Pemetrexed for non-Small-cell lung cancer

- Intrathecal pemetrexed efficacy and cerebrospinal fluid tumor marker response in refractory leptomeningeal metastasis of non-small-cell lung cancer: a single-arm phase II trial
- Insights into treatment-specific prognostic somatic mutations in NSCLC from the AACR NSCLC GENIE BPC cohort analysis
- Real-World Survival of First-Line Immune Checkpoint Inhibitor Treatment Versus Chemotherapy in Older Patients With Non-Small-Cell Lung Cancer and Synchronous Brain Metastases
- Pemetrexed combined with dual immune checkpoint blockade enhances cytotoxic T lymphocytes against lung cancer
- Cerebrospinal fluid exosomal microRNAs as biomarkers for diagnosing or monitoring the progression of non-small cell lung cancer with leptomeningeal metastases
- Safety, Pharmacokinetic and Clinical Activity of Intrathecal Chemotherapy With Pemetrexed via the Ommaya Reservoir for Leptomeningeal Metastases From Lung Adenocarcinoma: A Prospective Phase I Study
- Pulmonary Resection after Radiosurgery and Neoadjuvant Immunochemotherapy for NSCLC Patients with Synchronous Brain Metastasis-A Case Series of Three Patients
- Stereotactic Body Radiotherapy and Systemic Dose Chemotherapy for Locally Advanced Lung Cancer: Single Arm Phase 2 Study

Pemetrexed is an FDA-approved chemotherapy drug used for non-small cell lung cancer treatment, which is the most common type of lung cancer. Pemetrexed is used in combination with other chemotherapy drugs, such as cisplatin or carboplatin, and it is typically administered intravenously.

Pemetrexed works by inhibiting the synthesis of purines and pyrimidines, which are building blocks of DNA and RNA. This disrupts the cancer cell's ability to grow and divide, leading to cell death.

Pemetrexed is indicated for the first-line treatment of locally advanced or metastatic non-squamous NSCLC, and it has been shown to increase survival rates and improve quality of life in patients with this type of lung cancer. However, it is not effective in the treatment of squamous cell NSCLC.

Like all chemotherapy drugs, pemetrexed can have significant side effects, including fatigue, nausea, vomiting, diarrhea, anemia, low platelet counts, and decreased white blood cell counts. Patients receiving pemetrexed may also be given folic acid and vitamin B12 supplements to help reduce the risk of certain side effects.

Treatment with pemetrexed should only be administered under the close supervision of a qualified healthcare provider, and patients should be closely monitored for any adverse reactions or changes in their condition.

Chen et al. evaluated the induction of HLA-G as well as PD-L1 by sub-lethal doses of chemotherapeutics including pemetrexed in different Non-small cell lung cancer cell lines. Except for gefitinib, most of the chemotherapeutic agents enhanced HLA-G and PD-L1 expression in a dose-dependent manner, whereas pemetrexed and carboplatin treatments showed the most consistent upregulation of PD-L1 and HLA-G in each cell line. In addition to protein levels, a novel finding of this study is that pemetrexed enhanced the glycosylation of HLA-G and PD-L1. Pemetrexed potentiated the cytotoxicity of cytotoxic T cells (CTLs) to treat NSCLC. Both in vitro and in vivo experiments revealed that the CTL-mediated cytotoxicity was most pronounced when both anti-PD-L1 and anti-

HLA-G ICBs were combined with pemetrexed treatment. In conclusion, anti-HLA-G could be an intervention strategy in addition to the anti-PD-1/PD-L1 pathway for NSCLC. Moreover, dual targeting of PD-L1 and HLA-G combined with pemetrexed may have a better extent of cytotoxic T cells (CTLs)-based immunotherapy [1].

Intrathecal pemetrexed at a dose of 30 mg via Ommaya reservoirs on Days 1 and 8 every 21 days achieved promising disease control and satisfactory survival with moderate toxicities in resistant lung adenocarcinoma-leptomeningeal metastasis, providing a feasible and effective option, especially for the patients who cannot tolerate LP [2].

Cagney et al., identified 149 patients with lung adenocarcinoma and newly diagnosed brain metastases without a targetable mutation receiving stereotactic radiation. Kaplan-Meier plots and Cox regression were employed to assess whether the use of pemetrexed was associated with intracranial disease control and radiation necrosis.

Among the entire cohort, 105 patients received pemetrexed while 44 did not. Among patients who were chemotherapy-naïve, use of pemetrexed (n = 43) versus alternative regimens after stereotactic radiation (n = 24) was associated with a reduced likelihood of developing new brain metastases (HR 0.42, 95% CI 0.22-0.79, p = 0.006) and a reduced need for salvage brain-directed radiation therapy (HR 0.36, 95% CI 0.18-0.73, p = 0.005). Pemetrexed use was associated with increased radiographic necrosis. (HR 2.70, 95% CI 1.09-6.70, p = 0.03).

Patients receiving pemetrexed after brain-directed stereotactic radiation appear to benefit from improved intracranial disease control at the possible expense of radiation-related radiographic necrosis. Whether symptomatic radiation injury occurs more frequently in patients receiving pemetrexed requires further study [3].

Pemetrexed and gemcitabine preferentially inhibited G3 Medulloblastoma proliferation in vitro compared to control neurospheres and substantially inhibited G3 MB proliferation in vivo. When combined, these two drugs significantly increased survival of mice bearing cortical implants of mouse and human G3 MBs that overexpress MYC compared to each agent alone, while having little effect on mouse MBs of the sonic hedgehog subgroup. The findings strongly suggest that combination therapy with pemetrexed and gemcitabine is a promising treatment for G3 MBs [4].

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