Review Article

A Scoping Review to Evaluate Different Treatments Used in Advanced Nonsmall-cell Lung Cancer in India

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Summary

Background: Nonsmall-cell lung cancer (NSCLC) accounts for nearly 85% of all lung cancers and represents a major global health burden. In India, treatment strategies must be optimized through a customized approach that considers genetic and environmental differences. **Objectives:** To provide evidence from Indian RCTs with valuable insights into effective and cost effective treatment options. **Materials and Methods:** This review, conducted according to the Cochrane Handbook guidelines, identified 179,960 studies across databases—PubMed (26,383), Google Scholar (17,100), ScienceDirect/Embase (136,458), and the Clinical Trials Registry of India (19). **Results:** After screening, 11 primary studies involving 3,470 patients were included. Treatment regimens studied included platinum-based chemotherapy (carboplatin and cisplatin), taxanes (paclitaxel and docetaxel), epidermal growth factor receptor tyrosine kinase inhibitors (EGFR TKIs), and combination therapies. Carboplatin and cisplatin were the most frequently used agents; gefitinib plus cisplatin showed better efficacy in EGFR-mutated patients; pemetrexed plus carboplatin was more tolerable than paclitaxel plus carboplatin; and chemoimmunotherapy demonstrated superior survival outcomes compared to chemotherapy alone. Targeted therapies such as EGFR TKIs were equally effective with fewer toxicities. **Conclusion:** In conclusion, platinum-based chemotherapy remains the mainstay of NSCLC treatment, but patient tolerance, mutational status, and toxicity profiles must be carefully considered. Chemoimmunotherapy and EGFR TKIs are promising alternatives with improved results, while personalized treatment approaches and novel drug combinations should be the focus of future research.

Key words: Chemoimmunotherapy, chemotherapy, epidermal growth factor receptor tyrosine kinase inhibitors, India, lung cancer treatment, nonsmall-cell lung cancer, randomized controlled trials, targeted therapy

Introduction

Nonsmall-cell lung cancer (NSCLC) casts a long shadow on global health, claiming countless lives each year. It stands as the undisputed champion of lung cancers, accounting for a staggering 85% of all diagnosed cases.[1] This translates to a significant burden on healthcare systems worldwide, with a ripple effect impacting families, communities, and economies.

As researchers delve deeper into the complexities of NSCLC, the development of novel treatment approaches continues. Optimizing treatment for advanced NSCLC in India requires a deep understanding of what works best for the country's specific population.[2] The reviews of randomized controlled trials (RCTs) become a powerful tool in this fight. These reviews analyze data from multiple high-quality RCTs, providing robust evidence on the effectiveness and safety of various treatment options. This evidence-based approach is crucial, as treatment responses and side effects can differ based on genetics and environmental factors.[3]

Since data from western populations might not perfectly translate to India, focusing on RCTs conducted within the country or including Indian participants offers more relevant insights.[4] These reviews can then guide healthcare decision-making by highlighting the most effective and cost-effective treatments for

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advanced NSCLC. This not only optimizes resource allocation but also translates into improved patient outcomes such as better survival rates, enhanced quality of life, and improved treatment tolerability. Furthermore, these reviews can address the specific needs of Indian patients by identifying targeted therapies or treatment combinations that are most effective for their unique genetic makeup or coexisting medical conditions.

In essence, reviews of RCTs empower healthcare professionals in India to deliver the best possible care for patients battling advanced NSCLC. NSCLC may be a formidable opponent, but it is not an invincible one. By raising awareness, encouraging preventive measures like smoking cessation, and promoting early detection strategies, we can work toward a future where this disease claims fewer lives. Furthermore, ongoing research holds immense promise for developing more effective and targeted therapies, offering a brighter outlook for patients battling NSCLC.

Objectives

Since patient responses vary, evidence from Indian RCTs provides valuable insights into effective and cost effective treatment options.

Materials and Methods

The scoping review followed a structured format outlined in the Cochrane Handbook for reviews.

Eligibility criteria

The inclusion criteria for the review: (1) RCTs on advanced NSCLC, (2) published in English language, (3) Peer-reviewed, (4) open access, (5) studies conducted in India. Quasi-RCTs were excluded from the review.

Information sources

The search covered databases such as PubMed, Google Scholar, and ScienceDirect/Embase. Additional sources included gray literature comprising articles from peer-reviewed sources such as conferences, theses, and reports. Trial registries such as the Clinical Trials Registry of India (CTRI) were also searched for a better output [Table 1].

The flow diagram [Figure 1] illustrates the study selection process, including the number of records identified through database searches, duplicates removed, articles screened, and those ultimately included in the review.[5] The study followed a structured format outlined in the Cochrane Handbook for systematic reviews, with strict inclusion and exclusion criteria to select relevant studies.

