

## Non-Small-Cell Lung Cancer: Optimizing Immune Checkpoint Inhibitor Therapy

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## Editorial

**1. Non-small-cell lung cancer (NSCLC) is a type of lung cancer that accounts for approximately 85% of all lung cancer cases. Immune checkpoint inhibitors (ICIs) have emerged as a promising form of immunotherapy for NSCLC, providing durable responses and improved survival outcomes in some patients. Here are some strategies for optimizing ICI therapy in NSCLC:**

**1.1. Patient Selection:** Proper patient selection is crucial for optimizing ICI therapy in NSCLC. ICIs are most effective in patients with advanced NSCLC who have high levels of programmed death-ligand 1 (PD-L1) expression in their tumors, as PD-L1 is the target of ICIs. PD-L1 testing should be performed on tumor samples to determine the PD-L1 expression level and guide ICI therapy decisions.

**1.2. Combination Therapy:** Combination therapy with ICIs and other agents can enhance the effectiveness of ICI therapy in NSCLC. For example, combining an ICI with chemotherapy, such as platinum-based chemotherapy, has been shown to improve response rates and overall survival compared to chemotherapy alone. Other combinations, such as ICIs with targeted therapies or radiation therapy, are also being investigated in clinical trials.

**1.3. Treatment Duration:** Optimal treatment duration with ICIs in NSCLC is an area of ongoing research. In some patients, ICIs can be discontinued after achieving a durable response, while in others, longer-term maintenance therapy may be needed. Balancing the risks and benefits of long-term ICI therapy, including the potential for immune-related adverse events, is important in optimizing treatment duration.

**1.4. Monitoring and Management of Immune-Related Adverse Events (irAEs):** ICIs can cause immune-related adverse events (irAEs) in various organs, such as the skin, gastrointestinal tract, liver, and lungs. Prompt recognition and management of irAEs are essential for optimizing ICI therapy in NSCLC. Close monitoring of patients for irAEs and appropriate management, including the use of corticosteroids or other immunosuppressive agents, is necessary to prevent severe complications and ensure continuation of ICI therapy when appropriate.

**1.5. Biomarker-Guided Therapy:** Emerging evidence suggests that biomarker-guided therapy can help optimize ICI therapy in NSCLC. Beyond PD-L1 expression, other biomarkers, such as tumor mutational burden (TMB), microsatellite instability (MSI), and the presence of specific genetic alterations, may also impact response to ICIs. Biomarker testing should be considered to identify patients who are most likely to benefit from ICI therapy and guide treatment decisions.

**1.6. Clinical Trials:** Participation in clinical trials is essential for optimizing ICI therapy in NSCLC. Clinical trials offer access to novel ICI-based combinations, biomarker-driven therapies, and other innovative treatment strategies that can potentially improve outcomes for NSCLC patients. Patients should be encouraged to consider participation in clinical trials whenever feasible.

**1.7. Multidisciplinary Approach:** A multidisciplinary approach involving collaboration among medical oncologists, radiation oncologists, pathologists, radiologists, and other healthcare providers is crucial in optimizing ICI therapy in NSCLC. Close communication and coordination among different specialties can help ensure appropriate patient selection, treatment sequencing, and management of irAEs, leading to optimal outcomes.

## **Chemotherapy is indicated in several scenarios for non-small-cell lung cancer (NSCLC), including**

**2.1. Advanced or Metastatic NSCLC:** Chemotherapy is often used as a standard treatment option for patients with advanced or metastatic NSCLC who are not candidates for targeted therapies or immunotherapy, or in cases where these treatments have not been effective. Platinum-based chemotherapy regimens, such as cisplatin or carboplatin in combination with other chemotherapy drugs, are commonly used in this setting. Chemotherapy can help shrink tumors, relieve symptoms, and improve overall survival in advanced NSCLC.

**2.2. Neoadjuvant Chemotherapy:** Neoadjuvant chemotherapy, which is given before surgery, may be considered in certain cases of locally advanced NSCLC to shrink tumors and increase the chances of successful surgical resection. It can be used as part of a multimodal treatment approach that includes surgery and/or radiation therapy.

**2.3. Adjuvant Chemotherapy:** Adjuvant chemotherapy, which is given after surgery, may be recommended for patients with resected early-stage NSCLC who are at high risk of disease recurrence. Adjuvant chemotherapy can help reduce the risk of cancer recurrence and improve overall survival in select patients.

**2.4. Combination Therapy:** Chemotherapy may also be used in combination with other treatment modalities, such as immunotherapy or targeted therapies, in certain cases of NSCLC. For example, combination chemotherapy and immunotherapy regimens, such as pembrolizumab plus platinum-based chemotherapy, have shown improved outcomes in advanced NSCLC patients with high PD-L1 expression.

**2.5. Palliative Care:** In some cases, chemotherapy may be used as part of palliative care for patients with advanced NSCLC to help manage symptoms, such as pain or difficulty breathing, and improve quality of life.

The decision to use chemotherapy in NSCLC depends on several factors, including the stage and extent of the disease, the patient's overall health and performance status, and other individualized considerations. The treatment plan should be determined by a multidisciplinary team of healthcare providers, including medical oncologists, radiation oncologists, and thoracic surgeons, based on the specific characteristics of each patient's NSCLC.

