Riluzole Indications

Riluzole, a glutamate release inhibitor, has been in use for the treatment of amyotrophic lateral sclerosis for over two decades since its approval by the Food and Drug Administration. Recently, riluzole has been evaluated in cancer cells and indicated to block cell proliferation and/or induce cell death. Riluzole has been proven effective as an anti-neoplastic drug in cancers of various tissue origins, including the skin, breast, pancreas, colon, liver, bone, brain, lung and nasopharynx. While cancer cells expressing glutamate receptors frequently respond to riluzole treatment, numerous types of cancer cell lacking glutamate receptors unexpectedly responded to riluzole treatment as well. Riluzole was demonstrated to interfere with glutamate secretion, growth signaling pathways, Ca2+ homeostasis, glutathione synthesis, reactive oxygen species generation and integrity of DNA, as well as autophagic and apoptotic pathways. Of note, riluzole is highly effective in inducing cell death in cisplatin-resistant lung cancer cells. Furthermore, riluzole pretreatment sensitizes glioma and melanoma to radiation therapy. In addition, in triple-negative breast cancer, colorectal cancer, melanoma and glioblastoma, riluzole has synergistic effects in combination with select drugs. In an effort to highlight the therapeutic potential of riluzole, the current study reviewed the effect and outcome of riluzole treatment on numerous cancer types investigated thus far [1)].

Depressive disorder

Glutamatergic modulators may have therapeutic potential in the treatment of depressive disorder (DD), riluzole, as a modulating drug of the glutamatergic system, its antidepressant efficacy and safety of riluzole for DD are inconsistent. This meta-analysis was performed to determine the efficacy and safety of riluzole used for DD. A systematic literature search was performed using PubMed, Embase, Cochrane Library, Web of Science, VIP and other databases from 1980 to 2019. The primary outcome was change in depression severity and meta-analysis was performed using comprehensive meta-analysis software. Seven randomized controlled trials (RCTs) were included. There was some difference in depression severity change in riluzole-citalopram therapy. No significant differences were observed in response rate, remission rate, relapse rate and adverse events, while, the relapse time in riluzole group was longer than placebo group. In this meta-analysis riluzole showed no antidepressant efficacy compared to placebo in monotherapy or riluzole-ketamine combined therapy, while it might relieve depression severity to some extent in riluzole-citalopram therapy. Furthermore, riluzole showed favorable safety for DD. The longer relapse time of riluzole group might have clinical significance to some extent, although this had no statistical difference. More studies are needed to clarify the potential association between riluzole and DD [2)].

Riluzole (Rilutek) is a drug used to treat amyotrophic lateral sclerosis and is marketed by Sanofi Pharmaceuticals. It delays the onset of ventilator-dependence or tracheostomy in selected patients and may increase survival by approximately two to three months.

In terms of safety and efficacy, systemic hypothermia and glibenclamide were superior to riluzole.

Glioblastoma

see Riluzole for Glioblastoma.

Degenerative Cervical Myelopathy

Dettori JR. Spine Treatment Appraisal Report (STAR): Does Riluzole Improve Outcomes in Patients Undergoing Decompression Surgery for Degenerative Cervical Myelopathy? Global Spine J. 2021 Mar 4:2192568221997401. doi: 10.1177/2192568221997401. Epub ahead of print. PMID: 33657901.

A double blind study and Placebo controlled study, Randomized controlled trial did not show a significant change in the clinical outcome and DTI Indices with the use of Riluzole as a standalone pharmacotherapeutic agent for early cervical myelopathy. More studies may be needed to confirm the usefulness of Riluzole as a treatment option for cervical myelopathy [3].

To shed light on the mechanisms and to test a combination therapeutic strategy for cervical spondylotic myelopathy (CSM), Karadimas et al. performed surgical decompression in a rat model of CSM, randomizing some animals to also receive the U.S. Food and Drug Administration-approved drug riluzole. Spinal cord blood flow measurements increased after decompression surgery in rats. CSM rats showed a transient postoperative neurological decline akin to that seen in some CSM patients, suggesting that ischemia-reperfusion injury may occur after decompression surgery. Riluzole treatment attenuated oxidative DNA damage in the spinal cord and postoperative decline after decompression surgery. Mechanistic in vitro studies also demonstrated that riluzole preserved mitochondrial function and reduced oxidative damage in neurons. Rats receiving combined decompression surgery and riluzole treatment displayed long-term improvements in forelimb function associated with preservation of cervical motor neurons and corticospinal tracts compared to rats treated with decompression surgery alone [4].

1)
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4)
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