Experiences with Smo antagonist vismodegib for the treatment of locally advanced basal cell carcinoma

András Bánvolgyi¹, Kende Lőrincz¹, Norbert Kiss¹, Anker Pálma¹, Nóra Gyöngyösi¹, Dalma Márton¹ and Norbert Wikonkal¹
¹ Department of Dermatology, Semmelweis University, Budapest, Hungary

Basal cell carcinoma (BCC) is the most common skin tumor in humans [1]. Although surgical excision is considered gold standard treatment, locally invasive advanced forms are difficult to treat. Gorlin-Goltz syndrome is an inherited disorder which is characterized by the occurrence of multiple BCC-s [2]. Vismodegib is the first Smo inhibitor agent which is indicated in otherwise untreatable BCC [3]. We treated 11 BCC patients with vismodegib in our department in the last 4 years. 2 male and 9 female patients with mean age of 73±15 years were included, 4 patients had Gorlin-Goltz syndrome and the rest had locally advanced BCC with no metastasis. Vismodegib was given for an average of 15 months. 2 patients showed complete remission, and no relapse has been seen after the discontinuation of the drug. 2 patients first showed remission, then the treatment had to be suspended due to side effects. When we re-administered the drug, its efficacy was lost. The last group of 5 patients improved considerably, and they are still on-treatment despite the side effects. The main side effects were muscle cramps, dysgeusia, nausea, loss of appetite and hair loss. We experienced a significant improvement of the side effects with an individual combination of calcium channel blocker amlodipine, muscle relaxant tizanidine, H2 antagonists and antiemetics for each patient. Our results show that vismodegib has a remarkable effect in the treatment of BCC. However, it has serious side effects, which can lead to a temporary discontinuation of vismodegib therapy. Side effects should be managed carefully, as suspension of the treatment can induce the development of therapy resistance against vismodegib. Based on our experience, we emphasize the importance of the adequate treatment of side effects of vismodegib to achieve long-term remission.

Fig. 3 54-year-old female patient with Gorlin-Goltz syndrome before treatment (A) and after 47 months of treatment (B)

Fig. 4 84-year-old male patient with Gorlin-Goltz syndrome before treatment (A-B), after 8 months of treatment (C-D) and after 15 months of treatment (E-F)

Fig. 5 Changes in tumor size after treatment in 5 well documented patients

Fig. 1 Average number of tumors before and after treatment (*p<0.05)

Fig. 2 Average diameter of tumors before and after treatment (*p<0.05)

Fig. 6 Moderate and severe adverse effects of vismodegib treatment

References

- 1 Diepgen TL, Mahler V. The epidemiology of skin cancer. The British journal of dermatology. 2002;146 Suppl 61:1-6.
- 2 Cakir BO et al.. Epidemiology and economic burden of nonmelanoma skin cancer. Facial plastic surgery clinics of North America. 2012;20(4):419-22.
- 3 Gould SE et al. Discovery and preclinical development of vismodegib. Expert opinion on drug discovery. 2014;9(8):969-84.