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Research Article

The 200 Most Cited Articles in EGRF Mutant Non-small Cell Lung Cancer Bibliometric Analysis

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Abstract

Objectives: We analyzed the top 200 most cited EGFR mutant metastatic non-small cell lung cancer (NSCLC) articles. We aimed to highlight advancements and provide easy access to researchers in this dynamic field.

Methods: This research was conducted using the Web of Science (WoS) Core Collection database. The following keywords were used: "lung cancer" and (treat* or medic* or remedy or cure or therapy) and (mutant or mutation) and (egfr or “epidermal growth factor receptor”). The top 200 most cited articles were analyzed by topic, journal, author, year, country, keywords, and average citations per article.

Results: A total of 16.165 eligible articles were identified, and the top 200 most cited articles in the EGFR-mutant NSCLC field were selected. The average number of citations for these articles was 724.95. The most cited article (number of citations: 8,899) was by Chmielecki et al. The Journal of Clinical Oncology contributed the most to the top 200 list with 50 articles, while the most cited article was published in *Science Translational Medicine*.

Conclusion: The top 200 articles in our study not only reflect the most impactful studies in the EGFR-mutant NSCLC field but also highlight the most productive authors, journals, and countries contributing to this list.

Keywords: EGFR, Lung Cancer, NSCLC, Erlotinib, Bibliometric Analysis

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Lung cancer is the second most common cancer worldwide and the leading cause of cancer-related deaths.[1] Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer cases and is divided into three subtypes: adenocarcinoma, large cell carcinoma, and squamous cell carcinoma.[2,3] NSCLC is highly heterogeneous due to a variety of driver genetic mutations. In recent years, breakthroughs in NSCLC treatment, particularly with the discovery of targeted therapies and immunotherapy, have revolutionized the field. Personalized treatment approaches based on genetic profiles are gaining popularity. In general, treatment options for NSCLC primarily include surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy.[4,5] Most advancements in lung cancer treatment have occurred in the field of targeted therapies, especially for NSCLC patients with EGFR (epidermal growth factor receptor) mutations.[6] The use of targeted therapies has led to significant benefits in both progression-free survival and overall survival rates. EGFR is a transmembrane receptor with a crucial role in cancer cell proliferation, neoangiogenesis, and inhibition of apoptosis.[7] Overexpression of EGFR is associated with poor prognosis, making it a key target in cancer treatment.[8] Mutations in the EGFR gene are among the most common driver mutations in metastatic NSCLC. The incidence of EGFR mutations in advanced non-squamous NSCLC varies significantly, with

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approximately 10% in Western Europe, while in East Asian populations, this rate can reach as high as 64%.[9-11] Approximately 45% of EGFR mutations consist of exon 19 deletions, and 40% involve the L858R point mutation in exon 21.6 Exon 20 T790M is a rarer mutation, commonly detected in cases of resistance following treatment with first- or second-generation EGFR tyrosine kinase inhibitors.[12] The remaining mutations, known as rare mutations, account for approximately 10-15% of all EGFR mutations.[13]

Thousands of articles have been published on EGFR-mutant NSCLC, covering research areas such as treatment agents, resistance mechanisms, and treatment planning. It is essential, yet challenging, for researchers to identify the most popular articles and stay informed about research trends. Therefore, a comprehensive study is needed to systematically compile significant developments, present current research centers, and propose directions for future research. Bibliometrics is a statistical analysis of scientific publications related to a specific topic or field of study, helping identify the most influential countries, authors, publications, and active journals in that field.[14,15] Additionally, it provides summarized data, offering readers an opportunity to assess the current state of research.[16]

This study adopted a scientific analysis via the Web of Science (WoS) database to provide researchers with an advanced review of studies on EGFR-mutant NSCLC. This approach has the advantage of holistically gathering information to highlight the progress, key aspects, and limitations of the publications. In this study, newly developed visualization tools (such as VOSviewer) were used to map the global research landscape and leading trends in EGFR-mutant NSCLC from multiple perspectives.

Methods

For this analytical research, a search was conducted in the WoS Core Collection database on May 27, 2024. Publications from all result pages of the systematic search on the WoS interface were saved into a file and reviewed by the researcher. The search was performed using the terms "lung cancer" and (treat* or medic* or remedy or cure or therapy) and (mutant or mutation) and (egfr or "epidermal growth factor receptor") in the topic field. From a total of 16,165 articles, an initial assessment was concluded with the 200 most highly cited relevant articles after applying exclusion criteria based on citation rankings. No date limitation was applied during the filtering process. Only original articles were included, while reviews, abstracts, case reports, book chapters, editorial materials, meeting abstracts, and letters to the editor were excluded from the study. Articles not in English, duplicate articles, or irrelevant ones were also excluded.