Search strategy

We took assistance from the available literature to design an optimal search strategy. To eliminate the inconsistencies in terminology, the terms "*advance*" *or* "*advanced*"* and "*randomized*" *or* "*randomized*"* were used. A detailed table outlining the databases, keywords, MeSH terms, and Boolean operators is given in Table 1.

Selection and data collection process

The articles retrieved from the search were imported into Mendeley, a reference manager tool, and organized into groups for better management. These retrieved articles were compiled, and duplicates within the group were removed with the help of Mendeley. Four reviewers independently screened the remaining articles for titles and abstracts and assessed them for eligibility against the predetermined inclusion criteria. All manuscripts with titles and abstracts meeting the inclusion criteria were then downloaded for further review. Each article was then reviewed by two independent reviewers to maintain robustness [Table 1].

Data items

The data from these studies were systematically extracted, covering key data items according to our study objective. These data items contain both primary and secondary outcome domains, ensuring a comprehensive assessment of the study characteristics, treatment outcomes, demographic details, and methodological quality [Table 2 and Supplementary Table 1]. The systematic extraction and organization of this data allow for a thorough analysis and synthesis of the evidence on the effectiveness and safety of treatments for NSCLC in the Indian context.

Data extraction

Each study has distinct sample sizes, age ranges, genders, cancer stages, and histological types, providing a comprehensive understanding of the approaches undertaken. The study with the largest sample size, Sharma *et al*.,[6] includes a total of 506 participants. On the other hand, the studies with the smallest sample size were Beniwal *et al*.[7] and Kumar *et al.* (2020)[8] with 60 participants [Table 2].

Quality assessment of the studies

In this study, we used the CONSORT guideline to evaluate our articles instead of the more recent Cochrane bias tool.

Table 1: Databases, keywords, MeSH terms, and Boolean operators

Database	Keywords and MeSH terms	Boolean operator	Filters applied
PubMed	Advanced nonsmall cell lung cancer, randomized controlled trials	AND	Language: English, article type: RCTs, research article, open access
ScienceDirect	Advanced nonsmall cell lung cancer, randomized controlled trials	AND	Language: English, article type: RCTs, research article, open access
Google Scholar	Advanced nonsmall cell lung cancer, randomized controlled trials	AND	Language: English, article type: RCTs, research article, open access, title: allintitle
CTRI	Nonsmall cell lung cancer		Language: English, scientific title

