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Case Report

Experiences on the Treatment of Locally Advanced Basal Cell Carcinoma with Vismodegib

Rauno J Harvima[1,2]*, Antti P. Kaukinen[1] and Ilkka T Harvima[1,2]

[1]Department of Dermatology, Kuopio University Hospital, Kuopio, Finland

[2]Department of Dermatology, University of Eastern Finland, Kuopio, Finland

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***Corresponding author:** Rauno J Harvima, Department of Dermatology, Kuopio University Hospital, Kuopio, Finland, Tel: +358-40-9309150, Fax: +358-17-174420

ABSTRACT

Basal cell carcinoma (BCC) is the most common skin cancer. At early stages, various topical treatments or light surgical procedures will give effective results. However, when the commonly used treatments are not appropriated, the hedgehog signaling inhibitor may be considered. We describe our experience on the treatments of locally advanced BCCs with vismodegib.

Keywords: Basal cell carcinoma; Gorlin Syndrome; Hedgehog signaling pathway inhibitor; Vismodegib

Introduction

Basal cell carcinoma (BCC) is the most common skin cancer with annually about 9,000 cases recorded annually by the Finnish Cancer Registry. However, due to underreporting, it is likely that the real number is around 30,000 to 35,000 cases in Finland with population of about 5.5 million.

BCC is often easily accessible and thus, topical treatments on superficial variants include cryotherapy with liquid nitrogen, photodynamic therapy (PDT), imiquimod or 5-fluorouracil. Nodular forms may be excised by a curette (curettage debulking) followed by cryotherapy or PDT or by surgery. Also, various lasers are used. Morpheaformic, infiltrative BCC and basosquamous carcinoma are targets for surgery[1]. In some cases, oncologic treatments by radiation therapy or cytostatic drugs may be used. In addition, various combination of the treatments may be applied. The newest treatment option is immunotherapies by anti-PD1- drugs[2].

When surgery or other treatments are not applicable, Hedgehog signaling pathway inhibitors may be considered. Presently, there are two drugs in this group: vismodegib (Erivedge) 150 mg capsules and sonidegib (Odomzo) 200 mg capsules[2]. Both are very effective drugs, but are extremely teratogenic necessitating extreme cautions in handling of drug capsules.

Vismodegib and sonidegib demonstrate >99% binding to plasma proteins. Binding of vismodegib to proteins was concentration-dependent, whereas that of sonidegib was non-concentration-dependent. Vismodegib has a volume of distribution of 16-27 L, suggesting it is confined to the plasma and has limited tissue penetration. In contrast, sonidegib is more lipophilic and has a volume distribution of >9,000 L, indicating extensive distribution in tissues. Consequently, the concentration of sonidegib is 6 times higher in skin than in plasma. This might explain potential differences in efficacy and toxicity between these drugs. Vismodegib has an elimination half-life of 4-12

days achieving steady-state situation after 7-21 days. In contrast, sonidegib 's elimination half-life is longer 28-30 days achieving steady-state after 3-4 months[3].

The efficacy of vismodegib (N=63) was reported in the BOLT and Erivance studies being 22.2% (complete clearance), 25.4% (partial clearance), 34,9% (stable disease), 12.7% (progressive disease) and 4.8% (unknown). These figures for sonidegib (N=66) were 21.2% (CR), 39.4% (PR), 30.3% (SD), 1.5% (PD) and 7.6% (unknown)[3,4].

Vismodegib came available in Finland for patients in 2016 and sonidegib later in 2022. Sonidegib shares about the same efficacy, tolerability and adverse event profile as vismodegib. However, sonidegib has a better skin penetrance than vismodegib[3]. Financial monthly costs are at the same level.

Here we describe our experiences on the use of vismodegib for the treatment of locally advanced BCC, before sonidegib was available for our patients.

Case Reports

Case 1: A male born in 1951 started to develop multiple mainly superficial BCCs in the 1970s mainly in the head area. He experienced numerous surgical operations in Oto-Rhino-Laryngology and Surgery clinics and finally he was referred to Dermatology Clinic in the 1990s. Gorlin Syndrome diagnosis was set. About 10 to 15 new BCCs developed during follow-up at about 1-to-2-month intervals. He was treated by cryotherapy with liquid nitrogen and/or PDT.

In May 2013, an investigational Phase-III Study by vismodegib was started until Oct 2016. At the start he had 26 BCCs mainly in the head area, some in the upper trunk and extremities, of which 4 target lesions were selected to be followed-up **(Table 1)**. BCCs reduced in number and size very rapidly. In the following years he could interrupt the medication for variable periods of 5 months to 1.5 years. When 1 to 2 BCCs appeared, often excision and cryotherapy were performed. When 2 to 4 BCCs appeared, they were often excised with cryotherapy followed by vismodegib for 2 to 3 months. When 14 BCCs were detected at a follow-up visit, vismodegib was used for 6 months. PDT-treatment was used only once.

