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For UK medical and trade media only

For immediate release

RYBREVANT®▼ (amivantamab) plus chemotherapy shows positive overall survival trend versus chemotherapy in patients with previously treated EGFR-mutated lung cancer

Post-progression outcomes showed significant and sustained improvement for amivantamab plus chemotherapy, versus chemotherapy alone[1]

High Wycombe, UK (14 September 2024) – Johnson & Johnson today announced updated results from the Phase 3 MARIPOSA-2 study which showed RYBREVANT®▼ (amivantamab) combined with chemotherapy led to a favourable trend toward improved overall survival (OS) compared to chemotherapy alone.[1] The data also reveal consistent benefits across post-progression outcomes in adult patients with previously treated non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions (ex19del) or L858R Exon21 (L858R) substitution mutations.[1] Results were presented at the European Society of Medical Oncology (ESMO) 2024 Congress, taking place in Barcelona, Spain from 13-17 September.[1]

“The positive overall survival trend seen in MARIPOSA-2 suggests that amivantamab combined with chemotherapy could potentially change the treatment landscape for a population that has historically faced limited options,” said Prof Sanjay Popat, M.D., Ph.D., Medical Oncologist at the Royal Marsden Hospital and the Institute of Cancer Research in the United Kingdom, and presenting author.* “Building on the strong progression-free survival data previously reported from this study and by helping more patients stay on treatment for longer, we are improving their chances for better outcomes.”

At the second interim analysis for the MARIPOSA-2 clinical trial, with a median follow-up of 18.1 months, 50 percent of patients treated with amivantamab plus chemotherapy were still alive at the 18-month landmark, compared to 40 percent of those receiving chemotherapy alone (median OS, 17.7 vs 15.3 months, respectively; hazard ratio [HR], 0.73; [95 percent confidence interval [CI], 0.54–0.99]; nominal *P*=0.039**).[1] Amivantamab plus chemotherapy showed a significant improvement in treatment discontinuation rates (22 percent), with nearly five times as many patients remaining on therapy at 18 months compared to chemotherapy (4 percent) (median time-to-treatment discontinuation [TTD], 10.4 vs 4.5 months, respectively; HR, 0.42; [95 percent CI, 0.33–0.53]; nominal P<0.0001**).[1] Additionally,

patients treated with amivantamab plus chemotherapy experienced a 27 percent reduction in the risk of symptomatic progression (median time to symptomatic progression [TTSP] 16.0 vs 11.8 months; HR, 0.73; [95 percent CI, 0.55–0.96]; nominal P=0.026**).[1] The time to subsequent therapy was significantly prolonged with the amivantamab plus chemotherapy combination compared to chemotherapy (median time to subsequent therapy [TTST], 12.2 vs 6.6 months, respectively; HR, 0.51; [95 percent CI, 0.39–0.65]; nominal P<0.0001**), which also reduced the risk of second disease progression or death by 39 percent (median progression-free survival 2 [PFS2], 16.0 vs 11.6 months, respectively; HR, 0.64; [95 percent CI, 0.48–0.85]; nominal P=0.002**).[1]

“While diverse resistance mechanisms in treated EGFR-mutant non-small cell lung cancer can present a challenge in relapsed disease, the latest findings from the MARIPOSA-2 study reveal that combining amivantamab with chemotherapy markedly extends progression-free survival and holds promise for improving overall survival compared to chemotherapy alone in the relapsed setting,” said Dr John Fleming, Country Medical Director, Johnson & Johnson Innovative Medicine, UK. “These results reaffirm J&J’s focus on advancing precision medicine across all lines of NSCLC, with the goal of offering novel treatment options and more durable therapies to better support patients in need.’’

In the primary analysis of the MARIPOSA-2 study, presented at the European Society for Medical Oncology (ESMO) 2023 Congress, adverse events (AEs) of Grade 3 or higher, mainly due to haematologic toxicities, were reported by 72 percent of patients treated with amivantamab plus chemotherapy, and 48 percent with chemotherapy alone.[2] The most common Grade 3 or higher AEs included neutropenia, thrombocytopenia, anaemia, and leukopenia.[2] Grade 3 or 4 bleeding events were seen in 1 percent of patients treated with amivantamab plus chemotherapy, and in no patients with chemotherapy.[2] Serious treatment-emergent AEs (TEAEs) were observed in 32 percent of patients treated with amivantamab plus chemotherapy and 20 percent with chemotherapy.[2] Infusion-related reactions in the amivantamab plus chemotherapy arm were 58 percent (all grades) and 5 percent (Grade >3 or above).[2] Treatment-related AEs leading to death were infrequent in all arms (2 percent vs. 1 percent) in the amivantamab plus chemotherapy and chemotherapy alone arms respectively.[2] Permanent discontinuation of all study agents in amivantamab plus chemotherapy arm due to adverse reactions occurred in 11 percent of patients.[2]

