RYBREVANT® (amivantamab) ▼ + LAZCLUZE® (lazertinib) ▼

Impact of 1L RYBREVANT® plus LAZCLUZE® vs osimertinib on 2L progression-free survival (PFS)

KEY TAKEAWAY

With clinically meaningful increases in 1L PFS and 2L PFS vs osimertinib, initiating treatment with **RYBREVANT® + LAZCLUZE® provides long-term durable efficacy**[1]

BACKGROUND

In c*EGFR*m NSCLC, 1L RYBREVANT® + LAZCLUZE® vs osimertinib demonstrated:[2,3]

Significant mPFS benefit
23.7M vs 16.6M
HR: 0.70 (95% CI: 0.58–0.85); *p*<0.001

Significant OS benefit with a difference shown at 3 years
60% vs 51%
Median OS: NR vs 36.7 months. HR: 0.75 (95%) CI: 0.61–0.92); *p*<0.005

METHODS[1]

MARIPOSA patients with previously untreated *EGFR*m aNSCLC

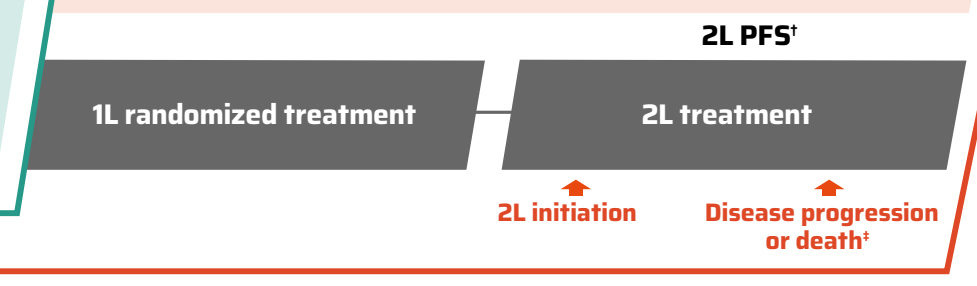
Key eligibility criteria
- aNSCLC
- Treatment-naïve for advanced disease
- Documented *EGFR* Ex19del or L858Rsub
- ECOG PS 0 or 1

RYBREVANT® + LAZCLUZE® (n=429; open-label)

Osimertinib (n=429; blinded)

***Post hoc* exploratory endpoint:**
2L PFS
- By treatment arm
- By resistance mechanisms*

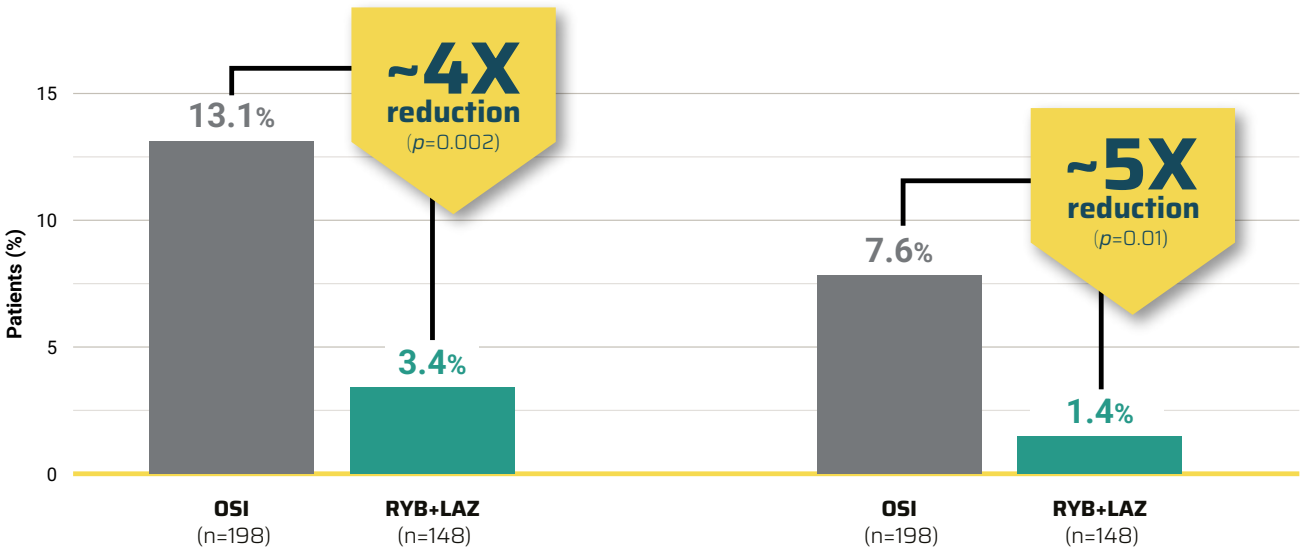
Dosing (in 28-day cycles):
RYBREVANT® 1,050 mg (1,400 mg if ≥80 kg) weekly for the first 4 weeks, then every 2 weeks; LAZCLUZE® 240 mg daily; osimertinib 80 mg daily



