COMBINED POWER TO CHANGE THE GAME

RYBREVANT® + LAZCLUZE™, a New 1L Approach for *EGFR*+* Locally Advanced or Metastatic NSCLC

***Ex19del/L858R.**
1L, first-line; EGFR, epidermal growth factor receptor; ex19del, exon 19 deletion; NSCLC, non-small cell lung cancer.

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Please see Important Safety Information throughout this presentation.
Please see the full Prescribing Information for RYBREVANT® and LAZCLUZE™ at www.RYBREVANTHCP.com.

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

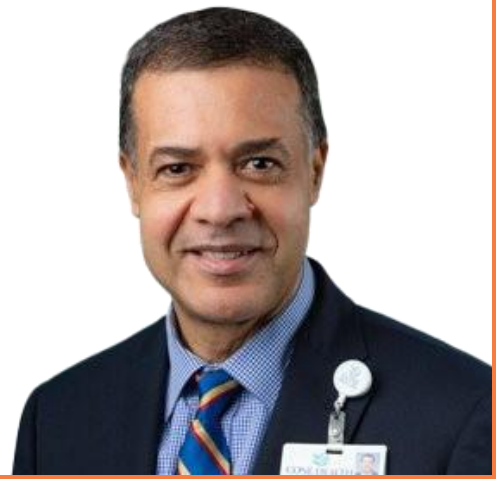
Panel Introductions

Ralph Boccia, MD

The Center for Cancer and Blood Disorders
Bethesda, Maryland

Mohamed K. Mohamed, MD, Ph.D.

Cone Health Cancer Center at Wesley Long Hospital
Greensboro, North Carolina



Sharon Zhong, Pharm.D., BCOP

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Program disclosures

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Objectives

Examine unmet needs for *EGFR*+ locally advanced or mNSCLC

Evaluate the clinical evidence from the phase 3 MARIPOSA trial that supports the combination RYBREVANT® (amivantamab-vmjw) and LAZCLUZE™ (lazertinib) as a 1L treatment for patients with *EGFR*+* locally advanced or mNSCLC

Highlight treatment outcomes with RYBREVANT® plus LAZCLUZE™, proactive supportive care strategies that may mitigate adverse reactions (ARs), and management of ARs through a patient case study and expert panel discussion

*Ex19del/L858R.
mNSCLC, metastatic NSCLC.

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UNMET NEEDS

in 1L Treatment of *EGFR*+ Locally Advanced or mNSCLC

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Despite advancements, there are many challenges associated with treating *EGFR*+ mNSCLC

Disease progression is inevitable and PFS outcomes are limited[1-9]

<20% of patients survive 5 years as demonstrated by real-world data[10]

PFS, progression-free survival.

1. Sequist LV et al. *J Clin Oncol*. 2013;31(27):3327-3334. 2. Rosell R et al. *Lancet Oncol*. 2012;13(3):239-246. 3. Wu Y-L et al. *Lancet Oncol*. 2017;18(11):1454-1466. 4. Park K et al. *Lancet Oncol*. 2016;17(5):577-589. 5. Passaro A et al. *Nat Cancer*. 2021;2(4):377-391. 6. Saito H et al. *Lancet Oncol*. 2019;20(5):625-635. 7. Nakagawa K et al. *Lancet Oncol*. 2019;20(12):1655-1669. 8. Soria J-C et al. [Supplementary material]. *N Engl J Med*. 2018;378(2):113-125. 9. Maemondo M et al. *N Engl J Med*. 2010;362(25):2380-2388. 10. Bazhenova L et al. *Lung Cancer*. 2021;162:154-161.

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Disease progression is inevitable and PFS outcomes are limited[1-9]

~25% to 40%

of patients with *EGFR*+ mNSCLC

never receive 2L therapy[10-12]*

*Range includes patients who died or discontinued the assigned therapy without receiving 2L therapy during follow-up.[10-12]

2L, second-line.

1. Sequist LV et al. *J Clin Oncol*. 2013;31(27):3327-3334. 2. Rosell R et al. *Lancet Oncol*. 2012;13(3):239-246. 3. Wu Y-L et al. *Lancet Oncol*. 2017;18(11):1454-1466. 4. Park K et al. *Lancet Oncol*. 2016;17(5):577-589. 5. Passaro A et al. *Nat Cancer*. 2021;2(4):377-391. 6. Saito H et al. *Lancet Oncol*. 2019;20(5):625-635. 7. Nakagawa K et al. *Lancet Oncol*. 2019;20(12):1655-1669. 8. Soria J-C et al. [Supplementary material]. *N Engl J Med*. 2018;378(2):113-125. 9. Maemondo M et al. *N Engl J Med*. 2010;362(25):2380-2388. 10. Nieva J et al. *Ann Oncol*. 2023;34(suppl 2):S774. 11. Lee JY et al. Presented at: IASLC 2022 World Lung Conference on Lung Cancer; August 69, 2022; Vienna, Austria. 12. Girard N et al. Presented at: the European Lung Cancer Congress; March 29-April 1, 2023; Copenhagen, Denmark. Poster 19P.

In a survey, patients with NSCLC ranked extending their lives as the most important attribute of treatment[1]*

MARIPOSA OS results were immature at the current analysis. As a result, no conclusions can be drawn on RYBREVANT® and LAZCLUZE™ OS benefit at this time.[2]

*Data come from a cross-sectional online survey of 160 adult patients, 30 care partners, and 150 clinicians conducted between March and May 2023. Survey questions were informed by a targeted literature review, qualitative interviews, and input from a steering committee that included 2 lung cancer physicians, an oncology nurse practitioner, a patient advocate, a patient, anda care partner. Descriptive statistics were generated and reported in aggregate. In addition to "extending their lives," patients ranked "quality of life" and "functional independence" as the next most important treatment attributes.[1]

OS, overall survival.

1. Data on file. Janssen Biotech, Inc. 2. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

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Maria

A spotlight on Maria’s journey: baseline presentation

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Maria

Diagnosis

1L Treatment

Follow-up

Clinical Information

History	Never smoker
Presentation	Fatigue; occasional back and hip pain; ECOG PS 0
Radiographic findings	4.7-cm mass in the left lower lobe, a right ischium metastasis
Histologic findings	Poorly differentiated adenocarcinoma. Diagnosis was confirmed using a CT-guided biopsy of the left lower lobe
Diagnosis	Stage IV NSCLC
Molecular findings	*EGFR* exon 19 deletion

Hypothetical patient and case.

CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status.

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RYBREVANT® (amivantamab-vmjw) in Combination With LAZCLUZE™ (lazertinib)

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

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.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

The safety population of RYBREVANT® with LAZCLUZE™ described in Warnings and Precautions was based on 421 patients in the MARIPOSA study.

Warnings and Precautions for RYBREVANT® with LAZCLUZE™ include infusion-related reactions, interstitial lung disease/pneumonitis, venous thromboembolism, dermatologic adverse reactions, ocular toxicity, and embryo-fetal toxicity.

RYBREVANT® + LAZCLUZE™ achieve multitargeted inhibition of EGFR and MET, with the addition of CNS penetration[1-3]

CNS, central nervous system; MET, mesenchymal-epithelial transition.

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. LAZCLUZE™. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 3. Yun J et al. *Clin Cancer Res*. 2019;25(8):2575-2587. 4. Cho BC et al. *Clin Lung Cancer*. 2023;24(2):89-97. 5. Press release. Johnson & Johnson. August 20, 2024. Accessed August 20, 2024. https://www.prnewswire.com/news-releases/rybrevant-amivantamab-vmjw-plus-lazcluze-lazertinib-approved-in-the-us-as-a-first-line-chemotherapy-free-treatment-for-patients-with-egfr-mutated-advanced-lung-cancer-302226047.html 6. Bettadapur A et al. *Infect Immun*. 2020;88(7):e00930-19. 7. Grugan KD et al. *MAbs*. 2017;9(1):114-126.

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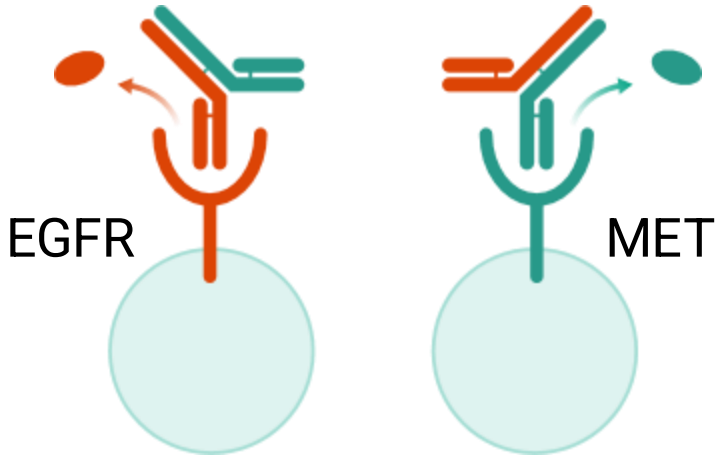
RYBREVANT®



Tumor Cells

BLOCKS[1]

EGFR and MET activity

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. LAZCLUZE™. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 3. Yun J et al. *Clin Cancer Res*. 2019;25(8):2575-2587. 4. Cho BC et al. *Clin Lung Cancer*. 2023;24(2):89-97. 5. Press release. Johnson & Johnson. August 20, 2024. Accessed August 20, 2024. https://www.prnewswire.com/news-releases/rybrevant-amivantamab-vmjw-plus-lazcluze-lazertinib-approved-in-the-us-as-a-first-line-chemotherapy-free-treatment-for-patients-with-egfr-mutated-advanced-lung-cancer-302226047.html 6. Bettadapur A et al. *Infect Immun*. 2020;88(7):e00930-19. 7. Grugan KD et al. *MAbs*. 2017;9(1):114-126.

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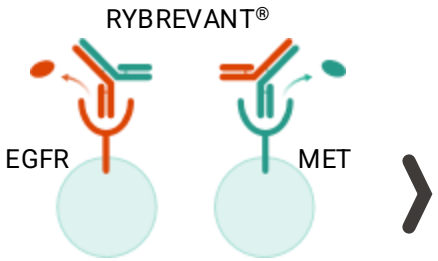
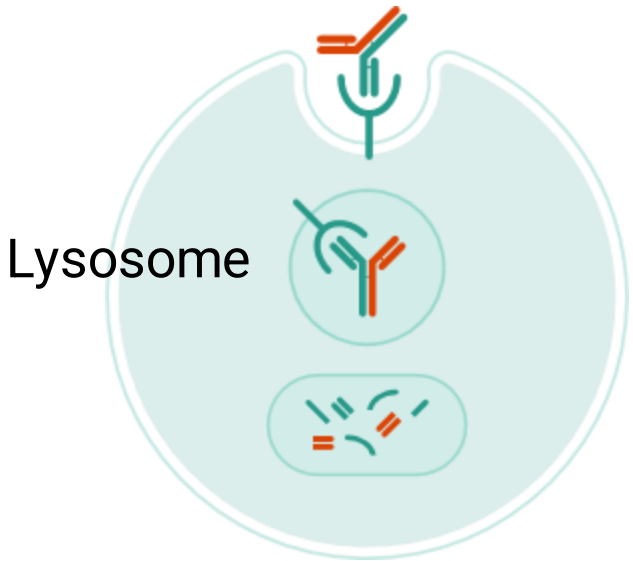


