Tocilizumab

Tocilizumab, also known as atlizumab, is an immunosuppressive drug, mainly for the treatment of rheumatoid arthritis (RA) and systemic juvenile idiopathic arthritis, a severe form of arthritis in children. It is a humanized monoclonal antibody against the interleukin-6 receptor (IL-6R). Interleukin 6 (IL-6) is a cytokine that plays an important role in immune response and is implicated in the pathogenesis of many diseases, such as autoimmune diseases, multiple myeloma and prostate cancer. It was developed by Hoffmann–La Roche and Chugai.

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOG-AD) is an immune-mediated neuroinflammatory disorder leading to demyelination of the CNS. Interleukin (IL)-6 receptor blockade is under study in relapsing MOGAD as a preventative strategy, but little is known about the role of such treatment for acute MOGAD attacks.

McLendon et al. discuss the cases of a 7-year-old boy and a 15-year-old adolescent boy with severe acute CNS demyelination and malignant cerebral edema with early brain herniation associated with clearly positive serum titers of MOG-IgG, whose symptoms were incompletely responsive to standard acute therapies (high-dose steroids, IV immunoglobulins (IVIGs), and therapeutic plasma exchange).

Both boys improved quickly with IL-6 receptor inhibition, administered as tocilizumab. Both patients have experienced remarkable neurologic recovery.

They propose that IL-6 receptor therapies might also be considered in acute severe life-threatening presentations of MOGAD [1)]

A study of the Medova Hospital, Necmettin Erbakan University in Konya, showed significant neuroprotective effects of tocilizumab on rabbit spinal cord ischemia reperfusion injury [2)].

The interleukin 6 signaling pathway plays an important role in glioma cell proliferation, and tocilizumab exerts an antitumor effect in U87MG glioma cells. These results may bring new insight into the molecular pathogenesis of glioma and may lead to a new therapeutic intervention [3)].

Enrichment of IL6 and STAT3 pathway genes were found to distinguish Group A Ependymoma (EPN) from Group B EPN and other brain tumors, implicating an IL6 activation of STAT3 mechanism. EPN tumor cell growth was shown to be dependent on STAT3 activity, as demonstrated using shRNA knockdown and pharmacologic inhibition of STAT3 that blocked proliferation and induced apoptosis. The inflammatory factors secreted by EPN tumor cells were shown to reprogram myeloid cells, and this paracrine effect was characterized by a significant increase in pSTAT3 and IL8 secretion. Myeloid polarization was shown to be dependent on tumor secretion of IL6, and these effects could be reversed using IL6-neutralizing antibody or IL6 receptor-targeted therapeutic antibody tocilizumab. Polarized myeloid cell production of IL8 drove unpolarized myeloid cells to upregulate CD163 and to produce a number of proinflammatory cytokines. Collectively, these findings indicate that constitutive

IL6/STAT3 pathway activation is important in driving tumor growth and inflammatory cross-talk with myeloid cells within the Group A EPN microenvironment. Effective design of Group A-targeted therapy for children with EPN may require reversal of this potentially immunosuppressive and protumor pathway [4].

see Tocilizumab for rheumatoid arthritis.

Thirty-two consecutive patients were intradiscally injected with 2 mL of 0.5% bupivacaine (control group). Another 31 consecutive patients were intradiscally injected with 40 mg tocilizumab and 1-2 mL of 0.5% bupivacaine (tocilizumab group) at the same time. Prior to treatment, the vertebral origin of low back pain was confirmed in all patients based on pain provocation during discography and pain relief with 1 mL of 1% xylocaine. Numeric rating scale and Oswestry disability index scores were used to evaluate pain level before and after treatment between the 2 groups. The association between pain relief with tocilizumab and intervertebral disc degeneration grade was also determined.

At the end of the study (8 weeks after treatment), 30 patients in each group were evaluable. In the tocilizumab group, numeric rating scale and Oswestry disability index scores improved significantly at 2 and 4 weeks after treatment, respectively. Intervertebral disc degeneration was not associated with improvement of numeric rating scale score in the tocilizumab group. Local infection (i.e., discitis) was observed in 1 patient in the tocilizumab group.

The results demonstrate the clinical relevance of interleukin-6 in discogenic low back pain. Intradiscal tocilizumab injection was shown to exert a short-term analgesic effect in patients with discogenic low back pain. Further research is required to determine the long-term effects of intradiscal tocilizumab therapy in patients with discogenic low back pain [5].

1)
McLendon LA, Gambrah-Lyles C, Viaene A, Fainberg NA, Landzberg EI, Tucker AM, Madsen PJ, Huh J, Silver MR, Arena JD, Kienzle MF, Banwell B. Dramatic Response to Anti-IL-6 Receptor Therapy in Children With Life-Threatening Myelin Oligodendrocyte Glycoprotein-Associated Disease. Neurol Neuroimmunol Neuroinflamm. 2023 Aug 15;10(6):e200150. doi: 10.1212/NXI.0000000000200150. PMID: 37582615.
2)
Karatas Y, Erdi MF, Kaya B, Keskin F, Cüce G, Kılınc I, Uyar M, Izci EK, Kalkan E. Neuroprotective effects of tocilizumab on experimentally induced spinal cord ischemia-reperfusion injury. World Neurosurg. 2018 Dec 26. pii: S1878-8750(18)32892-4. doi: 10.1016/j.wneu.2018.12.069. [Epub ahead of print] PubMed PMID: 30593966.
3)
Kudo M, Jono H, Shinriki S, Yano S, Nakamura H, Makino K, Hide T, Muta D, Ueda M, Ota K, Ando Y, Kuratsu J. Antitumor effect of humanized anti-interleukin-6 receptor antibody (tocilizumab) on glioma cell proliferation. Laboratory investigation. J Neurosurg. 2009 Aug;111(2):219-25. doi: 10.3171/2008.12.JNS081284. PubMed PMID: 19326989.
4)
Griesinger AM, Josephson RJ, Donson AM, Mulcahy Levy JM, Amani V, Birks DK, Hoffman LM, Furtek SL, Reigan P, Handler MH, Vibhakar R, Foreman NK. Interleukin-6/STAT3 Pathway Signaling Drives an Inflammatory Phenotype in Group A Ependymoma. Cancer Immunol Res. 2015 Oct;3(10):1165-74. doi: 10.1158/2326-6066.CIR-15-0061. Epub 2015 May 12. PubMed PMID: 25968456; PubMed Central PMCID: PMC4596749.
5)
Sainoh T, Orita S, Miyagi M, Inoue G, Yamauchi K, Suzuki M, Sakuma Y, Kubota G, Oikawa Y, Inage K, Sato J, Nakata Y, Aoki Y, Takahashi K, Ohtori S. Single intradiscal injection of the interleukin-6 receptor

antibody tocilizumab provides short-term relief of discogenic low back pain; prospective comparative cohort study. J Orthop Sci. 2015 Nov 19. pii: S0949-2658(15)00068-8. doi: 10.1016/j.jos.2015.10.005. [Epub ahead of print] PubMed PMID: 26755382.