Table 1: A 62-year-old male with Gorlin syndrome treated with vismodegib during Phase-III study (Case 1).

Visit day	Total number of BCCs	Target lesion 1 (mm)	Target lesion 2 (mm)	Target lesion 3 (mm)	Target lesion 4 (mm)
8.5.2013	26	11	11	11	18
4.6.2013	19	0	7	9	0
2.7.2013	15	0	0	9.5	0
30.7.2013	6	0	0	2.5	0
27.8.2013	3	7	0	0	0
23.9.2013	0	0	0	0	0
23.10.2013	0	0	0	0	0
19.11.2013	0	0	0	0	0
17.12.2013 (br)	0	0	0	0	0
14.1.2014 (br)	0	0	0	0	0
11.2.2014	0	0	0	0	0

br = break in vismodegib use started
Selected target BCC lesions according to Study Protocol

Case 2: A male born in 1953 started to develop multiple mainly superficial BCCs in the 1970s typically in the head area, but also in the upper trunk. He was the younger brother of Case 1 and experienced numerous surgical operations in Oto-Rhino-Laryngology and Surgery clinics. Finally, he was referred to Dermatology Clinic in the 1990s and Gorlin Syndrome diagnosis was established. About 10 to 15 new BCCs developed during follow-up at about 1-to-2-month intervals. The treatments included cryotherapy with liquid nitrogen and occasional PDTs. The biggest superficial BCC with a size of 8x15 cm located below the left clavicle and was treated in 6 visits by cryotherapy.

In May 2013, an investigational Phase-III Study by vismodegib was started. At the start he had 40 BCCs mainly in the head area, some in the upper trunk, of which 5 target lesions were selected to be followed-up **(Table 2)**. BCCs reduced in number and size very rapidly. However, his head skin was full of scars due to multiple operations and some target lesions responded in variable manner. When new occasional lesions developed, vismodegib was used without interruptions.

Table 2: A 60-year-old male with Gorlin syndrome treated with vismodegib during Phase-III study (Case 2).

Visit day	Total number of BCCs	Target lesion 1 (mm)	Target lesion 2 (mm)	Target lesion 3 (mm)	Target lesion 4 (mm)	Target lesion 5 (mm)
8.5.2013	40	33	10	13	12	17
4.6.2013	36	12	8	13	12	19
2.7.2013	32	15	8	17	14	16
30.7.2013	18	3.5	4	5	0	14
27.8.2013	10	6.5	4	9	0	0
23.9.2013	4	10	4	0	0	4
23.10.2013	1	0	3.5	0	0	0
19.11.2013	0	0	0	0	0	0
17.12.2013	0	0	0	0	0	0
14.1.2014	0	0	0	0	0	0
11.2.2014	1	0	0	0	0	0

Case 3: A male born in 1947 showed at the age of 46 in his left ear-cheek area a morpheaformic BCC that was operated numerous times with pure margins, but relapses were encountered. Also, radiation therapy was given in 2003. In 2007, petrosectomy and microvascular flap were performed and in preoperational pulmonary X-ray, a squamous cell carcinoma was detected and treated with cytostatic drugs. In 2013, a relapse BCC was detected infiltrating along the skull base being beyond surgery. It affected his jawbone and jaw joint causing difficulties in eating. Thus, vismodegib was initiated in March 2015 **(Figure 1a)** and the lesion shrank gradually during over 3 months **(Figure 1b)** and at 7 months it was clinically clear with the histopathology of scar. In addition, his yaw movement returned. Vismodegib was continued for a total of 1 year 3 months. At follow-up 6 months later **(Figure 1c)** in November 2016, a clinical remission was still noticed.