BLOCKS[1]
EGFR and MET activity

RYBREVANT®



Tumor Cell

DEGRADES[1]
EGFR and MET

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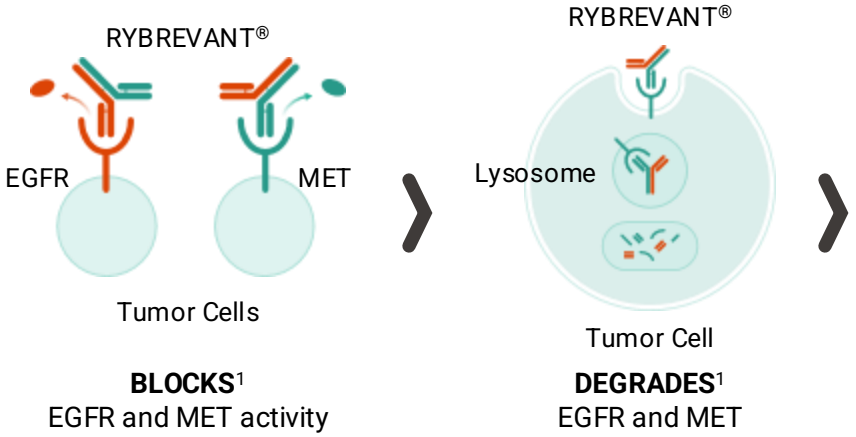

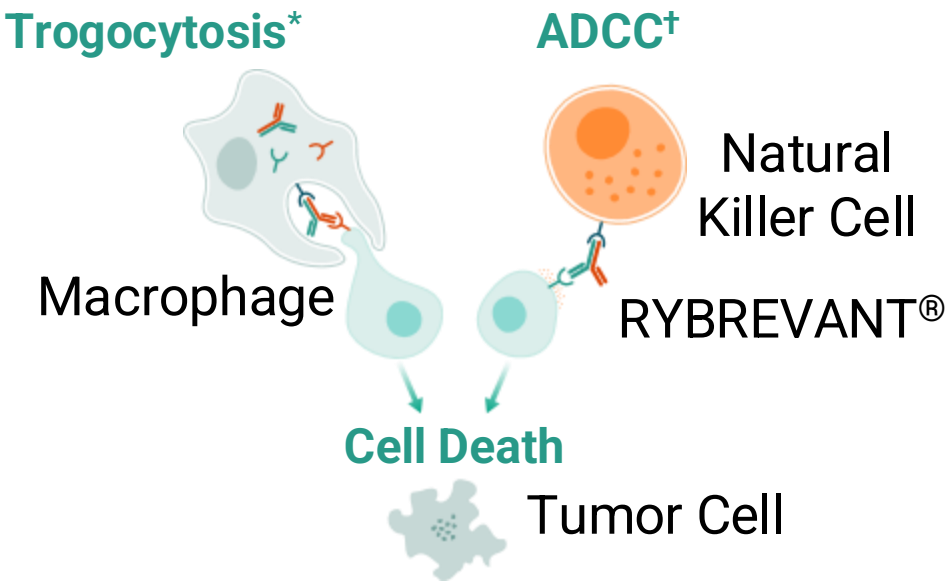

ACTIVATES[1,4*†] Immune cell responses

*Trogocytosis is a process in which 1 cell, in this case a macrophage, physically extracts and ingests cellular material of another cell.[6] †ADCC involves the release of cytotoxic granules that cause tumor cell death.[4,7] ADCC, antibody-dependent cellular cytotoxicity.

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. LAZCLUZE™. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 3. Yun J et al. *Clin Cancer Res*. 2019;25(8):2575-2587. 4. Cho BC et al. *Clin Lung Cancer*. 2023;24(2):89-97. 5. Press release. Johnson & Johnson. August 20, 2024. Accessed August 20, 2024. https://www.prnewswire.com/news-releases/rybrevant-amivantamab-vmjw-plus-lazcluze-lazertinib-approved-in-the-us-as-a-first-line-chemotherapy-free-treatment-for-patients-with-egfr-mutated-advanced-lung-cancer-302226047.html 6. Bettadapur A et al. *Infect Immun*. 2020;88(7):e00930-19. 7. Grugan KD et al. *MAbs*. 2017;9(1):114-126.

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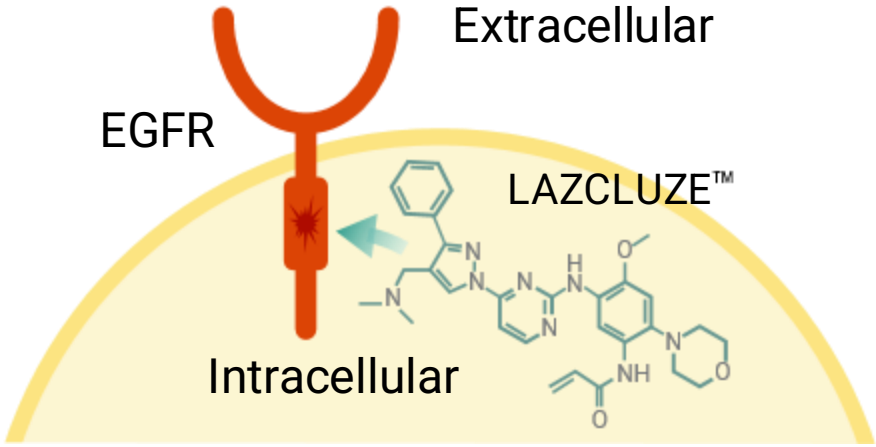
LAZCLUZE™ is a third-generation TKI that is a suitable combination partner for RYBREVANT® because of high selectivity for mutant EGFR, low selectivity for wild-type EGFR, and because it is CNS-penetrant[2,3]



INTRACELLULAR TARGETED[2-4]
EGFR inhibition

TKI, tyrosine kinase inhibitor.

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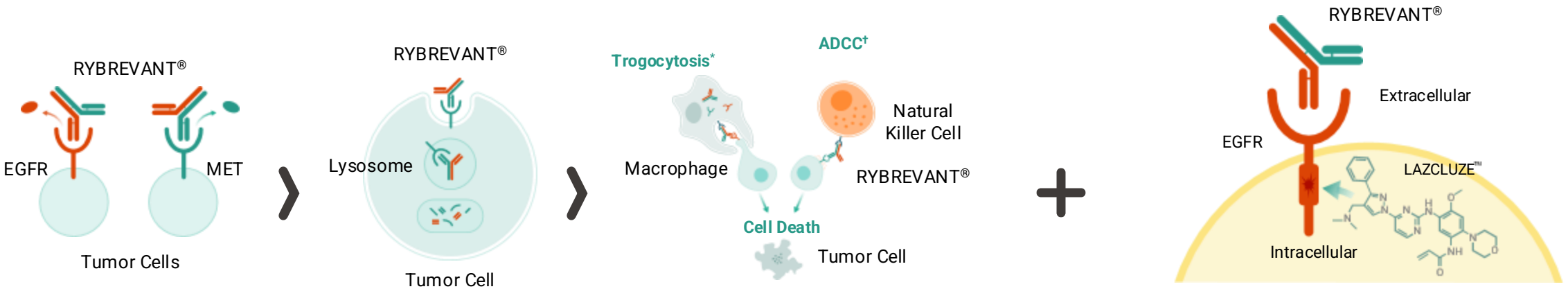

BLOCKS[1]
EGFR and MET activity

DEGRADES[1]
EGFR and MET

ACTIVATES[1,4*†]
Immune cell responses

INTRACELLULAR TARGETED[2-4]
EGFR inhibition

*Trogocytosis is a process in which 1 cell, in this case a macrophage, physically extracts and ingests cellular material of another cell.[6] †ADCC involves the release of cytotoxic granules that cause tumor cell death.[4,7]

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

Select a Panel Discussion Topic

A

What is the rationale for combining RYBREVANT® and LAZCLUZE™?

B

Why was LAZCLUZE™ chosen as a therapeutic partner for RYBREVANT®?

slido

Please download and install the Slido app on all computers you use

Select a Panel Discussion Topic

ⓘ Start presenting to display the poll results on this slide.

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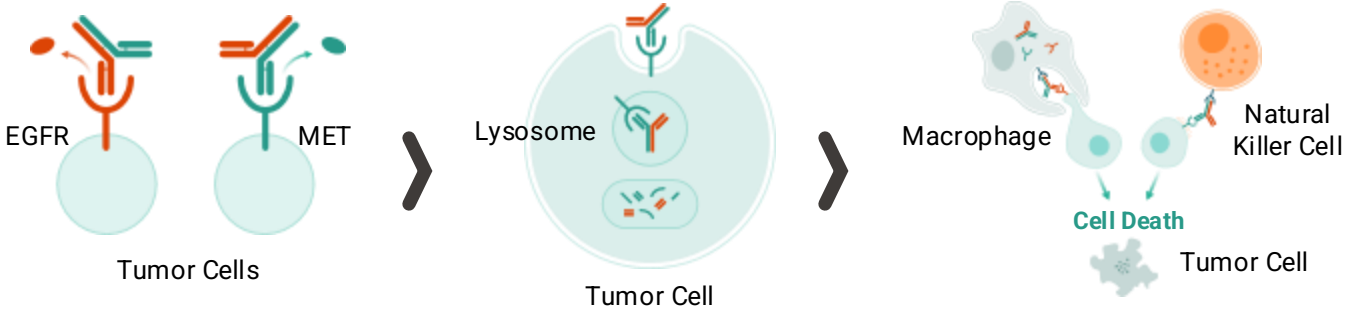

BLOCKS[1]
EGFR and MET activity

DEGRADES[1]
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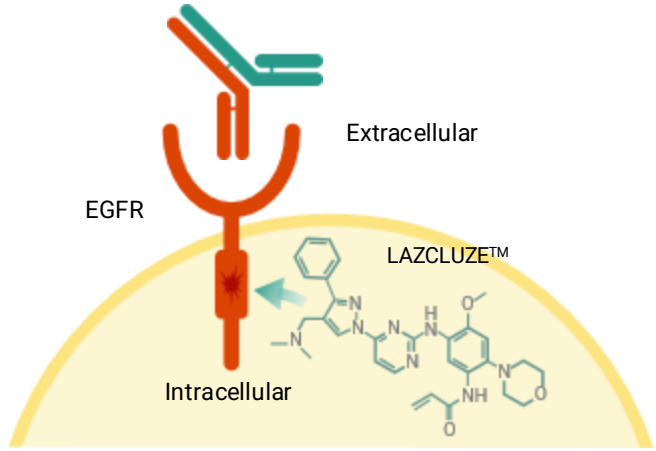
ACTIVATES[1,4*†]
Immune cell responses



INTRACELLULAR TARGETED[2-4]
EGFR inhibition

RYBREVANT® + LAZCLUZE™ is a chemotherapy-sparing combination that provides complementary extra- and intracellular antitumor activity and CNS penetration[1-4]

*Trogocytosis is a process in which 1 cell, in this case a macrophage, physically extracts and ingests cellular material of another cell.[6] †Antibody-dependent cellular cytotoxicity involves the release of cytotoxic granules that cause tumor cell death.[4,7]

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

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

First-line amivantamab-vmjw (RYBREVANT®) + lazertinib (LAZCLUZE™) is an NCCN category 1 therapy option in metastatic *EGFR*m (exon 19 deletion, exon 21 L858R mutation) NSCLC

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MARIPOSA: Evaluating the first and only 1L multitargeted combination in *EGFR*+ mNSCLC vs osimertinib

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MARIPOSA was a randomized, active-controlled, multicenter study and the largest phase 3 trial of patients with *EGFR*+ disease[1-13]*

Key Eligibility Criteria
- Locally advanced or mNSCLC
- Treatment-naive
- Documented *EGFR* ex19del or L858R
- ECOG PS 0 or 1

Randomization
2:2:1
(N=1,074)

- **RYBREVANT®† + LAZCLUZE™‡** (n=429; open-label)
- **Osimertinib§** (n=429; blinded)
- **Nonregistrational data set**: **LAZCLUZE™‡‖** (n=216; blinded)

Primary endpoint:
PFS by BICR per RECIST v1.1

Secondary endpoints:
- OS
- ORR by BICR
- DOR by BICR
- Safety

Baseline and serial brain MRI was conducted for all patients to assess intracranial response rate and duration¶

*MARIPOSA was the largest phase 3 trial that evaluated 1L treatment in patients with *EGFR*+ mNSCLC as of July 2024.[2,5-13] †RYBREVANT® 1,050 mg (patients <80 kg) or 1,400 mg (patients ≥80 kg) was administered intravenously (IV) once a week through 5 weeks, then every 2 weeks thereafter starting at Week 7 until disease progression or unacceptable toxicity.[1] ‡LAZCLUZE™ 240 mg was administered orally once daily.[1] §Osimertinib 80 mg was administered orally once daily.[1] ‖The LAZCLUZE™ monotherapy arm was included to assess the contribution of the components.[2] ¶Brain MRI was performed at baseline and either every 8 weeks for the first 30 months and every 12 weeks thereafter for patients with a history of brain metastases or every 24 weeks for patients without a history.[1,2]

BICR, blinded independent central review; DOR, duration of response; MRI, magnetic resonance imaging; ORR, overall response rate; RECIST, Response Evaluation Criteria in Solid Tumors.

