactions, Ocular Toxicity, and Embryo-Fetal Toxicity.

Please see Important Safety Information on pages 32-38. Please read full Prescribing Information for RYBREVANT® and full Prescribing Information for LAZCLUZE™.

What to expect

Consider RYBREVANT®-based regimens for mNSCLC across multiple indications

RYBREVANT® is approved for the following indications[1]

EGFR+ mNSCLC with exon 19 deletions or exon 21 L858R substitution mutations	*EGFR*+ mNSCLC with exon 20 insertion mutations
First line (in combination with LAZCLUZE™)	First line (in combination with carboplatin and pemetrexed)
Second line, after EGFR TKI (in combination with carboplatin and pemetrexed)	Second line, after platinum-based chemotherapy (as monotherapy)

This guide aims to review the proactive and reactive measures that may help you and your patients prepare for, identify, and manage ARs that may occur when treating with any RYBREVANT®-based regimen

AR, adverse reaction; EGFR, epidermal growth factor receptor; mNSCLC, metastatic non–small cell lung cancer; TKI, tyrosine kinase inhibitor.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

RYBREVANT® can cause infusion-related reactions (IRR) including anaphylaxis; 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™.

Please see Important Safety Information on pages 32-38. Please read full Prescribing Information for RYBREVANT® and full Prescribing Information for LAZCLUZE™.

Table of contents

1L, first-line; 2L, second-line; CTCAE, Common Terminology Criteria for Adverse Events; exon20ins, exon 20 insertion mutations; VTE, venous thromboembolism.

RYBREVANT® (amivantamab-vmjw) Injection for IV Use | 350 mg/7 mL (50 mg/mL) + LAZCLUZE™ (lazertinib) Tablets | 240 mg/80 mg

1L *EGFR*+ mNSCLC

RYBREVANT® (amivantamab-vmjw) + LAZCLUZE™ (lazertinib)

RYBREVANT® (amivantamab-vmjw) Injection for IV Use | 350 mg/7 mL (50 mg/mL)

LAZCLUZE™ (lazertinib) Tablets | 240 mg/80 mg

Please see Important Safety Information on pages 32-38. Please read full Prescribing Information for RYBREVANT® and full Prescribing Information for LAZCLUZE™.

What to expect

Safety: Majority of ARs were Grades 1 and 2[1]

ARs (≥10%) in patients in MARIPOSA[1]

Adverse Reaction	RYBREVANT® + LAZCLUZE™ (N=421)		Osimertinib (N=428)	
	All Grades (%)	Grades 3–4 (%)	All Grades (%)	Grades 3–4 (%)
Skin and subcutaneous tissue disorders				
Rash*	86	26	48	1.2
Nail toxicity*	71	11	34	0.7
Dry skin*	25	1	18	0.2
Pruritus	24	0.5	17	0.2
Injury, poisoning, and procedural complications				
Infusion-related reaction†	63	6	0	0
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain*	47	2.1	39	1.9
Gastrointestinal disorders				
Stomatitis*	43	2.4	27	0.5
Diarrhea*	31	2.6	45	0.9
Constipation	29	0	13	0
Nausea	21	1.2	14	0.2
Vomiting	12	0.5	5	0
Abdominal pain*	11	0	10	0
Hemorrhoids	10	0.2	2.1	0.2
General disorders and administration site conditions				
Edema*	43	2.6	8	0
Fatigue*	32	3.8	20	1.9
Pyrexia	12	0	9	0
Vascular disorders				
Venous thromboembolism*	36	11	8	2.8
Hemorrhage*	25	1	13	1.2
Nervous system disorders				
Paresthesia*	35	1.7	10	0.2
Dizziness*	14	0	10	0
Headache*	13	0.2	13	0
Infections and infestations				
COVID-19	26	1.7	24	1.4
Conjunctivitis	11	0.2	1.6	0
Metabolism and nutrition disorders				
Decreased appetite	24	1	18	1.4
Respiratory, thoracic, and mediastinal disorders				
Cough*	19	0	23	0
Dyspnea*	14	1.7	17	3.5
Eye disorders				
Ocular toxicity*	16	0.7	7	0
Psychiatric disorders				
Insomnia	10	0	11	0

*Grouped terms.
†Applicable for RYBREVANT® only.

To learn more about proactive therapy management and how to manage ARs, please see pages 17-31

What to expect

Laboratory abnormalities

Select laboratory abnormalities (≥20%) that worsened from baseline in MARIPOSA[1]*

Laboratory Abnormality	RYBREVANT® + LAZCLUZE™ (N=421)		Osimertinib (N=428)	
	All Grades (%)	Grades 3–4 (%)	All Grades (%)	Grades 3–4 (%)
Chemistry				
Decreased albumin	89	8	22	0.2
Increased ALT	65	7	29	2.6
Increased AST	52	3.8	36	1.9
Increased alkaline phosphatase	45	0.5	15	0.5
Decreased calcium (corrected)	41	1.4	27	0.7
Increased GGT	39	2.6	24	1.9
Decreased sodium	38	7	35	5
Decreased potassium	30	5	15	1.2
Increased creatinine	26	0.7	35	0.7
Decreased magnesium	25	0.7	10	0.2
Increased magnesium	12	2.6	20	4.8
Hematology				
Decreased platelet count	52	0.7	57	1.4
Decreased hemoglobin	47	3.8	56	1.9
Decreased white blood cell	38	1	66	0.7
Decreased neutrophils	15	1.4	33	1.4

*The denominator used to calculate the rate is the number of patients with a baseline value and at least one post-treatment value for the specific lab test.

