P504 Efficacy, tolerability, and quality of life (QoL) evaluation in six patients affected by Gorlin-Goltz syndrome and treated with Vismodegib 150mg/die: a retrospective monocentric cohort analysis

Biagio Scotti[1,2*], Barbara Melotti[3], Francesca Comito[3], Carlotta Baraldi[1,2], Federico Venturi[1,4], Martina Lambertini[1,2], Emi Dika[1,2]

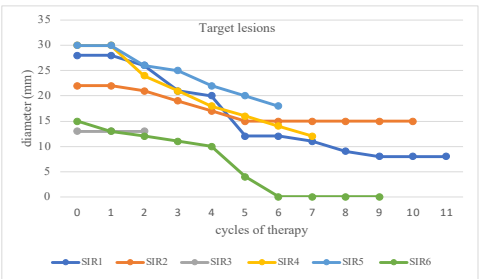
1 Oncologic Dermatology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy.
2 Dermatology, Department of Medical and Surgical Sciences *Alma Mater Studiorum*, University of Bologna, Italy.
3 Oncology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Policlinic of Sant'Orsola Italy.
4 Section of Dermatology, Department of Health Sciences, University of Florence, Florence, Italy.
*biagioscottimd@outlook.it

PATIENTS AND METHODS

Gorlin Goltz syndrome (GGS) is a genetic disorder predisposing patients to develop multiple basal cells carcinomas (BCCs). The literature data describing the efficacy and safety of vismodegib outside clinical trials are few and heterogeneous [1–5]. With the following study we would like to describe our experience using vismodegib 150 mg die in six patients (2 M and 4 F) diagnosed with GGS. During the screening phase for each patient we performed biopsies, complete blood chemistry, imaging and Skindex-16 questionnaire. Respecting the RECIST v1.1 guidelines, we considered clinically measurable lesions those with a greater diameter > 10 mm, target lesions those that are representative of all the organs involved and not-target lesions the rest not included in the above. The Follow-Up (FU) phase included a visit every 28 days (cycle of therapy) until discontinuation of the drug, and then every 6 months for 5 years after the last dose of vismodegib. Data on the efficacy (RECIST v1.1 criteria) and tolerability (CTCAE) were collected at the end of treatment and during FUs. Skindex-16 questionnaire was administrated also at the end of the 6th cycle of therapy and after 24 months from screening.

RESULTS

The diagnosis of GGS was established based on clinical and genetic criteria in all cases. Analyzing the global response for target and not-target lesions, in 66% of cases this appeared to be PR (Partial Response), while a CR (Complete Response) and a SD (Stable Disease) were found in 16.6% of cases each. There is a percentage reduction in the value of the target lesion's largest diameter, i.e. 50.5% in cases of PR after an average of 8.5 cycles of therapy and 100% in cases of CR after 9 cycles. The reduction of BCCs number for the entire cohort is 52.6%.



Patient		1	2	3	4	5	6
Sex		M	M	F	F	F	F
Age (years)		54	45	60	37	49	61
Genetic diagnosis		PTCH1	PTCH1	PTCH2	PTCH1	SUFU	PTCH1
Family history positive		No	No	No	Yes	Yes	No
Extracutaneous involvement		No	Hypertension	No	Maxillary odontogenic cyst	Pellucid septum cyst, calcification of the sickle and tentorium, corpus callosum aplasia, uterine fibroleiomyomas, endometriotic cysts	Maxillary odontogenic cyst, right breast cancer with total mastectomy plus RT and CHT
BCCs surgically treated (n.)		>10	>10	>10	>20	>30	>30
Number of vismodegib cycles		11	10	2	7	6	9
Reduction in the Target lesions diameter (%)		71.4	31.8	0	60	40	100
Overall response (12th month)	Target lesions	PR	PR	SD	PR	PR	CR
	Not-Target	PR	PR	SD	PR	PR	CR
New lesions	During treatment	No	No	No	No	No	No
New lesions	After vismodegib discontinuation	Yes	Yes	Yes	Yes	Yes	Yes
Skindex-16 questionnaire	Baseline (T0)	47	47	57	59	64	62
	6th cycle (T6)	24	26	0	39	44	29

Considering the 5-year FU data, all patients suffered a recurrence between 6 and 12 months after the last administration of the drug. Excluding patient n° 3 who definitively discontinued the drug after 2 cycles due to intolerable side effects (CTC grade 3), the most frequent adverse events (AEs) were muscle cramps mainly nocturnal, followed by alopecia/telogen effluvium and dysgeusia/metallic taste. Only patient n° 6 did not require any suspension of therapy. Overall, the AEs recorded were considered grade 2/moderate. The evaluation of the Skindex-16 questionnaire showed a decrease in terms of disease's discomfort during therapy and a worsening after disease' recurrence [mean (T0) 56 vs (T6) 27 vs (T24) 47.2].

CONCLUSIONS

Our data confirm that vismodegib has a favorable risk ratio improving the QoL even in patients with GGS.

1. Mesti, T., Sever, M. & Ocvirk, J. Vismodegib in Locally Advanced Basal Cell Carcinoma in Slovenia. *Dermatology* 239, (2023). **2.** Russo, F. *et al.* Long-term efficacy of a Vismodegib regime including a 1-week drug holiday every month in two patients with Gorlin Goltz syndrome. *Dermatologic Therapy* 35, (2022). **3.** Yang, X. & Dinehart, S. M. Intermittent vismodegib therapy in basal cell nevus syndrome. *JAMA Dermatology* 152, (2016). **4.** Tang, J. Y. *et al.* Inhibiting the Hedgehog Pathway in Patients with the Basal-Cell Nevus Syndrome. *N. Engl. J. Med.* 366, (2012). **5.** Dréno, B. *et al.* Two intermittent vismodegib dosing regimens in patients with multiple basal-cell carcinomas (MIKIE): a randomised, regimen-controlled, double-blind, phase 2 trial. *Lancet Oncol.* 18, (2017).