FOR EUROPEAN MEDICAL AND TRADE MEDIA ONLY

Johnson&Johnson

Media contact:
Zayn Qureshi
zqureshi@its.jnj.com
+44 7760 334666

Investor contact:
Raychel Kruper
investor-relations@its.jnj.com

For Immediate Release

CHMP adopts positive opinion for BALVERSA® (erdafitinib) for the treatment of adult patients with unresectable or metastatic urothelial carcinoma with susceptible FGFR3 genetic alterations

Pending approval, erdafitinib would become the first therapy targeting FGFR3 alterations in patients with metastatic urothelial carcinoma, one of Europe's most common cancers[1]

The CHMP's recommendation is based on results from Cohort 1 of the Phase 3 THOR study, which showed a 36 percent reduction in the risk of death with erdafitinib versus chemotherapy[2]

BEERSE, Belgium (28 June, 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended marketing authorisation for BALVERSA® (erdafitinib) as a once-daily oral monotherapy for the treatment of adult patients with unresectable or metastatic urothelial carcinoma (UC), harbouring susceptible FGFR3 genetic alterations who have previously received at least one line of therapy containing a PD-1 or PD-L1 inhibitor in the unresectable or metastatic treatment setting.[3] Erdafitinib is the first targeted therapy to receive a positive CHMP recommendation in this patient population.[3]

"FGFR alterations are important oncogenic drivers in urothelial carcinoma and can be associated with adverse clinical outcomes," said Yohann Loriot, M.D., Ph.D., Institut Gustave Roussy and University of Paris-Saclay, France.‡ "As we aim to optimise treatment outcomes for patients, there is a significant unmet need for novel, targeted therapies that enable treatment decisions tailored according to a patient's individual genetic and disease characteristics."

Europe has one of the highest rates of bladder cancer in the world, with nearly 225,000 patients diagnosed in 2022[1] representing a 10 percent increase from 2020.[4] The most common form of bladder cancer is UC,[5] and up to 20 percent of patients with metastatic UC (mUC) have FGFR alterations.[6] Unfortunately, prognoses remain poor for patients with mUC, with only eight percent of people diagnosed at a late metastatic stage surviving for five years or more.[7,8]

"Today's recommendation from the CHMP marks important progress towards transforming outcomes for patients diagnosed with bladder cancer with FGFR alterations. There is a critical need for a multidisciplinary care team approach, to identify patients who may benefit from erdafitinib through biomarker testing, ensuring the right treatment reaches the right patient at the right time," said Henar Hevia, Ph.D., Senior Director, EMEA Therapeutic Area Lead, Oncology, Johnson & Johnson Innovative Medicine. "Pending approval, we look forward to providing eligible patients across the region with a new treatment option as soon as possible."

The positive CHMP opinion is supported by data from Cohort 1 of the randomised, controlled, open-label multicentre Phase 3 THOR study (NCT03390504),[9] evaluating the efficacy and safety of erdafitinib (n=136) versus chemotherapy (n=130) in patients with advanced or mUC with select FGFR alterations who have progressed on or after one or two prior treatments, at least one of which includes an anti-PD-(L) 1 agent.[9] In June 2023, based on the recommendation of the independent data safety monitoring committee, the THOR study was stopped at the interim analysis for efficacy and all patients randomised to chemotherapy (docetaxel or vinflunine) were offered the opportunity to cross over to erdafitinib.[2] The results demonstrate median overall survival (OS) of over one year at the data cut-off, marking a significant increase as compared to those in the chemotherapy arm (12.1 months vs. 7.8 months; hazard ratio [HR], 0.64; 95 percent confidence interval [CI], 0.44 to 0.93; P=0.0050).[10] Treatment with erdafitinib also showed an improvement in median progression-free survival [PFS] compared to chemotherapy of 5.6 months versus 2.7 months (HR 0.58; 95 percent CI, 0.41 to 0.82; P=0.0002) and overall response rate [ORR] of 35.3 percent versus 8.5 percent.[10]

Serious treatment-related adverse events (TRAEs) were observed in 13.3 percent of patients who received erdafitinib and 24.1 percent of patients randomised to chemotherapy.[2] Grade 3 or higher adverse events were observed in 45.9 percent of patients on erdafitinib and 46.4 percent on chemotherapy.[2] Amongst patients who received erdafitinib, 8.1 percent had TRAEs that led to discontinuation of therapy, versus 13.4 percent of patients who received chemotherapy.[2] TRAEs leading to death were reported in one patient who received erdafitinib and six patients who received chemotherapy.[2]

“Erdafitinib has been shown to significantly improve outcomes for patients with FGFR3-altered urothelial carcinoma based on the THOR study results and represents an important new therapeutic option for these patients,” said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumours, Johnson & Johnson Innovative Medicine. “We are dedicated to advancing precision medicine approaches in oncology to improve patient outcomes, and this positive CHMP opinion is a significant milestone in our efforts to combat bladder cancer.”