CTRI: Clinical Trials Registry of India, MeSH; Medical subject headings

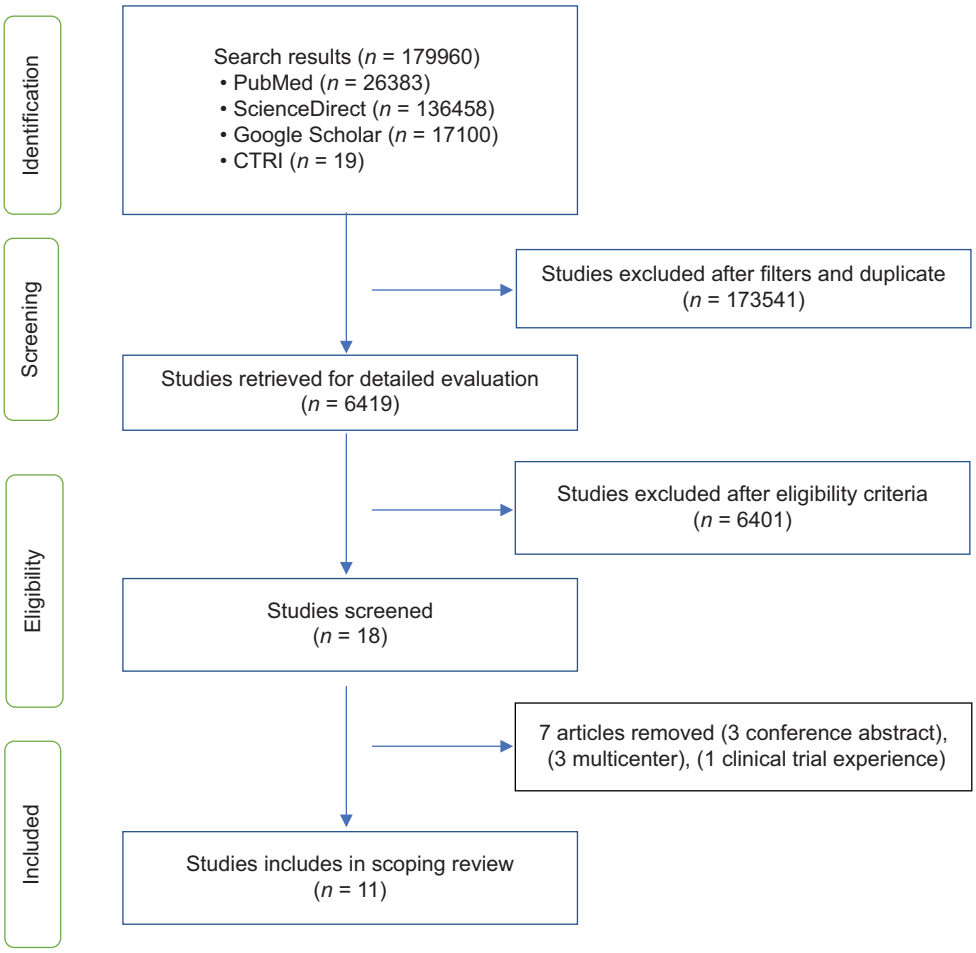

Figure 1: PRISMA flowchart for selection of studies.

Table 2: Demographic details of selected studies

Study name	Sample size	Age/age group	Gender	Stage of cancer	Histology
Noronha *et al*.[14]	246	Adults (not specified)	Male and female	Stage III and IV	Adenocarcinoma, squamous carcinoma, adenosquamous carcinoma
Yadav *et al*.[11]	171	18–65 years	Male and female	Stage III and IV	Adenocarcinoma, NSCLC - NOS
Noronha *et al*.[10]	350	18 years or older	Male and female	Stage III and IV	Adenocarcinoma, adenosquamous, carcinoma, sarcomata carcinoma
Kumar *et al*.[8]	60	18–75 years	Male and female	Stage III A and III B	Squamous cell carcinoma, adenocarcinoma
Belani *et al*[24]	221	Both sex >18 years	Male and female	Stage III and IV	Adenocarcinoma, squamous cell carcinoma, large-cell carcinoma
Roy *et al*.[23]	229	>70 years	Male and female	Stage III A and III B	Squamous cell carcinoma
Beniwal *et al*.[7]	60	up to 70 years	Male and female	Stage III B and IV	Squamous, adenocarcinoma, undifferentiated
Parikh *et al*.[12]	100	27–78 years	Male and female	Stage III B and IV	Squamous cell, nonsquamous cell
Digumarti *et al*.[13]	110	Approx. 55 years	Male and female	Stage III B and IV	Not specified
Dasgupta *et al*.[22]	103	up to 75 years	Male and female	Stage III A and III B	Squamous cell carcinoma, adenocarcinoma, large-cell carcinoma, anaplastic carcinoma
Sharma *et al*.[6]	506	33–76 years	Male and female	Stage III A and B	Squamous cell, adenocarcinoma, large-cell

NSCLC: Nonsmall cell lung cancer, NOS: Non-squamous

CONSORT guidelines, although not a direct measure of assessing the quality of RCTs, are helpful in assessing the quality of clinical trials. The Cochrane bias tool focuses on applying the tool at the outcome level rather than the study level, which often does not include details and key indicators. This tool also has high interrater agreement. We reviewed each article against the CONSORT checklist and documented our findings in an Excel sheet.[9]

Studies such as Noronha *et al*. (2020)[10] and Yadav *et al*.[11] demonstrate a robust approach to reducing biases and enhancing the reliability of outcomes by implementing allocation concealment. Blinding was notably rare, Parikh M *et al*. (2011)[12] and Digumarti *et al*.[13] due to the nature of the study. The per-protocol/intention-to-treat (PP/ITT) analysis was not mentioned in studies such as Noronha *et al*. (2024)[14] and Yadav *et al*.[11] As for the reporting of side effects, only one study failed to elaborate on it, Parikh *et al*. (2011)[12] [Supplementary Table 2].

Results

Our search strategy yielded a total of 179,960 studies: 26,383 from PubMed, 17,100 from Google Scholar, 136,458 from ScienceDirect/Embase, and 19 from CTRI. From this initial pool, we identified 18 potentially relevant articles. After excluding seven articles (three conference papers, three multicenter studies, and one clinical trial experience)[15-21] [Supplementary Table 2], we included 11 manuscripts that met our inclusion and exclusion criteria [Figure 1].

Included studies

We included a total of 11 primary studies encompassing 3470 patients across RCTs. Among these studies, three were Phase III RCTs, two were Phase II RCTs, and six were parallel-arm prospective RCTs [Table 3]. The management of NSCLC most frequently involved the use of paclitaxel, carboplatin, and cisplatin. However, other treatment regimens, including Talactoferrin (TLF), were also identified.

