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Letter to the Editor

Navigating a paradigm shift; food and drug administration approved Tarlatamab-dlle redefining the landscape of small cell lung cancer therapy

Sir,

Small cell lung cancer (SCLC) constitutes 10% of lung cancer.[1] It is the leading cause of death due to cancer in men and the second most prevalent cause of cancer related death in women worldwide.[2] It is an extremely hostile tumor with early development, spread, and fatal as it is typically found too late. Early-stage patients are usually treated with chemotherapy and thoracic radiation and surgery is rarely used to treat this malignancy. The addition of immunotherapy to first-line chemotherapy has improved survival for the first time in the decennary. It has demonstrated promise in producing significant, long-lasting responses. The disease is still challenging to treat but adding radiation therapy to a patient's care at certain intervals may enhance illness control. Platinum-based chemotherapy is initially quite effective, eliciting prompt and often substantial responses, however, they are transient effects, and when SCLC recurs, treatment resistance is strong.[3]

The specific biology of SCLC has been revealed in recent years, due to the rapid development of modern molecular biology tools.[1] Lurbinectedin inhibition may reduce the proliferation of cancer cells, mainly by preventing mitosis. It is an inhibitor of RNA polymerase II, which is commonly hyperactivated in SCLC, resulting in excessive transcription in tumor cells.[4] Ipilimumab is a human anti-CTLA-4 monoclonal antibody that stimulates T cell activation and proliferation by blocking CTLA-4 and its ligands (CD80/CD86).[5] It has shown long lasting suppression in multiple tumor types.[6,8] Atezolizumab and pembrolizumab are humanized monoclonal antibodies. Atezolizumab is an inhibitory ligand that binds to the PD-1 receptor and adversely controls T cell activation and proliferation. However, pembrolizumab binds to the PD-1 receptor and prevents the negative signaling that is brought about by the interaction of PD-1 with its ligands.[9,10] Another humanized monoclonal antibody that targets PD-L1 is Durvalumab.[11] A completely human PD-1 immune checkpoint inhibitor antibody, nivolumab is safe and effective in SCLC patients.[12,13]

Drug resistance and cancer cell's resistance to genotoxic stimuli have been linked with overexpression of poly (ADP-ribose) polymerase (PARP).[14] The PARP enzyme is substantially expressed in SCLC in comparison to normal lung epithelial cells and other histologic subtypes of lung cancer.[15] For the past 10 years, platinum-etoposide chemotherapy has been the accepted standard of care. However, persistent thoracic lesions are seen in 75% of the patients, and these lesions frequently reoccur in the first year.[16] Brain metastasis (BM) is quite common in patients with SCLC. According to prior research, 50% of SCLC patients had a chance of developing BM following systemic medication. Whole-brain radiation therapy (WBRT) is the usual course of treatment for BM in SCLC. Nevertheless, WBRT worsens quality of life and cognitive function.[17]

Amgen researchers have developed a first in class immunotherapy called IIMDELLTRA. It binds to CD3 on T cells and DLL3 on tumor cells, causing T cells to become activated and destroy DLL3-expressing SCLC cells. As a result, the cancer cell is lysed and a cytolytic synapse is formed.[18,19] DLL3 is an interesting target since it is a protein that is expressed on the surface of SCLC cells in approximately 85-96% of patients with SCLC but is little expressed on normal healthy cells.[20,21]

In pivotal DeLLphi-301 study in the DeLLphi-301 trial IIMDELLTRA showed an impressive 40% objective response rate, 9.7-month median duration of response, and 14.3-month median. Overall survival, the patients responded well to tarlatamab treatment in 40% of cases, with a median overall survival of 14.3 months. These effects were exceptionally long-lasting, signifying a significant shift in the paradigm for treating SCLC.[22]

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REFERENCES

1. Hayashi R, Inomata M. Small cell lung cancer; recent advances of its biology and therapeutic perspective. Respir Investig. 2022;60(2):197-204.
2. Yang S, Zhang Z, Wang Q. Emerging therapies for small cell lung cancer. J Hematol Oncol. 2019;12(1):47.

