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PRESCRIBER FORUM

Thank you for entrusting in the compounding services at Madison Medical Compounding Pharmacy to help meet the unique medication needs of your patients. We are excited to share our monthly newsletter with you and look forward to working with you. Please don't hesitate to let us know how we can assist you and your practice.

LeAnn Chambers, Pharm.D. and Matthew Chambers, Pharm.D.

Low Doses Naltrexone (LDN): Promising Treatment for Patients with Cancer and Immune-Related Diseases

Naltrexone (NTX), a non-selective antagonist of opioid receptors, is commonly used at standard doses, ranging from 50-100mg daily, as rehabilitation therapy for discharged opiate addicts to eliminate addiction in order to maintain a normal life and prevent or reduce relapse. NTX is also used off-label for the treatment of amphetamine and cocaine addictions, impulse control disorders, eating disorders, and autism spectrum disorders.[1]

Decades of research have now shown that Low-Dose Naltrexone (LDN), in doses of 1.5-4.5mg/day, has immunomodulatory and anticancerogenic effects, and exhibits remarkable inhibition of DNA synthesis, cell proliferation, viability, and other functions in numerous cancers.2 LDN can act as an immunomodulator in multiple autoimmune diseases and malignant tumors as well as alleviate the symptoms of some mental disorders. LDN can reduce tumor growth by interfering with cell signaling as well as by modifying the immune system. The results of increasing studies indicate that LDN exerts its immunoregulatory activity by binding to opioid receptors in or on immune cells and tumor cells. These discoveries indicate that LDN may become a promising therapeutic agent for cancer and many immune-related diseases.[2]

LDN acts as an Opioid Growth Factor receptor (OGFr) antagonist. The OGF-OGFr axis is an inhibitory biological pathway present in human cancer cells and tissues and therefore a target

for the treatment with low-dose naltrexone (LDN). LDN positively regulates OGF, impairing cancer cell proliferation, blocking tumor mitosis, and preventing uncontrolled proliferation, without interfering with cell apoptosis. McLaughlin and Zagon observed through preclinical studies that the duration of opioid receptors blockade is responsible for the effect produced by LDN, and the intermittent blocking of OGFr by LDN (4-6 hours per day) determined the cell proliferative response in ovarian cell carcinoma, pancreatic, colorectal and human squamous cell carcinoma of head and neck, in addition to autoimmune diseases. Clinical trials have proposed unique mechanisms allowing LDN to affect tumors, and LDN shows promising results for people with primary cancer of the bladder, breast, liver, lung, lymph nodes, colon, and rectum. (In contrast, at standard higher dosages of 50-100mg/day, naltrexone invokes a continuous receptor blockade of the OGF-OGFr axis that results in enhanced cell proliferation and cancer progression[1], so commercially available forms of naltrexone do not have potential benefits for cancer or autoimmune diseases.)

Ask our compounding professionals about customized medications to meet specific patient needs.

Low-Dose Naltrexone May Delay Cervical and Colorectal Cancer Progression

The incidence of cervical cancer and colorectal cancer is increasing annually worldwide. Low-dose naltrexone (LDN) has been reported to delay tumor progression, and the mechanisms continue to be researched. Studies explored the mechanisms underlying the inhibitory effect of LDN on cervical and colorectal cancer progression in vivo and in vitro. Researchers found that LDN could upregulate the expression of OGFr. Additionally, LDN could suppress the abilities of colony formation, migration, and invasion in cervical cancer cells. LDN could also inhibit cervical cancer progression in mice model. Moreover, LDN indirectly reduced the expressions of PI3K, pAKT, and mTOR in vitro and in vivo. In a study of colorectal cancer, researchers speculated that LDN reduces tumor size by increasing levels of M1-like macrophages and activating the Bax/Bcl-2/caspase-3/PARP signaling pathway to induce apoptosis. Therefore, LDN may be considered a potential adjunctive treatment option for cervical and colorectal cancer.[4, 5]

LDN Prescribing Pearls

LDN is not commercially available but can be prescribed and compounded by our pharmacy in the best dose and dosage form for each patient.

Start Low and Go Slow. Doses of LDN need to be titrated and increased slowly over time. Talk to our pharmacist for more information about prescribing LDN.

References:
[1] Current Drug Research Reviews, 2021, 13, 86-89
[2] Int Immunopharmacol. 2021 Jul;96:107714.
[3] Int Immunopharmacol. 2018 Aug;61:178-184.
[4] Transl Oncol. 2021 Apr;14(4):101028.
[5] Int Immunopharmacol. 2020 Jun;83:106388.
http://www.lowdosenaltrexone.org