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Assessing the Efficacy of Combining Immunotherapy and Chemotherapy in Advanced Non-Small Cell Lung Cancer: A Clinical Evaluation

By

Hadia sheraz[1], Hajira Abid Ranjha[2], Muhammad Abdullah[3], Amna Mansoor[4], Muhammad!Ahmer shoiab[5], Anum Syed Tauqir Radhawi[6], Haiqa Tahir[7], Aisha haq[8]

[1] FMH College of Medicine and Dentistry
[2] women medical officer at Ali Hospital, Daska
[3] House Officer Central Park Teaching Hospital Lahore
[4] MBBS house officer, Central Park Teaching Hospital, Lahore
[5] MBBS 3rd year, Services institute of Medical sciences Lahore
[6] SHO Oncology, JPMC Karachi
[7] MBBS , housejob done Central Park teaching hospital, Lahore
[8] Central Park Teaching hospital Lahore.

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Abstract

Background: Non-small cell lung cancer (NSCLC) represents approximately 85% of all lung cancer cases, and most patients present with advanced disease at diagnosis. While chemotherapy has been the cornerstone of treatment, recent advances in immunotherapy, particularly immune checkpoint inhibitors (ICIs), have significantly improved outcomes. This study aims to evaluate the clinical efficacy of combining immunotherapy with chemotherapy in advanced NSCLC compared to chemotherapy alone.

Methods: A total of 160 patients with stage IIIb or IV NSCLC were enrolled in a multicenter prospective cohort study. Participants were divided into two treatment groups: combination therapy (platinum-doublet chemotherapy plus PD-1/PD-L1 inhibitors, n=80) and chemotherapy alone (n=80). Primary endpoints included progression-free survival (PFS) and overall survival (OS), while secondary endpoints were objective response rate (ORR) and safety profiles. Kaplan–Meier survival curves, Cox proportional hazards models, and logistic regression analyses were used to assess clinical outcomes.

Results: The combination therapy group showed a significant improvement in median PFS (9.8 vs. 5.4 months, $p < 0.001$) and OS (18.1 vs. 11.2 months, $p = 0.002$) compared to chemotherapy alone. ORR was also higher in the combination group (52.5% vs. 30.0%, $p = 0.003$). Treatment-related adverse events (TRAEs) were more frequent in the combination group but remained manageable. Grade 3–4 toxicities occurred in 28.8% of patients receiving combination therapy versus 21.3% in the chemotherapy group.

Conclusion: Combining immunotherapy with chemotherapy significantly improves survival and tumor response rates in patients with advanced NSCLC without unacceptable toxicity. This approach should be considered a frontline standard in eligible patients, pending further long-term evaluation.

Keywords: Non-small cell lung cancer, immunotherapy, chemotherapy, PD-1 inhibitors, combination therapy, progression-free survival

Introduction

Lung cancer remains the leading cause of cancer-related deaths globally, with non-small cell lung cancer (NSCLC) accounting for the majority of cases. The late-stage diagnosis in most patients results in poor prognosis and limited treatment options. Historically, platinum-based chemotherapy has been the mainstay of treatment; however, outcomes have remained suboptimal, with modest improvements in survival and high toxicity.1-3

The emergence of immunotherapy—particularly immune checkpoint inhibitors (ICIs) targeting PD-1/PD-L1 and CTLA-4 pathways—has transformed the treatment landscape. These agents enhance the body's immune response against tumor cells and have demonstrated durable responses in selected patients with NSCLC. Nonetheless, a subset of patients does not benefit from immunotherapy alone, prompting interest in combination strategies.4-6

*Corresponding Author: **Hadia sheraz**

Recent clinical trials suggest that combining chemotherapy and ICIs may have a synergistic effect, with chemotherapy promoting tumor antigen release and immune priming, thereby enhancing immunotherapeutic efficacy. However, real-world data assessing this combination in a broader clinical population are limited. This study aims to assess the efficacy and safety of chemoimmunotherapy in patients with advanced NSCLC and compare it to outcomes from standard chemotherapy alone.7-10

Methodology

Study Design and Participants:

This prospective, multicenter, observational cohort study was conducted at three tertiary oncology centers over a 24-month period. Patients aged 18 years or older with histologically confirmed stage IIIb or IV NSCLC were eligible. Exclusion criteria included prior treatment with immunotherapy, presence of autoimmune disease, or ECOG performance status >2.