The survival rates for patients with advanced non-small cell lung cancer (NSCLC) can vary widely depending on several factors, including the stage of the disease, the patient's overall health, and the specific treatment regimens used. With advancements in treatment options, including targeted therapies and immunotherapies, the prognosis for advanced NSCLC has improved in recent years, but it can still be variable.

According to recent data, the median overall survival for patients

with advanced NSCLC treated with standard platinum-based chemotherapy regimens is around 9-12 months on average. However, with the advent of immune checkpoint inhibitors, such as pembrolizumab, nivolumab, and atezolizumab, as well as targeted therapies for specific genetic mutations, the survival rates for certain subsets of NSCLC patients have improved significantly. For example, in patients with NSCLC that harbors certain driver mutations, such as EGFR, ALK, or ROS1 mutations, targeted therapies have shown median overall survival ranging from 2-5 years or more, depending on the specific mutation and treatment used. It's important to note that survival rates can vary widely depending on individual patient factors, and some patients may experience longer or shorter survival than the average.

In terms of clinical trials, there are various research protocols available for admission of patients with NSCLC, depending on the stage, molecular characteristics, and other factors. Clinical trials are critical for advancing the field of oncology and improving treatment outcomes for patients with NSCLC. Some common types of clinical trials for NSCLC include:

**2.6. Phase I Trials:** These trials are typically the first step in testing new treatments in humans and involve a small number of patients to evaluate the safety, dosage, and side effects of a new treatment.

**2.7. Phase II Trials:** These trials involve a larger number of patients and are designed to assess the effectiveness of a new treatment in a specific population, as well as further evaluate its safety and side effects.

**2.8. Phase III Trials:** These trials involve a larger number of patients and compare the new treatment to standard treatments or placebos to determine its efficacy and safety in a larger population.

**2.9. Biomarker-Driven Trials:** These trials focus on patients with specific molecular characteristics, such as genetic mutations or other biomarkers, and evaluate the effectiveness of targeted therapies or immunotherapies that specifically target those biomarkers.

**2.10. Combination Therapy Trials:** These trials explore the use of multiple treatments in combination, such as chemotherapy with immunotherapy, targeted therapy with immunotherapy, or other combinations, to determine if the combined treatments are more effective than individual treatments alone.

To be admitted to a clinical trial, patients typically need to meet certain eligibility criteria, which may include factors such as stage of disease, previous treatments received, overall health status, and molecular characteristics of the tumor. Patients interested in participating in clinical trials should consult with their healthcare provider or a clinical trials specialist to discuss available options and determine if they meet the eligibility criteria for any ongoing trials.

The future of non-small cell lung cancer (NSCLC) is promising with ongoing research and advancements in various areas of treatment. Some potential areas that hold promise for the future of NSCLC include:

**2.11. Immunotherapy:** Immune checkpoint inhibitors, such as pembrolizumab, nivolumab, and atezolizumab, have revolutionized the treatment landscape for NSCLC by harnessing the body's immune system to attack cancer cells. As our understanding of the complex immune system and tumor microenvironment continues to evolve, there may be further advancements in immunotherapy for NSCLC, including the development of new immune checkpoint inhibitors, combination immunotherapy regimens, and personalized immunotherapy approaches based on individual patient characteristics.

**2.12. Targeted Therapies:** Targeted therapies have shown significant efficacy in NSCLC patients with specific genetic mutations, such as EGFR, ALK, ROS1, and others. As our understanding of the molecular drivers of NSCLC improves, there may be further development of targeted therapies that can effectively treat a wider range of genetic mutations, as well as the identification of novel molecular targets for treatment.

**2.13. Liquid Biopsy and Molecular Profiling:** Liquid biopsy, a non-invasive method of obtaining genetic information from a patient's blood, has shown great potential in guiding treatment decisions for NSCLC patients. As liquid biopsy technology continues to advance, it may become a standard part of routine clinical practice for NSCLC patients, allowing for more precise molecular profiling and personalized treatment selection based on real-time genetic information.

**2.14. Combination Therapies:** Combination therapies, such as combining chemotherapy with immunotherapy or targeted therapies, have shown promising results in NSCLC patients. Further research and clinical trials may identify optimal combination approaches to improve treatment outcomes and overcome resistance mechanisms.

**2.15. Early Detection and Screening:** Early detection and screening strategies, such as low-dose computed tomography (LDCT) screening for high-risk individuals, have the potential to identify NSCLC at earlier stages when it is more treatable. Continued research and efforts to identify high-risk populations and implement effective screening programs may lead to earlier diagnosis and improved outcomes for NSCLC patients.

**2.16. Personalized Medicine:** Advances in genomic profiling, liquid biopsy, and other molecular techniques may allow for more personalized treatment approaches for NSCLC patients, tailoring treatments based on the unique genetic characteristics of an individual's tumor. Precision medicine and individualized treatment plans may become more widespread in the future, leading to improved outcomes for NSCLC patients.

It's important to note that the future of NSCLC will likely continue to evolve as new research emerges and technology advances. Collaboration between researchers, healthcare providers, and patients will be critical in driving progress and improving outcomes for

NSCLC patients in the coming years.

In conclusion, optimizing ICI therapy in NSCLC requires careful patient selection, consideration of combination therapies, monitoring and management of irAEs, biomarker-guided therapy, participation in clinical trials, and a multidisciplinary approach. With ongoing research and advancements in the field of immunotherapy, optimizing ICI therapy has the potential to significantly improve outcomes for patients with NSCLC.

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