COMBINED* POWER TO CHANGE THE GAME in *EGFR*+ ADVANCED NSCLC†

RYBREVANT® liquid treatment options provide a targeted approach that's proven to change the game in EGFR+ mutated advanced NSCLC

*RYBREVANT® (amivantamab-vmjw) + platinum-based chemotherapy

RYBREVANT® + PLATINUM-BASED CHEMOTHERAPY: LEGIR RECRUITONS AT 2L+

RYBREVANT® is indicated in combination with carboplatin and pemetrexed for the treatment of adult patients with advanced NSCLC with *EGFR* Exon 19 deletions or Exon 21 L858R substitution mutations after failure of prior therapy including an EGFR TKI

HEALTHCARE PROFESSIONALS ONLY

Prescribing information and adverse events reporting

For RYBREVANT® SmPC

- This medicinal product is subject to additional monitoring. Adverse events and product quality complaints should be reported. Healthcare professionals must refer to their country specific prescribing information for company contact details.

MARIPOSA-2 study design

MARIPOSA-2 is a randomized, open-label, multicentre Phase III study in patients with locally advanced or metastatic NSCLC with *EGFR* Exon 19 deletions or Exon 21 L858R substitution mutations,[4] assessing the efficacy and safety of RYBREVANT® + platinum-based chemotherapy vs. platinum-based chemotherapy alone after failure of prior therapy including a 3rd generation EGFR TKI.[1]

*Mutation testing could have been performed at or after the time of locally-advanced or metastatic disease diagnosis. Testing did not need to be repeated at the time of study entry once EGFR mutation status was previously established.

Efficacy benefits with RYBREVANT® + platinum-based chemotherapy vs. platinum-based chemotherapy alone[1–3]

Superior PFS benefit‡,1,2

52% reduction in the risk of progression or death
6.3 vs. 4.2 months
HR=0.48 (95% CI: 0.39–0.59); p<0.0001

Prolonged PFS2‡,1
13.9 vs. 11.3 months
HR=0.69 (95% CI: 0.54–0.89); p=0.0037

Higher ORR‡,1
64% vs. 36% patients
(95% CI: 57.9%–70.3% vs. 29.8%–42.5%)

Durable response‡,1
6.90 vs. 5.55 months
(95% CI: 5.55–8.28 months vs. 4.73–5.62 months, respectively)

Adverse events are consistent with treatment components1,2

RYBREVANT® + platinum-based chemotherapy ADLT were predominantly haematologic, EGFR-, MET-, or infusion-related and were consistent with the known AE profiles of the individual components.[1,2]

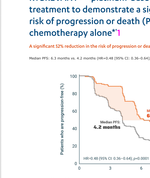
Permanent discontinuation of RYBREVANT® due to AEs occurred in 8% of RYBREVANT® + platinum-based chemotherapy patients.[1] The most frequent adverse reactions leading to treatment discontinuation were IRR (2.7%), rash (2.3%), ILD (2.3%), and nail toxicity (1.0%).[1]

Multi-targeted

RYBREVANT® is the first and only approved EGFR-MET bispecific antibody with 3 mechanisms of action[1]

Works synergistically with platinum-based chemotherapy to address post-osimertinib resistance[1,2,4,5]

RYBREVANT®'s multi-targeted MoA has demonstrated efficacy against a broad range of *EGFR*- and MET-based alterations,[1] whilst the DNA-interfering effect of platinum-based chemotherapy provides activity against resistance mechanisms that are *EGFR*- and MET-independent.[2,5]



Visualization of RYBREVANT® MoA' mechanism of action description.[1]

The RYBREVANT® + platinum-based chemotherapy mechanisms of action work synergistically to provide broad coverage of the diverse and polyclonal tumour resistance arsing after disease progression on osimertinib.[2]

*95% was the primary endpoint assessed by RECIST and the data shown are at a median follow-up of 8.7 months.[1]
†PFS2 was a secondary endpoint assessed by RECIST and the data shown are at a median follow-up of 8.7 months.[1]
‡‡The cytotoxic platinum agent in combination, as the DNA-damaging agent, is active against both EGFR- and MET-independent resistance.[2]
§§Data from a Phase I study of RYBREVANT® + lazertinib in patients with EGFR+ advanced NSCLC.[3]
¶¶ 321 patients with advanced NSCLC exposed to RYBREVANT® + platinum-based chemotherapy, from MARIPOSA-2, MARIPOSA and CHRYSALIS combined datasets.[1,2]
The median exposure to RYBREVANT® + platinum-based chemotherapy was 7.7 months.[1]