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Cho BC et al; MARIPOSA Investigators. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614 3. Cho BC et al; MARIPOSA Investigators. *N Engl J Med*. 2024. Supplementary Appendix. doi:10.1056/NEJMoa2403614 4. Yang JCH et al. *Lancet Oncol*. 2015;16(2):141-151. 5. Wu YL et al. *Lancet Oncol*. 2017;18:1454-1466. 6. Rosell R et al. *Lancet Oncol*. 2012;13:239-246. 7. Nacagawa K et al. *Lancet Oncol*. 2019;20(12):1655-1669. 8. Kawashima Y et al. *Lancet Respir Med*. 2022;10(1):72-82. 9. Douillard JY et al. *Br J Cancer*. 2014;110(1):55-62. 10. Mok TS et al. *N Engl J Med*. 2009;361:947-957. 11. Soria JC et al. *N Engl J Med*. 2018;378(2):113-125. 12. Planchard D et al. *N Engl J Med*. 2023;389(21):1935-1948. 13. Mok TS et al. *N Engl J Med*. 2017;376(7):629-640.

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

Baseline characteristics were well-balanced across treatment types

Cho BC et al; MARIPOSA Investigators. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614

Characteristic	RYBREVANT® + LAZCLUZE™ (n=429)	Osimertinib (n=429)
Median age, years (range)	64 (25–88)	63 (28–88)
Female, n (%)	275 (64)	251 (59)
Race, n (%)		
Asian	250 (58)	251 (59)
White	164 (38)	165 (38)
Other*	15 (3)	13 (3)
ECOG PS 0, n (%)	141 (33)	149 (35)
ECOG PS 1, n (%)	288 (67)	280 (65)
History of smoking, n (%)	130 (30)	134 (31)
History of brain metastases, n (%)	178 (41)	172 (40)
EGFR mutation type,† n (%)		
Ex19del	258 (60)	257 (60)
L858R	172 (40)	172 (40)
Adenocarcinoma subtype, n (%)	417 (97)	415 (97)

*Other includes American Indian or Alaska Native, Black or African American, Native Hawaiian or Pacific Islander, multiple, and unknown.
†One patient in the RYBREVANT® + LAZCLUZE™ arm had both ex19del and L858R.
Cho BC et al; MARIPOSA Investigators. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614

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

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Cho BC et al; MARIPOSA Investigators. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614

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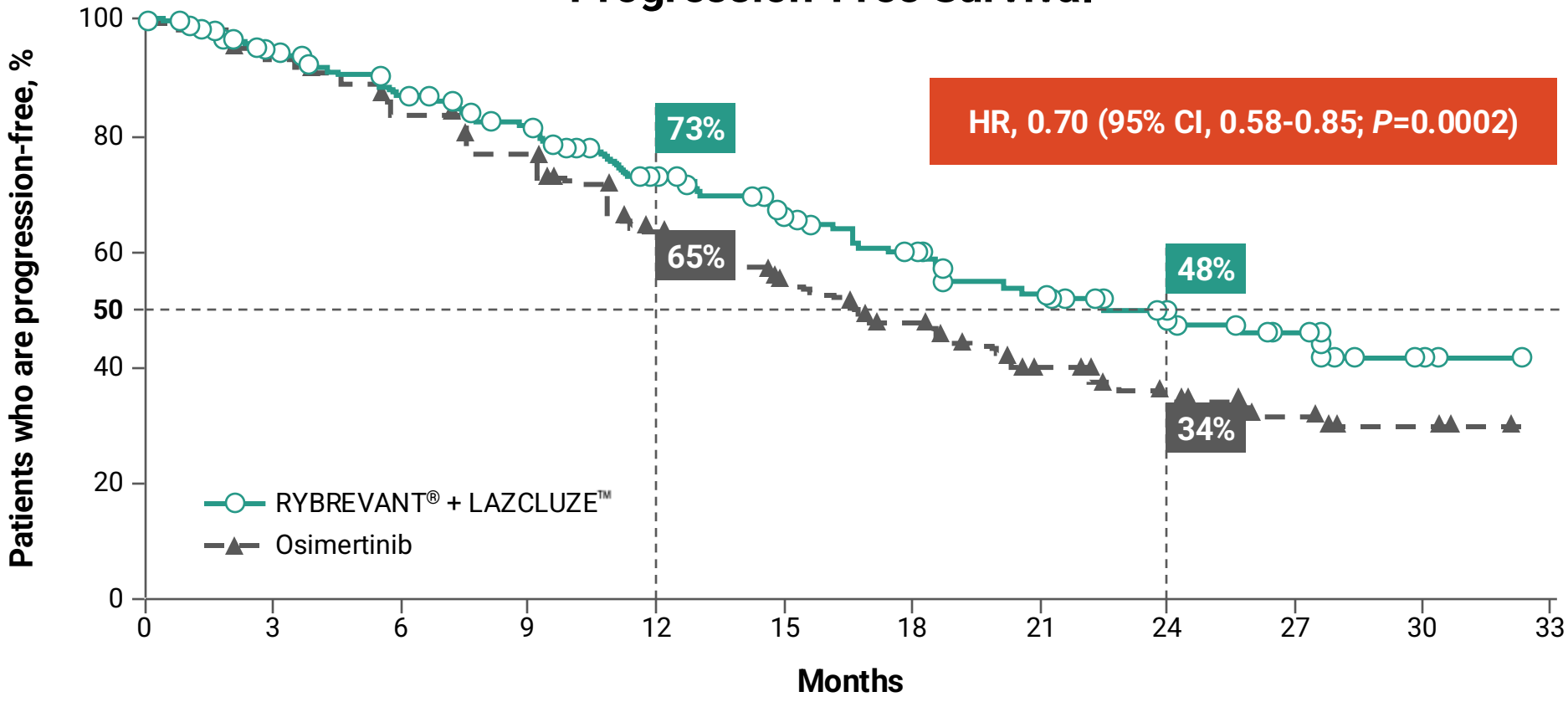
Please see Important Safety Information throughout this presentation.
Please see the full Prescribing Information for RYBREVANT® and LAZCLUZE™ at www.RYBREVANTHCP.com.

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

Progression-Free Survival[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

CI, confidence interval; HR, hazard ratio.

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Cho BC et al; MARIPOSA Investigators. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614

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

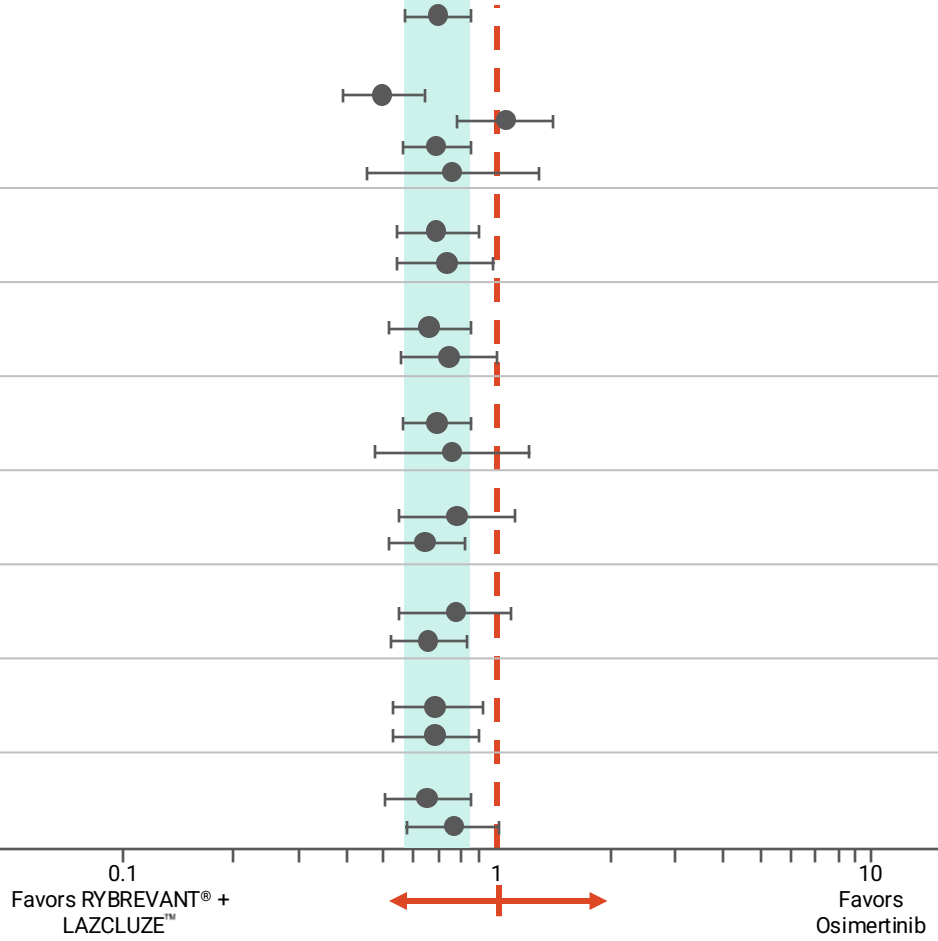
- **7.1-month improvement in mPFS vs osimertinib**[1]
  - **23.7 months** (95% CI: 19.1, 27.7) mPFS with RYBREVANT® + LAZCLUZE™ vs **16.6 months** (95% CI: 14.8, 18.5) with osimertinib
- **In the nonregistrational LAZCLUZE™ arm, mPFS was 18.5 months (95% CI: 14.8, 20.1)**[2]

mPFS, median progression-free survival.

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Cho BC et al; MARIPOSA Investigators. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614

PFS Results in Prespecified Subgroups

Subgroup	HR for disease progression or death (95% CI)	Events/n: RYBREVANT® + LAZCLUZE™	Events/n: Osimertinib
All randomized patients	0.70 (0.58–0.85)	192/429	252/429
Age category			
<65 years	0.50 (0.39–0.65)	94/235	153/237
≥65 years	1.06 (0.80–1.41)	98/194	99/192
<75 years	0.70 (0.57–0.85)	165/378	220/376
≥75 years	0.77 (0.46–1.30)	27/51	32/53
Sex			
Female	0.70 (0.55–0.90)	112/275	140/251
Male	0.74 (0.55–0.98)	80/154	112/178
Race			
Asian	0.67 (0.52–0.86)	105/250	144/251
Non–Asian	0.75 (0.56–0.99)	85/117	108/177
Weight category			
<80 kg	0.70 (0.57–0.86)	161/376	209/368
≥80 kg	0.77 (0.48–1.22)	31/53	43/61
ECOG PS			
0	0.79 (0.56–1.12)	56/141	76/149
1	0.66 (0.52–0.82)	136/288	176/280
History of smoking			
Yes	0.78 (0.56–1.08)	67/130	79/134
No	0.67 (0.53–0.84)	125/299	173/295
History of brain metastases			
Yes	0.69 (0.53–0.92)	94/178	111/172
No	0.69 (0.53–0.89)	98/251	141/257
***EGFR* mutation**			
Ex19del	0.65 (0.51–0.85)	101/257	142/257
L858R	0.78 (0.59–1.02)	90/171	110/172



This was a prespecified analysis and was not powered to show statistical significance.