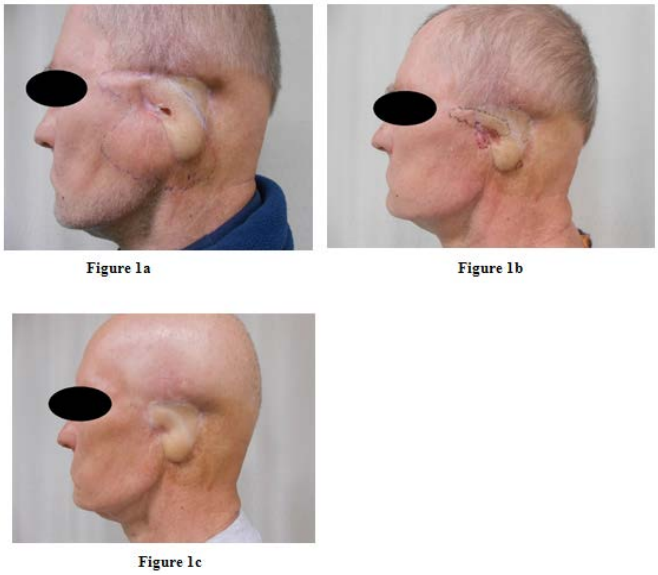

Figure 1a Figure 1b

Figure 1c

Figure 1: Treatment of morpheaformic basal cell carcinoma with vismodegib in a 68-year-old male (Case 3). Blue/black margins show the localization of tumor. At start in February-March 2015 **(Figure 1a)**, after 3 months **(Figure 1b)**, after 7 months being clinically and histopathologically clear. Vismodegib was continued for 1 year 3 months. At follow-up at 1 year 9 months later from start **(Figure 1c)**, a clinical remission was noticed in November 2016.

Case 4: A 52-year-old male had on the lateral right cheek in front of ear a nodular infiltrative BCC growing gradually for 5 years with Staphylococcus aureus colonization. A Computer Tomography revealed tumor tissue to be in close contact to mastoid part of the occipital bone, dorsal part of temporal bone to lateral edge of infratemporal fossa and to occipital and bone ear canal **(Figure 2a)**. At a multiprofessional meeting, surgery and radiation therapies were not considered and vismodegib was started in September 2015 for 10 months at a standard dose of 150 mg/day. The response started in a few weeks, at follow-up a marked healing **(Figure 2b)** was noted and later after 5.5 months his skin was clinically clear. Three years later, a relapse **(Figure 2c)** was confirmed by Magnetic Resonance Image (MRI) and vismodegib was used for 3 months. At the follow-up of 5 months later the skin was clinically and by MRI clear of disease. Two years later he was clinically in remission. The last follow-up 5 years later in January 2025 **(Figure 2d)** still showed remission, that is, over 9 years from the start of treatment.

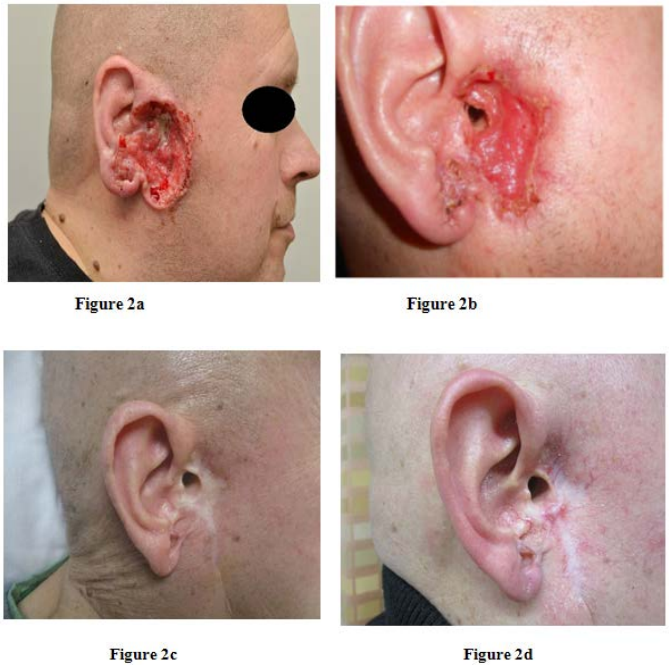

Figure 2a Figure 2b

Figure 2c Figure 2d

Figure 2: Treatment of nodular infiltrative basal cell carcinoma with vismodegib in a 52-year-old male (Case 4) with Staphylococcus aureus colonization. At the start in February 2015 **(Figure 2a)** and after 2 months **(Figure 2b)** with a marked improvement. Vismodegib was used for 10 months. A relapse 3 years later **(Figure 2c)** was treated with vismodegib for 3 months. The last follow-up **(Figure 3d)** in January 2025 still showed clinical remission.

Case 5: A 72-year-old man had suffered from wide superficial excoriations and wounds in his left leg for 3 years, despite adequate oral and topical treatments. In the bacterial culture, Escheria coli was repeatedly found with an Extended Spectrum Beta Lactamase (ESBL) resistency. Numerous skin biopsies revealed chronic wound and regenerative tissue. However, BCC was finally confirmed in skin biopsy **(Figure 3a)**. The patient participated in Phase-III Study by vismodegib and after 4 months a clear response was obtained **(Figure 3b)** and soon later the skin was complete healed, without the need of leg amputation.