Safety profile

- **Serious ARs** occurred in 49% of patients with RYBREVANT® + LAZCLUZE™ and 33% with osimertinib[1,2]
- **Serious ARs in ≥2% of patients** included VTE (11%), pneumonia (4%), rash (2.9%), ILD/pneumonitis (2.9%), COVID-19 (2.4%), pleural effusion (2.1%), and IRR (2.1%)[1]
- **Fatal ARs** occurred in 7% of patients who received RYBREVANT® + LAZCLUZE™ and 7% with osimertinib[1,2]
- **The most common ARs** (≥20%) were rash, nail toxicity, IRR, edema, musculoskeletal pain, stomatitis, VTE, paresthesia, fatigue, diarrhea, constipation, COVID-19, dry skin, hemorrhage, decreased appetite, pruritus, nausea, and ocular toxicity[1]
- **Clinically relevant ARs** in <10% of patients who received RYBREVANT® + LAZCLUZE™ included ILD/pneumonitis (3.1%)[1]
- **The most common Grade 3 or 4 laboratory abnormalities** (≥2%) were decreased albumin, decreased sodium, increased ALT, decreased potassium, decreased hemoglobin, increased AST, increased GGT, and increased magnesium[1]

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; ILD, interstitial lung disease; IRR, infusion-related reaction.

What to expect

Discontinuation rates/Dose modifications

RYBREVANT® + LAZCLUZE™: First-line treatment of locally advanced or metastatic NSCLC with *EGFR* exon 19 deletions or exon 21 L858R substitution mutations[1]

Discontinuation rates:

- Median duration of treatment was 18.5 months for RYBREVANT® + LAZCLUZE™ and 18 months for osimertinib[2]
- Permanent discontinuation of RYBREVANT® due to an AR occurred in 34% of patients[1]
  - ARs leading to RYBREVANT® discontinuation in ≥1% of patients included rash, IRRs, nail toxicity, VTE, ILD/pneumonitis, pneumonia, edema, hypoalbuminemia, fatigue, paresthesia, and dyspnea
- Permanent discontinuation of LAZCLUZE™ due to an AR occurred in 21% of patients[3]
  - ARs that resulted in permanent discontinuation of LAZCLUZE™ in ≥1% of patients included ILD/pneumonitis, pneumonia, VTE, rash, respiratory failure, and sudden death

Dose interruptions:

- Dose interruptions of RYBREVANT® due to an AR occurred in 88% of patients. ARs requiring dose interruptions in ≥5% of patients were IRRs, rash, nail toxicity, COVID-19, VTE, increased ALT, edema, and hypoalbuminemia[1]
- Dose interruptions of LAZCLUZE™ due to an AR occurred in 72% of patients. ARs requiring dose interruptions in ≥5% of patients were rash, nail toxicity, COVID-19, VTE, increased ALT, increased AST[3]

Dose reductions:

- Dose reductions of RYBREVANT® due to an AR occurred in 46% of patients. ARs requiring dose reductions in ≥5% of patients were rash and nail toxicity[1]
- Dose reductions of LAZCLUZE™ due to an AR occurred in 42% of patients. ARs requiring dose reductions in ≥5% of patients were rash and nail toxicity[3]

The rate of discontinuation of all agents due to treatment-related ARs was 10% for RYBREVANT® + LAZCLUZE™[2]

Learn more about first-line *EGFR*+ mNSCLC (MARIPOSA) efficacy and safety results at www.RYBREVANThcp.com

NSCLC, non–small cell lung cancer.

Please see Important Safety Information on pages 32-38. Please read full Prescribing Information for RYBREVANT® and full Prescribing Information for LAZCLUZE™.

2L *EGFR*+ mNSCLC

RYBREVANT® (amivantamab-vmjw) + chemotherapy*

*Chemotherapy is carboplatin and pemetrexed.

RYBREVANT® (amivantamab-vmjw) Injection for IV Use | 350 mg/7 mL (50 mg/mL)

What to expect

Safety: Majority of ARs were Grades 1 and 2[1]

ARs (≥10%) in patients in MARIPOSA-2[1]

Adverse Reaction	RYBREVANT® + Chemotherapy (N=130)		Chemotherapy (N=243)	
	All Grades (%)	Grades 3–4 (%)	All Grades (%)	Grades 3–4 (%)
Skin and subcutaneous tissue disorders				
Rash*	72	11	12	0
Nail toxicity*	45	2.3	0.4	0
Pruritus	15	0	7	0
Dry skin*	15	0	2.5	0
General disorders and administration site conditions				
Infusion-related reaction	59	5.4	0.4	0
Fatigue*	51	3.8	35	3.7
Edema*	36	1.5	11	0.4
Pyrexia	12	0	10	0
Gastrointestinal disorders				
Nausea	45	0.8	37	0.8
Constipation	39	0.8	30	0
Stomatitis*	35	2.3	11	0
Vomiting	25	0.8	17	0.4
Diarrhea*	15	1.5	7	0.8
Metabolism and nutrition disorders				
Decreased appetite	31	0	21	1.2
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain*	30	3.1	19	0.8
Infections and infestations				
COVID-19	21	1.5	10	0
Eye disorders				
Ocular toxicity*	17	0	3.7	0
Vascular disorders				
Hemorrhage*	14	0.8	4.9	0
Venous thromboembolism*	10	2.3	4.5	2.9
Respiratory, thoracic, and mediastinal disorders				
Cough*	14	0	16	0.4
Dyspnea*	13	1.5	8	1.2

*Grouped terms.

To learn more about proactive therapy management and how to manage ARs, please see pages 17-31

What to expect

Laboratory abnormalities

Select laboratory abnormalities (≥20%) that worsened from baseline in MARIPOSA-2[1]

Laboratory Abnormality	RYBREVANT® + Chemotherapy (N=130)		Chemotherapy (N=243)	
	All Grades (%)	Grades 3–4 (%)	All Grades (%)	Grades 3–4 (%)
Hematology				
Decreased white blood cells	91	42	85	19
Decreased neutrophils	74	49	64	25
Decreased platelets	74	17	58	9
Decreased hemoglobin	71	12	77	9
Decreased lymphocytes	69	28	58	18
Chemistry				
Decreased albumin	73	3.8	26	0.4
Decreased sodium	49	11	30	6
Increased aspartate aminotransferase	47	0.8	52	0.9
Increased alkaline phosphatase	42	0	29	0.4
Increased alanine aminotransferase	39	3.9	56	6
Decreased magnesium	38	0.8	17	0.4
Decreased potassium	37	11	12	3.4
Increased gamma-glutamyl transferase	30	3.1	41	1.3
Decreased calcium (corrected)	25	0	11	0.9