Cho BC et al; MARIPOSA Investigators. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614

Biomarkers of high-risk disease: a secondary analysis*

High-risk features at baseline were identified in 89% of patients with baseline ctDNA available for NGS of pathogenic alterations (n=636).[1,2]

This analysis is not included in the Prescribing Information for RYBREVANT® and LAZCLUZE™. This was a post hoc exploratory analysis and was not powered to show statistical significance.

*In MARIPOSA, pathogenic alterations were identified by NGS using ctDNA from blood with Guardant360 CDx at baseline. Ex19del and L858R ctDNA in blood was analyzed at baseline with Biodesix ddPCR. This exploratory analysis included all randomized patients who had 1 or more biomarker assessments. Subgroup analyses of efficacy endpoints were carried out using statistical methods for the primary analysis of the general MARIPOSA population.

ctDNA, circulating tumor DNA; ddPCR, droplet digital polymerase chain reaction; NGS, next-generation sequencing.

1. Felip E et al. *Ann Oncol*. 2024. doi:10.1016/j.annonc.2024.05.541 2. Cho BC et al; MARIPOSA Investigators. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614

31%

reduction*

in risk of progression or death in patients with **brain metastases** at baseline treated with RYBREVANT® + LAZCLUZE™ (n=178) vs osimertinib (n=172) (HR: 0.69 [95% CI: 0.53, 0.92])[1,2]

- mPFS of RYBREVANT® + LAZCLUZE™ was 18.3 months (95% CI: 16.6, 23.7) and 13.0 months (95% CI: 12.2, 16.4) with osimertinib

This analysis is not included in the Prescribing Information for RYBREVANT® and LAZCLUZE™. This was a post hoc exploratory analysis and was not powered to show statistical significance.

*In MARIPOSA, pathogenic alterations were identified by NGS using ctDNA from blood with Guardant360 CDx at baseline. Ex19del and L858R ctDNA in blood was analyzed at baseline with Biodesix ddPCR. This exploratory analysis included all randomized patients who had one or more biomarker assessments. Subgroup analyses of efficacy endpoints were carried out using statistical methods for the primary analysis of the general MARIPOSA population.

1. Felip E et al. Ann Oncol. 2024. doi:10.1016/j.annonc.2024.05.541 2. Cho BC et al; MARIPOSA Investigators. *N Engl J Med.* 2024. Supplementary Appendix. doi:10.1056/NEJMoa2403614

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Please see the full Prescribing Information for RYBREVANT® and LAZCLUZE™ at www.RYBREVANTHCP.com.

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

42%

reduction*

in risk of progression or death in patients with **liver metastases** at baseline treated with RYBREVANT® + LAZCLUZE™ (n=64) vs osimertinib (n=72) (HR: 0.58 [95% CI: 0.37, 0.91])

- mPFS of RYBREVANT® + LAZCLUZE™ was 18.2 months (95% CI: 13.1, NE) and 11.0 months (95% CI: 7.4, 12.8) with osimertinib

This analysis is not included in the Prescribing Information for RYBREVANT® and LAZCLUZE™. This was a post hoc exploratory analysis and was not powered to show statistical significance.

*In MARIPOSA, pathogenic alterations were identified by NGS using ctDNA from blood with Guardant360 CDx at baseline. Ex19del and L858R ctDNA in blood was analyzed at baseline with Biodesix ddPCR. This exploratory analysis included all randomized patients who had one or more biomarker assessments. Subgroup analyses of efficacy endpoints were carried out using statistical methods for the primary analysis of the general MARIPOSA population.

NE, not estimable.

Felip E et al. *Ann Oncol*. 2024. doi:10.1016/j.annonc.2024.05.541

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35%

reduction*

in risk of progression or death in patients with ***TP53* co-mutations** treated with RYBREVANT® + LAZCLUZE™ (n=149) vs osimertinib (n=144) (HR: 0.65 [95% CI: 0.48, 0.87])

- mPFS of RYBREVANT® + LAZCLUZE™ was 18.2 months (95% CI: 15.3, 22.1) and 12.9 months (95% CI: 11.1, 14.7) with osimertinib

This analysis is not included in the Prescribing Information for RYBREVANT® and LAZCLUZE™. This was a post hoc exploratory analysis and was not powered to show statistical significance.

*In MARIPOSA, pathogenic alterations were identified by NGS using ctDNA from blood with Guardant360 CDx at baseline. Ex19del and L858R ctDNA in blood was analyzed at baseline with Biodesix ddPCR. This exploratory analysis included all randomized patients who had one or more biomarker assessments. Subgroup analyses of efficacy endpoints were carried out using statistical methods for the primary analysis of the general MARIPOSA population.

TP53, tumor protein 53.

Felip E et al. *Ann Oncol*. 2024. doi:10.1016/j.annonc.2024.05.541

32%

reduction*

in risk of progression or death in patients with **ctDNA** at baseline by ddPCR† treated with RYBREVANT® + LAZCLUZE™ (n=231) vs osimertinib (n=240) (HR: 0.68 [95% CI: 0.53, 0.86])

- mPFS of RYBREVANT® + LAZCLUZE™ was 20.3 months (95% CI: 16.6, 24.0) and 14.8 months (95% CI: 12.9, 16.5) with osimertinib

This analysis is not included in the Prescribing Information for RYBREVANT® and LAZCLUZE™. This was a post hoc exploratory analysis and was not powered to show statistical significance.

*In MARIPOSA, pathogenic alterations were identified by NGS using ctDNA from blood with Guardant360 CDx at baseline. Ex19del and L858R ctDNA in blood was analyzed at baseline with Biodesix ddPCR. This exploratory analysis included all randomized patients who had one or more biomarker assessments. Subgroup analyses of efficacy endpoints were carried out using statistical methods for the primary analysis of the general MARIPOSA population. †Consistent results were seen in patients with detectable ctDNA using the NGS assay (HR: 0.71 [95% CI: 0.57, 0.89]).

Felip E et al. *Ann Oncol*. 2024. doi:10.1016/j.annonc.2024.05.541

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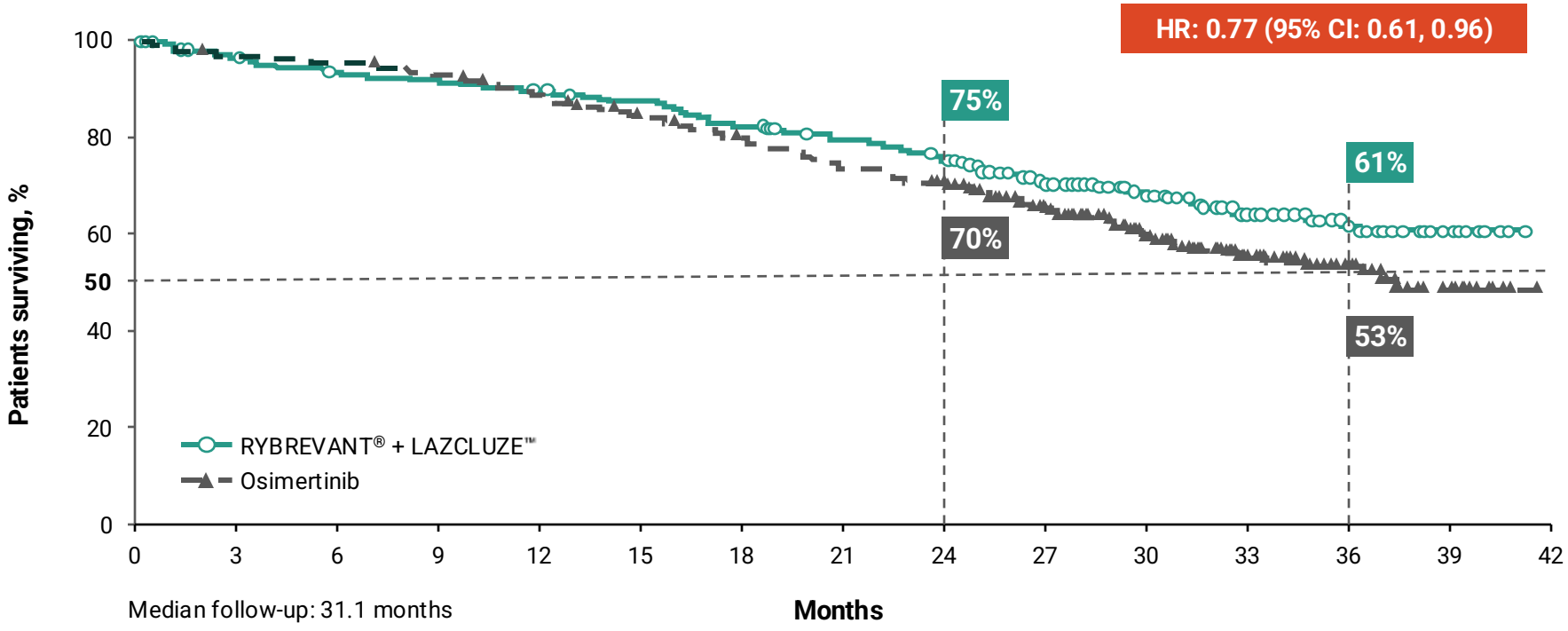
Interim OS results

Overall Survival[1-3]

OS results were immature at this interim analysis (55% of prespecified events); no trend towards a detriment was observed. In a longer follow-up (82% of prespecified events), updated OS results were:



No. at risk															
RYBREVANT® + LAZCLUZE™	429	404	390	383	375	363	343	327	307	245	173	112	51	15	0
Osimertinib	429	416	409	396	373	353	331	310	285	224	145	91	45	13	0

61% of patients were alive at 36 months with RYBREVANT® + LAZCLUZE™ and 53% with osimertinib

The final OS analysis has not yet been formally tested.

1. RYBREVANT® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Gadgeel SM et al. Presented at: World Conference on Lung Cancer 2024; September 7-10, 2024; San Diego, CA. 3. Data on file. Janssen Biotech, Inc.