3. Chauhan AF, Liu SV. Small Cell Lung Cancer: Advances in Diagnosis and Management. Semin Respir Crit Care Med. 2020;41(3):435-46.
4. Fernandez-Teruel C, Gonzalez I, Troconiz IF, Lubomirov R, Soto A, Fudio S. Population-pharmacokinetic and covariate analysis of lurbinectedin (PM01183), a new RNA polymerase II inhibitor, in pooled phase I/II trials in patients with cancer. Clin Pharmacokinet. 2018;58(3):363-74.
5. Hoos A, Ibrahim R, Korman A, Abdallah K, Berman D, Shahabi V, et al. Development of ipilimumab: contribution to a new paradigm for cancer immunotherapy. Semin Oncol. 2010;37(5):533-46.
6. Small EJ, Tchekmedyian NS, Rini BI, Fong L, Lowy I, Allison JP. A pilot trial of CTLA-4 blockade with human anti-CTLA-4 in patients with hormone-refractory prostate cancer. Clin Cancer Res. 2007;13(6):1810-15.
7. Ansell SM, Hurvitz SA, Koenig PA, LaPlant BR, Kabat BF, Fernando D, et al. Phase I study of ipilimumab, an anti-CTLA-4 monoclonal antibody, in patients with relapsed and refractory B-cell non-Hodgkin lymphoma. Clin Cancer Res. 2009;15(20):6446-53.
8. Hodi FS, Butler M, Oble DA, Seiden MV, Haluska FG, Kruse A, et al. Immunologic and clinical effects of antibody blockade of cytotoxic T lymphocyte-associated antigen 4 in previously vaccinated cancer patients. Proc Natl Acad Sci U S A. 2008;105(8):3005-10.
9. Herbst RS, Soria JC, Kowanetz M, Fine GD, Hamid O, Gordon MS, et al. Predictive correlates of response to the anti-PD-L1 antibody MPDL3280A in cancer patients. Nature. 2014;515(7528):563–567.
10. Sul J, Blumenthal GM, Jiang X, He K, Keegan P, Pazdur R. FDA approval summary: pembrolizumab for the treatment of patients with metastatic non-small cell lung cancer whose tumors express programmed death-ligand. Oncologist. 2016;5(21):643-50.
11. Cho DC, Mahipal A, Dowlati A, Chow WA, Segal NH, Chung KY, et al. Safety and clinical activity of durvalumab in combination with tremelimumab in extensive disease small-cell lung cancer (ED-SCLC) J Clin Oncol. 2018;36(15):8517.
12. Borghaei H, Paz-Ares L, Horn L, Spigel DR, Steins M, Ready NE, et al. Nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer. N Engl J Med. 2015;373(17):1627-39.
13. Brahmer J, Reckamp KL, Baas P, Crino L, Eberhardt WE, Poddubskaya E, et al. Nivolumab versus docetaxel in advanced squamous-cell non-small-cell lung cancer. N Engl J Med. 2015;373(2):123-35.
14. Singh R, Kaur B, Farmer PB. Detection of DNA damage derived from a direct acting ethylating agent present in cigarette smoke by use of liquid chromatography-tandem mass spectrometry. Chem Res Toxicol. 2005;18(2):249-56.
15. Byers LA, Wang J, Nilsson MB, Fujimoto J, Saintigny P, Yordy J, et al. Proteomic profiling identifies dysregulated pathways in small cell lung cancer and novel therapeutic targets including PARP1. Cancer Discov. 2012;2(9):798-811.
16. Hurwitz JL, McCoy F, Scullin P, Fennell DA. New advances in the second-line treatment of small cell lung cancer. Oncologist. 2009;14(10):986-94.
17. Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, et al. Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. N Engl J Med. 2017;377(20):1919-29.
18. Giffin MJ, Cooke K, Lobenhofer EK, Juan E, Jinghui Z, Petra D, et al. AMG 757, a Half-Life Extended, DLL3-Targeted Bispecific T-Cell Engager, Shows High Potency and Sensitivity in Preclinical Models of Small-Cell Lung Cancer. Clin Cancer Res. 2021;27(5):1526-37.
19. Baeuerle PA, Kufer P, Bargou R. BiTE: Teaching antibodies to engage T-cells for cancer therapy. Curr Opin Mol Ther. 2009;11(1):22-30.
20. Ahn MJ, Cho BC, Felip E, Ippokratis K, Kadoaki O, Margarita M, et al. Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer. N Engl J Med. 2023;389(22):2063-75.
21. Rojo F, Corassa M, Mavroudis D, Aysim BÖ, Bonne B, Luka B, et al. International real-world study of DLL3 expression in patients with small cell lung cancer. Lung Cancer. 2020;147:237-43.
22. FDA approves IMDELLTRATM (Tarlatamab-DLLE), the first and only T-cell engager therapy for the treatment of extensive-stage small cell lung cancer. Amgen. 2024. Available at: https://www.amgen.com/newsroom/press-releases/2024/05/fda-approves-imdelltra-tarlatamabdlle-the-first-and-only-tcell-engager-therapy-for-the-treatment-of-extensivestage-small-cell-lung-cancer. Accessed on 31 May 2024.

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