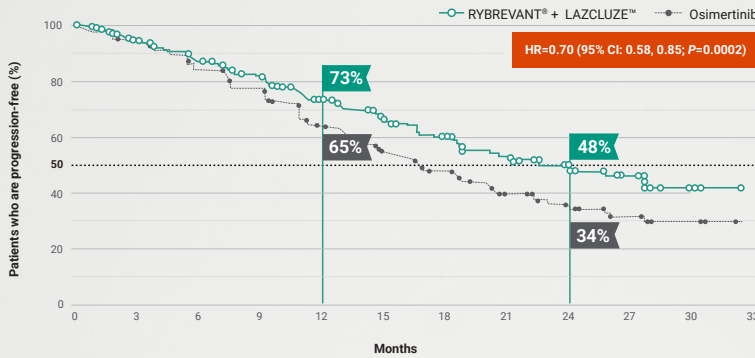




IS APPROVED¹

PROGRESSION-FREE SURVIVAL DATA^{1,2}

RYBREVANT® + LAZCLUZE™ demonstrated a statistically significant reduction in the risk of progression or death by 30% vs osimertinib^{1,2}



7.1-MONTH IMPROVEMENT IN MEDIAN PFS¹

23.7 months (95% CI: 19.1, 27.7) mPFS for RYBREVANT® + LAZCLUZE™ vs **16.6 months (95% CI: 14.8, 18.5)** for osimertinib (HR=0.70 [95% CI: 0.58, 0.85]; P=0.0002)

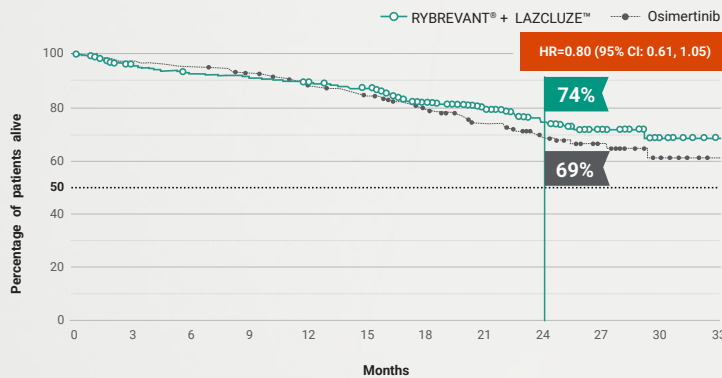
• In the non-registrational LAZCLUZE™ arm, mPFS was 18.5 months (95% CI: 14.8, 20.1)²

	No. at risk											
RYBREVANT® + LAZCLUZE™	429	391	357	332	291	244	194	106	60	33	8	0
Osimertinib	429	404	358	325	266	205	160	90	48	28	10	0

Secondary endpoint

INTERIM OVERALL SURVIVAL DATA^{1,2}

OS results were immature at this interim analysis (55% maturity); no trend towards detriment was observed.¹



74% of patients were alive at 24 months with RYBREVANT® + LAZCLUZE™ and 69% with osimertinib²

	No. at risk											
RYBREVANT® + LAZCLUZE™	429	403	389	382	374	360	293	201	122	58	14	0
Osimertinib	429	416	409	395	372	349	280	186	110	54	13	0

Study design: MARIPOSA was a randomized, active-controlled, multicenter Phase 3 trial assessing the efficacy of RYBREVANT® in combination with LAZCLUZE™. Eligible patients were required to have untreated locally advanced or metastatic NSCLC with either exon 19 deletions or exon 21 L858R substitution EGFR mutations identified by local testing, not amenable to curative therapy. Patients with asymptomatic or previously treated and stable intracranial metastases were eligible to enroll. Patients were randomized (2:2:1) to receive RYBREVANT® in combination with LAZCLUZE™ (N=429), osimertinib monotherapy (N=429), or LAZCLUZE™ monotherapy (an unapproved regimen for NSCLC) until disease progression or unacceptable toxicity. The evaluation of efficacy for the treatment of untreated metastatic NSCLC relied upon comparison between RYBREVANT® in combination with LAZCLUZE™, and osimertinib. The primary efficacy endpoint was PFS according to RECIST 1.1 as evaluated by BICR. OS was a secondary endpoint.^{1,2}

- **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, musculoskeletal pain, stomatitis, edema, VTE, paresthesia, fatigue, diarrhea, constipation, COVID-19, hemorrhage, dry skin, decreased appetite, pruritus, nausea, and ocular toxicity¹
- **Clinically relevant ARs** in <10% of patients who received RYBREVANT® + LAZCLUZE™ include ILD/pneumonitis (3.1%)¹

AR, adverse reaction; BICR, blinded independent central review; CI, confidence interval; EGFR, epidermal growth factor receptor; HR, hazard ratio; ILD, interstitial lung disease; IRR, infusion-related reaction; mPFS, median progression-free survival; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; VTE, venous thromboembolism.

INDICATION

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.

Please see Important Safety Information throughout. Please read full Prescribing Information for RYBREVANT® and full Prescribing Information for LAZCLUZE™.



IMPORTANT SAFETY INFORMATION

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™.

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.

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.

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™.

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, dose reduce or permanently discontinue both drugs 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.

Please see Important Safety Information throughout. Please read full [Prescribing Information](#) for RYBREVANT® and full [Prescribing Information](#) for LAZCLUZE™.



IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Promptly refer patients with new or worsening eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT® 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 ($\geq 20\%$) 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 ($\geq 2\%$) 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 $\geq 2\%$ 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).

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-464671v1

References:

1. RYBREVANT® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Cho BC, Lu S, Filip E, et al; MARIPOSA Investigators. Amivantamab plus lazertinib in previously untreated EGFR-mutated advanced NSCLC. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614