To see how RYBREVANT® + platinum-based chemotherapy work together to help patients with advanced NSCLC

Click here

MARIPOSA-2 study results

PFS | PFS2 | INTRACRANIAL PFS | ORR | DURABLE RESPONSE | OS

For patients progressing on or after osimertinib, RYBREVANT® + platinum-based chemotherapy is the first treatment to demonstrate a significant reduction in the risk of progression or death (PFS) vs. platinum-based chemotherapy alone*[1]

A significant 52% reduction in the risk of progression or death vs. platinum-based chemotherapy alone*[1]

Median PFS: 6.3 months vs. 4.2 months (HR=0.48 (95% CI: 0.36–0.64); p<0.0001‡)

*95% was the primary endpoint assessed by RECIST and the data shown are at a median follow-up of 8.7 months.[1]
‡95 events out from total cut-off 321 by ICR2 where hypothesis testing and final analysis for OS endpoint was performed.[1]

2L treatment efficacy is limited after progression, including after an EGFR-TKI, with patients having a poor prognosis[6]

Eventually, osimertinib treated patients develop resistance mechanisms and progress, facing limited treatment options and reduced DOR and OSB

32%
Up to 32% of *EGFR*-mutated patients receiving osimertinib in 2L die before reaching 2L treatment**.[6,7]

Osimertinib resistance is a key driver of progression and is associated with diverse, polyclonal and *EGFR*-independent genomic alterations.[8]

50%
MET amplifications are the most common genomic alterations, accounting for **up to 50%‡‡** tumour resistance.[8]

Limited evidence exists to support EGFR-TKI retreatment or the addition of immunotherapy,[8,9] leaving limited effective options beyond platinum-based chemotherapy[6,8]

Studies investigating chemotherapy + immunotherapy regimens have not demonstrated a benefit vs. chemotherapy alone in patients with TKI resistance.[8]

Patients with brain metastases have increased symptom burden[6]

Compared to those without, patients with brain metastases have:[6,9]

The incidence of brain metastases in EGFR-mutated advanced NSCLC increases over time:[6,9]

24.4% at diagnosis

52.9% after 5 years

A NEW APPROACH IS AVAILABLE

There is a new therapeutic option available for *EGFR*-mutated advanced NSCLC patients who have progressed on prior therapy, including an EGFR TKI, with a multi-targeted mechanism of action to counter the *EGFR* and *MET* gene alterations and potentially delay progression!

*In a real-world study with 777 *EGFR*-mutated advanced NSCLC patients.[10]
†Data from a Phase I study of RYBREVANT® + lazertinib in advanced NSCLC patients. 467 treated with first-line osimertinib.[11]
‡Data are from a prospective study of 204 patients with disease progression after EGFR TKI therapy including first- or second-generation TKI for those with an *ITGB4* mutation and/or comorbid regardless of *ITGB4* mutations.[12]
§Data from a retrospective study of 1,662 patients with metastatic chronic health record study of 402 *EGFR*-mutated advanced NSCLC patients, 201 with brain metastases.[13]
¶In a retrospective cohort study of 96 patients with *EGFR* mutations with no standardized protocol for CNS evaluation.[14]

ADVERSE EVENTS | LIFESTYLE MANAGEMENT

AEs are consistent with treatment components[1,2]

RYBREVANT® + platinum-based chemotherapy ADLT were predominantly haematologic, EGFR-, MET-, or infusion-related and were consistent with the known AE profiles of the individual components.[2]

The most frequent AEs* in all grades were:††					
Rash‡	83%	**Fatigue‡**	45%	**Oedema‡**	40%
Neutropenia	57%	**Nausea**	43%	**Stomatitis‡**	39%
Nail toxicity‡	53%	**Thrombocytopenia**	40%	**Decreased appetite**	35%
IRRs	51%	**Constipation**	40%	**Hypoalbuminaemia**	33%
Diarrhoea/enterocolitis increased	39%	**Increased aminotransferase**	33%	**Vomiting**	33%
Cytokinaemia	33%				