Drugs used

Carboplatin

Noronha *et al*. (2019)[10] showed gefitinib + cisplatin (Gef + C) regimen as the best option for patients prioritizing efficacy and long-term survival. It is particularly advantageous for patients with epidermal growth factor receptor (EGFR)-sensitizing mutations who can manage higher toxicity risks. Another study done by Beniwal *et al*.[7] estimated that the gemcitabine regimens in combination of carboplatin offer a viable alternative with a better-tolerated safety profile, though with modest efficacy.

Yadav *et al*.[11] compared two standard chemotherapy regimens for advanced-stage cancer: pemetrexed plus carboplatin versus paclitaxel plus carboplatin. Pemetrexed appears to be the better treatment option due to its comparable efficacy in progression-free survival (PFS) and overall survival (OS), along with a more favorable toxicity profile.

Cisplatin

Sharma *et al*.[6] investigated the efficacy of a combination chemotherapy regimen (cisplatin, ifosfamide, and mitomycin C) followed by radiotherapy in patients with locally advanced NSCLC. The study found that combining chemotherapy with chest irradiation appears promising due to its higher response rate. Dasgupta *et al*.[22] estimated for patients prioritizing initial tumor control and delay in progression, the concomitant chemoradiotherapy (CCRT) using cisplatin offers the best outcomes in terms of response rate and metastasis reduction.

Paclitaxel

Digumarti *et al*.[13] used cisplatin/pemetrexed/trial drug (C/P/T) (oral TLF) for the treatment of advanced cancer; the study found that the C/P/T was a better option due to its improved efficacy in terms of response rates and potentially longer PFS and OS. Kumar *et al*. (2020)[8] randomized patients into two arms – Continuous hyperfractionated accelerated radiotherapy week end-less (CHARTWEL) and Concomitant chemo-radiotherapy (CCRT), after 3 weeks of the fourth cycle of Neoadjuvant chemotherapy (NACT). CHARTWEL in combination with NACT proved to be an effective strategy to treat patients with locally advanced lung cancer, with the advantage of a smaller dose and shorter duration. Roy *et al*.[23] estimated that neoadjuvant chemotherapy followed by external beam radiotherapy with concomitant cisplatin appears to be the better treatment option due to its higher metabolic response rate and greater reduction in maximum standardized uptake value, although survival outcomes (PFS and OS). Belani *et al*. (2017)[24] compared the efficacy of a standard chemotherapy regimen (cisplatin and paclitaxel) to a combination of chemotherapy and immunotherapy (chemoimmunotherapy) in treating a specific type of cancer, indicating that chemoimmunotherapy offers additional benefits in terms of survival and should be considered where feasible and appropriate. Noronha *et al*. (2023)[14] experimented with two arms: the first arm included a combination of gemcitabine, docetaxel, paclitaxel, or vinorelbine. The second arm involved the use of EGFR tyrosine kinase inhibitors (TKIs) (gefitinib or erlotinib). EGFR TKI is considered the better treatment option for NSCLC patients due to its comparable efficacy in survival outcomes and a more favorable toxicity profile.

Other combinations

In the study by Parikh *et al*.[12], patients received TLF and placebo. TLF demonstrated an apparent improvement in OS in patients with stages IIIB to IV NSCLC.

Toxicity

Carboplatin

- Gef + C arm (EGFR-mutated lung cancer) had severe side effects such as nephrotoxicity, infections, and gastrointestinal issues, leading to treatment discontinuation in some patients [Supplementary Table 3].

Cisplatin

- Both study and control groups reported grade III/IV toxicities, including anemia, neutropenia, fever, nausea, vomiting, and skin reactions. The study group had a higher incidence of severe toxicities [Supplementary Table 3].

Paclitaxel

- Both chemoimmunotherapy and chemotherapy arms reported various side effects such as nausea, vomiting, diarrhea, pain, neuropathy, and alopecia. Some patients

