

Company

Janssen

Drug or Device Name

RYBREVANT®

Category

Pharmaceutical

Compound/Technical Name

Amivantamab-vmjw

Trade Name

RYBREVANT®

Date of Approval

05/21/2021

Therapeutic Categories

Oncology: non-small cell lung cancer (NSCLC)

Indications

RYBREVANT® was approved in the United States in 2021 for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy. This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. As of March 1, 2023, RYBREVANT® is also approved in Australia, Brazil, Canada, the European Union, Hong Kong, India, Israel, Lichtenstein, Malaysia, Mexico, Philippines, Serbia, Singapore, South Korea, Switzerland, Taiwan, Thailand, and the United Kingdom, for use in adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations, after failure of platinum-based therapy.

Background

Lung cancer is the most common cause of death from cancer and non-small cell lung cancer (NSCLC) accounts for 85% of all lung cancers. Despite the development of many therapies targeted to NSCLC oncogenes and the promising outcomes that resulted from these therapies, there remain patient populations who have limited treatment options and whose prognosis remain poor. RYBREVANT®, a bispecific EGF receptor (EGFR)-directed and MET receptor-directed antibody, has the potential to fill this unmet need.

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approved test, whose disease has progressed on or after platinum-based chemotherapy. This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. As of March 1, 2023, RYBREVA[®] is also approved in Australia, Brazil, Canada, the European Union, Hong Kong, India, Israel, Lichtenstein, Malaysia, Mexico, Philippines, Serbia, Singapore, South Korea, Switzerland, Taiwan, Thailand, and the United Kingdom, for use in adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations, after failure of platinum-based therapy.

RYBREVA[®] has a novel mechanism of action, which includes EGFR/MET ligand blocking, EGFR/MET receptor degradation, and immune cell-directing activity. RYBREVA[®] has demonstrated efficacy and safety in a broad range of patient populations. Various clinical trials are ongoing to assess its use in varied patient populations.

Development

Amivantamab is a low-fucose, fully human, IgG 1-based bispecific antibody directed against the EGFR and MET receptors. The human Fcγ1_{3a} receptor on natural killer cells, critical for antibody-dependent cellular cytotoxicity (ADCC), binds low-fucose antibodies more tightly and consequently mediates more potent and effective ADCC killing of target cancer cells.

Amivantamab was developed for the treatment of EGFR-mutated NSCLC, based on the hypothesis that by targeting the extracellular domains of each receptor (EGFR and MET), this bispecific antibody would demonstrate activity against tumors resistant to EGFR TKIs, either through primary resistance, or via the two most frequent mechanisms of resistance to current EGFR therapies: (1) secondary/tertiary mutations in EGFR, and (2) MET amplification or mutation. Amivantamab has demonstrated preclinical activity against tumors with the primary activating EGFR mutations, the T790M and C797S second-site resistance EGFR mutations, overexpressed wild-type EGFR, and activation of the MET pathway. Preclinical studies have demonstrated in vitro and in vivo efficacy and safety using various models.

Notably, amivantamab's three MOAs are not required to occur simultaneously for amivantamab to be efficacious, broadening its use for diverse antitumor mechanisms. Thus, the clinical development program, which includes studies of amivantamab as both monotherapy and combination therapy, spans a vast range of patient populations.

Innovation

Amivantamab's novel mechanism of action, including its bispecificity and extracellular targets, and its preclinical and early clinical antitumor efficacy and safety, suggests that through continued trials and research, it has the potential to provide innovative treatment options as monotherapy and combination therapy. Amivantamab was developed for EGFR- and MET alteration-driven tumors, which are common resistance mechanisms to current therapies.

Several trials with multiple cohorts are underway to determine the efficacy of amivantamab monotherapy and combination therapy in diverse populations. CHRYSALIS (NCT02609776), CHRYSALIS-2 (NCT04077463), MARIPOSA (NCT04487080), MARIPOSA-2 (NCT04988295), and PAPILLON (NCT04538664) trials are studying amivantamab in combination with the 3rd-generation TKI lazertinib and/or chemotherapy in patients with common and uncommon EGFR and MET mutations. The phase 3 MARIPOSA, MARIPOSA-2, and PAPILLON trials are fully accrued. The MET-2 cohort of the CHRYSALIS (NCT02609776) trial is evaluating amivantamab monotherapy in treatment

naïve and previously treated patients with advanced or metastatic NSCLC MET exon 14 skipping mutations, with promising preliminary results. The METalmark/KALEIDOSCOPE (NCT05488314) trial is evaluating amivantamab plus capmatinib in metastatic NSCLC with MET mutations.

Another innovation of amivantamab research and development relates to its mode of delivery; the PALOMA (NCT04606381) trial is evaluating subcutaneous delivery amivantamab therapy aimed at improving the treatment experience of patients and medical providers. The PALOMA-2 (NCT05498428) and PALOMA-3 (NCT05388669) trials are evaluating subcutaneous amivantamab as combination therapies. Enrollment in these trials has been robust, reflecting enthusiasm for amivantamab among the clinical community. Continuation of this trend will lead to more innovation and more treatment options for patients.

RYBREVENT® has already received the British Pharmacological Society's prestigious annual award for Drug Discovery of the Year 2023.

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Attachments

- 1656636519Section_1_RYBREVANT_Product.pdf
- 1656636556Section_2_RYBREVANT_Background.pdf
- 1656636642Section_3_RYBREVANT_Development.pdf
- 1656636696Section_4_RYBREVANT_Innovation.pdf
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