The onset and severity of haematologic AEs were highest in Cycle 1, with more patients experiencing neutropenia and thrombocytopenia with RYBREVANT® + platinum-based chemotherapy vs. platinum-based chemotherapy alone.[2] Haematologic AEs decreased over time, and profiles were similar in both groups by Cycle 2 onwards.[2]

VTEs occurred in 14% of RYBREVANT® + platinum-based chemotherapy patients, with most VTE events being Grade 1 or 2.[1,2]

Among patients in 51% of patients treated with RYBREVANT® + platinum-based chemotherapy, in greater than 94% of cases, Grade 1 or 2.[1] The majority of IRRs occurred at the first infusion,[1] with time to onset of 50 minutes, and the majority occurred within 2 hours (range: 0–7 hours) of infusion start.[1] Occasionally an IRR can occur at reinitiation of RYBREVANT® after prolonged dose interruptions of more than 6 weeks.[1]

Administer premedications (antihistamine, antipyretics and glucocorticoids) prior to infusion (Week 1, Days 1 and 2) to reduce the risk of IRRs and at subsequent doses as indicated in the dosing table.[1] Antiemetics should be administered as needed. RYBREVANT® should be administered by a healthcare professional with access to appropriate medical support to manage IRRs if they occur.[1] For more information, see the SmPC.

Premedication*	Dose	Route of administration	Recommended dosing window prior to RYBREVANT® administration
Antihistamine†	Diphenhydramine (25 to 50 mg) or equivalent	Intravenous	15 to 30 minutes
		Oral	30 to 60 minutes
Antipyretic†	Paracetamol (acetaminophen (650 to 1000 mg)	Intravenous	15 to 30 minutes
		Oral	30 to 60 minutes
Glucocorticoid‡	Dexamethasone (10 mg) or equivalent	Intravenous	40 to 120 minutes
Glucocorticoid‡	Dexamethasone (10 mg) or equivalent	Intravenous	40 to 60 minutes

Limited discontinuations due to AEs1

*In 321 patients with advanced NSCLC exposed to RYBREVANT® + platinum-based chemotherapy, from MARIPOSA-2, MARIPOSA and CHRYSALIS combined datasets.[1,2]
The median exposure to RYBREVANT® + platinum-based chemotherapy was 7.7 months.[1]
†Permanent discontinuation of RYBREVANT® + platinum-based chemotherapy, at an incidence of ≥10%. For full list of AEs, refer to the SmPC.[1]
‡Grouped terms.
§MARIPOSA-2 data set only.[1]
¶Refer to Section 4.2 of the SmPC for further details.[1]
#For more information on the usage of premedications, refer to the respective SmPCs for each of the products included in the treatment combination.
††Reported at all doses.[1]
‡‡Reported at a dose of Week 1, Day 1+ at the next subsequent dose in the event of an IRR.[1]
§§Reported at second dose (Week 1, Day 1), optional for subsequent doses.[1]

To see the full safety profile of the regimen, see the SmPC
Click Here

For dosing and administration information
Click Here

To book a meeting with a J&J representative
Click Here

1L, first-line; 2L, second-line; 2L+, second-line plus; 3L, advanced; aaHR, BRCA, Bristol-Myla Squibb Medical Control Review; aDOR, common EGFR mutation; CI, confidence interval; CT, computed tomography; DNA, deoxyribonucleic acid; DOR, duration of response; EGFR, epidermal growth factor receptor; EGFR+, EGFR mutation positive; EGFRi, European Medicines Agency; ESMO, European Society for Medical Oncology; FDA, Food and Drug Administration; GI, gastrointestinal; HR, hazard ratio; IHC, immunohistochemistry; IRR, infusion-related reaction; mDOR, median duration of response; mOS, median overall survival; MRI, magnetic resonance imaging; NE, not estimable; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PFS2, second progression-free survival; SmPC, Summary of Product Characteristics; SoC, standard of care; TKI, tyrosine kinase inhibitor; VTE, venous thromboembolism.

