

Phase I study of cisplatin plus pemetrexed combined with salazosulfapyridine targeting cancer stem cells in advanced non-squamous non-small-cell lung cancer

Target disease: Advanced non-squamous non-small-cell lung cancer

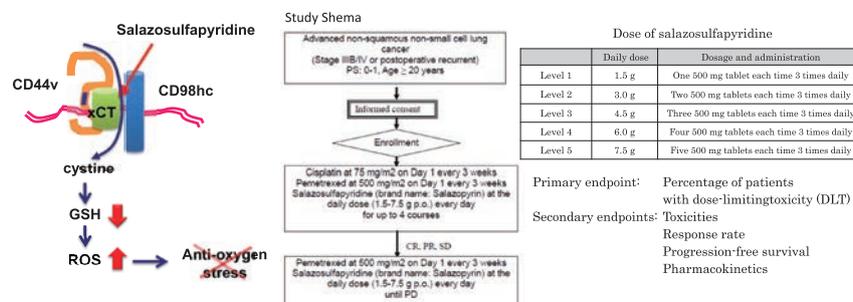
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Synopsis

It is known that cancer tissues contain a small cell population called cancer stem cells, which are capable of self-renewing and producing cells at various levels of differentiation. Cancer stem cells are resistant to anticancer drugs/radiotherapy and profoundly involved in treatment resistance and recurrence/metastasis of cancer. Accordingly, treatment strategies aimed at destroying cancer stem cells are critical to improvement in treatment outcomes and complete cure of cancer.

Saya et al. have recently found that CD44 variants (CD44v), an important cancer stem cell marker, binds to xCT protein, a cystine transporter subunit, on the cancer cell membrane, resulting in stable expression of the transporter on the cell surface, which stimulates the formation of glutathione, a strong antioxidant, by stimulating the uptake of extracellular cysteine and the release of intracellular glutamic acid, which results in reduced vulnerability to oxidative stress and thus tumor growth and treatment resistance are promoted. Furthermore, in vitro and vivo experiments demonstrate that salazosulfapyridine, a conventional small molecule agent for ulcerative colitis, selectively killed CD44v-expressing tumor cells. In a subsequent phase I study of salazosulfapyridine alone in previously treated patients with advanced gastric cancer, post-treatment immunostaining of tumor biopsy tissue revealed that CD44v-positive cancer cells were significantly decreased at a dose of 8 g/day, suggesting that salazosulfapyridine inhibited the CD44v-xCT pathway.

Since CD44v-expressing cancer stem cells are original cells of tumor cells, but account for a small percentage of all tumor cells, salazosulfapyridine alone can reduce the number of cancer stem cells, but may not be effective in reducing or eliminating tumor mass. Accordingly, concomitant use of conventional anticancer therapy may be necessary to enhance the efficacy of salazosulfapyridine in treatment of cancer stem cells. This study is a phase I open-label study designed to determine the recommended dose (RD) of salazosulfapyridine used in combination with combination therapy with cisplatin (75 mg/m²) and pemetrexed (500 mg/m²) in patients with advanced non-squamous non-small cell lung cancer.



Intellectual property information: Patent pending

Related keywords : Cancer Stem Cell, salazosulfapyridine Non-small-cell lung cancer