P505 Basal cell carcinomas' histological subtypes and relative response to Vismodegib in six patients diagnosed with Gorlin-Goltz syndrome

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PATIENTS AND METHODS

Gorlin Goltz syndrome (GGS) is a genetic disorder predisposing patients to develop cutaneous and extra-cutaneous anomalies. A patient with GGS could develop hundreds of basal cell carcinomas (BCCs), each with a different intrinsic biological behavior and thus equally variable response to HHI[1-3]. Herein, we would like to analyzes the response to HHI according to the histological subtypes of diagnosed BCCs. Six patients (2 M and 4 F) were included in the study and treated with vismodegib 150 mg/die after an average duration' therapy of 7.5 months (range 2-11). The treatment response was evaluated respecting the RECIST v1.1 guidelines and the 4th edition of the WHO classification of skin tumors was adopted for the histological subtypes analysis.

RESULTS

The number and subtypes of BCCs identified were various with 1 or 2 *target lesions* per patient and between 11 and 18 carcinomas as *not-target lesions* at screening phase [Table 1]. Overall, the clinical response of pigmented BCCs (pBCCs) was partial and temporally slower at 6 and 12 months compared to not-pBCCs (npBCCs) [Table 2]. We performed histological examination on not-completely responsive lesions 12 months after treatment start: the staining both of npBCC and pBCC showed no residual neoplastic cells. Among the four patients in partial response (PR), two of them diagnosed with basal squamous epithelioma and morpheiform BCC reported the least reduction in diameter of the cohort.

SIR	WHO (2018) HYSTOLOGICAL BCC SUBTYPES										TOTAL N° BCC		OTHER FEATURES for TL	
	Nodular	Superficial	Micro nodular	Infiltrating	Sclerosing/ morphoeic	Baso squamous	Pigmented	BCC with sarcomatoid differentiation	BCC with adnexal differentiation	Fibroepithelial	TARGET LESIONS (TL)	NOT TARGET LESIONS	Focal ulceration	Multifocal spreading
1	3	4	1	2	0	0	7	0	2	0	2 (Not-pigmented nodular)	17	yes	yes
2	4	1	0	0	0	1	9	0	1	0	2 (Pigmented nodular and basosquamous)	14	yes	no
3	3	9	1	1	0	0	5	0	0	0	1 (Pigmented nodular)	18	no	no
4	3	7	0	1	0	0	5	0	1	0	1 (Pigmented nodular)	16	yes	no
5	1	2	0	0	1	0	8	0	0	0	1 (Morpheic)	11	yes	yes
6	1	5	2	0	0	0	3	0	3	0	1 (Pigmented superficial)	13	no	no
TOTAL N°	15	28	4	4	1	1	37	0	7	0	8	89	/	/

ALL PATIENTS

	TARGET LESIONS	NOT-TARGET LESIONS	TL and NOT-TL (pigmented and not)
Screening	8	89	97
6th month	7	58	65
12th month	7	39	46

OVERALL RESPONSE

	TARGET LESIONS (% diameter reduction)	NOT-TARGET LESIONS
SIR 1	Partial Response (71.4)	Partial Response
SIR 2	Partial Response (31.8)	Partial Response
SIR 3	Stable Disease (0)	Stable Disease
SIR 4	Partial Response (60)	Partial Response
SIR 5	Partial Response (40)	Partial Response
SIR 6	Complete Response (100)	Complete Response

Table 1

SIR	pBCCs									npBCCs								
	Screening phase			6 months			12 months			Screening phase			6 months			12 months		
	TARGET	NOT TARGET	TOTAL	TARGET	NOT TARGET	TOTAL	TARGET	NOT TARGET	TOTAL	TARGET	NOT TARGET	TOT	TARGET	NOT TARGET	TOT	TARGET	NOT TARGET	TOT
1	0/2	7/17	7/19 (36.8%)	0/2	5/17	5/19 (26.3%)	0/2	4/17	4/19 (21%)	2/2	10/17	12/19 (63.2%)	2/2	6/17	8/19 (42.1%)	2/2	3/17	5/19 (26.3%)
2	1/2	8/14	9/16 (56.3%)	1/2	7/14	8/16 (50%)	1/2	5/14	6/16 (37.5%)	1/2	6/14	7/16 (43.7%)	1/2	2/14	3/16 (18.7%)	1/2	1/14	2/16 (12.5%)
3	1/1	4/18	5/19 (26.3%)	1/1	4/18	5/19 (26.3%)	1/1	4/18	5/19 STABLE DISEASE	0/1	14/18	14/19 (73.7%)	0/1	14/18	14/19 (73.7%)	0/1	14/18	14/19 STABLE DISEASE
4	1/1	4/16	5/17 (29.4%)	1/1	3/16	4/17 (23.5%)	1/1	2/16	3/17 (17.6%)	0/1	12/16	12/17 (70.6%)	0/1	6/16	6/17 (35.3%)	0/1	3/16	3/17 (17.6%)
5	0/1	8/11	8/12 (66.7%)	0/1	5/11	5/12 (41.6%)	0/1	3/11	3/12 (25%)	1/1	3/11	4/12 (33.3%)	1/1	1/11	2/12 (16.6%)	1/1	0/11	1/12 (8.3%)
6	1/1	2/13	3/14 (21.4%)	0/1	1/13	1/14 (7.1%)	0/1	0/13	0/14 (0%)	0/1	11/13	11/14 (78.6%)	0/1	4/13	4/14 (28.5%)	0/1	0/13	0/14 (0%)

Table 2

DISCUSSION

Patients with the highest number of pBCCs recorded the worst results in terms of response to therapy. Some of the pBCCs clinically resistant at 6 months were completely regressed at 12 months. The immunological response and tissue remodeling led to the lymphatic recirculation of the melanophages taking place of the tumor cells. However, pigmentation in BCCs can also be the result of a process of *melanization*, that is the transfer of melanosomes to the neoplastic cells[4]. We hypothesize that similarly to infectious processes, this is a way through which the competent immune system circumscribes the abnormal target, allowing its elimination in the superficial dermis by phagocytic cells[5].

CONCLUSIONS

The histological subtypes of BCCs with *higher risk* of recurrence and *pBCCs* showed in our cohort a greater tendency to PR during HHI treatment.

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