

The Medical Letter[®]

on Drugs and Therapeutics

Volume 66

Published online November 11, 2024

Online
Article

IN THIS ISSUE

In Brief: A New Non-Small Cell Lung Cancer Indication for Osimertinib (*Tagrisso*)

Important Copyright Message

FORWARDING OR COPYING IS A VIOLATION OF U.S. AND INTERNATIONAL COPYRIGHT LAWS

The Medical Letter, Inc. publications are protected by U.S. and international copyright laws. Forwarding, copying, or any distribution of this material without permission to a nonsubscriber is prohibited.

Sharing a password with a nonsubscriber or otherwise making the contents of this site available to third parties is prohibited.

By accessing and reading the attached content I agree to comply with U.S. and international copyright laws and these terms and conditions of The Medical Letter, Inc.

For further information click: [Subscriptions](#), [Site Licenses](#), [Reprints](#)
or call customer service at: 800-211-2769

The Medical Letter[®]

on Drugs and Therapeutics

Volume 66

Published online November 11, 2024

Online
Article

IN THIS ISSUE

In Brief: A New Non-Small Cell Lung Cancer Indication for Osimertinib (*Tagrisso*)

IN BRIEF

A New Non-Small Cell Lung Cancer Indication for Osimertinib (*Tagrisso*)

The oral kinase inhibitor osimertinib (*Tagrisso* – AstraZeneca), which has been available for years for treatment of non-small cell lung cancer (NSCLC) in adults with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, has now been approved for treatment of unresectable stage III EGFR-mutated NSCLC.¹ About 20-30% of patients with NSCLC have locally advanced stage III NSCLC, and 60-90% of these patients have unresectable disease. Osimertinib is the first targeted therapy to be approved for the new indication.

MECHANISM OF ACTION – Osimertinib is a kinase inhibitor of EGFR; it binds to certain mutant forms of EGFR and disrupts EGFR signaling functions.

CLINICAL STUDIES – FDA approval of osimertinib for the new indication was based on the results of a double-blind trial (LAURA) in 216 patients with unresectable EGFR-mutated stage III NSCLC who did not have disease progression during or after chemoradiotherapy. Patients were randomized to receive osimertinib or placebo once daily until disease progression or unacceptable toxicity occurred. Median progression-free survival, the primary endpoint, was significantly longer with osimertinib than with placebo (39.1 months vs 5.6 months). About 65% of patients in the osimertinib arm were alive and progression free at 24 months compared to 13% of those in the placebo arm. Osimertinib reduced the risk of disease progression and the incidence of distant metastases, including new brain and lung lesions, compared to placebo. The objective response rate was higher (57% vs 33%) and the median duration of response was longer (36.9 months vs 6.5 months) with osimertinib than with placebo.²

Table 1. FDA-Approved Indications of Osimertinib

- ▶ Adjuvant treatment of NSCLC after tumor resection in adults whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations.
- ▶ Treatment of locally advanced, unresectable stage III NSCLC in adults whose disease has not progressed during or following concurrent or sequential platinum-based chemoradiation therapy and whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations.
- ▶ First-line treatment of metastatic NSCLC in adults whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations.
- ▶ First-line treatment in combination with pemetrexed and platinum-based chemotherapy for locally advanced or metastatic NSCLC in adults whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations.
- ▶ Treatment of EGFR T790M mutation-positive NSCLC in adults whose disease progressed on or after EGFR tyrosine kinase inhibitor therapy.

ADVERSE EFFECTS – In the LAURA trial, the most common adverse effects of osimertinib were radiation pneumonitis, diarrhea, and rash. QT-interval prolongation and torsades de pointes, cardiomyopathy, keratitis, Stevens-Johnson syndrome, erythema multiforme major, cutaneous vasculitis, and aplastic anemia have been reported with use of the drug.

DRUG INTERACTIONS – Coadministration of CYP3A4 inducers³ can decrease serum concentrations of osimertinib and possibly its efficacy and should be avoided; if concurrent administration is necessary, the dosage of osimertinib should be increased to 160 mg once daily. Osimertinib can increase the exposure of drugs that are substrates of breast cancer resistant protein (BCRP) or P-glycoprotein (P-gp). Administration of other drugs that also prolong the QT interval can increase the risk of torsades de pointes.