For the final 200 articles, the publication year, country, time of publication, journal, institution, keywords, and citation data were recorded. VosViewer software was used to create network maps that include elements such as keywords, countries, authors, and citations, and to visualize and analyze trends through these maps.[17] In this study, VosViewer software (version 1.6.10) was employed for the bibliometric visualizations and analysis of these trend maps.[18]

Results

Using the WoS database, 500 articles were identified related to EGFR mutant NSCLC after excluding non-original articles and review papers. After filtering out non-English or articles not directly related to the English language, a final sample of 200 articles was selected. A significant increase in publications on this topic has been observed since 2004. The highest number of publications and citations comes from the United States. The five most cited articles on EGFR mutant NSCLC are: Paez, JG et al. (8899 citations), Mok, Tony S. et al. (7248 citations), Shepherd, FA et al. (4983 citations), Rosell, Rafael et al. (4719 citations), and Engelman, Jeffrey A. et al. (4314 citations). The Top 10 most commonly cited articles related to EGFR mutant NSCLC are summarized in Table 1.

The number of citations ranged from 8899 to 223. The average number of citations per article was 724.95. The most cited article, with 8899 citations, was by Paez, JG et al. titled "EGFR mutations in lung cancer: Correlation with clinical response to gefitinib therapy." The article with the fewest citations, at 223, was authored by Spigel, David R. et al., titled "Results From the Phase III Randomized Trial of Onartuzumab Plus Erlotinib Versus Erlotinib in Previously Treated Stage IIIB or IV Non-Small-Cell Lung Cancer: MET Lung," focusing on EGFR mutant NSCLC.

When examining the number of most-cited articles by year and applying regression analysis, it was found that the number of articles increased significantly from 6 in 2004 to 25 in 2005. An increasing trend in the number of publications over the years was observed. The distribution of articles by year is shown in Figure 1.

When analyzing based on the average number of citations per article, Plos Medicine had an average of 2792 citations per article. We can say that Plos Medicine is the most effective journal in terms of citation per published article. The top 10 journals by number of published articles are presented in Table 2.

The density map of the journals publishing articles on EGFR mutant NSCLC is shown in Figure 2.

When examining the authors of the most cited articles related to EGFR mutant NSCLC, we found that author PA

Table 1. Top-10 Most Commonly-cited Articles Related to EGRF Mutant NSCLC

Article Title	Authours	Institution	Journal	Year	Citations
EGFR mutations in lung cancer: Correlation with clinical response to gefitinib therapy	Paez, JG et al.	Harvard University	Science	2021	8899
Gefitinib or Carboplatin-Paclitaxel in Pulmonary Adenocarcinoma.	Mok, Tony S.et al.	Chinese University of Hong Kong	New England Journal of Medicine	2020	7248
Erlotinib in previously treated non-small-cell lung cancer	Shepherd, FA et al	University of Toronto	New England Journal of Medicine	2020	4983
Gefitinib or Chemotherapy for Non-Small-Cell Lung Cancer with Mutated EGFR.	Maemondo, Makoto et al.	Tohoku University	New England Journal of Medicine	2020	4862
Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): a multicentre, open-label, randomised phase 3 trial	Rosell, Rafael et al.	UNICANCER	Lancet Oncology	2020	4719
MET amplification leads to gefitinib resistance in lung cancer by activating ERBB3 signaling	Engelman, Jeffrey A et al.	Harvard University	Science	2020	4314
Erlotinib versus chemotherapy as first-line treatment for patients with advanced EGFR mutation-positive non-small-cell lung cancer (OPTIMAL, CTONG-0802): a multicentre, open-label, randomised, phase 3 study	Zhou, Caicun et al.	Tongji University	Lancet Oncology	2020	3674
Gefitinib versus cisplatin plus docetaxel in patients with non-small-cell lung cancer harbouring mutations of the epidermal growth factor receptor (WJTOG3405): an open label, randomised phase 3 trial	Mitsudomi, Tetsuya et al	Aichi Cancer Center	Lancet Oncology	2020	3514
Osimertinib in Untreated EGFR-Mutated Advanced Non-Small-Cell Lung Cancer	Soria, J. -C. Et al.	Universite Paris Cite	New England Journal of Medicine	2020	3420
Acquired resistance of lung adenocarcinomas to gefitinib or erlotinib is associated with a second mutation in the EGFR kinase domain	Pao, W et al.	Memorial Sloan Kettering Cancer Center	Plos Medicine	2019	3203