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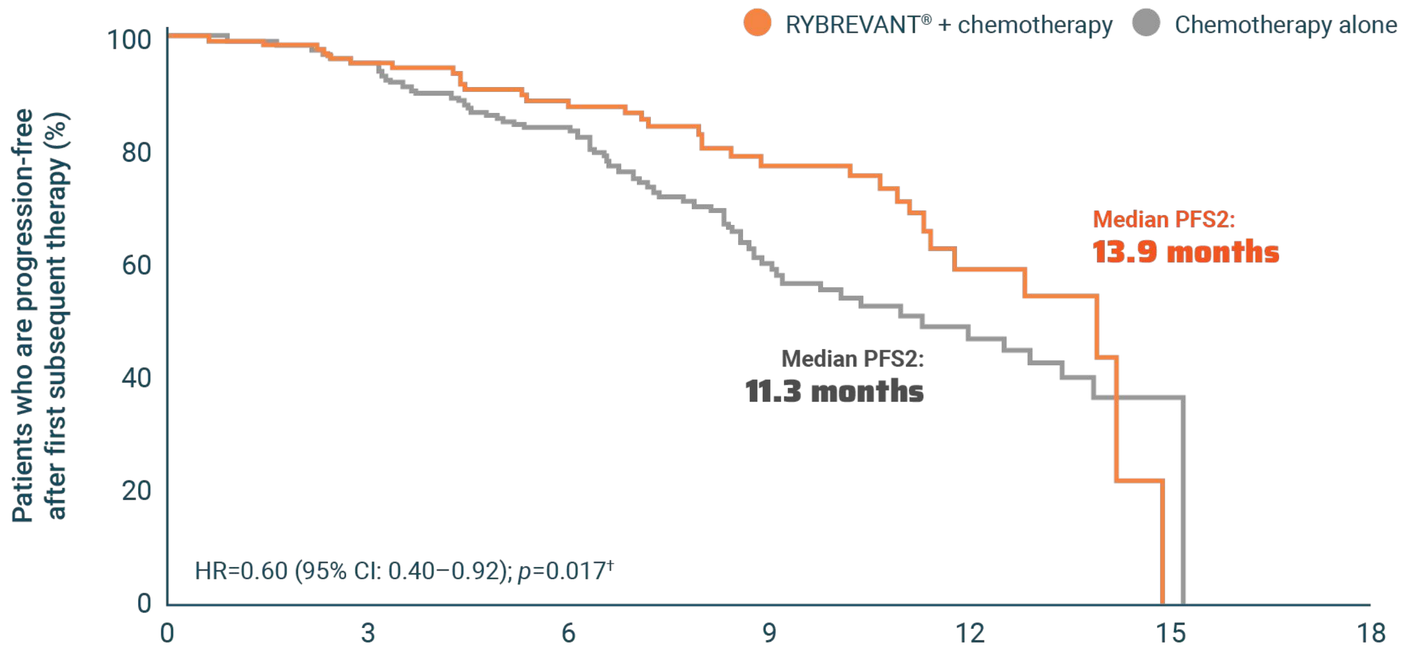
RYBREVANT® + platinum-based chemotherapy demonstrated prolonged progression-free survival after first subsequent therapy vs. platinum-based chemotherapy alone*[3]

40% reduction in the risk of progression or death after first subsequent therapy vs. platinum-based chemotherapy alone*[3]

Median PFS2: 13.9 months vs. 11.3 months (HR=0.60 [95% CI: 0.40–0.92]; *p*=0.017)†[3]



No. at risk							
RYBREVANT® + chemotherapy	131	109	83	48	16	0	0
Chemotherapy alone	263	209	136	56	23	1	0

Graph adapted from Gentzler R *et al.* 2024.[3]

*PFS2 was a secondary endpoint assessed by BICR and the data shown are at a median follow-up of 8.7 months.[2,3]

