Drugs (2025) 85:1055–1058
https://doi.org/10.1007/s40265-025-02184-y

ADISINSIGHT REPORT

Limertinib: First Approval

Arnold Lee[1]

Accepted: 7 April 2025 / Published online: 23 June 2025

Abstract
Limertinib (Aoyixin) is an orally available, third-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI), which has been developed for the treatment of non-small cell lung cancer (NSCLC). In clinical trials, limertinib demonstrated efficacy in patients who are positive for the T790M gatekeeper mutation. Limertinib received its first approval for the treatment of adults with locally advanced or metastatic NSCLC with disease progression following treatment with an EGFR TKI and are positive for the EGFR T790M mutation in China in January 2025. In April 2025, limertinib was also approved in China for first-line treatment for adult patients with locally advanced or metastatic NSCLC harbouring EGFR exon 19 deletions or exon 21 L858R mutations. This article summarizes the milestones in the development of limertinib leading to this first approval.

Digital Features for this AdisInsight Report can be found at https://doi.org/10.6084/m9.figshare.28728923.

Limertinib (Aoyixin): Key Points

A tyrosine kinase inhibitor is being developed by Jiangsu Aosaikang Pharmaceutical Co. Ltd. for the treatment of NSCLC

Received its first approval on 14 Jan 2025 in China

Approved for use for treatment of adults with locally advanced or metastatic NSCLC with disease progression following treatment with an EGFR TKI and are positive for the EGFR T790M mutation. In April 2025, limertinib was also approved in China for first-line treatment for adult patients with locally advanced or metastatic NSCLC harbouring EGFR exon 19 deletions or exon 21 L858R mutations

1 Introduction

Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) have been successfully used for the treatment of non-small cell lung cancer (NSCLC) [1]. However, the efficacy of earlier first-generation and second-generation EGFR TKIs is limited by resistance mutations, such as the T790M gatekeeper mutation that is frequently acquired following treatment with these early TKIs. Osimertinib was the first approved third-generation EGFR TKI that is effective for the treatment of *EGFR* T790M mutation-positive NSCLC, though a lack of other third-generation EGFR TKIs has limited the accessibility of treatment [1].

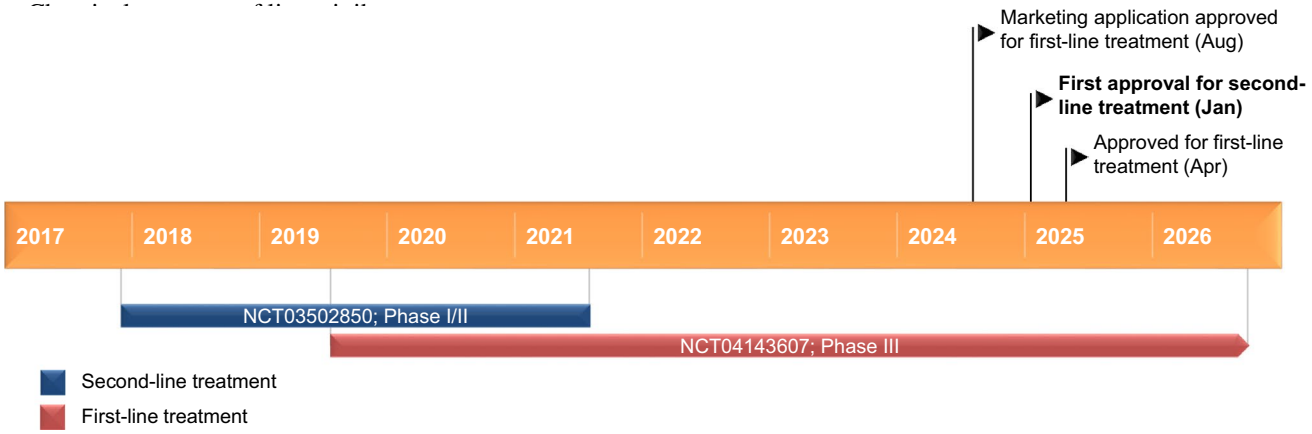
Limertinib (Aoyixin) is an orally available, third-generation EGFR TKI approved in January 2025 in China for the treatment of adults with locally advanced or metastatic NSCLC with disease progression following treatment with an EGFR TKI and are positive for the *EGFR* T790M mutation [2–4]. Limertinib has since been approved in April 2025 in China for the first-line treatment of adults with locally advanced or metastatic NSCLC harbouring EGFR exon 19 deletions (exon19del) or exon 21 L858R mutations [5].