Safety profile

- **Serious ARs** occurred in 32% of patients who received RYBREVANT® + chemotherapy and 20% of patients who received chemotherapy alone[1,4]
- **Serious ARs in >2% of patients** included dyspnea (3.1%), thrombocytopenia (3.1%), sepsis (2.3%), and pulmonary embolism (2.3%)[1]
- **Fatal ARs** occurred in 2.3% of patients who received RYBREVANT® + chemotherapy and 1% of patients who received chemotherapy alone[1,4]
- **The most common ARs** (occurring in ≥20% of patients) were rash, IRRs, fatigue, nail toxicity, nausea, constipation, edema, stomatitis, decreased appetite, musculoskeletal pain, vomiting, and COVID-19[1]
- **Clinically relevant ARs** in <10% of patients who received RYBREVANT® + chemotherapy include abdominal pain, hemorrhoids, dizziness, visual impairment, trichomegaly, keratitis, and ILD[1]
- **The most common Grade 3 or 4 laboratory abnormalities** (≥2%) were decreased neutrophils, decreased leukocytes, decreased platelets, decreased hemoglobin, decreased potassium, decreased sodium, increased alanine aminotransferase, increased gamma-glutamyl transferase, and decreased albumin[1]

Discontinuation rates/Dose modifications

RYBREVANT® + chemotherapy: Second-line treatment of previously treated locally advanced or metastatic NSCLC with *EGFR* exon 19 deletions or exon 21 L858R substitution mutations[1]

Discontinuation rates[1]**:**

- 11% of patients permanently discontinued RYBREVANT® due to ARs
- Most frequent ARs leading to treatment discontinuation in ≥5% of patients were IRRs

Dose interruptions[1]**:**

- Dose interruptions of RYBREVANT® due to an AR occurred in 60% of patients
- IRRs requiring infusion interruptions occurred in 52% of patients
- ARs requiring dose interruption in ≥5% of patients included IRR, rash, and fatigue

Dose reductions[1]**:**

- Dose reductions of RYBREVANT® due to ARs occurred in 17% of patients
- ARs requiring dose reductions in ≥2% of patients included rash

Learn more about second-line *EGFR*+ mNSCLC (MARIPOSA-2) efficacy and safety results at www.RYBREVANThcp.com

1L *EGFR*+ exon20ins mNSCLC

RYBREVANT® (amivantamab-vmjw) + chemotherapy*

NOTE: For second-line patients in the CHRYSALIS study, see the full Prescribing Information.

*Chemotherapy is carboplatin and pemetrexed.

RYBREVANT® (amivantamab-vmjw) Injection for IV Use | 350 mg/7 mL (50 mg/mL)

What to expect

Safety: Majority of ARs were Grades 1 and 2[1]

ARs (≥10%) observed in PAPILLON[1]

Adverse Reaction*	RYBREVANT® + Chemotherapy (N=151)		Chemotherapy (N=155)	
	All Grades (%)	Grades 3–4 (%)	All Grades (%)	Grades 3–4 (%)
Skin and subcutaneous tissue disorders				
Rash†	90	19	19	0
Nail toxicity†	62	7	3	0
Dry skin†	17	0	6	0
Gastrointestinal disorders				
Stomatitis†	43	4	11	0
Constipation	40	0	30	0.7
Nausea	36	0.7	42	0
Vomiting	21	3.3	19	0.7
Diarrhea	21	3	13	1.3
Hemorrhoids	12	1	1.3	0
Abdominal pain†	11	0.7	8	0
General disorders and administration site conditions				
Infusion-related reactions	42	1.3	1.3	0
Fatigue†	42	6	45	3.9
Edema†	40	1.3	19	0
Pyrexia†	17	0	6	0
Metabolism and nutrition disorders				
Decreased appetite	36	2.6	28	1.3
Infections and infestations				
COVID-19	24	2	14	0.6
Pneumonia†	13	5	6	1.9
Vascular disorders				
Hemorrhage†	18	0.7	11	1.9
Respiratory, thoracic, and mediastinal disorders				
Cough†	17	0	16	0
Dyspnea†	11	1.3	16	3.2
Investigations				
Weight decreased	14	0.7	8	0
Nervous system disorders				
Dizziness†	11	0	12	0
Psychiatric disorders				
Insomnia	11	0	13	0

*ARs were graded using CTCAE version 5.0.
†Grouped terms.

Safety profile

- **Serious ARs** occurred in 37% of patients who received RYBREVANT® + chemotherapy and 31% of patients who received chemotherapy alone. Serious ARs in ≥2% of patients included rash, pneumonia, ILD, pulmonary embolism, vomiting, and COVID-19[1,5]
- **Fatal ARs** occurred in 4.6% of patients who received RYBREVANT® + chemotherapy and 3% of patients who received chemotherapy alone[1,5]
- **The most common ARs** (≥20%) were rash, nail toxicity, stomatitis, IRR, fatigue, edema, constipation, decreased appetite, nausea, COVID-19, diarrhea, and vomiting[1]
- **Clinically relevant ARs** in <10% of patients who received RYBREVANT® + chemotherapy included pulmonary embolism, deep vein thrombosis, skin ulcer, conjunctivitis, and ILD/pneumonitis[1]

Please see Important Safety Information on pages 32-38. Please read full Prescribing Information for RYBREVANT®.