Table 3: Summary of selected studies

Study	Design	Study population	Sample size	Treatment	Findings
Noronha *et al*.[14]	Phase III, open-label, parallel-arm	Mumbai, India	246	IV chemotherapy with gemcitabine, docetaxel, paclitaxel, or vinorelbine on various weekly or 21-day cycles, and an EGFR TKI arm featuring daily oral Gefitinib or Erlotinib	Global health, physical, role, and social functions were similar between treatment groups, but cognitive function differed significantly, and chemotherapy had nonstatistically significant higher hematological toxicities
Yadav *et al*.[11]	Phase III	Northern India (New Delhi)	171	Patients received either pemetrexed with carboplatin (every 3 weeks) or paclitaxel with carboplatin (every 4 weeks) for four cycles, with optional maintenance pemetrexed	Both pemetrexed and paclitaxel showed similar progression-free survival and clinical benefit rates, though paclitaxel had higher objective response rates; maintenance treatment and toxicities were comparable between the groups
Noronha *et al*.[10]	Open-label, phase III study	Mumbai, India	350	The Gef+C group received daily gefitinib plus pemetrexed and carboplatin for four cycles, followed by maintenance pemetrexed, whereas the Gef group received daily gefitinib only	The Gef+C regimen significantly improved progression-free and OS with higher radiologic response rates compared to Gef alone, but also led to more severe toxicities
Kumar *et al*.[8]	Randomized, prospective single-institutional study	Bikaner (Rajasthan), India	60	All patients received neoadjuvant chemotherapy with cisplatin and paclitaxel, followed by randomization to either continuous accelerated hyper-fractionated radiotherapy or a control arm	The study arm had better complete response and locoregional disease control at 6 months post-RT than the control, with similar survival and toxicity, except for two cases of persistent severe esophagitis
Belani *et al*.[24]	Double-arm, Phase III trial	15 sites in India (Rajasthan, Punjab, West Bengal [5 sites]; Madhya Pradesh [2 sites]; Himachal Pradesh, Chandigarh, Gujarat, Kerala, Bihar, Andhra Pradesh)	221 (all sites total)	Chemotherapy group (cisplatin plus paclitaxel) or the chemoimmunotherapy group (cisplatin, paclitaxel, and weekly intradermal CADI-05)	Overall, there was no statistical difference in median OS between groups, but the chemoimmunotherapy group showed improved median OS and 1-year survival, significant PFS improvement in the PPA population (with a trend in ITT), and improved OS and PFS for patients completing at least two chemotherapy cycles
Roy *et al*.[23]	Parallel (RCT)	New Delhi, India	229	Arm A received neoadjuvant chemotherapy (paclitaxel and carboplatin), followed by 60 Gy EBRT, while Arm B received the same chemotherapy, followed by 48 Gy EBRT with concurrent cisplatin	Both treatment arms achieved significant reductions in SUVmax and metabolic response, with similar median PFS and OS for responders and nonresponders, and no significant outcome difference between the arms
Beniwal *et al*.[7]	Parallel group	Ahmedabad, India	60	Patients received gemcitabine with carboplatin either as a standard 30-min infusion or a prolonged 6-h low-dose infusion	Both treatment arms demonstrated comparable efficacy and safety, with similar overall response, progression-free and OS, and rare severe toxicity
Parikh *et al*.[12]	Randomized, double-blind, placebo-controlled Phase II	Mumbai, India	100	The study compared TLF 1.5 g twice daily plus standard supportive care to a placebo plus standard supportive care	TLF showed an apparent, well-tolerated improvement in OS for advanced NSCLC patients who had failed prior therapies, warranting confirmation in a global phase III trial
Digumarti *et al*.[13]	Double-blind, placebo-controlled, phase II trial	Total of 11 sites in India (Hyderabad, Chennai, Mumbai, Bangalore, Trivandrum, Jaipur; two sites in Pune; two sites in New Delhi)	110	Arm 1 received carboplatin and paclitaxel with oral TLF, while Arm 2 received carboplatin and paclitaxel with an oral placebo	TLF combined with C/P showed apparent improvements in RR, PFS, and OS for untreated advanced NSCLC patients without significant added toxicity, requiring Phase III confirmation

Contd...

Table 3: Contd...

Study	Design	Study population	Sample size	Treatment	Findings
Dasgupta *et al*.[22]	Parallel randomized trial	Kolkata, India	103	Patients were assigned to Group A (radiotherapy alone), Group B (sequential cisplatin and etoposide chemotherapy then radiotherapy), or Group C (concurrent cisplatin and etoposide chemoradiotherapy)	Groups B and C showed better initial treatment responses with reduced distant metastasis and improved time to tumor progression compared to Group A, but had no 2-year survival benefit and increased acute toxicities
Sharma *et al*.[6]	Prospective randomized trial	New Delhi, India	560	The study group received three cycles of cisplatin, ifosfamide with mesna, and mitomycin C, followed by radiotherapy up to 60 Gy	The combination of induction chemotherapy (mitomycin C, ifosfamide, and cisplatin) and radiotherapy is an excellent and manageable treatment for locally advanced NSCLC

NSCLC: Nonsmall cell lung cancer, RR: Response rate, PFS: Progression-free survival, ITT: Intention-to-treat, OS: Overall survival, RCTs: Randomized controlled trials, EGFR: Epidermal growth factor receptor, TKI: Tyrosine kinase inhibitor, TLF: Telcoterin, PPA: Per-protocol analysis, EBRT: External Beam Radiotherapy

in both arms experienced severe (grade 3/4) laboratory toxicities [Supplementary Table 3].