#ENDS#

ABOUT MARIPOSA-2

MARIPOSA-2 (NCT04988295), which enrolled 657 patients, is a randomised, open-label Phase 3 study evaluating the efficacy and safety of two combination regimens of amivantamab (with and without lazertinib) and chemotherapy.[5] Patients with locally-advanced or metastatic EGFR ex19del or exon 21 L858R substitution NSCLC who had disease progression on or after treatment with osimertinib were randomised to treatment with amivantamab plus chemotherapy, amivantamab plus chemotherapy with lazertinib, or chemotherapy alone.[5] The dual primary endpoint was used to compare the progression-free survival (PFS) (using RECIST v1.1 guidelines†) as assessed by blinded independent central review (BICR) for each experimental arm to chemotherapy alone.[5] Secondary endpoints included objective response as assessed by BICR, overall survival (OS), duration of response (DOR), time to subsequent therapy, PFS2 and intracranial PFS.[5]

All study participants underwent serial brain imaging to allow for the robust assessment of intracranial endpoints and to assess the CNS activity of amivantamab and platinum doublet chemotherapy with and without lazertinib.[5] Because brain metastases can lead to significant burden and poor outcomes for patients, this aspect of the study design provides critical information in an area of high unmet need.[3]

ABOUT AMIVAMTAMAB

Amivantamab is a fully-human EGFR-MET bispecific antibody that acts by targeting tumours with activating and resistant EGFR mutations and MET mutations and amplifications, and by harnessing the immune system.[4,5,6,7] Amivantamab is licensed for treating adults in Great Britain and Northern Ireland in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with advanced NSCLC with activating EGFR Exon 20 insertion mutations; and as monotherapy for treatment of adult patients with advanced NSCLC with activating EGFR Exon 20 insertion mutations, after failure of platinum-based therapy.[8,9]

Adverse events should be reported. ▼ This medicinal product is subject to additional monitoring, and it is therefore important to report any suspected adverse events related to this medicinal product. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Janssen-Cilag Limited, a Johnson & Johnson company on 01494 567447 or at dsafety@its.jnj.com.

ABOUT NON-SMALL CELL LUNG CANCER

Lung cancer is the third most common cancer in the UK, it is estimated that there are around 48,500 new lung cancer cases in the UK every year (2016-2018).[10] Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for 85 percent of all lung cancers.[11]

The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[12] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.[12,13] EGFR mutations are present in 10 to 15 percent of Western patients with NSCLC with adenocarcinoma histology and occur in 40 to 50 percent of Asian patients. [14,15,16,17] EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.[18] The five-year survival rate for patients with advanced NSCLC and EGFR mutations treated with EGFR tyrosine kinase inhibitors (TKIs) is less than 20 percent.[19]

ABOUT JOHNSON & JOHNSON

Janssen, the Pharmaceutical Companies of Johnson & Johnson, is evolving to become Johnson & Johnson Innovative Medicine. The Company is updating its brand and uniting both its pharmaceutical and MedTech segments under the Johnson & Johnson brand name.

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are

smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of amivantamab. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialise, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen-Cilag, S.A. and Janssen-Cilag International NV, and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behaviour and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 31, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at http://www.sec.gov/, http://www.jnj.com/ or on request from Johnson & Johnson. None of Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen-Cilag, S.A. and Janssen-Cilag International NV, nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

*Prof. Sanjay Popat has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.

**P-value is from a log-rank test stratified by osimertinib line of therapy (first-line vs second-line), history of brain metastases (yes or no), and Asian race (yes vs no). OS was evaluated at a 2-sided alpha of 0.0142.

†RECIST (version 1.1) refers to Response Evaluation Criteria in Solid Tumors, which is a standard way to measure how well solid tumours respond to treatment and is based on whether tumours shrink, stay the same or get bigger.

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CP-475905
September 2024

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