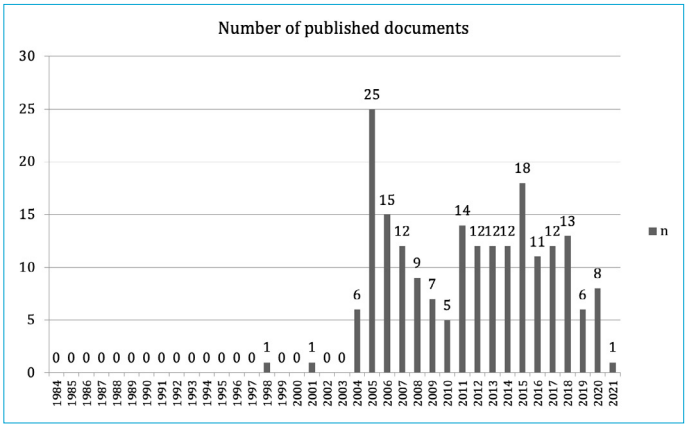

Figure 1. The Distribution of Articles by Year.

Jänne contributed to 27 articles. The top 10 authors who contributed the most to the 200 most cited articles are shown in Table 3.

The most frequently used keyword was "EGFR," followed by "NSCLC." In our study, a map was used to illustrate the keywords and their relationships, as shown in Figure 3.

The oldest article related to EGFR mutant NSCLC was published in 1998 in the Journal of Clinical Oncology. It is titled "Results From the Phase III Randomized Trial of Onartuzumab Plus Erlotinib Versus Erlotinib in Previously Treated Stage IIIB or IV Non-Small-Cell Lung Cancer: MET Lung" by Spigel, David R. et al., and has 223 citations. All of the top 200 articles were published in 32 different journals, with the majority appearing in the Journal of Clinical Oncology.

Discussion

Lung cancer is the leading cause of cancer-related deaths worldwide. Despite advancements in surgical methods and improvements in radiotherapy and chemotherapy, NSCLC remains a significant portion of lung cancers and is associated with a 5-year survival rate of about 15%.[19] In our rapidly evolving and information-rich era, it is quite challenging for researchers to keep track of developments in a particular field. Bibliometric analysis provides researchers with a comprehensive overview of the past, present, and even future of a field, offering insights into research trends over the past few decades. It also serves as a valuable resource for guiding future research directions.[20]

Table 2. Top 10 Journals by Number of Published Articles

Journal Name	Number of Articles	Number of Citations	Average Citations per Article
Journal of Clinical Oncology	50	20525	410
Clinical Cancer Research	31	9315	300
Lancet Oncology	19	12130	638
Journal of Thoracic Oncology	13	6908	531
Cancer Research	12	3265	272
Annals of Oncology	12	2788	232
New England Journal of Medicine	10	15741	1431
Cancer Discovery	7	1798	256
Plos Medicine	5	13960	2792
Nature Communications	3	2351	783

Table 3. Top 10 Authors With the Most Contributions

Author Name	Number of Articles	Percentage (%)
Jänne, PA	27	13.5
James Chih-Hsin Yang	23	11.5
Sequist, LV	21	10.5
Mok, TSK	19	9.5
Wu, YL	19	9.5
Miller, VA	17	8.5
Pao, W	16	8
Riely, GJ	12	6
Johnson, BE	12	6
Kris, MG	11	5.5

In this study, a visual analysis of research on EGFR-mutant NSCLC was conducted. No date limitations were applied during filtering, and the analysis was based on 16.165 research records obtained from the WoS Core Collection. Over the past decade, the number of articles on EGFR-mutant NSCLC has steadily increased, with this growth supported by a significant number of citations. Notably, a substantial increase in the number of publications was observed in highly cited journals, particularly from 2005 onwards.A total of 200 articles with 144.990 citations were examined. These top 200 EGFR-mutant NSCLC articles were published across 35 different journals. Of these articles, 35% were published within the last 10 years, while 65% were older than 10 years. It is typical for more highly cited articles to be older, as citation numbers generally increase over time. Although citation count is an important measure of a paper's quality and impact, it is not the sole indicator of quality; a paper generally requires time to accumulate citations.