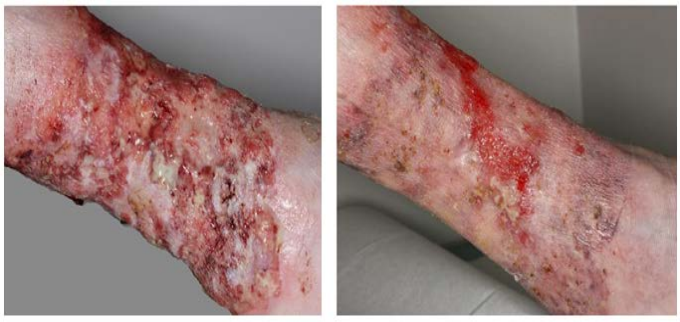

Figure 3a Figure 3b

Figure 3: Treatment of basal cell carcinoma with vismodegib in a 72-year-old male (Case 5) with Escheria coli colonization. At the start **(Figure 3a)** and after 4 months **(Figure 3b)**. The wide lesion healed without the need of leg amputation. Courtesy from Dr Sari Pitkänen at the Department of Dermatology of Helsinki University Central Hospital

Discussion

Hedgehog signaling pathway inhibitors are used only in locally advanced BCC lesions when operational or other

treatments are not adequate. Both vismodegib and sonidegib are on the same level in efficacy, as well as with adverse event profiles according to literature[3,4]. Most patients had experienced typical adverse effects like hair loss, leg cramps and loss of taste and thus, appetite. The patients with Gorlin syndrome felt it beneficial to use oral magnesium citrate and magnesium containing topical cream products.

Vismodegib is very effective for the treatment of locally advanced BCCs. The patient 2 with Gorlin syndrome had experienced numerous surgical operations and thus, the facial skin was full of operational scars. Consequently, it is possible that skin blood microcirculation was not sufficient for vismodegib to penetrate to the BCC tumor. This may explain, why some BCC lesions responded weakly or some new BCC tumors developed during vismodegib treatment, even though he used the drug continuously. However, individual properties are distinct, because the other Gorlin syndrome patient could have breaks in vismodegib treatments for several months, even up to 1.5 years.

The patient with morpheaformic BCC also responded well to vismodegib treatment, despite multiple wide surgeries previously.

The patient with right cheek-ear area BCC responded well without any heavy mutilating surgery and after a relapse he was treated again with another 3-month course with vismodegib. Of note, the patient was clinically clear as followed-up for 7years in January 2025. Cosmetically, the ear canal is now more visible but accepted by the patient.

Vismodegib treatment is usually not the 1st line treatment due to extreme teratogenicity, high costs (about 5,000 Eur/month) and to some extent the adverse events. It is an interesting question, when vismodegib should be used as the 1st line treatment.

The brothers with Gorlin syndrome responded well to vismodegib. However, it can be questioned what the efficacy would be without numerous previous surgical excisions and operations, when the skin blood vessel network is in a good condition delivering vismodegib to the BCC area. The results from the cases 4 and 5 (without earlier operations) might support the conclusion that vismodegib should be used earlier than recommended at the moment.

Another interesting question is, how long vismodegib treatment for each patient should go on without interruptions or if a break occurs, the length of such. We assume that it is neceessary to make an individual decision for each patient.

Ethical Approval

The patients have given their consent for this case report.

Conflict of Interests

Authors declare no conflicts of interests.

References

1. Kwasniak, LA, Garcia-Zuazaga J. Review: Basal cell carcinoma: evidence-based medicine and review of treatment modalities. Int J Dermatol 2011;50:645-658.
2. Peris K, Fargnoli MC, Kaufmann R, et al. On behalf of EADO, EDF, ESTRO, UEMS and EADV. European consensus-based interdisciplinary guideline for diagnosis and treatment of basal cell carcinoma-update 2023. Eur J Cancer 2023;192:1-35.
3. Dummer R, Ascierto PA, Basset-Seguin N, et al. Sonidegib and vismodegib in the treatment of patients with locally advanced basal cell carcinoma: a joint expert opinion. J Eur Acad Dermatol Venereol 2020;34:1944-1956.
4. Gutzmer R, Robert C, Loquai C, Schadendorf D, Squittieri N, Arntz R, Martelli S, Dummer R. Assessment of various efficacy outcomes using ERIVANCE-like criteria in patients with locally advanced basal cell carcinoma receiving sonidegib: results from a preplanned sensitivity analysis. BMC Cancer 2021;21(1):1-9.