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整合免疫療法促進肺癌治療之進展

Advancing Lung Cancer Treatment through Immunotherapy Integration

時間：114 年 6 月 28 日(星期六) 13:30~17:00
地點：臺北榮民總醫院 三門診 9 樓創意谷

13:30-13:40	Opening Remarks	陳育民教授 Yuh-Min Chen
	座長：陳育民 教授 (Prof. Yuh-Min Chen)	
13:40-14:20	非小細胞肺癌新輔助與輔助免疫治療的發展現狀 The Evolving Landscape of Neo-adjuvant and Adjuvant Immunotherapy for NSCLC	楊景堯醫師 Ching-Yao Yang
14:20-15:00	無法切除之第三期非小細胞肺癌的免疫療法新進展 Advances in Immunotherapy Approaches for Unresectable Stage III NSCLC	曾彥寒醫師 Yen-Han Tseng
15:00-15:30	Coffee Break	
	座長：羅永鴻 醫師 (Dr. Yung-Hung Luo)	
15:30-16:10	以免疫療法改變晚期非小細胞肺癌的治療 Transforming Advanced NSCLC Treatment with Immunotherapy	鍾福財醫師 Fu-Tsai Chung
16:10-16:50	小細胞肺癌免疫治療的新前景 New Horizons in SCLC Immunotherapy Treatments	黃煦晴醫師 Hsu-Ching Huang
16:50-17:00	Closing Remarks	羅永鴻醫師 Yung-Hung Luo

The evolving landscape of neo-adjuvant and adjuvant immunotherapy for NSCLC

非小細胞肺癌新輔助與輔助免疫治療的發展現狀

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Lung cancer remains the leading cause of cancer-related mortality worldwide. For patients with early-stage non-small-cell lung cancer (NSCLC), the treatment typically involves surgical resection followed by adjuvant chemotherapy. The use of platinum-based chemotherapy after surgery has been shown to enhance survival outcomes. However, a significant number of patients continue to experience disease recurrence, either locally or systemically, resulting in poor prognosis. Only a small proportion of individuals with resected NSCLC remain free of recurrence at the five-year mark. Given the proven benefits of immune checkpoint inhibitors in early-stage NSCLC, immunotherapy has been incorporated into the perioperative strategy to improve outcomes in this disease.

The role of immunotherapy in resectable NSCLC was shown in multiple randomized phase III trial of neoadjuvant and adjuvant immunotherapy-based regimen. For patients undergoing neoadjuvant treatment, this approach may be considered for those with potentially resectable disease, especially individuals with node-positive status. In cases where tumors are ≥ 4 cm and/or lymph node involvement is present, and no actionable mutations are detected in epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK), combining platinum-based doublet chemotherapy with one of the following immune checkpoint inhibitors, such as nivolumab, pembrolizumab, or durvalumab, is a treatment option. When pembrolizumab or durvalumab is used, therapy is typically continued in the adjuvant setting. If nivolumab is selected, continuation into the adjuvant phase is an option for patients who have tolerated it well, particularly those at increased risk of recurrence.

This review highlights both published and recent data from clinical studies investigating the use of immunotherapy in neoadjuvant and adjuvant treatment approaches for early-stage NSCLC. Ongoing and future clinical trials are needed to refine and optimize immunotherapeutic strategies for patients at this stage of the disease.

Advances in immunotherapy approaches for unresectable stage III NSCLC

無法切除之第三期非小細胞肺癌的免疫療法新進展

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Stage III non-small cell lung cancer (NSCLC) is a heterogeneous condition typically managed through a multimodal treatment strategy that may include chemotherapy, radiotherapy, and, in selected cases, surgical resection. For patients with unresectable, locally advanced (stage III) NSCLC, the standard treatment since the early 2000s has been definitive chemoradiotherapy, usually involving a platinum-based chemotherapy regimen administered concurrently with radiation.