RESULTS

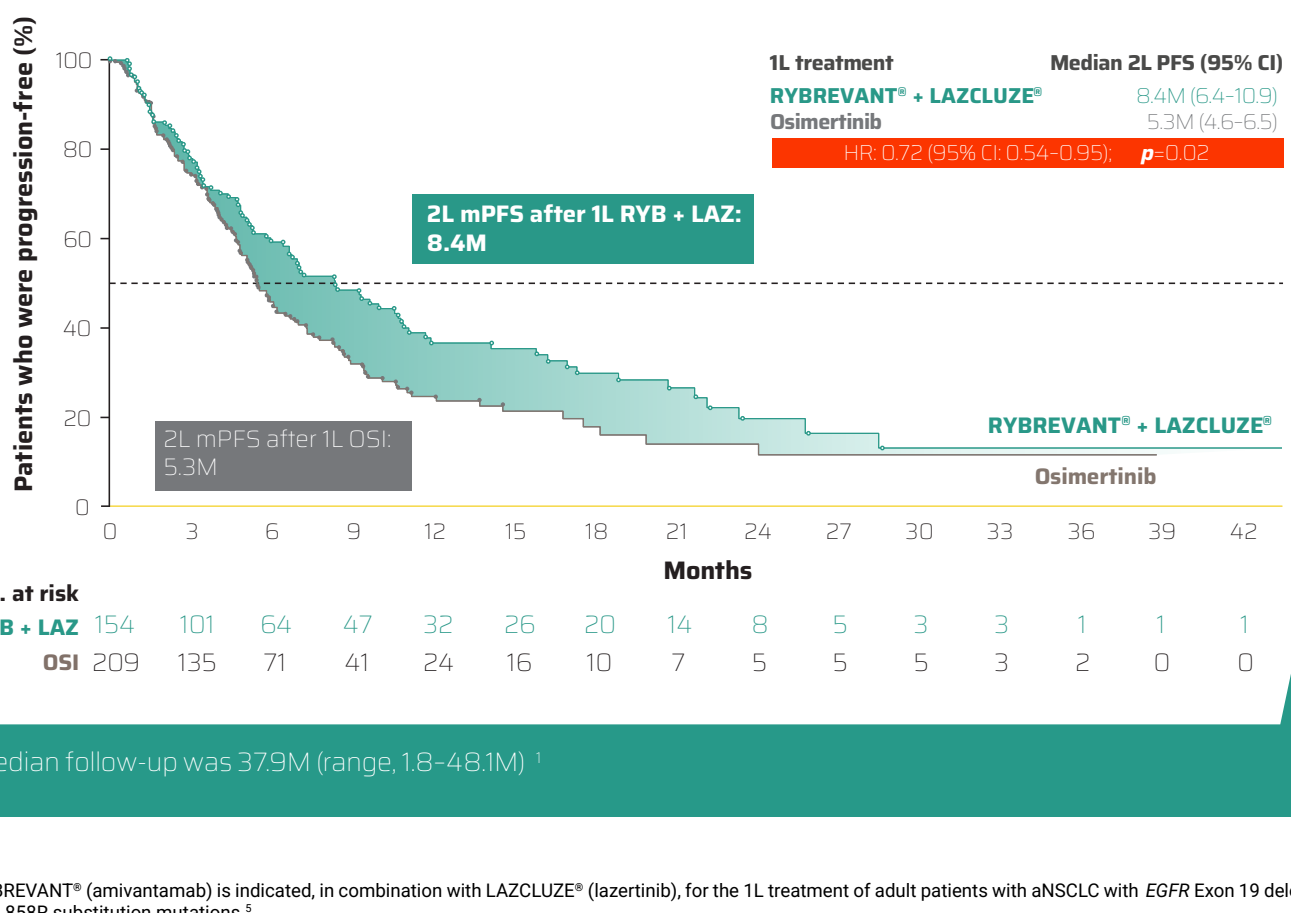
1L RYBREVANT® + LAZCLUZE® significantly reduces *EGFR*- and *MET*-dependent resistance mechanisms associated with poor prognosis vs osimertinib without significant increases in other known resistance pathways§[1,4]