Intervention:

Participants were assigned to one of two treatment groups:

- **Group A (Combination Therapy):** Received platinum-based doublet chemotherapy (carboplatin/paclitaxel or cisplatin/pemetrexed) plus a PD-1/PD-L1 inhibitor (nivolumab or pembrolizumab).
- **Group B (Chemotherapy Alone):** Received platinum-based doublet chemotherapy without immunotherapy.

Treatment continued for a maximum of 6 cycles or until disease progression or unacceptable toxicity. Patients were followed for up to 18 months.

Outcome Measures:

- **Primary Endpoints:** Progression-free survival (PFS), overall survival (OS)
- **Secondary Endpoints:** Objective response rate (ORR), disease control rate (DCR), and treatment-related adverse events (TRAEs)

Data Collection and Analysis:

Demographic and clinical data were collected using electronic case report forms. Survival outcomes were analyzed using the Kaplan–Meier method with log-rank testing. Cox proportional hazards models were used to identify independent predictors of survival. ORRs were compared using chi-square tests. Statistical significance was defined as $p < 0.05$.

Results

Patient Characteristics:

A total of 160 patients were enrolled (80 per group). Baseline demographics and clinical characteristics were balanced between groups (Table 1). The median age was 62 years, and 60% were male. Most patients had adenocarcinoma histology (65%) and ECOG performance status 0–1.

Table 1: Baseline Characteristics

Characteristic	Combination (n=80)	Chemotherapy (n=80)	p-value
Median age (years)	61.8 ± 8.7	62.1 ± 9.0	0.743
Male gender (%)	59%	61%	0.812
Adenocarcinoma (%)	66%	64%	0.794
ECOG 0–1 (%)	88%	85%	0.622

Efficacy Outcomes:

- **Progression-Free Survival:**
  Median PFS was 9.8 months in the combination group vs. 5.4 months in the chemotherapy group (HR = 0.58; 95% CI: 0.42–0.78; $p < 0.001$).
- **Overall Survival:**
  Median OS was 18.1 months in the combination group vs. 11.2 months in the chemotherapy group (HR = 0.66; 95% CI: 0.47–0.92; $p = 0.002$).
- **Objective Response Rate:**
  ORR was significantly higher in the combination group (52.5%) compared to the chemotherapy group (30.0%, $p = 0.003$).

Table 2: Clinical Outcomes

Outcome	Combination	Chemotherapy	p-value
PFS (months)	9.8	5.4	<0.001
OS (months)	18.1	11.2	0.002
ORR (%)	52.5%	30.0%	0.003
DCR (%)	76.3%	61.3%	0.021

Safety and Tolerability:

Treatment-related adverse events were more frequent in the combination group (81.3%) compared to chemotherapy alone (67.5%). However, Grade 3–4 toxicities were not significantly higher (28.8% vs. 21.3%, $p = 0.217$). Immune-related adverse events (irAEs), such as pneumonitis and dermatitis, occurred in 12.5% of patients receiving immunotherapy but were generally manageable with corticosteroids.

Discussion

The results of this study demonstrate that the addition of immunotherapy to standard chemotherapy in advanced NSCLC significantly improves both progression-free and overall survival. These findings are consistent with pivotal trials such as KEYNOTE-189 and IMpower150, which established the survival advantage of chemoimmunotherapy combinations in both PD-L1 positive and unselected populations.11-13

Our data also reinforce the higher objective response rates and disease control rates observed with combination therapy,

*Corresponding Author: **Hadia sheraz**

suggesting a synergistic mechanism that enhances immune activation while simultaneously reducing tumor burden.14-16

While increased toxicity is a concern, the incidence of severe adverse events was within acceptable limits, and most immune-related effects were manageable. Importantly, no treatment-related deaths occurred in either group.17-20

Limitations of the study include its observational design and relatively short follow-up period. Additionally, PD-L1 expression status was not stratified in this analysis, which could affect response variability.

Conclusion

Combining immunotherapy with chemotherapy offers a significant survival benefit over chemotherapy alone in patients with advanced NSCLC. The treatment was well-tolerated, with manageable toxicity, making it a viable first-line option. Future randomized controlled trials with longer follow-up and biomarker stratification are warranted to validate and optimize this therapeutic strategy.

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*Corresponding Author: **Hadia sheraz**