Other combinations

- Pemetrexed arm had unique side effects like excessive lacrimation, while paclitaxel caused alopecia and neuropathy. Both arms reported deaths related to toxicity
- TLF was well tolerated with mild musculoskeletal side effects
- CHARTWEL had grade I–III skin, lung, and gastrointestinal toxicities, while CCRT had grade II esophagitis and pneumonitis
- The trial drug (C/P/T) showed fewer severe side effects compared to the placebo arm (C/P/P) Supplementry Table 3.

Discussion

The treatment landscape for NSCLC is constantly evolving, offering renewed hope for patients. The course of treatment depends on various factors, including the stage and type of cancer, the patient's overall health, and the presence of any relevant mutations. The fight against NSCLC on a global scale involves a continuous stream of clinical trials evaluating promising new therapies. Chemotherapy remains a mainstay, with platinum-based drugs such as cisplatin and carboplatin forming the backbone of many treatment regimens. These drugs target the very core of cancer cells, their DNA, hindering their ability to grow and multiply. Taxanes like paclitaxel and docetaxel are another common weapon in the chemotherapeutic arsenal, disrupting cell division by interfering with the cellular scaffolding essential for movement and growth.

Platinum-based doublets

Carboplatin versus cisplatin

Both carboplatin and cisplatin are effective platinum-based chemotherapy drugs commonly used in the treatment of advanced NSCLC. While they share a similar mechanism of action, there are key differences to consider when selecting the optimal agent for a particular patient. Research by Noronha *et al*. (2020)[10] suggested that a combination of Gef + C offers superior efficacy and long-term survival, especially for patients with EGFR-positive tumors. However, Beniwal *et al*.[7] found that gemcitabine plus carboplatin provides a viable alternative with a better safety profile, although with potentially lower efficacy compared to cisplatin-based regimens. Therefore, the choice between carboplatin and cisplatin should be individualized based on factors such as patient tolerance, EGFR mutation status, and the desired balance between treatment efficacy and tolerability. Similar studies demonstrate a significant increase in morbidity associated with cisplatin compared to carboplatin-based regimens, which have important implications for the selection of platinum-based chemotherapy in advanced NSCLC.[25-27]

Efficacy versus toxicity

A recurring theme in NSCLC treatment is the balance between efficacy and toxicity. While some regimens may offer improved efficacy, they often come with an increased risk of side effects. Studies by Shantanu Sharma *et al*.[6] and Anirban Dasgupta *et al*.[22] highlighted the effectiveness of cisplatin-based combination chemotherapy with radiotherapy for locally advanced NSCLC, but they also emphasize the importance of patient tolerance to the associated toxicities. Similarly, Yadav *et al*.[11] suggested that pemetrexed + carboplatin provides comparable efficacy to paclitaxel + carboplatin, but with a more favorable toxicity profile. Therefore, when selecting a treatment regimen for advanced NSCLC, clinicians must carefully weigh the potential benefits of improved efficacy against the increased risk of side effects, taking into account individual patient factors and preferences.

Other study compared carboplatin and cisplatin regimens for advanced NSCLC, analyzing OS, PFS, overall response rate, and toxicity. The results showed no significant difference in OS or PFS between the two groups. This suggests that both carboplatin and cisplatin have similar efficacy in terms of disease control and survival in advanced NSCLC.[28]

However, the study found significant differences in toxicity profiles. Carboplatin was associated with higher hematologic

toxicity, while cisplatin led to more nonhematologic toxicity.[29] This confirms the importance of considering the trade-off between efficacy and toxicity when choosing between these two agents.

Newer treatment options

The landscape of advanced NSCLC treatment is constantly evolving, with newer drugs and treatment strategies emerging alongside established options. Several studies have explored these advancements. Digumarti *et al*.[13] found that adding a trial drug to the standard cisplatin/pemetrexed regimen improved efficacy. Kumar *et al*. (2020)[8] suggested that CHARTWEL combined with neoadjuvant chemotherapy is effective for locally advanced lung cancer, offering a smaller dose and shorter duration. Roy *et al*.[23] indicated that neoadjuvant chemotherapy followed by cisplatin-based radiotherapy might be superior due to a higher metabolic response rate. Belani *et al*. (2017)[24] showed that chemoimmunotherapy offers additional survival benefits compared to standard chemotherapy. Noronha *et al*. (2024)[14] suggested that EGFR TKIs have comparable efficacy and a more favorable toxicity profile than certain chemotherapy combinations. Finally, Parikh *et al*.[12] found that TLF demonstrated an apparent improvement in overall survival.