What to expect

Laboratory abnormalities

Summary of laboratory abnormalities (≥20%) that worsened from baseline in PAPILLON[1]

Laboratory Abnormality*	RYBREVANT® + Chemotherapy† (N=151)		Chemotherapy‡ (N=155)	
	All Grades (%)	Grades 3–4 (%)	All Grades (%)	Grades 3–4 (%)
Hematology				
Decreased white blood cells	89	17	76	10
Decreased hemoglobin	79	11	85	13
Decreased neutrophils	76	36	61	23
Decreased platelets	70	10	54	12
Decreased lymphocytes	61	11	49	13
Chemistry				
Decreased albumin	87	7	34	1
Increased aspartate aminotransferase	60	1	61	1
Increased alanine aminotransferase	57	4	54	1
Decreased sodium	55	7	39	4
Increased alkaline phosphatase	51	1	28	0
Decreased potassium	44	11	17	1
Decreased magnesium	39	2	30	1
Increased gamma-glutamyl transferase	38	4	43	4
Decreased calcium (corrected)	27	1	18	1

*ARs were graded using CTCAE version 5.0.
†The denominator used to calculate the rate varied from 113 to 150 based on the number of patients with a baseline value and at least one post-treatment value.
‡The denominator used to calculate the rate varied from 119 to 154 based on the number of patients with a baseline value and at least one post-treatment value.

- **Grades 3 to 4 laboratory abnormalities** (≥2%) were decreased albumin, increased alanine aminotransferase, increased gamma-glutamyl transferase, decreased sodium, decreased potassium, decreased magnesium, and decreases in white blood cells, hemoglobin, neutrophils, platelets, and lymphocytes[1]

To learn more about proactive therapy management and how to manage ARs, please see pages 17-31

What to expect

Discontinuation rates/Dose modifications

RYBREVANT® + chemotherapy: First-line treatment of locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations[1]

Discontinuation rates[1]**:**

- Permanent discontinuation of RYBREVANT® due to an AR occurred in 11% of patients
- ARs resulting in permanent discontinuation of RYBREVANT® in ≥1% of patients were rash and ILD

Dose interruptions[1]**:**

- Dose interruption of RYBREVANT® due to an AR occurred in 64% of patients. ARs requiring dose interruption in ≥5% of patients included rash and nail toxicity
- IRRs requiring infusion interruptions occurred in 38% of patients

Dose reductions[1]**:**

- Dose reductions of RYBREVANT® due to an AR occurred in 36% of patients
- ARs requiring dose reductions in ≥5% of patients included rash and nail toxicity

Learn more about first-line *EGFR*+ exon20ins mNSCLC (PAPILLON) efficacy and safety results at www.RYBREVANThcp.com

PROACTIVE THERAPY MANAGEMENT

Overview of proactive therapy management

Proactive therapy management is recommended and may help reduce the risk and severity of select ARs[6,7]

Mutated EGFR is a critical oncogenic driver for many patients with mNSCLC.[6]

- Treatments targeting EGFR such as RYBREVANT® or LAZCLUZE™ cause on-target ARs[6]
- EGFR inhibitor–related ARs can affect patients' quality of life[6]
- A proactive therapy management approach is needed to give patients the best chance of tolerating and staying on EGFR-targeting treatment[7]

Evaluating prophylactic strategies for RYBREVANT®-based regimens

SKIPPirr trial

SKIPPirr was a Phase 2 prospective study that assessed prophylactic strategies to reduce incidence and/or severity of first-dose IRRs with RYBREVANT®, with the dexamethasone 8 mg cohort reaching the expansion stage.* The primary endpoint was the incidence of IRR events on Week 1, Day 1.[8,9]

Limitations

- SKIPPirr was not a comparative study[8]
- The dexamethasone 8 mg oral cohort sample size was n=40[8]

COCOON trial

COCOON is a Phase 2, open-label, randomized study evaluating the effect of enhanced versus standard dermatologic management strategies in patients treated with RYBREVANT® + LAZCLUZE™ in 1L. The primary endpoint is incidence of Grade ≥2 dermatologic ARs of interest in the first 12 weeks after treatment initiation.[10]

COCOON is also the first trial using RYBREVANT® + LAZCLUZE™ that required 4 months of prophylactic anticoagulation, with a secondary endpoint of VTE incidence.[10,11]

*This was a Simon 2-stage design. Stage 1 n=6. Stage 2 n=16. Expansion stage n=40.[8] See full presentation for more details.

IMPORTANT SAFETY INFORMATION (cont'd)

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population (n=281), IRR occurred in 50% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (3.2%) adverse reactions. The incidence of infusion modifications due to IRR was 46%, and 2.8% of patients permanently discontinued RYBREVANT® due to IRR.

Impact of proactive therapy management

For IRRs: Premedicate with glucocorticoids and consider additional prophylaxis[1,8,12]

In the SKIPPirr trial, Cycle 1, Week 1, Day 1 had a

22.5% rate of IRRs.

In the RYBREVANT® + LAZCLUZE™ arm of MARIPOSA, the rate of IRRs on Cycle 1, Week 1, Day 1 was 52.5%.

For dermatologic ARs: Use skincare prophylaxis and consider the COCOON study[10]

At the time of prespecified interim analysis, COCOON demonstrated a

50% reduction in Grade ≥2 key dermatologic ARs.

- 38.6% with COCOON prophylactic skincare management vs 76.5% with standard skincare management (primary endpoint) (OR, 0.19 [95% CI: 0.09, 0.4]; *P*<0.0001)

For VTE: Use anticoagulants (only when combined with LAZCLUZE™)[10]*

The COCOON trial required 4 months of VTE prophylaxis.

A 6.5% average rate of VTE

was observed in the patient population with *EGFR*+ mNSCLC receiving RYBREVANT® + LAZCLUZE™ in 1L.

*Based on Prescribing Information for RYBREVANT®.

IMPORTANT SAFETY INFORMATION (cont'd)

RYBREVANT® as a Single Agent

In CHRYSALIS (n=302), 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.