Among the top 200 articles, only 5 were published in Plos Medicine, yet this journal had an average citation count of 2,792 per article. This high average citation count indicates that Plos Medicine is the most influential journal in research on EGFR-mutant NSCLC. The New England Journal of Medicine is also noted as the second most influential journal in this field. The United States was the leading country in terms of the number of EGFR-mutant NSCLC articles. The most recent article among the top 200 was published in 2021, while the oldest was published in 1998. The most cited paper is "Optimization of Dosing for EGFR-Mutant Non-Small Cell Lung Cancer with Evolutionary Cancer Modeling" by Chmielecki et al. from Memorial Sloan-Kettering Cancer Center. This cancer modeling study is among the highly cited papers and is likely to receive more citations in the future.The most frequently used keywords were "EGFR," "NSCLC," "Gefitinib," and "Erlotinib," which may guide future research directions in EGFR-mutant NSCLC. Prominent contributors to the field include researchers from various countries and institutions, such as Jänne, PA, James Chih-Hsin Yang, and Sequist, LV.

This study has several limitations. Although we identified the most influential articles in the field of EGFR-mutant NSCLC using bibliometric citation analysis and broad search terms, there is a possibility that some articles may have been overlooked. Specifically, recently published articles that might receive a high number of citations in the future but have not yet accumulated enough citations may not be included in our data. Additionally, since our data are sourced only from WoSCC, some publications indexed in other databases may not be listed. Databases such as Scopus or PubMed could be used in future research.

Conclusion

Oncology is a field characterized by continuous advancements, and we have witnessed remarkable developments in lung cancer treatment over the years. Bibliometric research presents improvements in a particular field from a nominative perspective. This bibliometric citation analysis covers a broad range of scientific areas related to EGFR-

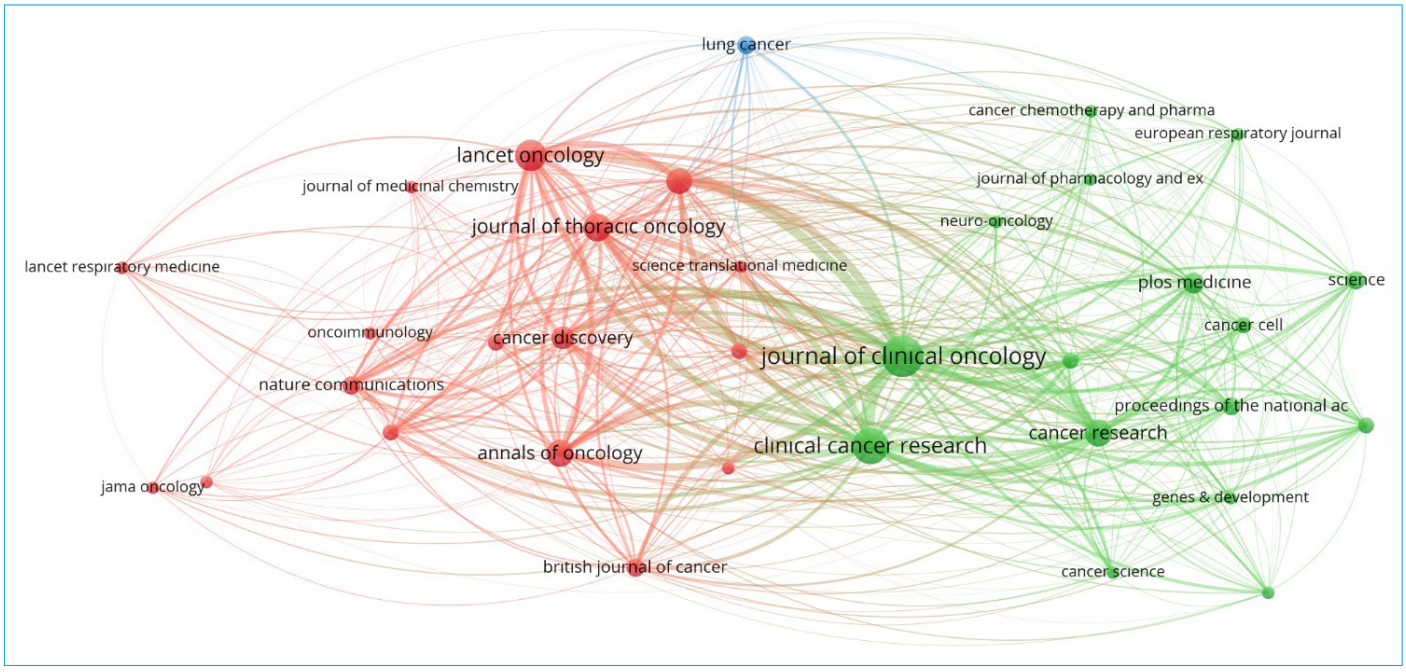

Figure 2. Matching Overlay Map of the Journals Where the Articles Are Published.