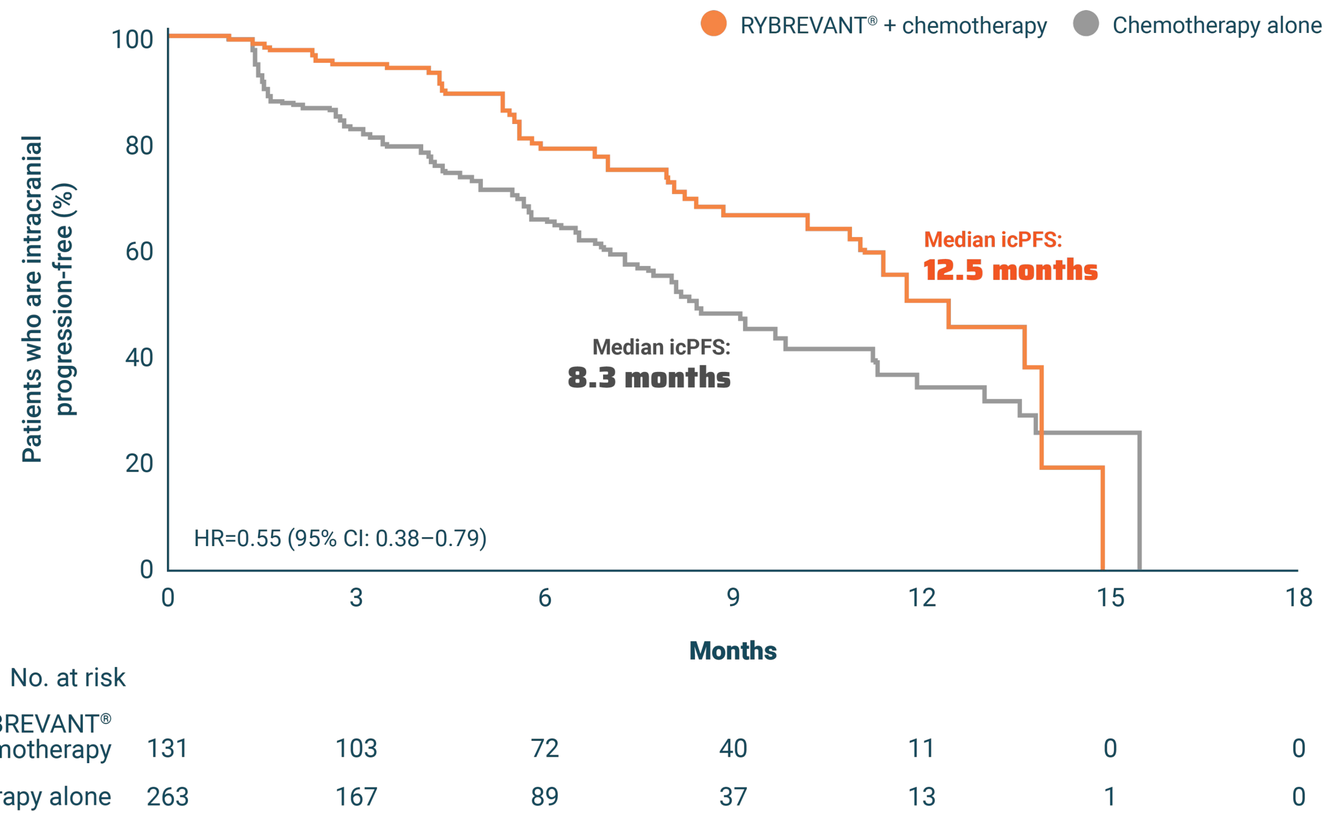
†The p-value reported here is nominal, as PFS2 was a secondary outcome and not subject to hypothesis testing.[2,3]

RYBREVANT® + platinum-based chemotherapy demonstrated an intracranial PFS benefit*2

45% reduction in intracranial progression or death in the ITT population vs. platinum-based chemotherapy alone*†2

Median icPFS: 12.5 months vs. 8.3 months (HR=0.55 [95% CI: 0.38–0.79])2

Serial brain MRIs were required for all patients. Those that could not have MRI were assessed through CT scans7



No. at risk							
RYBREVANT® + chemotherapy	131	103	72	40	11	0	0
Chemotherapy alone	263	167	89	37	13	1	0