In recent years, growing interest has emerged in the use of immunotherapy following definitive chemoradiotherapy in this setting. A phase III study, the PACIFIC trial, published in 2017, demonstrated that durvalumab significantly improved survival in patients with unresectable stage III NSCLC who did not experience disease progression after concurrent chemoradiotherapy (CCRT). A subsequent 4-year follow-up showed that 49.6% of patients treated with durvalumab were still alive at four years, compared to 36.3% in the placebo group. These findings have been further supported by multiple real-world studies confirming the clinical benefit. As a result, durvalumab consolidation therapy following CCRT is now considered the standard of care for managing unresectable stage III NSCLC.

Transforming advanced NSCLC treatment with immunotherapy

以免疫療法改變晚期非小細胞肺癌的治療

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Lung cancer remains the leading cause of cancer-related deaths globally. Despite ongoing advancements in the diagnosis and treatment of non-small cell lung cancer (NSCLC), the prognosis for patients with late-stage disease remains poor. Metastatic NSCLC is typically managed with systemic therapies or palliative care. In recent years, immunotherapeutic approaches, particularly immune checkpoint inhibitors, have demonstrated notable survival benefits in select patient groups. Inhibitors targeting PD-1, PD-L1, and CTLA-4 have shown promising efficacy and have been integrated into the standard treatment protocols for advanced NSCLC.

For patients whose tumors with $\geq 50\%$ PD-L1 expression and lack targetable oncogenic driver mutations, monotherapy with pembrolizumab or atezolizumab is commonly recommended. In cases of rapidly progressing disease or high tumor burden, a combination of pembrolizumab with platinum-based chemotherapy is often used. When PD-L1 expression is below 50%, the current standard of care includes platinum-based doublet chemotherapy combined with pembrolizumab. For non-squamous NSCLC, a regimen of bevacizumab and atezolizumab along with platinum-based chemotherapy offers an alternative treatment option. Additionally, nivolumab paired with ipilimumab is considered a viable choice for metastatic NSCLC patients with PD-L1 expression of at least 1%. Combining nivolumab and ipilimumab with two cycles of platinum-based chemotherapy also represents a reasonable treatment strategy for metastatic disease.

Ongoing clinical trials continue to explore novel immunotherapy combinations aimed at further improving outcomes for patients with lung cancer. In this review, we summarize key evidence supporting the efficacy of immunotherapy-containing regimens in advanced NSCLC and discuss the clinical relevance of combination strategies currently in practice or under investigation.

New horizons in SCLC immunotherapy treatments

小細胞肺癌免疫治療的新前景

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Small cell lung cancer (SCLC) remains a highly aggressive and lethal malignancy, with standard chemotherapy offering only limited survival benefits. Unlike lung adenocarcinoma, which has multiple effective targeted therapies aimed at specific oncogenic drivers, SCLC continues to be treated as a single clinical entity. SCLC typically presents widespread disease, and systemic therapy remains the primary treatment approach. Despite initial sensitivity to chemotherapy and radiotherapy, relapses often occur within a few months following treatment.

The integration of immune checkpoint inhibitors, such as the anti-PD-L1 antibodies atezolizumab or durvalumab, into chemotherapy regimens has demonstrated significant improvements in both overall survival and progression-free survival compared to treatment with platinum and etoposide alone. These combination therapies have now been established as the standard first-line treatment for extensive-stage SCLC (ES-SCLC). Nevertheless, the clinical benefit remains modest, and only a fraction of patients appears to respond favorably.

Tarlatamab is a bispecific T-cell engager immunotherapy that redirects a patient's T cells to target cancer cells expressing delta-like ligand 3 (DLL3), a protein overexpressed in approximately 90% of SCLCs. The U.S. Food and Drug Administration (FDA) has granted approval for Tarlatamab. In phase II study, Tarlatamab demonstrated encouraging efficacy in patients whose disease had either progressed after or was refractory to prior platinum-based therapy and at least one additional line of treatment. When administered at 10 mg intravenously biweekly, the overall response rate reached 40%, with a median progression-free survival of 4.9 months and a median overall survival of 14.3 months. With extended follow-up (median 12.1 months), the response rate was 35%, and median overall survival increased to 20 months.

Building on the chemoimmunotherapy backbone, ongoing research is focused on identifying additional therapeutic approaches to extend survival for patients facing this devastating disease. Further developments in immunotherapy for SCLC will be discussed in this presentation.