#ENDS#

About the THOR Study

THOR (NCT03390504) is a Phase 3 randomised, open-label, multicentre study evaluating the efficacy and safety of erdafitinib. All patients included in the study had metastatic or unresectable UC,[9] with selected FGFR genetic alterations and showed disease progression during or after one or two prior lines of treatment.[9] The study compared erdafitinib in two cohorts; erdafitinib versus standard of care chemotherapy (investigators choice of docetaxel or vinflunine) after at least one line of treatment including an anti-PD-(L)1 agent (Cohort 1);[9] and erdafitinib compared to pembrolizumab after one prior treatment not containing an anti-PD-(L)1 agent (Cohort 2).[9] The trial consists of a screening step, a treatment phase (from randomisation until disease progression, intolerable toxicity, withdrawal of consent or decision by investigator to discontinue treatment) and a post-treatment follow-up (from end-of-treatment to participants death, withdraws consent, lost to follow-up study completion for the respective cohort, whichever comes first).[9] A long-term extension period is already operational following the clinical cut-off date of the final analysis of each cohort and eligible patients are continuing to benefit from the study intervention.[9] The primary endpoint of the study is OS, with secondary endpoints being PFS, ORR, duration of response (DOR), patient-reported outcomes, safety and pharmacokinetics (PK).[9]

Results from Cohort 1 were presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting,[2] with findings from Cohort 2 presented at the 2023 European Society of Medical Oncology (ESMO) congress.[11]

About Erdafitinib

Erdafitinib is a pan-fibroblast growth factor receptor (FGFR) tyrosine kinase inhibitor being evaluated by Janssen Research & Development, LLC in clinical trials in patients with advanced urothelial cancer.[12]

In addition to the Phase 3 THOR/BLC3001 (NCT03390504) study,[9] erdafitinib is being studied as a once-daily oral tablet in: the Phase 2 THOR-2/BLC2003 (NCT04172675)[13] study examining erdafitinib versus investigator choice of intravesical chemotherapy in participants who received Bacillus Calmette-Guérin and recurred with high risk non-muscle-invasive bladder cancer; the Phase 1b/2 NORSE/BLC2002 (NCT03473743)[14] study of erdafitinib in combination with cetrelimab in patients with locally advanced or mUC and FGFR3 or FGFR2 gene alterations; and the Phase 2 RAGNAR/CAN2002 (NCT04083976)[15] study evaluating the safety and efficacy of erdafitinib in patients with advanced solid tumours, regardless of cancer type or tumour location (tumour-agnostic), driven by FGFR1–4 alterations.

Erdafitinib is also being investigated in the Phase 1 study/BLC1003 (NCT05316155)[16] evaluating erdafitinib in patients with non-muscle invasive or muscle invasive bladder cancer with selected FGFR alterations, given via the intravesical targeted releasing system (TAR-210)[16] ; and the Phase 3 MoonRISe-1 /BLC3004 (NCT06319820) study evaluating TAR-210 versus single agent intravesical cancer treatment in participants with bladder cancer.[17]

In addition to the marketing authorisation submitted to the EMA in September 2023, in January 2024 Johnson & Johnson obtained U.S. Food and Drug Administration (FDA) approval of erdafitinib for the treatment of adult patients with locally advanced or mUC with susceptible FGFR3 genetic alterations, whose disease has progressed on or after at least one line of prior systemic therapy, based upon Cohort 1 of the Phase 3 THOR study.[18]

In 2008, Janssen Pharmaceutica NV entered into an exclusive worldwide licence and collaboration agreement with Astex Therapeutics Limited to develop and commercialise erdafitinib.[19]

About Urothelial Carcinoma

Urothelial carcinoma (UC), also known as transitional cell carcinoma, starts in the innermost lining of the bladder.[20] Almost all bladder cancers – more than 90 percent – are UCs.[21] Up to one in five patients (20 percent) diagnosed with mUC have a fibroblast growth factor receptor (FGFR) genetic alteration.[8] FGFRs are a family of receptor tyrosine kinases that can be activated by genetic alterations in a variety of tumour types, and these alterations may lead to increased tumour cell growth and survival.[22] FGFRs play a key role in several biological processes, including tissue repair, inflammatory response and metabolism.[23] Fusions or mutations in the genes that control FGFR (known as FGFR1–4 alterations) may lead to the development and progression of certain cancers by increasing tumour cell growth and survival.[24] Patients with advanced UC, including FGFR-driven tumours, face a poor prognosis and the need for innovative therapies remains high.[25] The five-year survival rate for patients with metastatic bladder cancer that has spread to distant parts of the body is currently 8 percent.[26]

