Persistent Alopecia Induced by Vismodegib

S. Alkeraye, C. Maire, E. Desmedt, C. Templier, L. Mortier
Department of Dermatology, University Hospital of Lille, Hôpital Claude-Huriez, Lille, France

Introduction

Vismodegib is a known inhibitor of the Sonic Hedgehog pathway (Shh) approved by the US FDA and the EMEA. It is the first systemic treatment for patients with locally advanced or metastatic basal cell carcinoma. We have treated 65 patients (between July 2011- March 2014) with vismodegib for locally advanced basal-cell carcinomas. All patients received 150 mg of oral vismodegib daily. Among those, 4 patients presented with persistent alopecia (grade 2) even after several months (mean=15 months) of stopping the treatment.

Patients

Case1: a 54 year old female with history of xeroderma pigmentosum, was treated by vismodegib between February 2010 and November 2010, for multiple BCCs. The treatment was interrupted due to alopecia (grade 2) which persisted for more than 22 months after stopping the treatment. (Figure1,2)

Case2: a 48 year old male, presented with a retro-auricular BCC associated with multiple lymph nodes involvement and pulmonary metastases. Vismodegib between October 2011 and April 2012. The response to treatment was excellent clinically. Treatment interrupted because of alopecia (grade 2) which persisted up to 18 months after stopping the treatment.

Case3: a 27 year old male, diagnosed with Gorlin’s syndrome. vismodegib between September 2011 and August 2012 for multiple BCCs. The treatment suspended due to alopecia (grade 2) which persisted up to 1 year after stopping the treatment.

Case 4: a 92 year old female with right lower eye-lid BCC, treated with vismodegib between August 2011 and February 2013. The lesion has completely disappeared but the patient developed alopecia (grade 2) which persisted for 14 months after stopping the treatment.

Discussion

Reversible alopecia is a well-known side-effect of vismodegib. Less than 50% hair loss is considered as grade 1 alopecia, and 50% or more hair loss is considered as grade 2 alopecia (according to CTCAE). Shh pathway has an essential role during hair follicle morphogenesis, where it is required for normal advancement beyond the hair germ stage of development. Epidermis-derived Shh functions as a paracrine signal regulating development of the mesenchymal component of hair follicle. Shh may regulate early folliculogenesis through its two general targets, Ptc1 and Gli1.

Up to our knowledge persistent alopecia as a side effect of vismodegib therapy was never reported up to date.

Conclusion

Our experience suggests that vismodegib’s side effects are reversible after treatment cessation. However, we recognize that persistent alopecia has been reported in 4 out of 65 patients. Recent data suggest that amenorrhea is a potential side effect of unknown reversibility. These two side effects should be considered in the young subjects.

References