The Editor’s Choice

A multicenter, open-label, uncontrolled, single-arm phase 2 study of tirabrutinib, an oral Bruton’s tyrosine kinase inhibitor, in pemphigus

The treatment of pemphigus is based on systemic corticosteroid use and adjuvant therapies, but some patients are resistant to conventional therapy. Tirabrutinib is a highly selective oral Bruton’s tyrosine kinase inhibitor that may be clinically effective in treating pemphigus by suppressing B-cell signaling. Yamagami J et al investigated the efficacy and safety of tirabrutinib in patients with refractory pemphigus.

In total, 16 patients were evaluated. The complete remission rate after 24 weeks of treatment (primary endpoint) was 18.8%. By week 52, eight patients (50.0%) achieved complete remission and 10 patients (62.5%) achieved remission. Over 52 weeks of treatment, the mean prednisolone dose decreased from 17.03 to 7.65 mg/day. Incidences of adverse events (AEs) and adverse drug reactions were 87.5% and 43.8%, respectively. A relationship with tirabrutinib was ruled out for all serious AEs and Grade ≥3 AEs. Treatment with tirabrutinib enabled remission and reduced oral corticosteroid exposure over time and did not result in any major safety concerns in patients with refractory pemphigus.

Fig. 1. Cyclobutane pyrimidine dimer formation and pyrimidine-pyrimidone (6-4) formation in the epidermis after UV irradiation. Immunohistochemistry of cyclobutane pyrimidine dimers (CPDs) and pyrimidine-pyrimidone 6—4 photoproducts (6—4PPs) in B6 mice and in BALB/c mice after narrowband UVB (NB) or broadband UVB (BB).

Fig. 2. Changes in cumulative complete remission rate and cumulative remission rate (A) and changes in PDAI score and oral prednisolone dose (B). In Fig. 2A, error bars show 95% confidence intervals, N = 16. In Fig. 2B, data are mean (standard deviation). PDAI, n = 16, 15, and 14 for baseline—Week 8, Weeks 12–20, and Weeks 24–52, respectively. Prednisolone, n = 16, 15, and 14 for baseline—Week 16, Weeks 16–<24, and Weeks 24–<52, respectively. PDAI: pemphigus disease area index.

Time kinetics of cyclobutane pyrimidine dimer formation by narrowband and broadband UVB irradiation

Maximum cyclobutane pyrimidine dimer (CPD) formation in the skin induced by UVB irradiation is thought to occur within a few minutes and is immediately decreased by the DNA repair system. Toriyama E et al evaluated the time course and differential effects of narrowband (NB-UVB) and broadband (BB-UVB) UVB on CPD formation. CPDs induced by UVB irradiation (1 minimum erythemal dose) in epidermal skin were detected in the nucleus. Although the CPD levels increased immediately after irradiation (3min), the highest level was detected at 1 h and the increase lasted 24 to 48 h after irradiation. BB-UVB tended to induce greater CPD levels than NB-UVB in both mouse strains. CPDs were induced immediately after UV irradiation, with the maximum level observed 1 h after irradiation. BB-UVB irradiation tended to induce greater levels of CPD formation. In addition to the direct effects of UVB, the presence of CPDs in hair follicles, which were not irradiated by UVB, suggests that reactive oxygen species are also involved in CPD formation in the skin.

A novel circular RNA (circRNA) has been confirmed to play a vital role in melanoma progression. The regulatory function of circ_0062270, a novel circRNA, in melanoma progression is unclear. The expression of circ_0062270 was increased in melanoma tissues and cells. Knockdown of circ_0062270 inhibited proliferation, promoted apoptosis, and repressed metastasis in melanoma. Moreover, circ_0062270 could serve as miR-331-3p sponge, and miR-331-3p could target EPHA2. Furthermore, miR-331-3p inhibitor and EPHA2 overexpression reversed the inhibitory effect of circ_0062270 silencing on melanoma progression. In addition, silenced circ_0062270 also could inhibit melanoma tumor growth in vivo. Circ_0062270 accelerated the progression of melanoma through regulating the miR-331-3p/EPHA2 axis, suggesting that circ_0062270 might be a novel potential therapeutic target for melanoma.

Circ_0062270 upregulates EPHA2 to facilitate melanoma progression via sponging miR-331-3p

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Fig. 1. Circ_0062270 was upregulated in melanoma tissues and cells. (A) The expression of circ_0062270 in normal skin tissues (n = 55) and melanoma tissues (n = 55) was detected by qRT-PCR. (B) QRT-PCR was used to measure the expression of circ_0062270 in tissues of melanoma patients at different TNM stages (I: n = 17; II: n = 26; III: n = 12). (C) Kaplan-Meier analysis was used to analyze the correlation between circ_0062270 expression and the overall survival rate of melanoma patients.