High and durable responses with a chemotherapy-sparing combination

RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

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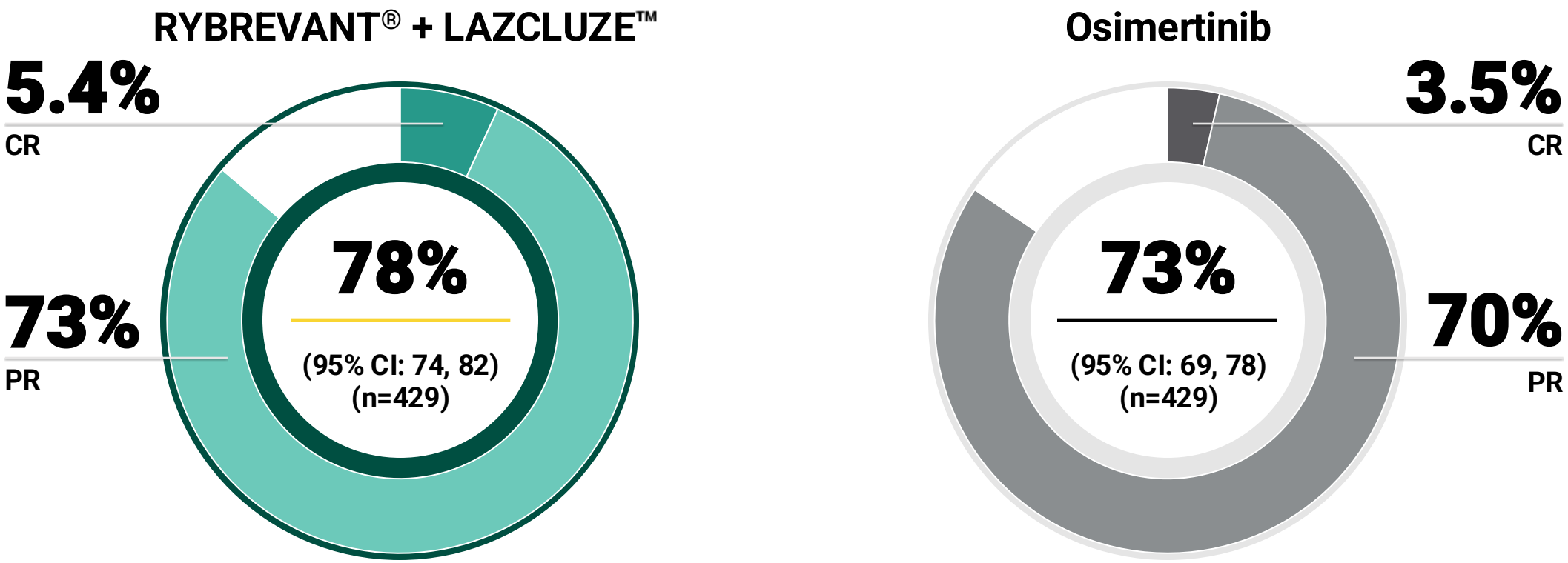
Overall Response Rate



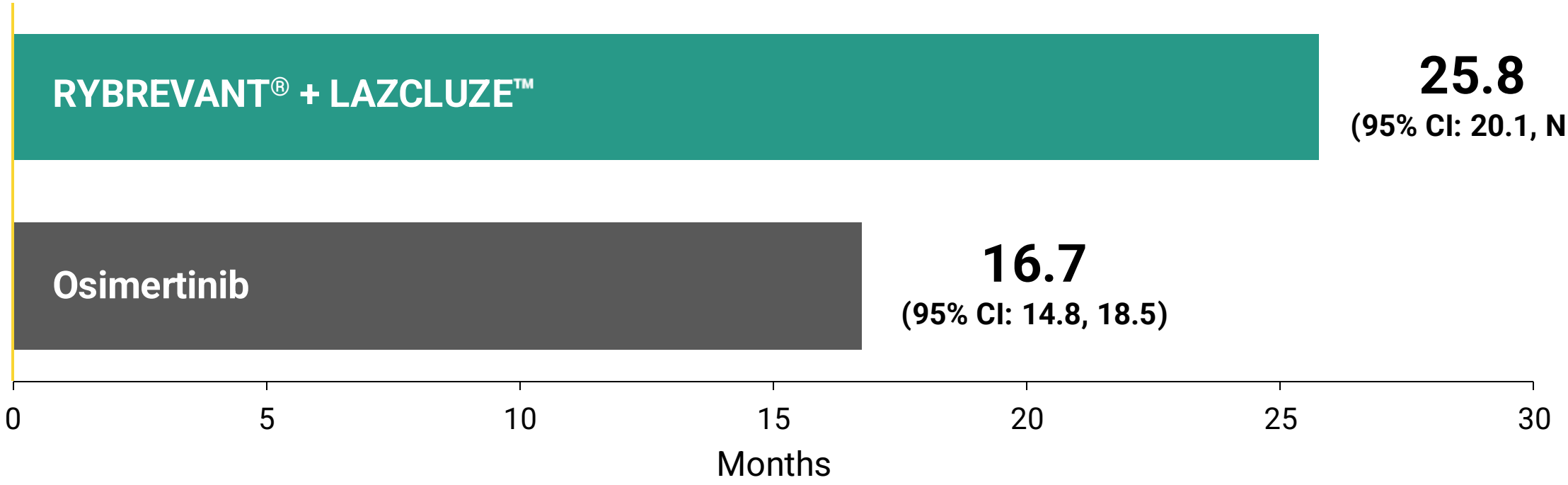
~1.5X CR with RYBREVANT® + LAZCLUZE™

This was a prespecified analysis and was not powered to show statistical significance.

CR, complete response; PR, partial response.

RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

Median Duration of Response



~1.5X mDOR with RYBREVANT® + LAZCLUZE™

This was a prespecified analysis and was not powered to show statistical significance.

mDOR, median duration of response.

RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

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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

High intracranial ORR with durable intracranial DOR

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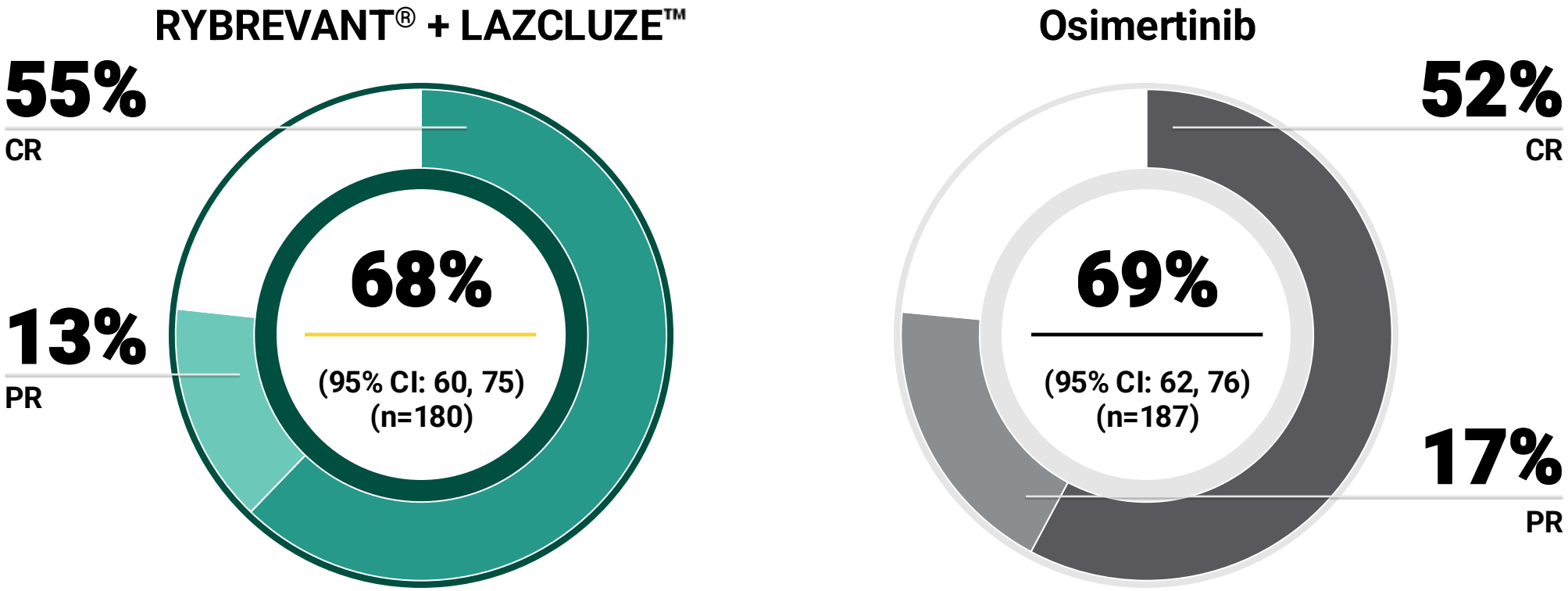
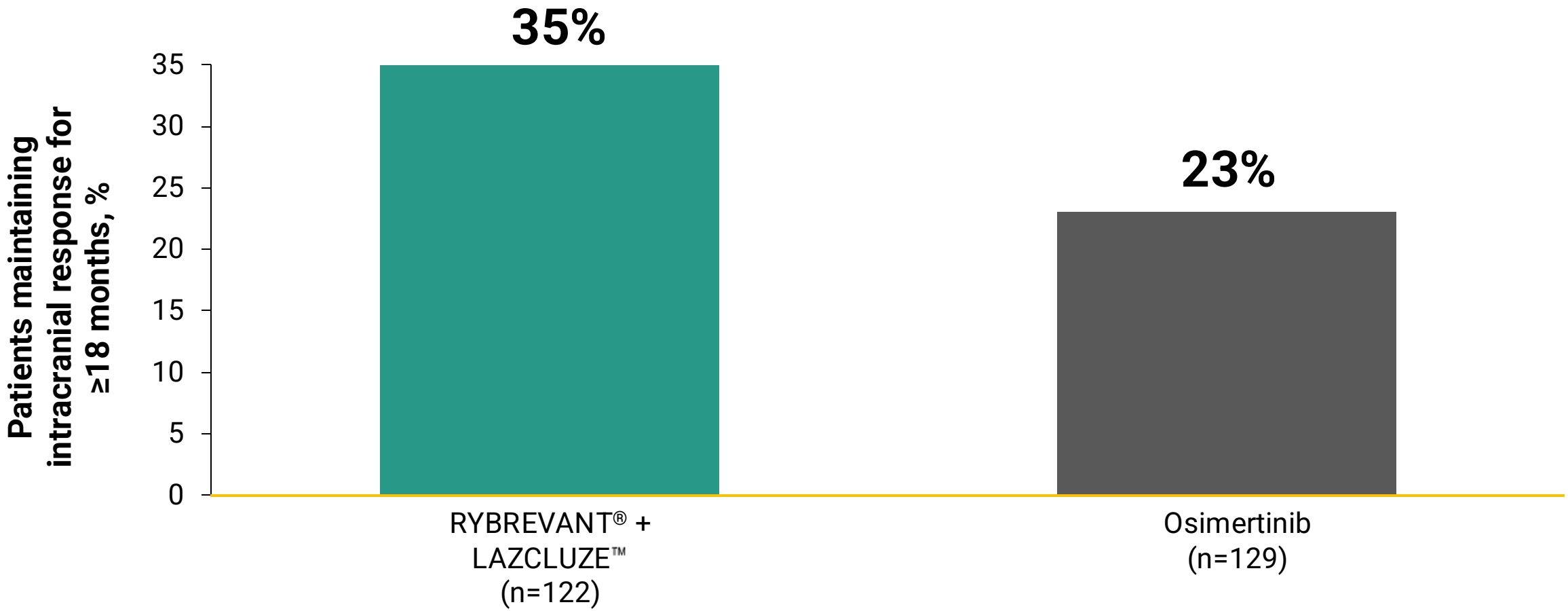
Intracranial Overall Response Rate in Patients With Intracranial Lesions at Baseline



This was a prespecified exploratory analysis and was not powered to show statistical significance.

RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

Intracranial Duration of Response in Confirmed Responders With Intracranial Lesions at Baseline



This was a prespecified exploratory analysis and was not powered to show statistical significance.

RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

Safety profile of RYBREVANT® + LAZCLUZE™

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ARs occurring in ≥10% of patients

	RYBREVANT® + LAZCLUZE™ (n=421)		Osimertinib (n=428)	
	All Grades, %	Grades 3 or 4, %	All Grades, %	Grades 3 or 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				
IRR†	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

*Grouped terms. †Applicable for RYBREVANT only.
IRR, infusion-related reaction.
RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

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ARs occurring in ≥10% of patients (cont)

	RYBREVANT® + LAZCLUZE™ (n=421)		Osimertinib (n=428)	
	All Grades, %	Grades 3 or 4, %	All Grades, %	Grades 3 or 4, %
Vascular disorders				
VTE*	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.
VTE, venous thromboembolism.
RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

- **The majority of ARs were Grades 1 and 2**[1]
- **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 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)[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 toxicity[1]
- **Clinically relevant ARs** in <10% of patients who received RYBREVANT® + LAZCLUZE™ included ILD/pneumonitis (3.1%)[1]

ILD, interstitial lung disease.