***MET* amplification**



Secondary *EGFR* resistance mutations

The substantially improved 1L mPFS, 2L mPFS, and OS vs osimertinib may reflect RYBREVANT®'s ability to modify the underlying disease biology‖[1-4]



Median follow-up was 37.9M (range, 1.8–48.1M) [1]

RYBREVANT® (amivantamab) is indicated, in combination with LAZCLUZE® (lazertinib), for the 1L treatment of adult patients with aNSCLC with *EGFR* Exon 19 deletions or Exon 21 L858R substitution mutations.[5]

▼These medicinal products are subject to additional monitoring. This will allow quick identification of new safety information. HCPs are asked to report any suspected adverse reactions. See section 4.8 of the SmPCs for how to report adverse reactions.[5,6]

*Guardant360® next-generation sequencing of ctDNA may have limited sensitivity and may not detect histologic transformations.

†2L PFS: Patients who died and/or did not receive 2L treatment were excluded.[1]
‡Disease progression or death could occur during later lines of treatment.[1]
§*MET* amplification was significantly reduced in participants receiving RYBREVANT® + LAZCLUZE® vs osimertinib (3.4% vs 13.1%; *p*=0.002). Further, *MET* amplifications were enriched among osimertinib-treated participants who experienced early disease progression (≤6 months post-randomisation); there were too few *MET* amplifications to draw conclusions for RYBREVANT® + LAZCLUZE®. Secondary *EGFR* mutations (e.g., C797S, L718X, G724X) were also significantly lower in the RYBREVANT® + LAZCLUZE® arm vs osimertinib arm (1.4% vs 7.6%; *p*=0.01). The two participants in the RYBREVANT® + LAZCLUZE® arm with acquired *EGFR* mutations only received RYBREVANT® for one cycle and continued LAZCLUZE®. Differences between arms for other known resistance pathways were not significant. Other acquired resistance pathways analysed included *HER2* amplification, *PI3K*, *RAS/RAF*, other *RTK*, cell cycle, and *TP53/RB1* loss.[4]
‖Subsequent therapies were similar after 1L RYBREVANT® + LAZCLUZE® and osimertinib, minimising impact on 2L PFS; most patients started a subsequent regimen with chemotherapy (52% vs 66%) and/or an EGFR-targeting agent (47% vs 32%); some patients received radiation after 1L RYBREVANT® + LAZCLUZE® and osimertinib (11% vs 12%), or concurrently with initiation of 2L treatment (1% each).[1]

1L, first-line; **2L,** second-line; **AACR,** American Association for Cancer Research; **aNSCLC,** advanced non-small cell lung cancer; **BICR,** blinded independent central review; **cEGFRm**, common EGFR-mutated; **CI,** confidence interval; **ctDNA,** circulating tumour DNA; **ECOG PS,** Eastern Cooperative Oncology Group Performance Status; **EGFR,** epidermal growth factor receptor; **Ex19del,** exon 19 deletion; **HCP,** healthcare professional; **HER2,** human epidermal growth factor receptor 2; **HR,** hazard ratio; **L858Rsub,** exon 21 L858R substitution; **LAZ,** LAZCLUZE®; **M,** month; **MET,** mesenchymal-epithelial transition factor; **mPFS,** median PFS; **NSCLC,** non-small cell lung cancer; **OS,** overall survival; **OSI,** osimertinib; **PFS,** progression-free survival; **PI3K,** phosphoinositide 3-kinase; **RAF,** rapidly accelerated fibrosarcoma; **RAS,** rat sarcoma; **RB1,** retinoblastoma 1; **RECIST,** response evaluation criteria in solid tumours; **RTK,** receptor tyrosine kinase; **RYB,** RYBREVANT®; **SPC:** Summary of Product Characteristics; **TP53,** tumour protein 53.

Click **here** to learn more about the benefits of RYBREVANT® + LAZCLUZE®

References: 1. Spigel D, et al. Presented at the American Association for Cancer Research (AACR) Annual Meeting; 17–22 April 2026; San Diego, CA, USA (Poster LB474). **2.** Cho BC, et al. *N Engl J Med.* 2024;391(16):1486–1498. **3.** Yang JC, et al. *N Engl J Med.* 2025;393(17):1681–1693. **4.** Hayashi, et al. Presented at World Conference on Lung Cancer (WCLC); 6–9 September 2025; Barcelona, Spain (Abstract PT1.03.06). **5.** RYBREVANT® Saudi Summary of Product Characteristics. April 2025. **6.**LAZCLUZE® Saudi Summary of Product Characteristics. November 2024.

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Date of preparation: October 2026
Date of expiry: October 2028.

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