About FGFR Testing

Testing for somatic mutations and fusions in FGFR genes can identify patients with urothelial carcinoma who may be eligible for treatment with FGFR-targeted therapies such as erdafitinib.[27] Identification of actionable FGFR alterations may allow for utilisation of biomarker-guided therapy.[28] FGFR testing to detect gene mutations, fusions and amplifications can be performed using validated laboratory developed tests involving polymerase chain reaction (PCR) and next-generation sequencing (NGS) techniques as recommended in the ESMO 2024 and EAU 2024 guidelines.[28,29,30] These guidelines recommend early molecular/genomic testing, ideally at diagnosis of advanced bladder cancer, to facilitate treatment decision-making and prevent delays in administering later lines of therapy.[30,31]

About Johnson & Johnson

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.

Learn more at https://www.twitter.com/JNJInnovMedEMEA. Follow us at https://www.linkedin.com/company/jnj-innvoative-medicine-emea for our latest news. Janssen-Cilag International NV, Janssen Pharmaceutica NV and Janssen Research & Development, LLC are Johnson & Johnson companies.

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 erdafitinib. 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-Cilag International NV, Janssen Pharmaceutica NV, Janssen Research & Development, LLC 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; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes in behavior 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-Cilag International NV, Janssen Pharmaceutica NV, Janssen Research & Development, LLC nor Johnson & Johnson undertake to update any forward-looking statement as a result of new information or future events or developments.

‡ Professor Loriot has provided consulting, advisory, and speaking services to Johnson & Johnson; they have not been paid for any media work.