IRRs: Premedications

Premedicate with antihistamines, antipyretics, and glucocorticoids and administer RYBREVANT® as recommended.[1]

Medication	Dose	Route of Administration	Dosing Window Prior to RYBREVANT® Administration	Frequency
Antihistamine	Diphenhydramine (25 to 50 mg) or equivalent	Intravenous	15 to 30 minutes	All doses
		Oral	30 to 60 minutes	
Antipyretic	Acetaminophen (650 to 1,000 mg)	Intravenous	15 to 30 minutes	All doses
		Oral	30 to 60 minutes	
Glucocorticoid	Dexamethasone (20 mg) or equivalent	Intravenous	45 to 60 minutes	Week 1, Day 1
Glucocorticoid	Dexamethasone (10 mg) or equivalent	Intravenous	45 to 60 minutes	Week 1, Day 2 (optional for subsequent doses)

- Due to the risk of IRR, administer premedications prior to initial infusion of RYBREVANT® (Week 1, Day 1 and 2) as described in the table above[1]
- Glucocorticoid administration is required for Week 1, Days 1 and 2 dose only and upon reinitiation after prolonged dose interruptions, then as necessary for subsequent infusions[1]
- Administer both antihistamine and antipyretic prior to all infusions[1]

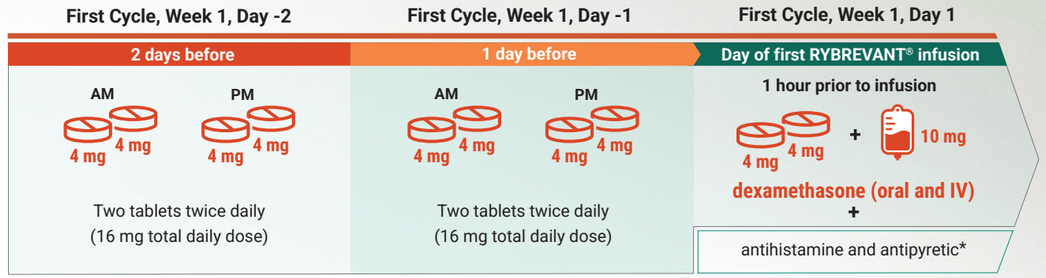
Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity[1]

IMPORTANT SAFETY INFORMATION (cont'd)

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. If an anaphylactic reaction occurs, permanently discontinue RYBREVANT®.

IRRs: SKIPPirr protocol and results

One cohort tested in SKIPPirr reached the expansion stage: dexamethasone 8 mg oral cohort[1,8]



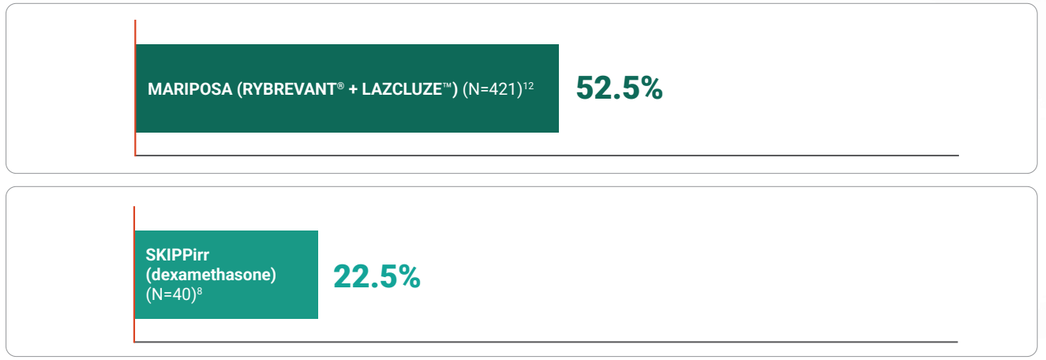
*These are given based on RYBREVANT® Prescribing Information recommendations, per the Premedications for RYBREVANT® table.[1]

In SKIPPirr, the Week 1, Day 1 dexamethasone dose is 10 mg IV. In the Prescribing Information for RYBREVANT®, the Week 1, Day 1 dexamethasone dose is 20 mg IV.[1,8]

SKIPPirr IRR rates

In the SKIPPirr dexamethasone 8 mg oral cohort, the incidence rate of patients experiencing IRRs on Week 1, Day 1 was 22.5% (9/40). All IRRs were Grade 1 and 2.[8]

All-Grade IRRs on Week 1, Day 1 infusion (%)



Prophylaxis regimen from the SKIPPirr trial is not included in the Prescribing Information.

IV, intravenous.

IMPORTANT SAFETY INFORMATION (cont'd)

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® (amivantamab-vmjw) Injection for IV Use | 350 mg/7 mL (50 mg/mL) + LAZCLUZE™ (lazertinib) Tablets | 240 mg/80 mg

Dermatologic ARs: COCOON skincare management

COCOON prophylactic skincare management reduced key dermatologic ARs[10,13]

Weeks 1-12

Oral antibiotic
Doxycycline or minocycline
100 mg twice daily

Weeks 13+

Topical antibiotic lotion
Topical clindamycin lotion 1%
on the scalp before bedtime

Daily

Antiseptic skin cleanser
Chlorhexidine 4% on the fingernails and toenails once daily

Moisturizer
Ceramide-based (eg, La Roche-Posay*) moisturizer on the body and face at least once daily

Limit direct exposure to sunlight
Wear protective clothing and broad-spectrum sunscreen (SPF ≥30)

*All trademarks are property of their respective owners.

SPF, sun protection factor.

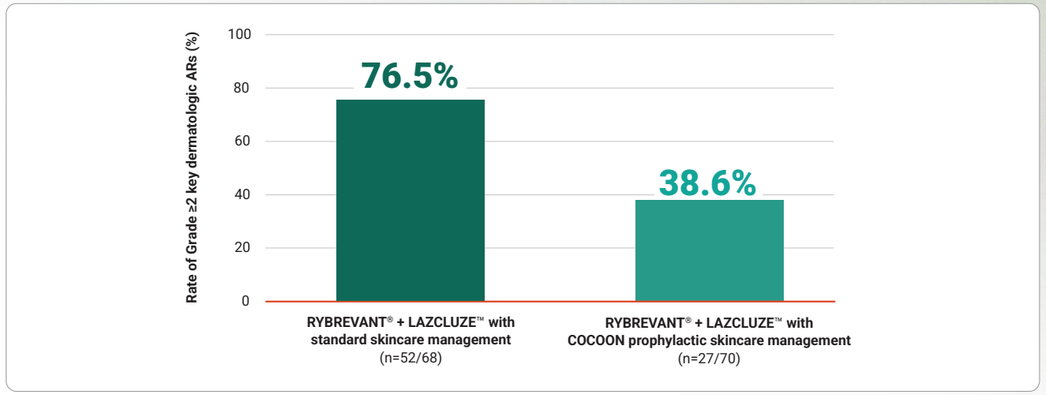
IMPORTANT SAFETY INFORMATION (cont'd)

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population, ILD/pneumonitis occurred in 2.1% treated with RYBREVANT® in combination with carboplatin and pemetrexed with 1.8% of patients experiencing Grade 3 ILD/pneumonitis. 2.1% discontinued RYBREVANT® due to ILD/pneumonitis.