Our study evaluates various treatments used in advanced NSCLC in India. It analyzed data from several high-quality RCTs to provide evidence on the effectiveness and safety of different treatment options for a specific population. The Indian consensus statement guidelines (2019) provide an update on the 2017 consensus statement on the treatment of advanced NSCLC. It includes recommendations for oncologists based on a review of published evidence, expert input, and practical experience.[30]

Together, both documents contribute to the evolving landscape of NSCLC management by offering different but complementary perspectives: one focused on guiding clinical practice and the other on summarizing and interpreting the available scientific data. This parallel effort highlights the need of evidence-based strategies to enhance patient outcomes in advanced NSCLC. The evidence synthesized in this review also suggests a need for greater emphasis on cost-effectiveness studies in the Indian context to inform resource allocation decision.

Limitations

This review has certain limitations. The focus on English-language publications may have introduced a language bias, potentially missing relevant studies in other languages. In addition, the restriction to studies conducted in India limits the generalizability of the findings to other populations. The emphasis on peer-reviewed and open-access publications might have led to publication bias. Due to the substantial heterogeneity observed across the included studies, particularly in terms of sample sizes, cancer stages, and treatment regimens, we were unable to conduct a meta-analysis.

Conclusion

This review investigated treatments for advanced NSCLC in India, analyzing 11 studies comprising 3470 patients. While the CONSORT guidelines were used for quality assessment, blinding and reporting of PP/ITT analysis and side effects in some studies were noted.

Chemotherapy remains a primary approach, with platinum-based drugs such as cisplatin and carboplatin, and taxanes like paclitaxel, forming the backbone of many regimens. This scoping review provides a comprehensive overview of advanced NSCLC treatments in India, highlighting the growing evidence for personalized medicine and the continued need for research on cost-effective strategies tailored to the Indian healthcare setting. The choice of treatment should be individualized based on patient and tumor characteristics, with careful consideration of the balance between efficacy and toxicity. Newer treatment options, such as chemoimmunotherapy and EGFR TKIs, show promise in improving survival and reducing toxicity but require further evaluation in the Indian context. This review highlights the need for continued research to optimize treatment strategies and improve outcomes for patients with advanced NSCLC in India.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Quality assessment of selected studies

Study	Randomization	Allocation concealment	Blinding	PP/ITT (As mentioned in study)	Harms (side effects)
Noronha *et al*.[14]	Yes	No	No	No	Yes
Yadav *et al*.[11]	Yes	Yes	No	No	Yes
Noronha *et al*.[10]	Yes	Yes	No	Yes	Yes
Kumar *et al*.[8]	Yes	No	No	Yes	Yes
Belani *et al*[24]	Yes	No	No	Yes	Yes
Roy *et al*.[23]	Yes	No	No	Yes	Yes
Beniwal *et al*.[7]	Yes	No	No	No	Yes
Parikh *et al*.[12]	Yes	No	Yes	Yes	Yes
Digumarti *et al*.[13]	Yes	No	Yes	Yes	Yes
Dasgupta *et al*.[22]	Yes	No	No	Yes	Yes
Sharma *et al*.[6]	Yes	No	No	Yes	Yes