References

CP-457588
June 2024

[1] Globocan 2022. Europe Cancer Factsheet. Available at: https://gco.iarc.who.int/media/globocan/factsheets/cancers/30-bladder-fact-sheet.pdf. Accessed June 2024.
[2] Loriot Y, et al. Phase 3 THOR study: Results of erdafitinib (erda) versus chemotherapy (chemo) in patients (pts) with advanced or metastatic urothelial cancer (mUC) with select fibroblast growth factor receptor alterations (*FGFRalt*). J Clin Oncol 2023;41(17). Available at: https://doi.org/10.1200/JCO.2023.41.17_suppl.LBA4619. Accessed June 2024.
[3] European Medicines Agency. Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 24 – 27 June 2024. Available at:https://www.ema.europa.eu/en/news/meeting-highlights-committee-medicinal-products-human-use-chmp-24-27-june-2024. Accessed June 2024.
[4] Globocan 2020. Europe Cancer Factsheet. Available at: https://gco.iarc.fr/today/data/factsheets/populations/908-europe-fact-sheets.pdf. Accessed June 2024.
[5] Cancer.net. Bladder cancer: introduction. Available at: https://www.cancer.net/cancer-types/bladder-cancer/introduction#:~:text=Urothelial%20carcinoma%20(or%20UCC)%20accounts,that%20line%20the%20urinary%20tract. Accessed: June 2024.
[6] Fernandez E, et al. Prognostic value and clinical significance of FGFR genomic alterations (GAs) in metastatic urothelial cancer patients. J Clin Med 2022;11(15):4483.
[7] Cancer.gov. Bladder Cancer Prognosis and Survival Rates – NCI (2023). Available at: https://www.cancer.gov/types/bladder/survival. Accessed: June 2024.
[8] Montazeri K & Bellmunt J. Erdafitinib for the treatment of metastatic bladder cancer. Expert Review of Clinical Pharmacology. 2020;13(1):1-6.
[9] Clinicaltrials.gov. A Study of Erdafitinib Compared With Vinflunine or Docetaxel or Pembrolizumab in Participants With Advanced Urothelial Cancer and Selected Fibroblast Growth Factor Receptor (FGFR) Gene Aberrations (THOR). Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03390504?term=NCT03390504&draw=2&rank=1. Accessed June 2024.
[10] European Medicines Agency. Balversa Summary of Product Characteristics. June 2024. Accessed: June 2024.
[11] Loriot Y, et al. Erdafitinib Prolongs Survival in Patients with Metastatic Urothelial Carcinoma and FGFR Alterations After Previous Anti–PD1(-L1) Treatment. Available at: https://www.esmo.org/oncology-news/erdafitinib-prolongs-survival-in-patients-with-metastatic-urothelial-carcinoma-and-fgfr-alterations-after-previous-anti-pd1-l1-treatment. Accessed June 2024.
[12] Tabernero J, et al. Phase I dose-escalation study of JNJ-42756493, an oral pan-fibroblast growth factor receptor inhibitor, in patients with advanced solid tumours. J Clin Oncol. 2015;33:3401–3408.5
[13] Clinicaltrials.gov. A Study of Erdafitinib Versus Investigator Choice of Intravesical Chemotherapy in Participants Who Received Bacillus Calmette-Guérin (BCG) and Recurred With High Risk Non-Muscle-Invasive Bladder Cancer (NMIBC). Available at: https://clinicaltrials.gov/study/NCT04172675. Accessed June 2024.
[14] Clinicaltrials.gov. A Study of Erdafitinib in Participants With Metastatic or Locally Advanced Urothelial Cancer. Available at: https://clinicaltrials.gov/study/NCT03473743. Accessed June 2024.
[15] Clinicaltrials.gov. A Study of Erdafitinib in Participants With Advanced Solid Tumors and Fibroblast Growth Factor Receptor (FGFR) Gene Alterations (RAGNAR). Available at: https://clinicaltrials.gov/study/NCT04083976. Accessed June 2024.
[16] Clinicaltrials.gov. Study of Erdafitinib Intravesical Delivery System for Localized Bladder Cancer. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05316155. Accessed June 2024.
[17] Clinicaltrials.gov. A study to evaluate TAR-210 versus single agent intravesical cancer treatment in participants with bladder cancer. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT06319820. Accessed June 2024.
[18] JnJ.com. Janssen Submits Marketing Authorisation Application to the European Medicines Agency Seeking Approval of Erdafitinib for the Treatment of Patients with Locally Advanced or Metastatic Urothelial Cancer with Susceptible FGFR Alterations. Available at: https://www.jnj.com/media-center/press-releases/janssen-submits-marketing-authorisation-application-to-the-european-medicines-agency-seeking-approval-of-erdafitinib-for-the-treatment-of-patients-with-locally-advanced-or-metastatic-urothelial-cancer-with-susceptible-fgfr-alterations. Accessed June 2024.
[19] Astex Therapeutics Limited. Astex Announces New Drug Discovery Alliance with Janssen Pharmaceutica N.V. 2008. Available at: https://astx.com/wp-content/uploads/2016/11/ASTX_News_2008_6_9_General_Releases.pdf. Accessed June 2024.
[20] Tanaka M, Sonpavde G. Diagnosis and Management of Urothelial Carcinoma of the Bladder. Postgraduate Medicine 2011;123(3):43-55.
[21] Milojevic B, et al. Urothelial carcinoma: Recurrence and risk factors. J BUON 2015;20(2):391-8.
[22] Presta M, et al. Fibroblast growth factors (FGFs) in cancer: FGF traps as a new therapeutic approach. Pharmacol Ther 2017;179:171-187.
[23] Xie Y, et al. FGF/FGFR signaling in health and disease. Sig Transduct Target Ther 2020;5(181):1-38.
[24] Katoh M. Fibroblast growth factor receptors as treatment targets in clinical oncology. Nat Rev Clin

Oncol 2019;16(2):105-122.
[25] Loriot Y, et al. Erdafitinib in Locally Advanced or Metastatic Urothelial Carcinoma. N Engl J Med 2019;381(4):338-348.
[26] American Cancer Society. Survival Rates for Bladder Cancer. Available at: https://www.cancer.org/cancer/types/bladder-cancer/detection-diagnosis-staging/survival-rates.html. Accessed June 2024.
[27] De Luca A, et al. FGFR fusions in cancer: from diagnostic approaches to therapeutic intervention. Int J Mol Sci 2020;21(18):6856.
[28] Schmidt KT, et al. Precision oncology medicine: the clinical relevance of patient-specific biomarkers used to optimize cancer treatment. J Clin Pharmacol 2016;56(12):1484–1499.
[29] Witjes J.A., et al. EAU guidelines on muscle-invasive and metastatic bladder cancer. Available at: https://uroweb.org/guidelines/muscle-invasive-and-metastatic-bladder-cancer. Accessed June 2024.
[30] Powles T, et al. ESMO Clinical Practice Guideline interim update on first-line therapy in advanced urothelial carcinoma. Annals of Oncology 2024;35(6):485-490.
[31] Powles T, et al. Bladder cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. Ann Oncol 2022;33(3):244–258.