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Cho BC et al; MARIPOSA Investigators. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614

Select laboratory abnormalities (≥20%) that worsened from baseline

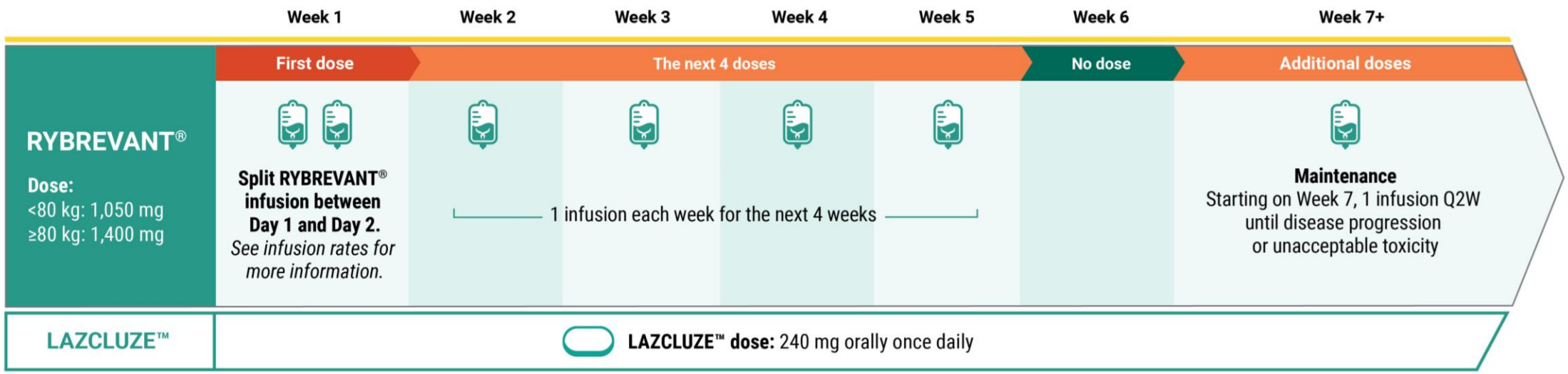
Laboratory abnormality*	RYBREVANT® + LAZCLUZE™ (n=421)		Osimertinib (n=428)	
	All Grades, %	Grades 3 or 4, %	All Grades, %	Grades 3 or 4, %
Chemistry				
Decreased albumin	89	8	22	0.2
Increased ALT	65	7	29	2.6
Increased AST	52	3.8	36	1.9
Increased alkaline phosphatase	45	0.5	15	0.5
Decreased calcium (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 1 posttreatment value for the specific lab test.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase.
RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

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

RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

Recommended dosing schedule for RYBREVANT® + LAZCLUZE™ [1,2]



RYBREVANT®[1]

- **The recommended dose of RYBREVANT® is based on baseline body weight and administered as an IV infusion after dilution**

With LAZCLUZE™[1,2]

- **When given with LAZCLUZE™, administer LAZCLUZE™ any time before RYBREVANT® when given on the same day**

Refer to the full Prescribing Information for LAZCLUZE™ for recommended dosing information
Refer to the full Prescribing Information for RYBREVANT® and LAZCLUZE™ for recommended dose modifications in the event of ARs.

Q2W, every 2 weeks.

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. LAZCLUZE™. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

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Please see the full Prescribing Information for RYBREVANT® and LAZCLUZE™ at www.RYBREVANTHCP.com.

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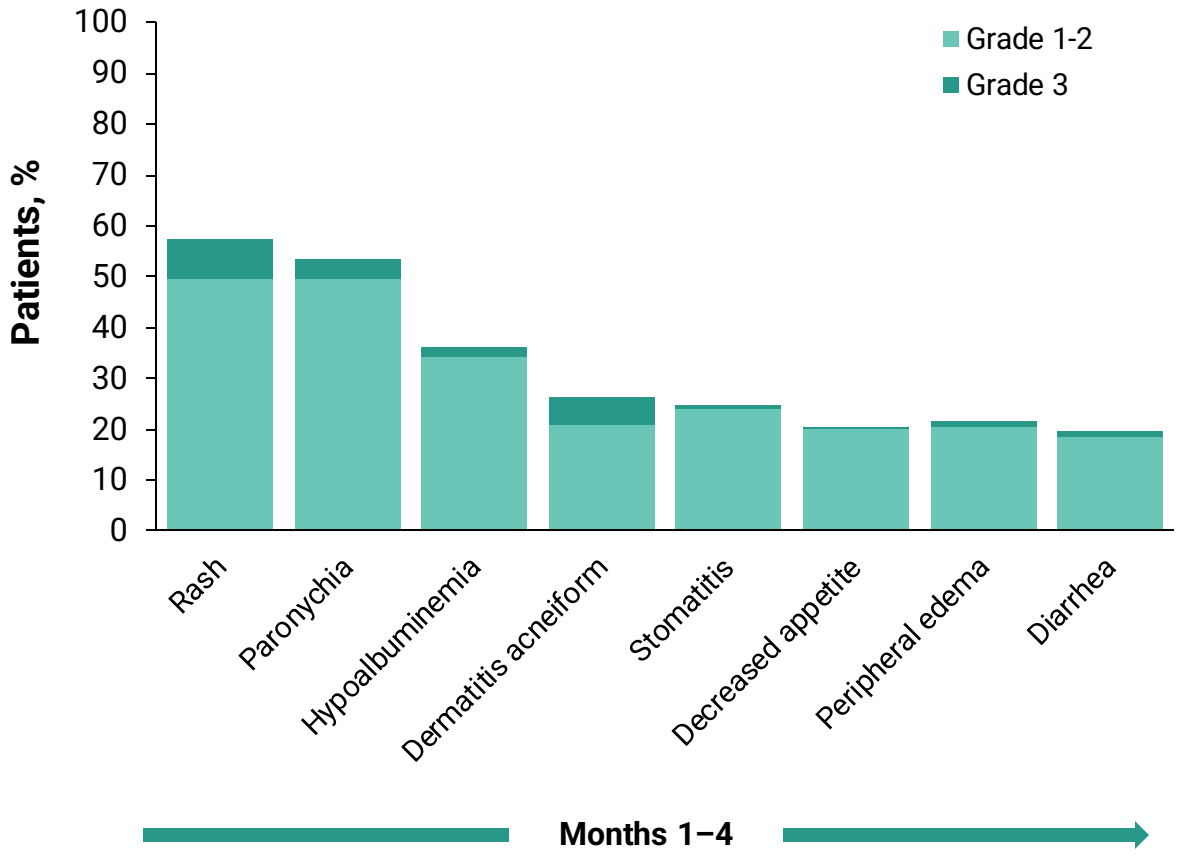
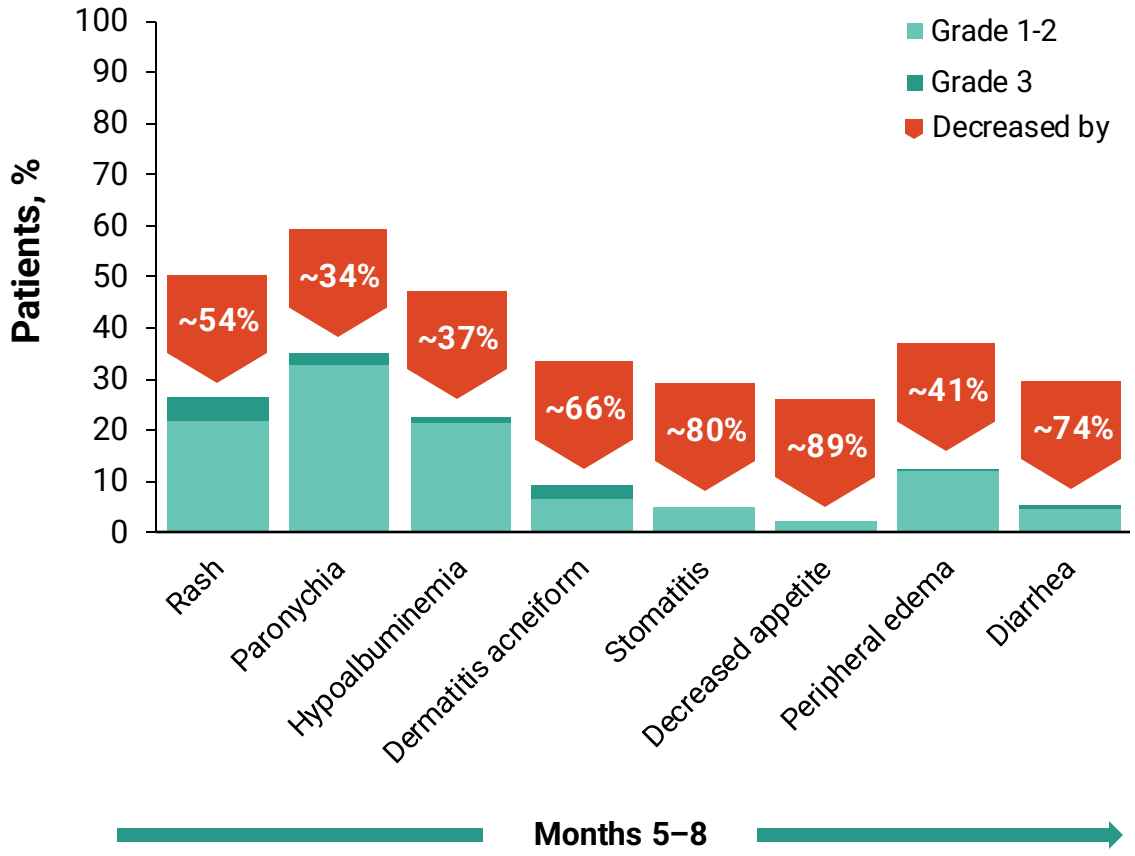
Key ARs occurred most frequently during the first 4 months and declined over the next 4 months*

These analyses are not in the Prescribing Information for RYBREVANT® and LAZCLUZE™. These are post hoc exploratory analyses.

*Patients with PFS events or censored in the first 4 months were excluded from this analysis.
Data on file. Janssen Biotech, Inc.

Rates of Key ARs During Months 1–4 and 5–8*





These analyses are not in the Prescribing Information for RYBREVANT® and LAZCLUZE™. These are post hoc exploratory analyses.

*Patients with PFS events or censored in the first 4 months were excluded from this analysis.
Data on file. Janssen Biotech, Inc.

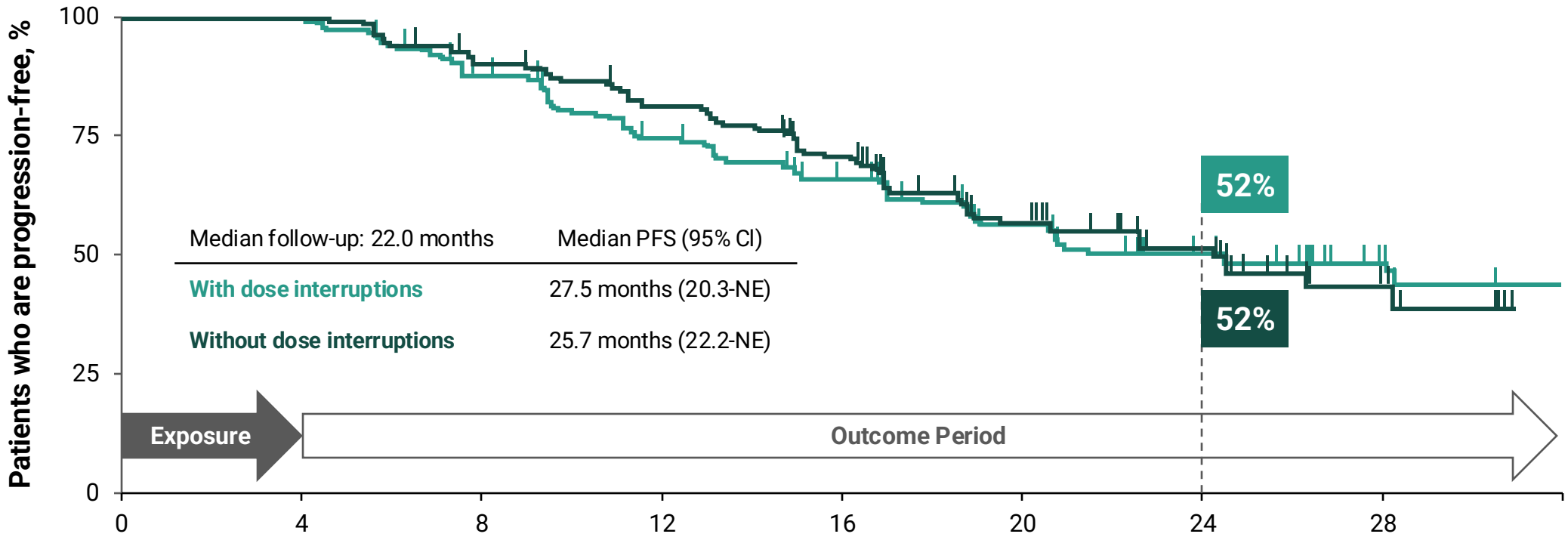
Association of dose interruptions with PFS after 4 months*†

These analyses are not in the Prescribing Information for RYBREVANT® and LAZCLUZE™. These are post hoc exploratory analyses.