Dermatologic ARs: COCOON interim analysis results

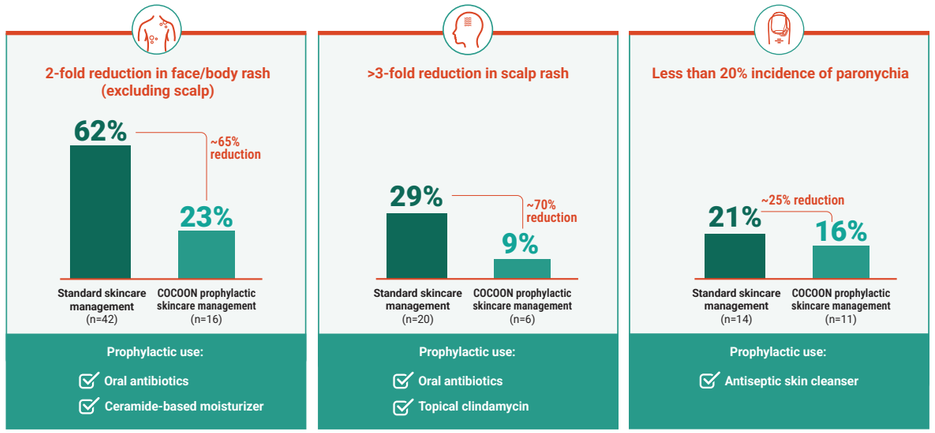
Primary endpoint[10]



At the time of prespecified interim analysis, COCOON prophylactic skincare management significantly reduced the incidence of Grade ≥2 dermatologic ARs for the first 12 weeks vs standard skincare management by 50% (OR, 0.19 [95% CI: 0.09, 0.4]; *P*<0.0001)[10]

- 4.3% rate of Grade 3 reactions with the COCOON skincare management vs 8.8% for patients receiving standard skincare management

Improvements seen with the COCOON prophylactic skincare management across areas of interest[10]



IMPORTANT SAFETY INFORMATION (cont'd)

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%) permanently discontinued RYBREVANT® due to ILD/pneumonitis.

RYBREVANT® (amivantamab-vmjw) Injection for IV Use | 350 mg/7 mL (50 mg/mL) + LAZCLUZE™ (lazertinib) Tablets | 240 mg/80 mg

VTE

Overview

VTE, which includes DVT and PE, is a key cause of morbidity among patients with lung cancer[14]

People living with cancer are at **9 times the risk** of developing VTE compared with the general population.[15]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommendations for cancer-associated VTE disease[16]

Anticoagulant options for VTE prophylaxis for ambulatory patients with cancer include direct oral anticoagulants (DOACs) and low molecular weight heparins (LMWHs).*†‡

For RYBREVANT® only when combined with LAZCLUZE™

VTE prophylaxis protocol

Drug-related prophylaxis for VTE

Prophylactic treatment with an anticoagulation medicine is recommended for the first 4 months of treatment with RYBREVANT® + LAZCLUZE™.[1]

- The use of Vitamin K antagonists is not recommended
- If there are no signs or symptoms of VTE during the first 4 months of treatment, consider discontinuation of anticoagulant prophylaxis at the discretion of the healthcare provider

~97% of patients in the RYBREVANT® + LAZCLUZE™ arm of MARIPOSA did not receive prophylactic anticoagulation for the first 4 months.[12]

Impact of VTE prophylaxis

COCOON is the first trial that required 4 months of prophylactic anticoagulation at treatment initiation, leading to a low incidence of VTE[10]

- A 6.5% average rate of VTE was observed in the patient population with *EGFR*+ mNSCLC receiving RYBREVANT® + LAZCLUZE™

*Recommendations derived from clinical trials of ambulatory patients with cancer with high thrombosis risk (>18 years, Khorana VTE Risk Score of ≥2, initiating new course of chemotherapy) and are not included in product labeling. Prophylaxis duration should be 6 months or longer if risk persists.[16]

†Always refer to the NCCN Guidelines for the comprehensive and most up-to-date recommendations on cancer-associated VTE when considering prophylaxis.

‡When using RYBREVANT® in combination with LAZCLUZE™, please refer to the Prescribing Information for VTE prophylaxis recommendation.

DVT, deep vein thrombosis; NCCN, National Comprehensive Cancer Network; PE, pulmonary embolism.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

Please see Important Safety Information on pages 32-38. Please read full Prescribing Information for RYBREVANT® and full Prescribing Information for LAZCLUZE™.

MONITORING & MANAGEMENT

Adverse event CTCAE grades

Based on the Common Terminology Criteria for Adverse Events (CTCAE) v5.0[17]*

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated	Moderate; minimal, local, or noninvasive intervention indicated; limiting age-appropriate instrumental ADL†	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL‡	Life-threatening consequences; urgent intervention indicated	Death related to AE

*CTCAE definition may differ from the Prescribing Information.
†Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
‡Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

ADL, activities of daily living; AE, adverse event.