PP/ITT: Per-protocol/intention-to-treat

Supplementary Table 2: Excluded studies from systematic review

Study	Design	Study population	Sample size	Treatment	Findings
Khan (2023) (abstract)[15]	Parallel group	not mention	90	Participants in Arm A underwent 30 min of yoga session daily besides standard fractionation radiotherapy with concurrent weekly chemotherapy. Participants in Arm B received the same schedule of concurrent chemoradiotherapy but without the daily yoga session	21 participants in Arm A recorded positive changes in their FEV1 values, compared to just three patients in Arm B (P=0.0002), suggesting daily yoga sessions during treatment can actually help in improvement of lung function among locally advanced NSCLC patients
Stroyakovskiy (multicenter)[16]	Parallel group	India, Russia, Ukraine, Belarus	Total=357, In India=219	Patients received BCD-021 or bevacizumab (15 mg/kg) plus paclitaxel (175 mg/m²) and carboplatin (AUC 6)	The study found no significant differences in efficacy, safety, and pharmacokinetics between BCD-021 and reference bevacizumab, with similar response rates and robust primary analysis outcomes confirmed by sensitivity analyses
Trukhin (multicenter)[17]	Phase III	Brazil, Bulgaria, Chile, Georgia, Greece, Hungary, India (Visakahapatnam), Lebanon, Malaysia, Mexico, Philippines, Russia, Serbia, Thailand, Turkey, Ukraine	627	MB02 with EU-bevacizumab (15 mg/kg), both administered with chemotherapy (paclitaxel 200 mg/m² and carboplatin AUC6) on day 1 of each 3-week cycle for six cycles	MB02 demonstrated similar efficacy to EU-bevacizumab, in combination with carboplatin and paclitaxel, in subjects with advanced nonsquamous NSCLC, with comparable safety and immunogenicity profiles
Shtivelband (abstract)[18]	Phase II	not mention	120	Study group receives 75 mg/m² of D every 21 days for up to six cycles combined with weekly blinded infusions of P, 1 mg/kg B or 3 mg/kg B until disease progression or unacceptable toxicity	This randomized, placebo-controlled phase II trial demonstrated a positive trend favoring 3 mg/kg B+D in ORR, PFS, and OS. 3 mg/kg B in combination with D was well tolerated and is the planned dose for phase III
Belani (abstract)[19]	Phase II	not mention	221	Study group receives paclitaxel 175 mg/m² IV 3-h infusion and cisplatin 100 mg/m² IV with or without Cadi-05 administered intradermally, 0.1 ml on each deltoid on the first visit at least 1 week prior to the first cycle and then on days 8 and 15 of each cycle of chemotherapy	Addition of Cadi-05 to paclitaxel plus cisplatin in patients with advanced NSCLC is safe and results in both improvement in PFS and OS. The study is supported by Cadila Pharmaceuticals Ltd. and is being presented on behalf of the Cadi-05 investigator study group
Blumenschein (multicenter)[20]	Phase II	USA (Houston, Los Angeles, Fayetteville, Greenville, Memphis), China (Hong Kong), Duarte, Thousand Oaks, India (Bengaluru, Mumbai)	Total=186	In group A, patients received radiotherapy alone. In group B, patients were treated by sequential chemotherapy and radiotherapy. In group C, patients received concurrent radiotherapy and chemotherapy	Initial treatment responses were significantly higher in group "B" (P<0.05) and "C" (P<0.03), compared to group "A." Follow-up observations showed that the addition of chemotherapy brought down distant metastasis from 62.5% (group "A") to 48.6% (group "B") and 44.4% (group "C")
Parikh (clinical experience)[21]	Parallel group	Europe, Asia, Central and South America, Australia, and Canada	Total=1692, In India=77	Comparison of gefitinib and placebo	Among Indian patients enrolled in the ISEL study, median survival was 6.4 months with gefitinib and 5.1 months with placebo. The objective response rate in Indian patients was 14% with gefitinib versus 0% with placebo. In ISEL, tolerability data from Indian patients were consistent with the overall study population. In the Indian gefitinib expanded-access program, median survival was 6 months, and gefitinib was well tolerated

FEV1: Forced expiratory volume in 1 s, NSCLC: Nonsmall cell lung cancer, AUC: Area under the curve, PFS: Progression-free survival, OS: Overall survival, ISEL: IRESSA survival evaluation in lung, BCD: Bevacizumab biosimilar

Supplementary Table 3: Reported toxicities in selected studies

Studies	Year	Stage	Toxicity
Noronha *et al*.[14]	2024	Grade III	Anemia, neutropenia, and thrombocytopenia
Yadav *et al*.[11]	2021	Grade I to IV	Excessive lacrimation, renal dysfunction, alopecia, and peripheral neuropathy
Noronha *et al*.[10]	2020	Grade III and IV	Nephrotoxicity, nonneutropenic infection, febrile neutropenia, and gastrointestinal toxicity like vomiting and diarrhea
Kumar *et al*.[8]	2020	Grade I to III	Skin, pneumonitis, gastrointestinal, esophagitis, and acute pneumonitis
Belani *et al*.[17]	2017	Grade III and IV	Nausea, vomiting, diarrhea, pain, weakness, weight loss, anorexia, neuropathy, and alopecia
Roy *et al*.[16]	2016	Not mention	Lymph node, kidney, contralateral lung, and bone metastasis
Beniwal *et al*.[7]	2012	Grade I to IV	Anemia, leukopenia, thrombocytopenia, vomiting, diarrhea, constipation, mucositis, and febrile neutropenia
Parikh *et al*.[12]	2011	Not mentioned	Nausea, vomiting, constipation, anemia, cough, and hypoglycemia
Digumarti *et al*.[13]	2011	Grade III and IV	Myelotoxicity, gastrointestinal disorders, respiratory disorders, and alopecia
Dasgupta *et al*.[15]	2006	Grade III	Primarily cutaneous, upper gastrointestinal, oropharyngeal, and hematological
Sharma *et al*.[6]	2003	Grade III and IV	Anemia, neutropenia, fever, nausea, vomiting, esophagitis, and skin reaction