*In this descriptive analysis of PFS, the HR by multivariable analysis (via multivariate Cox proportional hazards model, which only included patients still at risk of PFS at 4 months) adjusted for age, ECOG PS, *EGFR* mutation type, Asian race, and history of brain metastases was 1.06 (95% CI: 0.73, 1.44). †To minimize bias, outcomes (such as progression events or deaths, which could occur before interruptions leading to outcome-based selection bias) were evaluated after the first 4 months. Patients who discontinued the study, had disease progression, or died in the first 4 months were not evaluated, as they were not in the study by the cutoff timepoint (and the outcome event may have occurred prior to the interruption).

Campelo MRG et al. Presented at: European Lung Cancer Congress 2024; March 20-23, 2024; Prague, Czech Republic.

PFS With and Without Dose Interruption*†



No. at risk								
With dose interruptions	188	188	163	136	116	71	32	3
Without dose interruptions	190	190	171	154	125	79	33	6

These analyses are not in the Prescribing Information for RYBREVANT® and LAZCLUZE™. These are post hoc exploratory analyses.

*In this descriptive analysis of PFS, the HR by multivariable analysis (via multivariate Cox proportional hazards model, which only included patients still at risk of PFS at 4 months) adjusted for age, ECOG PS, *EGFR* mutation type, Asian race, and history of brain metastases was 1.06 (95% CI: 0.73, 1.44). †To minimize bias, outcomes (such as progression events or deaths, which could occur before interruptions leading to outcome-based selection bias) were evaluated after the first 4 months. Patients who discontinued the study, had disease progression, or died in the first 4 months were not evaluated, as they were not in the study by the cutoff timepoint (and the outcome event may have occurred prior to the interruption).

Campelo MRG et al. Presented at: European Lung Cancer Congress 2024; March 20-23, 2024; Prague, Czech Republic.

Association of dose interruptions with PFS*†

- **For patients who were treated with RYBREVANT® + LAZCLUZE™, median PFS after 4 months was similar between those with and without dose interruptions**
  - In this analysis, dose interruption is defined as a skipped dose that is not made up; this population may also include patients who had a dose reduction or drug discontinuation

These analyses are not in the Prescribing Information for RYBREVANT® and LAZCLUZE™. These are post hoc exploratory analyses.

*In this descriptive analysis of PFS, the HR by multivariable analysis (via multivariate Cox proportional hazards model, which only included patients still at risk of PFS at 4 months) adjusted for age, ECOG PS, *EGFR* mutation type, Asian race, and history of brain metastases was 1.06 (95% CI: 0.73, 1.44). †To minimize bias, outcomes (such as progression events or deaths, which could occur before interruptions leading to outcome-based selection bias) were evaluated after the first 4 months. Patients who discontinued the study, had disease progression, or died in the first 4 months were not evaluated, as they were not in the study by the cutoff timepoint (and the outcome event may have occurred prior to the interruption).

Campelo MRG et al. Presented at: European Lung Cancer Congress 2024; March 20-23, 2024; Prague, Czech Republic.

IMPORTANT SAFETY INFORMATION:
Infusion-Related Reactions

Occurrence

RYBREVANT® can cause IRRs

- Signs and symptoms of IRRs include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting
- The median time to IRR onset is approximately 1 hour
- In MARIPOSA, IRRs were Grade 3 in 5% of patients and Grade 4 in 1% of patients

IRR Events in MARIPOSA leading to:	%
Infusion modifications	54
Dose reduction of RYBREVANT®	0.7
Permanent discontinuation of RYBREVANT®	4.5

In MARIPOSA, most IRRs occurred during the first infusion (Week 1, Day 1) and rarely during subsequent infusions

Management

- 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 any 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

Premedications for RYBREVANT®

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

- Prior to the initial infusion of RYBREVANT® (Week 1, Day 1 and 2), administer premedication to reduce the risk of IRRs
- Glucocorticoid administration is required for Week 1, Day 1 and 2 dose only, and upon re-initiation after prolonged dose interruptions, then as necessary for subsequent infusions. Administer both antihistamine and antipyretic prior to all infusions
- Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity

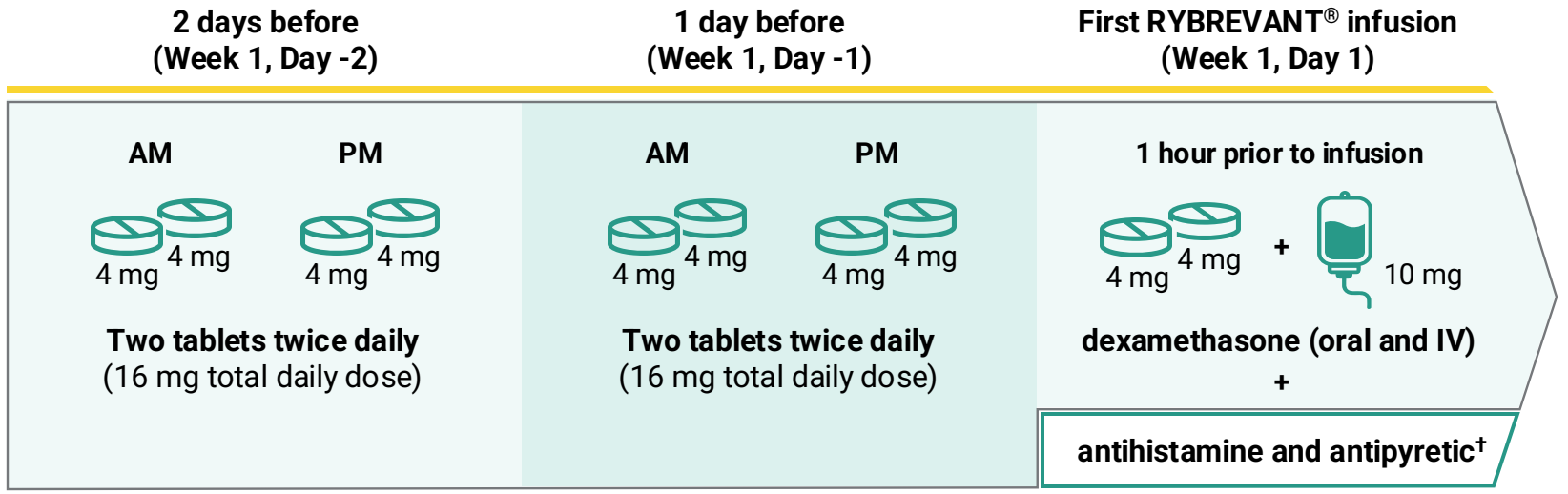
RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

SKIPPirr: Evaluating prophylactic strategies to reduce the incidence of IRRs With RYBREVANT®

Study design

SKIPPirr is a Phase 2 prospective study (NCT05663866) that assesses prophylactic strategies administered prior to RYBREVANT® infusion in order to reduce the incidence and/or severity of first-dose IRRs. This Simon's 2-stage study design evaluates prophylactic approaches in 4 cohorts, with the dexamethasone 8 mg oral cohort reaching the expansion stage.* The primary endpoint is the incidence of IRR events on Week 1, Day 1.[1,2]

One cohort tested in SKIPPirr reached the expansion stage: dexamethasone 8 mg oral cohort[1,3,4]



In SKIPPirr, the Week 1, Day 1 dexamethasone dose is 10 mg IV.[4] In the Prescribing Information for RYBREVANT®, the Week 1, Day 1 dexamethasone dose is 20 mg IV.[3]

Limitations:

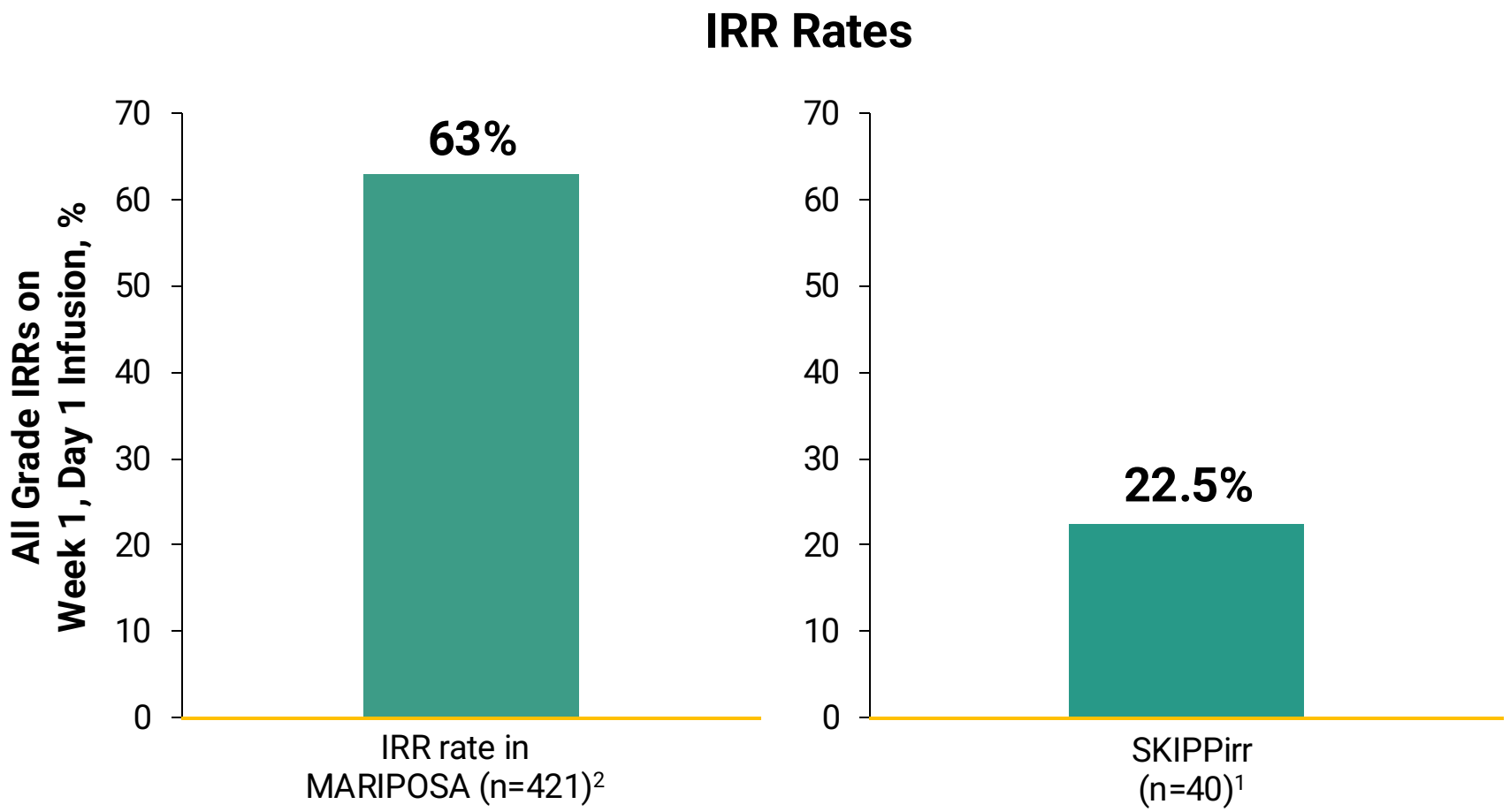
- **The dexamethasone 8 mg oral cohort sample size is n=40. Further studies are needed to determine prophylactic regimens[1]**

*Stage 1, n=6; stage 2, n=16; expansion stage, n=40.[1,2] †These are given based on recommendations in the Prescribing Information of RYBREVANT®, per the Premedications for RYBREVANT® table.