Dose reductions

Recommended RYBREVANT® dose reductions for ARs[1]

Dose reductions for ARs			
Dose at which the AR occurred	1st Dose Reduction	2nd Dose Reduction	3rd Dose Reduction
1,050 mg	700 mg	350 mg	Discontinue RYBREVANT®
1,400 mg	1,050 mg	700 mg	
1,750 mg	1,400 mg	1,050 mg	
2,100 mg	1,750 mg	1,400 mg	

Recommended LAZCLUZE™ dose reductions for ARs[3]

Dose reductions for ARs			
Dose at which the AR occurred	1st Dose Reduction	2nd Dose Reduction	3rd Dose Reduction
240 mg once daily (one 240 mg tablet)	160 mg once daily (two 80 mg tablets)	80 mg once daily (one 80 mg tablet)	Discontinue LAZCLUZE™

Dosage modifications & management

Recommended dosage modifications and management for ARs for RYBREVANT® and LAZCLUZE™[1,3]

For RYBREVANT® + LAZCLUZE™, refer to **both** the RYBREVANT® and LAZCLUZE™ recommendations. For RYBREVANT® + chemotherapy or RYBREVANT® as a single agent, refer only to the RYBREVANT® recommendations.

Adverse Reaction	Severity	Dosage Modifications
VTE events (applies to RYBREVANT® + LAZCLUZE™ combination only)	**Grade 2 or 3**	**RYBREVANT® + LAZCLUZE™** • Withhold RYBREVANT® and LAZCLUZE™ • Administer anticoagulant treatment as clinically indicated • Once anticoagulant treatment has been initiated, resume RYBREVANT® and LAZCLUZE™ at the same dose level, at the discretion of the healthcare provider
	Grade 4 or recurrent Grade 2 or 3 despite therapeutic level anticoagulation	**RYBREVANT® + LAZCLUZE™** • Withhold LAZCLUZE™ and permanently discontinue RYBREVANT® • Administer anticoagulant treatment as clinically indicated • Once anticoagulant treatment has been initiated, treatment can continue with LAZCLUZE™ at the same dose level at the discretion of the healthcare provider
IRR	**Grade 1 to 2**	**RYBREVANT®** • Interrupt RYBREVANT® infusion if IRR is suspected and monitor patient until reaction symptoms resolve • Resume the infusion at 50% of the infusion rate at which the reaction occurred • If there are no additional symptoms after 30 minutes, the infusion rate may be escalated • Include corticosteroid with premedications for subsequent dose
	Grade 3	**RYBREVANT®** • Interrupt RYBREVANT® infusion and administer supportive care medications. Continuously monitor patient until reaction symptoms resolve • Resume the infusion at 50% of the infusion rate at which the reaction occurred • If there are no additional symptoms after 30 minutes, the infusion rate may be escalated • Include corticosteroid with premedications for subsequent dose. For recurrent Grade 3, permanently discontinue RYBREVANT®
	Grade 4 or any Grade anaphylaxis/ anaphylactic reactions	**RYBREVANT®** • Permanently discontinue RYBREVANT®

Dosage modifications & management (cont'd)

Adverse Reaction	Severity	Dosage Modifications
ILD/pneumonitis	**Any Grade**	**RYBREVANT®** • Withhold RYBREVANT® if ILD/pneumonitis is suspected • Permanently discontinue RYBREVANT® if ILD/pneumonitis is confirmed **LAZCLUZE™** • Withhold LAZCLUZE™ and RYBREVANT® if ILD/pneumonitis is suspected • Permanently discontinue LAZCLUZE™ and RYBREVANT® if ILD/pneumonitis is confirmed
Dermatologic ARs (including dermatitis acneiform, pruritus, dry skin)	**Grade 1**	**RYBREVANT®** • Initiate supportive care management • Reassess after 2 weeks; if rash does not improve, consider dose reduction **LAZCLUZE™** • Initiate supportive care management
	Grade 2	**RYBREVANT®** • Initiate supportive care management • Reassess after 2 weeks; if rash does not improve, consider dose reduction **LAZCLUZE™** • Initiate supportive care management • If there is no improvement after 2 weeks, reduce RYBREVANT® dose and continue LAZCLUZE™ at the same dose • Reassess every 2 weeks; if no improvement, reduce LAZCLUZE™ dose until ≤Grade 1, then may resume previous dose of LAZCLUZE™ at the discretion of the healthcare provider

Dosage modifications & management (cont'd)

Recommended dosage modifications and management for ARs for RYBREVANT® and LAZCLUZE™[1,3]

For RYBREVANT® + LAZCLUZE™, refer to **both** the RYBREVANT® and LAZCLUZE™ recommendations. For RYBREVANT® + chemotherapy or RYBREVANT® as a single agent, refer only to the RYBREVANT® recommendations.

Adverse Reaction	Severity	Dosage Modifications
Dermatologic ARs (including dermatitis acneiform, pruritus, dry skin)	**Grade 3**	**RYBREVANT®** • Withhold RYBREVANT® and initiate supportive care management • Upon recovery to ≤Grade 2, resume RYBREVANT® at a reduced dose • If no improvement within 2 weeks, permanently discontinue treatment **LAZCLUZE™** • Withhold LAZCLUZE™ and RYBREVANT® • Initiate supportive care management • Upon recovery to ≤Grade 2, resume LAZCLUZE™ at the same dose or consider dose reduction, resume RYBREVANT® at a reduced dose • If there is no improvement within 2 weeks, permanently discontinue both LAZCLUZE™ and RYBREVANT®
	Grade 4 (including severe bullous, blistering, or exfoliating skin conditions, including TEN for RYBREVANT®)	**RYBREVANT®** • Permanently discontinue RYBREVANT® **LAZCLUZE™** • Initiate supportive care management • Permanently discontinue RYBREVANT® • Withhold LAZCLUZE™ until recovery to ≤Grade 2 or baseline • Upon recovery to ≤Grade 2, resume LAZCLUZE™ at a reduced dose, at the discretion of the healthcare provider

TEN, toxic epidermal necrolysis.