The recommended dosage of limertinib is 160 mg twice daily taken on an empty stomach until disease progression or unacceptable toxicity; consult local prescribing information for recommendations regarding dose modification for the management of adverse reactions [2]. The presence of an *EGFR* T790M mutation should be determined from tumour tissue samples or from circulating tumour DNA prior to initiating limertinib. The use of limertinib is contraindicated in patients who have hypersensitivity reactions to limertinib or its excipients [2].

This profile has been extracted and modified from the *AdisInsight* database. *AdisInsight* tracks drug development worldwide through the entire development process, from discovery, through pre-clinical and clinical studies to market launch and beyond.

✉ Arnold Lee
dru@adis.com

[1] Springer Nature, Private Bag 65901, Mairangi Bay, Auckland 0754, New Zealand



Key milestones in the development of limertinib for the treatment of locally advanced or metastatic non-small cell lung cancer in China.

1.1 Company Agreements

In October 2024, Jiangsu Aosaikang Pharmaceutical Co. Ltd. entered a strategic partnership with Innovent Biologics, Inc., where Innovent Biologics gained exclusive commercialization rights for limertinib in mainland China [6].

2 Scientific Summary

2.1 Pharmacodynamics

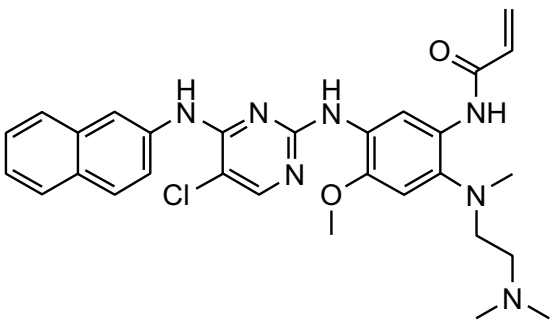
Limertinib selectively inhibits EGFR mutant variants including L858R/T790M (IC_{50} 0.3 nM), T790M (0.5 nM) and exon19del (0.5 nM) in comparison with wild-type EGFR (6.0 nM), as determined by ELISA [7]. In cell lines, limertinib potently inhibited the growth of cells with the *EGFR* T790M mutation (IC_{50} 12 nM; NCI-H1975 cell line) and those with sensitizing mutations (2–6 nM; PC-9 and HCC-827), and less potently inhibited lines with wild-type EFGR (388–1916 nM; A431, LoVo and A549) [7].

Limertinib inhibited the growth of a cell line with an *EGFR* exon20 D770-N771 NPG insertion mutation (IC_{50} 0.15 μM; BaF3-EGFR insNPG cell line), with a shift in dose-response curves in comparison with gefitinib (3.51 μM) and erlotinib (4.11 μM) [8]. Furthermore, in a xenograft model with this cell line, limertinib demonstrated significant ($p < 0.05$) and dose-dependent inhibition of tumour growth in comparison with controls [8].

2.2 Pharmacokinetics

The maximum plasma concentration (C_{max}) and area under the plasma-time curve (AUC) of limertinib increases proportionally with higher doses over a range of 40–320 mg [2]. The time to maximum plasma concentration (T_{max}) following a single oral dose of limertinib is 2.02–3.50 h. Administration with a high-fat meal increases the T_{max} by ≈1.25 h, the C_{max} by 45.45% and AUC by 45.39%. Steady state is reached after 5 days of twice daily dosing, with an accumulation ratio of ≈ 2. The volume of distribution (V_D) is ≈ 162.8–229.3 L over a dose range of 40–320 mg, with > 99.5% plasma protein binding [2].

The terminal half-life of limertinib is 12.105–19.947 h and the plasma clearance is 7.303–12.928 L/h over a dose range of 40–320 mg [2]. It is predominantly metabolised by CYP3A4, with a minor active metabolite (CCB4580030) representing 2.32% of the radioactivity following a single radiolabelled dose of limertinib. The coadministration of a strong CYP3A4 inhibitor increases the C_{max} of limertinib by 89.65% and the AUC by 289.80%, and decreases the respective pharmacokinetic parameters of CCB4580030 by 75.28% and 35.96%. When coadministered with a strong CYP3A4 inducer, the C_{max} and AUC of limertinib decreases by 73.44% and 87.86%, and the C_{max} and AUC of CCB4580030 decreases by 19.76% and 66.86%. Following a single oral radiolabelled dose, 8.39% of the radioactivity was recovered from the urine and 76.40% in the faeces [2].