DOSAGE, ADMINISTRATION, AND COST – *Tagrisso* is supplied in 40- and 80-mg tablets. The recommended dosage for the new indication is 80 mg taken once daily until disease progression or unacceptable toxicity

occurs. The label contains dosage adjustments that should be made if adverse effects occur. Osimertinib should be discontinued if interstitial lung disease/pneumonitis occurs. The wholesale acquisition cost (WAC) of a 30-day supply of *Tagrisso* is \$17,117.30.⁴

CONCLUSION – In one clinical trial, the oral kinase inhibitor osimertinib (*Tagrisso*) significantly extended progression-free survival and reduced the risk of disease progression in patients with unresectable stage III EGFR-mutated non-small cell lung cancer (NSCLC). ■

1. Osimertinib (Tagrisso) for adjuvant treatment of NSCLC. *Med Lett Drugs Ther* 2023; 65:e131.
2. S Lu et al. Osimertinib after chemoradiotherapy in stage III EGFR-mutated NSCLC. *N Engl J Med* 2024; 391:585.
3. Inhibitors and inducers of CYP enzymes, P-glycoprotein, and other transporters. *Med Lett Drugs Ther* 2023 January 25 (epub). Available at: www.medicalletter.org/downloads/CYP_PGP_Tables.pdf.
4. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. October 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2024. www.fdbhealth.com/policies/drug-pricing-policy.

PRESIDENT: Mark Abramowicz, M.D.; **VICE PRESIDENT, EDITOR IN CHIEF:** Jean-Marie Pflomm, Pharm.D.; **ASSOCIATE EDITORS:** Susan M. Daron, Pharm.D., Amy Faucard, MLS, Michael P. Viscusi, Pharm.D. **CONSULTING EDITORS:** Joanna Esterow, PA-C, Mordechai Sacks, DMSc, PA-C, Brinda M. Shah, Pharm.D., F. Peter Swanson, M.D.

CONTRIBUTING EDITORS: Carl W. Bazil, M.D., Ph.D., Columbia University College of Physicians and Surgeons; Ericka L. Crouse, Pharm.D., B.C.P.P., C.G.P., F.A.S.H.P., F.A.S.C.P., Virginia Commonwealth University; Vanessa K. Dalton, M.D., M.P.H., University of Michigan Medical School; Eric J. Epstein, M.D., Albert Einstein College of Medicine; David N. Juurlink, BPhM, M.D., Ph.D., Sunnybrook Health Sciences Centre; Richard B. Kim, M.D., University of Western Ontario; Sandip K. Mukherjee, M.D., F.A.C.C., Yale School of Medicine; Dan M. Roden, M.D., Vanderbilt University School of Medicine; Esperance A.K. Schaefer, M.D., M.P.H., Harvard Medical School; Arthur M. F. Yee, M.D., Ph.D., F.A.C.R., Weill Medical College of Cornell University

MANAGING EDITOR AND DIRECTOR OF CONTENT OPERATIONS: Susie Wong; **EDITORIAL ASSISTANT:** Karrie Ferrara

FULFILLMENT AND SYSTEMS MANAGER: Cristine Romatowski; **EXECUTIVE DIRECTOR OF SALES:** Elaine Reaney-Tomaselli

EXECUTIVE DIRECTOR OF MARKETING AND COMMUNICATIONS: Joanne F. Valentino; **INTERIM PUBLISHER:** Jean-Marie Pflomm, Pharm.D.

Founded in 1959 by Arthur Kallet and Harold Aaron, M.D.

Copyright and Disclaimer: The Medical Letter, Inc. is an independent nonprofit organization that provides healthcare professionals with unbiased drug prescribing recommendations. The editorial process used for its publications relies on a review of published and unpublished literature, with an emphasis on controlled clinical trials, and on the opinions of its consultants. The Medical Letter, Inc. does not sell advertising or receive any commercial support. No part of the material may be reproduced or transmitted by any process in whole or in part without prior permission in writing. The Medical Letter, Inc. does not warrant that all the material in this publication is accurate and complete in every respect. The Medical Letter, Inc. and its editors shall not be held responsible for any damage resulting from any error, inaccuracy, or omission.

Subscription Services

Address:

The Medical Letter, Inc.
145 Huguenot St. Ste. 312
New Rochelle, NY 10801-7537
www.medicalletter.org

Customer Service:

Call: 800-211-2769 or 914-235-0500
Fax: 914-632-1733
E-mail: custserv@medicalletter.org

Permissions:

To reproduce any portion of this issue, please e-mail your request to: permissions@medicalletter.org

Subscriptions (US):

1 year - \$159; \$65 per year for students, interns, residents, and fellows in the US and Canada. Reprints - \$45 per issue or article

Site License Inquiries:

E-mail: SubQuote@medicalletter.org
Call: 800-211-2769
Special rates available for bulk subscriptions.