Dosage modifications & management (cont'd)

Adverse Reaction	Severity	Dosage Modifications
Other ARs	**Grade 3**	**RYBREVANT®** • Withhold RYBREVANT® until recovery to ≤Grade 1 or baseline • Resume at the same dose if recovery occurs within 1 week • Resume at reduced dose if recovery occurs after 1 week but within 4 weeks • Permanently discontinue if recovery does not occur within 4 weeks **LAZCLUZE™** • Withhold LAZCLUZE™ and RYBREVANT® until the AR resolves to ≤Grade 1 or baseline • Resume both drugs at a reduced dose or LAZCLUZE™ alone • Consider permanently discontinuing both LAZCLUZE™ and RYBREVANT® if recovery does not occur within 4 weeks
	Grade 4	**RYBREVANT®** • Withhold RYBREVANT® until recovery to ≤Grade 1 or baseline • Resume at reduced dose if recovery occurs within 4 weeks • Permanently discontinue if recovery does not occur within 4 weeks • Permanently discontinue for recurrent Grade 4 reactions **LAZCLUZE™** • Withhold LAZCLUZE™ and RYBREVANT® until the AR resolves to ≤Grade 1 or baseline • Resume both drugs at a reduced dose or LAZCLUZE™ alone • Consider permanently discontinuing both LAZCLUZE™ and RYBREVANT® if recovery does not occur within 4 weeks

Recommended dosage modifications for ARs for RYBREVANT® in combination with LAZCLUZE™[1]

When administering RYBREVANT® in combination with LAZCLUZE™, if there is an AR requiring dose reduction after withholding treatment and resolution, reduce the dose of RYBREVANT® first.

Recommended dosage modifications for ARs for RYBREVANT® in combination with carboplatin and pemetrexed[1]

When administering RYBREVANT® in combination with carboplatin and pemetrexed, modify the dosage of one or more drugs. Withhold or discontinue RYBREVANT® as shown in the table above. Refer to Prescribing Information for carboplatin and pemetrexed for additional dosage modification information.

RYBREVANT® (amivantamab-vmjw) Injection for IV Use | 350 mg/7 mL (50 mg/mL) + LAZCLUZE™ (lazertinib) Tablets | 240 mg/80 mg

INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

RYBREVANT® (amivantamab-vmjw) is indicated:

- in combination with LAZCLUZE™ (lazertinib) for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.
- in combination with carboplatin and pemetrexed for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor.
- in combination with 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.
- as a single agent 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.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

RYBREVANT® can cause infusion-related reactions (IRR) including anaphylaxis; 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

Based on the pooled safety population (n=281), IRR occurred in 50% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (3.2%) adverse reactions. The incidence of infusion modifications due to IRR was 46%, and 2.8% of patients permanently discontinued RYBREVANT® due to IRR.

RYBREVANT® as a Single Agent

In CHRYSALIS (n=302), 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

IMPORTANT SAFETY INFORMATION (cont'd)

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. If an anaphylactic reaction occurs, permanently discontinue RYBREVANT®.

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

Based on the pooled safety population, ILD/pneumonitis occurred in 2.1% treated with RYBREVANT® in combination with carboplatin and pemetrexed with 1.8% of patients experiencing Grade 3 ILD/pneumonitis. 2.1% discontinued RYBREVANT® due to ILD/pneumonitis.

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%) permanently 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.

IMPORTANT SAFETY INFORMATION (cont'd)

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

RYBREVANT® in combination with LAZCLUZE™ can cause serious and fatal venous thromboembolic (VTE) 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

Based on the pooled safety population, rash occurred in 82% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (15%) adverse reactions. Rash leading to dose reductions occurred in 14% of patients, and 2.5% permanently discontinued RYBREVANT® and 3.1% discontinued pemetrexed.

IMPORTANT SAFETY INFORMATION (cont'd)

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® or LAZCLUZE™ in combination 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, reduce the dose, 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

Based on the pooled safety population, ocular toxicity occurred in 16% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed. All events were Grade 1 or 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, reduce the dose, or permanently discontinue RYBREVANT® based on severity.

IMPORTANT SAFETY INFORMATION (cont'd)

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%), ILD/pneumonitis and rash (2.9% each), COVID-19 (2.4%), and 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 130 patients in the MARIPOSA-2 clinical trial who received RYBREVANT® in combination with carboplatin and pemetrexed, the most common adverse reactions (≥20%) were rash (72%), infusion-related reactions (59%), fatigue (51%), nail toxicity (45%), nausea (45%), constipation (39%), edema (36%), stomatitis (35%), decreased appetite (31%), musculoskeletal pain (30%), vomiting (25%), and COVID-19 (21%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased neutrophils (49%), decreased white blood cells (42%), decreased lymphocytes (28%), decreased platelets (17%), decreased hemoglobin (12%), decreased potassium (11%), decreased sodium (11%), increased alanine aminotransferase (3.9%), decreased albumin (3.8%), and increased gamma-glutamyl transferase (3.1%).

IMPORTANT SAFETY INFORMATION (cont'd)

In MARIPOSA-2, serious adverse reactions occurred in 32% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed. Serious adverse reactions in >2% of patients included dyspnea (3.1%), thrombocytopenia (3.1%), sepsis (2.3%), and pulmonary embolism (2.3%). Fatal adverse reactions occurred in 2.3% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed; these included respiratory failure, sepsis, and ventricular fibrillation (0.8% each).

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%).

In PAPILLON, 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.

IMPORTANT SAFETY INFORMATION (cont'd)

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™.

cp-213274v7

Help your patients get the most out of their treatment from the start

Prepare for, identify, and proactively manage RYBREVANT® adverse reactions

For additional support, reach out to an Oncology Clinical Educator (OCE). OCEs are oncology nurses who are employed by Johnson & Johnson and can educate Patient Care Teams (PCTs) on product-specific and disease state information to share with their team and patients.

Reach out to Oncology Clinical Educators by visiting
www.RYBREVANThcp.com

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RYBREVANT® (amivantamab-vmjw) Injection for IV Use | 350 mg/7 mL (50 mg/mL) + LAZCLUZE™ (lazertinib) Tablets | 240 mg/80 mg