Graph adapted from Passaro A *et al.* 2023.2

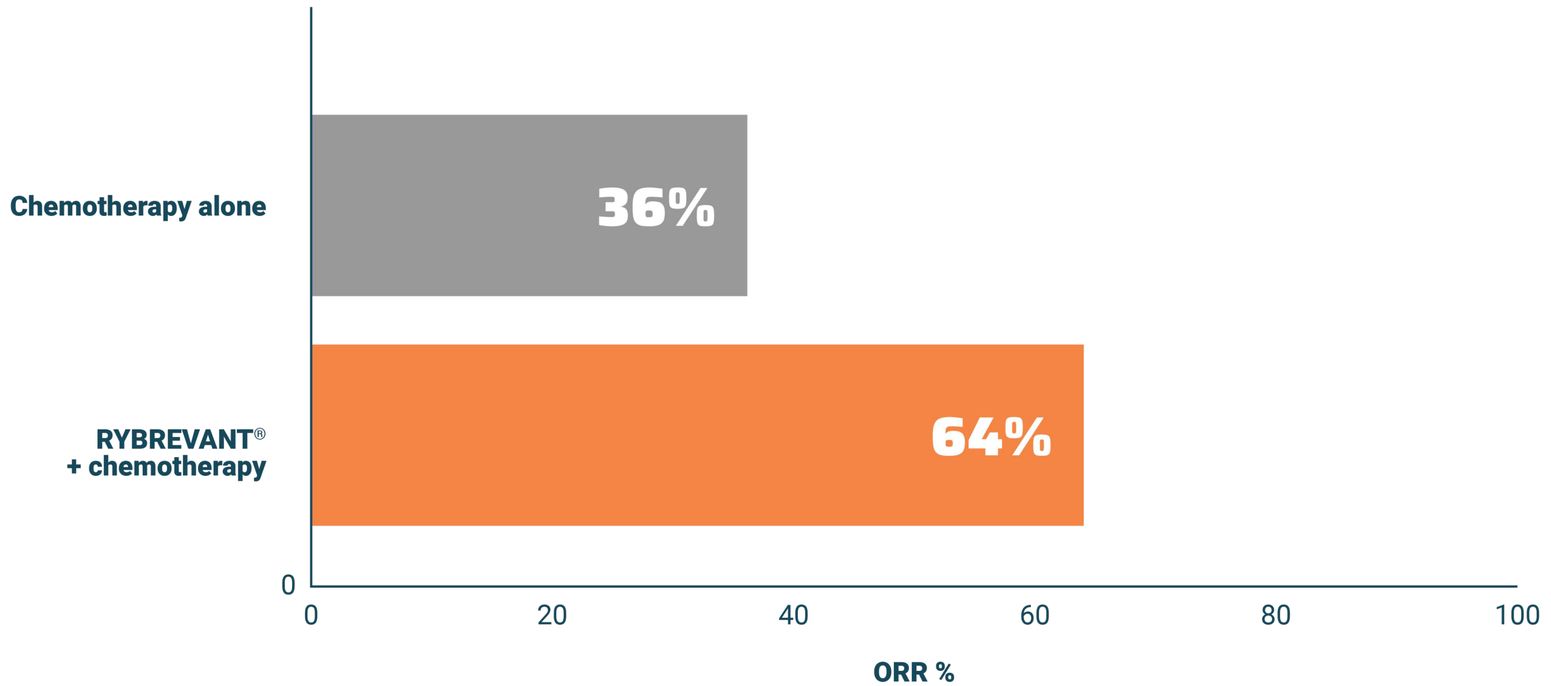
*icPFS was a secondary endpoint assessed by BICR and the data shown are at a median follow-up of 8.7 months.2 Patients with asymptomatic or previously treated and stable intracranial metastases were eligible to be randomised in MARIPOSA-2.1

†The icPFS endpoint was not part of the hypothesis testing in the MARIPOSA-2 study therefore only point estimates and 95% CIs are reported.2

RYBREVANT® + platinum-based chemotherapy delivered higher ORR vs. platinum-based chemotherapy alone*[1]

Almost double objective response rate vs. platinum-based chemotherapy alone*†[1]

ORR: 64% vs. 36% (OR=3.1 [95% CI: 2.0–4.8]; $p<0.0001$)



Graph adapted from RYBREVANT® Summary Product of Characteristics 2024.[1]

*ORR was a secondary endpoint assessed by BICR and the data shown are at a median follow-up of 8.7 months.[2]

†ORR results are from data cut-off 10 July 2023 when hypothesis testing and final analysis for this endpoint was performed.[1]

RYBREVANT® + platinum-based chemotherapy demonstrated a durable response*[1]

Demonstrated more durable responses vs. platinum-based chemotherapy alone*[1]

MEDIAN DOR:[1]

RYBREVANT® + PLATINUM-BASED CHEMOTHERAPY

6.90
months
(95% CI: 5.52–NE)

vs.