Chemical structure of limertinib

Features and properties of limertinib

Alternative names	Aoyixin, ASK 120067, Li'etini Pian
Class	Amides, anilides, aniline compounds, anisoles, antineoplastics, aromatic hydrocarbons, chlorinated hydrocarbons, ethylenediamines, naphthalenes, pyrimidines, small molecules
Mechanism of action	Epidermal growth factor receptor antagonist
Route of administration	Oral
Pharmacodynamics	Inhibits mutant EGFR kinases including L858R/T790M (IC_{50} 0.3 nM), T790M (0.5 nM) and exon19del (0.5 nM) plus wild-type EGFR (6.0 nM); inhibits cell lines with the EGFR T790M mutation (IC_{50} 12 nM), with sensitizing mutations (2–6 nM), EGFR exon20 insertion mutation (0.15 μM) and wild-type EFGR (388–1916 nM)
Pharmacokinetics	C_{max} and AUC ↑ proportionally with ↑ doses over a range of 40–320 mg; T_{max} 2.02–3.50 h; high fat meal ↑ T_{max} by ≈1.25 h, C_{max} by 45.45% and AUC by 45.39%; steady state is reached after 5 days of twice daily dosing; accumulation ratio ≈ 2; V_D ≈ 162.8–229.3 L; > 99.5% plasma protein binding; $t_{½}$ 12.105–19.947 h; CL 7.303–12.928 L/h; predominantly metabolised by CYP3A4, with a minor active metabolite; following a single dose 8.39% is excreted into the urine and 76.40% in the faeces
Most frequent adverse reactions	Diarrhoea, anaemia, nausea, loss of appetite, rash, vomiting
ATC codes	
WHO ATC code	L01 (antineoplastic agents)
EphMRA ATC code	L1 (antineoplastics)
Chemical name	N-[5-[[5-chloro-4-(naphthalen-2-ylamino)pyrimidin-2-yl]amino]-2-[2-(dimethylamino)ethyl-methylamino]-4-methoxyphenyl]prop-2-enamide

2.3 Therapeutic Trials

The objective response rate as determined by independent central review (ICR) was 68.8% (all partial responses) in 301 patients with previously treated, locally advanced or metastatic *EGFR* T790M-positive NSCLC (primary endpoint) [9]. In the open-label, single-arm, multicentre phase IIb portion of the NCT03502850 phase I/II trial, patients aged ≥ 18 years were treated with limertinib 160 mg twice daily in continuous 21-day cycles until disease progression or unacceptable toxicity. The disease control rate was 92.4% as determined by ICR. Median progression-free survival (PFS) was 11.0 months and median overall survival was not reached. As of the data cutoff date (9 Sep 2021), the median follow-up duration was 10.4 months [9].

Positive preliminary results for limertinib have been announced for the randomised, double-blind, positive-controlled phase III trial (NCT04143607) that investigated limertinib versus gefitinib for the first-line treatment of locally advanced or metastatic NSCLC in adults (n = 337) [5]. The NCT04143607 trial enrolled treatment-naïve patients with EGFR-sensitive mutation-positive locally advanced or metastatic NSCLC [5]; patients were randomized 1:1 receive twice-daily limertinib 80 mg plus placebo or twice-daily gefitinib 250 mg plus placebo [5, 10]. The primary outcome measure was median PFS [5].

Key clinical trials of limertinib (sponsored by Jiangsu Aosaikang Pharmaceutical Co., Ltd.)Key clinical trials of limertinib (sponsored by Jiangsu Aosaikang Pharmaceutical Co., Ltd.)

Drug(s)	Indication	Phase	Status	Location	Identifier
Limertinib, gefitinib	1L locally advanced or metastatic EGFR mutation-positive NSCLC	III	Ongoing	China	NCT04143607
Limertinib	2L locally advanced or metastatic T790M-positive NSCLC	I/II	Ongoing	China	NCT03502850

1/2L first/second line, *EGFR* epidermal growth factor receptor, *NSCLC* non-small cell lung cancer

2.4 Adverse Reactions

In 366 patients who received a dosage of limertinib ≥ 320 mg/day, the most common (incidence ≥ 20%) adverse reactions were diarrhoea (any-grade incidence 83.3%, grade ≥ 3 incidence 13.7%), anaemia (32.5%, 4.1%), nausea (30.3%, 0.5%), loss of appetite (29.8%, 1.1%), rash (29.5%, 3.0%) and vomiting (24.9%, 0.8%) [2].