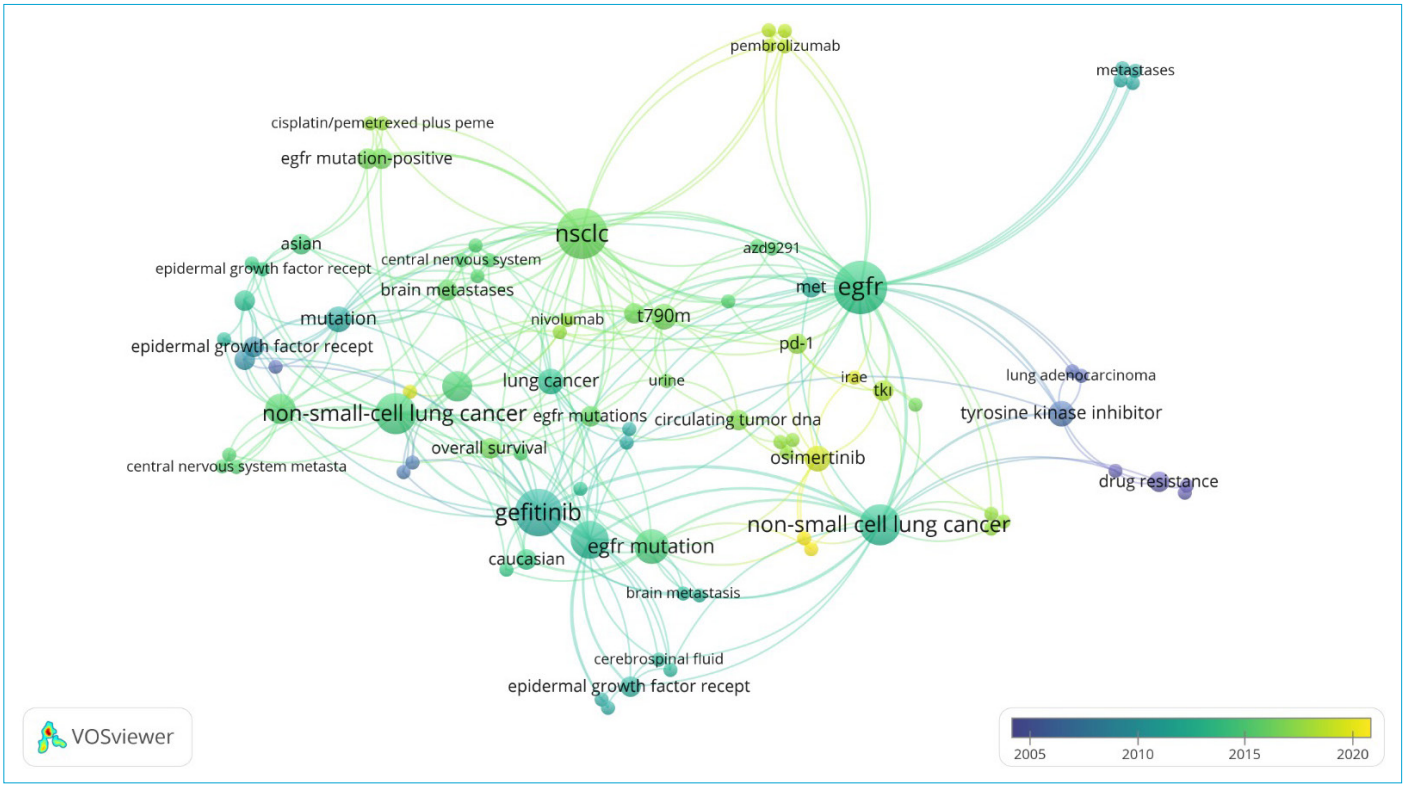

Figure 3. Keyword Co-occurence Overlay Map.

mutant NSCLC. It systematically identifies publications and analyzes their citation distribution by year, topic, institution, and scientific journal. Consequently, it provides a significant contribution to oncological research.

Disclosures

Ethics Committee Approval: The data in the study are in the public domain, so Ethics Committee approval was not required.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None of the authors has any conflicts of interest to declare.

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