1. Lopes G et al. Presented at: World Conference on Lung Cancer 2024; September 7-10, 2024; San Diego, CA. 2. ClinicalTrials.gov. Updated July 17, 2024. Accessed August 5, 2024. https://clinicaltrials.gov/study/NCT05663866 3. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.
4. Data on file. Janssen Biotech, Inc.

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)[1]



SKIPPirr is not a comparative study. Please refer to the limitations section on the previous slide for additional content.

1. Lopes G et al. Presented at: World Conference on Lung Cancer 2024; September 7-10, 2024; San Diego, CA. 2. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

Maria

Diagnosis

1L Treatment

Follow-up

Clinical Information

Dosing	• RYBREVANT® 1,050 mg/week for 5 weeks, then 1,050 mg every 2 weeks starting at Week 7 until disease progression or unacceptable toxicity • LAZCLUZE™ 240 mg orally once daily before treatment with RYBREVANT® if given on the same day
Pre-infusion medication (Week 1, Day 1)	Prior to initial infusion, 20 mg dexamethasone, 650 mg acetaminophen, and 25 mg diphenhydramine were given
RYBREVANT® infusion (Week 1, Day 1)	350 mg of RYBREVANT® was administered after LAZCLUZE™ 240 mg: • Maria experienced a mild grade 1 IRR of flushing and chest discomfort at 1 hour into the first infusion • Once symptoms resolved, RYBREVANT® infusion was resumed at 50% of the infusion rate

Hypothetical patient and case.

Maria

Diagnosis

1L Treatment

Follow-up

Clinical Information

Pre-infusion medication (Week 1, Day 2 and Week 2)	10 mg dexamethasone, 650 mg acetaminophen, and 25 mg diphenhydramine were given as pre-infusion medications
RYBREVANT® infusion (Week 1, Day 2 and Week 2)	Maria received 700 mg RYBREVANT® on Week 1, Day 2 and 1,050 mg RYBREVANT® on Day 1 of Week 2. She did not experience another IRR
Pre-infusion medication (subsequent infusions)	Only the required 650 mg acetaminophen and 25 mg diphenhydramine were given subsequent to Week 2

Hypothetical patient and case.

IMPORTANT SAFETY INFORMATION:
Dermatologic ARs

Occurrence

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

- In MARIPOSA, rash was Grade 3 in 26% of patients
- In MARIPOSA, the median time to onset of rash was 14 days (range: 1 to 556 days)

Events in MARIPOSA leading to:	RYBREVANT®, %	LAZCLUZE™, %
Dose interruptions	37	30
Dose reductions	23	19
Permanent discontinuation	5	1.7

Management

- Consider prophylactic measures (eg, 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

Proactive supportive care information for dermatologic ARs is presented on the next slides.

Proactive supportive care may reduce the risk and severity of dermatologic ARs

Proactive supportive care was not mandatory across RYBREVANT® studies. Some recommendations are based on the clinical trial experience while others are from guidelines.

Use of prophylactic antibiotics, with or without topical skin therapies, has demonstrated*

- 64% reduction in the risk of developing Grades 2 to 4 skin rash eruptions
- 46% reduction in the risk of all grades skin rash
- 39% reduction in the risk of paronychia

Proactive supportive care was not mandatory across RYBREVANT® studies. Some recommendations are based on the clinical trial experience while others are from guidelines.

*Based on a systematic review and meta-analysis of 13 studies, including 1073 patients.

Petrelli F et al. *Br J Dermatol*. 2016;175(6):1166-1174.

Multinational Association of Supportive Care in Cancer (MASCC) guidelines recommend proactive measures (Weeks 1 to 6) and ongoing monitoring to reduce the risk of severe reactions

- Hydrocortisone 1% cream with moisturizer and sunscreen twice daily
- Minocycline 100 mg daily OR doxycycline 100 mg twice daily

Proactive supportive care was not mandatory across RYBREVANT® studies. Some recommendations are based on the clinical trial experience while others are from guidelines.

Lacouture ME et al. *Support Care Cancer*. 2011;19(8):1079-1095.

IMPORTANT SAFETY INFORMATION:
Dermatologic ARs

Proactive lifestyle approach to help reduce the severity of dermatologic ARs*

Use alcohol-free (eg, isopropanol-free, ethanol-free) emollient cream

Limit time in the sun during and for 2 months after treatment

Wear protective clothing and use broad-spectrum UVA/UVB sunscreen

Proactive supportive care was not mandatory across RYBREVANT® studies. Some recommendations are based on the clinical trial experience while others are from guidelines.

*Based on RYBREVANT® Prescribing Information.

UVA, ultraviolet A; UVB, ultraviolet B.

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Please see the full Prescribing Information for RYBREVANT® and LAZCLUZE™ at www.RYBREVANTHCP.com.

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

IMPORTANT SAFETY INFORMATION:
Venous Thromboembolism

Occurrence

RYBREVANT® in combination with LAZCLUZE™ can cause serious and fatal VTE, including deep vein thrombosis and pulmonary embolism

- The majority of these events occurred during the first 4 months of therapy
- The median time to onset of VTEs was 84 days (range: 6 to 777)
- In MARIPOSA, VTEs were Grade 3 in 10% of patients, Grade 4 in 0.5% of patients, and fatal in 0.5% (2) of patients

Events in MARIPOSA	% (n)
On-study VTE while receiving anticoagulation therapy	1.2 (5)

Events in MARIPOSA leading to:	RYBREVANT®, %	LAZCLUZE™, %
Dose interruptions	9	7
Dose reductions	1	0.5
Permanent discontinuation	3.1	1.9

Management

- Administer prophylactic anticoagulation for the first 4 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

IMPORTANT SAFETY INFORMATION:

Interstitial Lung Disease (ILD)/Pneumonitis and Ocular Toxicity

ILD

Occurrence

RYBREVANT® can cause severe and fatal ILD/pneumonitis. In MARIPOSA

- ILD/pneumonitis occurred in 3.1% of patients and was Grade 3 in 1.0% and Grade 4 in 0.2%
- There was 1 fatal case (0.2%) of ILD/pneumonitis and 2.9% of patients permanently discontinued RYBREVANT® and LAZCLUZE™ due to ILD/pneumonitis

Management

- Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (eg, 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

Ocular Toxicity

Occurrence

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

Management

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

IMPORTANT SAFETY INFORMATION:

Embryo-Fetal Toxicity and LAZCLUZE™ Drug Interactions

Embryo-Fetal Toxicity

Occurrence

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

Management

- 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

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 ARs 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

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Select a Panel Discussion Topic

A

Management of dermatologic ARs

B

Management of VTE

slido

Please download and install the Slido app on all computers you use

Select a Panel Discussion Topic

ⓘ Start presenting to display the poll results on this slide.

Maria

Diagnosis

1L Treatment

Follow-up

Clinical Information

- To help reduce the risk of dermatologic ARs, Maria's oncologist recommended the following proactive supportive care measures:
  - Limit sun exposure by wearing protective clothing and use a broad-spectrum UVA/UVB sunscreen
  - Apply hydrocortisone 1% cream with an alcohol-free emollient cream twice daily for the first 6 weeks of treatment
  - Take a prophylactic antibiotic for the first 6 weeks of treatment
- Maria developed a grade 1 rash 2 weeks after initiation of RYBREVANT® + LAZCLUZE™. Maria's care team will continue to monitor her rash and take additional steps, if necessary
- To prevent VTE, Maria's oncologist prescribed a prophylactic anticoagulant for the first 4 months of treatment with RYBREVANT® + LAZCLUZE™

Hypothetical patient and case.

Maria

Diagnosis

1L Treatment

Follow-up

Clinical Information	
3 months	Radiographic partial response
10 months	Response ongoing with RYBREVANT® + LAZCLUZE™
Ongoing treatment	• RYBREVANT® treatment continued every 2 weeks (starting at Week 7) until disease progression or unacceptable toxicity • LAZCLUZE™ treatment continued daily until disease progression or unacceptable toxicity

Hypothetical patient and case.

SUMMARY

Choose the Combined Power of RYBREVANT® + LAZCLUZE™ First

RYBREVANT® + LAZCLUZE™ form the first and only multitargeted combination to show statistically significant mPFS improvement vs osimertinib[1,2]

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Press release. Johnson & Johnson. August 20, 2024. Accessed August 20, 2024. https://www.prnewswire.com/news-releases/rybrevant-amivantamab-vmjw-plus-lazcluze-lazertinib-approved-in-the-us-as-a-first-line-chemotherapy-free-treatment-for-patients-with-egfr-mutated-advanced-lung-cancer-302226047.html

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Superior efficacy vs osimertinib

- 30% reduction in the risk of progression or death vs osimertinib (HR: 0.70 [95% CI: 0.58, 0.85]; *P*=0.0002)[1]
- mPFS was 23.7 months (95% CI: 19.1, 27.7) for RYBREVANT® + LAZCLUZE™ vs 16.6 months (95% CI: 14.8, 18.5) for osimertinib[1]

Interim OS data

- 61% of patients were alive at 36 months with RYBREVANT® + LAZCLUZE™ and 53% with osimertinib[2]

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Gadgeel SM et al. Presented at: World Conference on Lung Cancer 2024; September 7-10, 2024; San Diego, CA.

Multitargeted inhibition with a chemotherapy-sparing regimen

- RYBREVANT® is the first and only approved EGFR-MET bispecific antibody with immune cell–directing activity[1-3]
- LAZCLUZE™ is a third-generation TKI that is a suitable combination partner for RYBREVANT® because of high selectivity for mutant EGFR, low selectivity for wild type EGFR, and because it is CNS-penetrant[4-6]
- A chemotherapy-sparing combination that provides complementary extra- and intracellular antitumor activity and CNS penetration[1,2,4,6]

1. RYBREVANT®. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Cho BC et al. *Clin Lung Cancer*. 2023;24(2):89-97. 3. Press release. Johnson & Johnson. August 20, 2024. Accessed August 20, 2024. https://www.prnewswire.com/news-releases/rybrevant-amivantamab-vmjw-plus-lazcluze-lazertinib-approved-in-the-us-as-a-first-line-chemotherapy-free-treatment-for-patients-with-egfr-mutated-advanced-lung-cancer-302226047.html 4. LAZCLUZE™. [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 5. Cho BC et al. *J Clin Oncol.* 2023;41(26):4208-4217. 6. Yun J et al. *Clin Cancer Res*. 2019;25(8):2575-2587.

Demonstrated safety profile

- 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 toxicity
  - The majority of ARs were Grade 1 and Grade 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%)
- Proactive supportive care may help reduce the risk and severity of ARs

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THANK YOU

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Diana Nyad

American author, journalist,
and long-distance swimmer

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