Limertinib was discontinued due to an adverse reaction in 24.6% of patients who received a dosage of limertinib ≥ 320 mg/day [2]. The most common reactions (incidence ≥ 1%) associated with discontinuation were diarrhoea (discontinuation in 9.3% of patients), rash (1.9%), hypokalaemia (1.9%), decreased appetite (1.4%) and decreased platelet count (1.4%) [2].

2.5 Ongoing Clinical Trials

There is one ongoing clinical trial assessing the efficacy and safety of limertinib. The phase III NCT04143607 trial is investigating limertinib as first line treatment of locally advanced or metastatic EGFR mutation-positive NSCLC [10]. This trial is investigating the efficacy and safety of limertinib in comparison with gefitinib; preliminary results have been reported [5].

3 Current Status

Limertinib received its first approval on 14 Jan 2025 for the treatment of adults with locally advanced or metastatic NSCLC with disease progression following treatment with an EGFR TKI and are positive for the *EGFR* T790M mutation in China [3, 4]. Limertinib has since been approved in April 2025 in China for the first-line treatment of adults with locally advanced or metastatic NSCLC harbouring EGFR exon19del or exon 21 L858R mutations [5].

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40265-025-02184-y.

Declarations

Funding The preparation of this review was not supported by any external funding.

Authorship and Conflict of interest During the peer review process the manufacturer of the agent under review was offered an opportunity to comment on the article. Changes resulting from any comments received were made by the authors on the basis of scientific completeness and accuracy. Arnold Lee is a contracted employee of Adis International Ltd/Springer Nature, and declares no relevant conflicts of interest. All authors contributed to this article and are responsible for its content.

Ethics Approval, Consent to Participate, Consent to Publish, Availability of Data and Material, Code Availability Not applicable.

References

1. Lau SCM, Ou SI. And still they come over troubled waters: can Asia's third-generation EGFR tyrosine kinase inhibitors (furmonertinib, aumolertinib, rezivertinib, limertinib, befotertinib, SH-1028, and lazertinib) affect global treatment of EGFR+ NSCLC. J Thorac Oncol. 2022;17(10):1144–54.
2. Innovent Biologics Inc. Limertinib: Chinese prescribing information [Chinese]. 2025. https://img.innoventbio.com/25.02/Limertinib.pdf. Accessed 4 Apr 2025.
3. National Medical Products Administration. Limertinib tablets: NMPA approval details [Chinese]. 2025. https://www.nmpa.gov.cn. Accessed 4 Apr 2025.
4. National Medical Products Administration. NMPA approval announcement [Chinese] [media release]. 16 Jan 2025. https://www.nmpa.gov.cn/zhuanti/cxylqx/cxypxx/20250116195204142.html.
5. Innovent announces NMPA approval of limertinib, a third-generation EGFR TKI collaborated with ASK Pharma, for the first-line treatment of lung cancer [media release]. 25 Apr 2025. https://www.innoventbio.com.
6. Innovent Biologics Inc. Innovent and ASK Pharm announce strategic collaboration for limertinib, a third-generation EGFR TKI for the treatment of lung cancer [media release]. 8 Oct 2024. https://www.innoventbio.com.
7. Zhang T, Qu R, Chan S, et al. Discovery of a novel third-generation EGFR inhibitor and identification of a potential combination strategy to overcome resistance. Mol Cancer. 2020;19(1):90.
8. Zhang T, Feng F, Tong L, et al. ASK120067 (limertinib) exerts pre-clinical anti-tumor activity by inhibiting EGFR exon20 insertion. Front Drug Discov. 2022;2. https://doi.org/10.3389/fddsv.2022.1050687.
9. Shi Y, Li B, Wu L, et al. Efficacy and safety of limertinib (ASK120067) in patients with locally advanced or metastatic EGFR Thr790Met-mutated NSCLC: a multicenter, single-arm, phase 2b study. J Thorac Oncol. 2022;17(10):1205–15.
10. ClinicalTrials.gov. ASK120067 versus gefitinib as first-line treatment for EGFRm locally advanced or metastatic NSCLC. 2024. https://clinicaltrials.gov/study/NCT04143607. Accessed 2 Apr 2025.