PLATINUM-BASED CHEMOTHERAPY ALONE

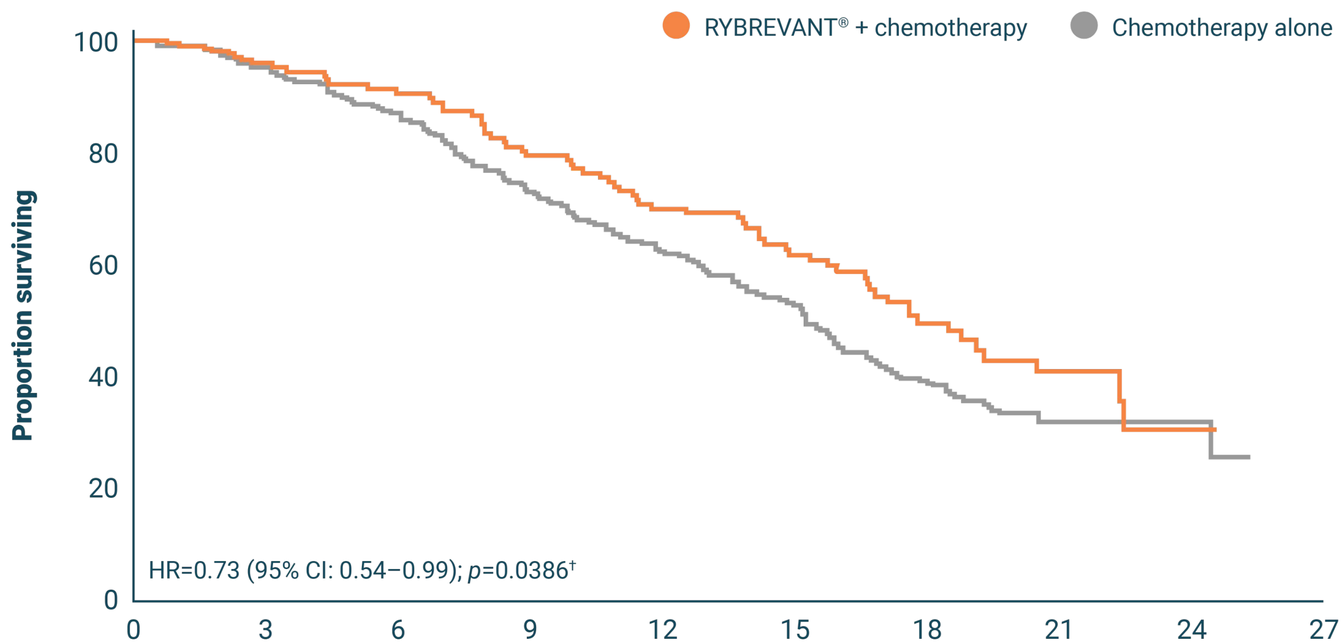
5.55
months
(95% CI: 4.17–9.56)

*DOR was a secondary endpoint assessed by BICR and the data shown is at a median follow-up of 8.7 months.[2]

RYBREVANT® + platinum-based chemotherapy demonstrated a trend to extended survival*[1]

At a second interim analysis, RYBREVANT® + platinum-based chemotherapy demonstrated a favourable trend towards OS benefit vs. platinum-based chemotherapy alone*[1]

(HR=0.73; 95% CI: 0.54–0.99; *p*=0.0386)†



No. at risk										
RYBREVANT® + chemotherapy	131	124	115	101	88	63	39	15	2	0
Chemotherapy alone	263	242	213	174	147	103	49	21	6	0

*OS results are from data cut-off 26 April 2024 from the second interim OS analysis. This second OS analysis occurred at a median follow-up of 18.6 months for RYBREVANT® + platinum-based chemotherapy arm and 17.8 months for platinum-based chemotherapy alone.[1]

†The p-value is compared to a 2-sided significance level of 0.0142. Thus, the OS results are not significant as of the second interim analysis.[1]

A proactive approach to rash prevention should be considered[1,18]

Proactive measures in line with ESMO Clinical Practice Guidelines are recommended to reduce the risk and severity of dermatologic AEs, including but not limited to acneiform rash, hand-foot skin reaction and nail toxicity:[19]

Oral antibiotics[19,20]
6 weeks at the start of therapy with or without topical low/moderate strength steroid to face and chest

Alcohol-free OTC moisturising creams or ointment[19]
Twice a day, preferably with urea-containing (5%–10%) moisturisers to the body

Sunscreen SPF >15[19]
Applied to exposed areas of body and every 2 hours when outside

Preventive nail care instructions[19]

A proactive lifestyle approach[19,20]
Including avoidance of excessive sun exposure, frequent washing with hot water, chemical or physical stress, biting or cutting nails too short and skin irritants