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Adjuvant immunotherapy in mucosal melanoma: an observational retrospective study from the Italian Melanoma Intergroup.

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Background

Anti PD-1 immunotherapy is considered a standard of care for patients with stage III melanoma. However, few data are available regarding subjects with mucosal melanoma (MM) who were originally excluded from registrational studies.

Patient n.	Age	Sex	Stage TNM AJCC 8th	Site of primary melanoma	Duration of treatment	Type of Progression	Death
1	48	M	IIIA	Glans	9		
2	82	F	IIIB	Anal	12	Distance	Yes
3	80	F	IIIA	Vulva	12		
4	70	M	IIIA	Conjunctiva	7	Distance	
5	73	F	IIIC	Vulva	10	Local	Yes
6	73	M	IIIC	Nasal mucosa	4	Local and Distance	
7	75	M	IIIC	Glans	11	Distance	Yes
8	76	F	IIIA	Vulva	2		
9	48	F	IIID	Vulva	12	Distance	
10	52	F	IIIC	Vulva	12		
11	77	F	IIIA	Anal	12		
12	51	F	IIIC	Anal	12	Distance	Yes
13	80	F	IIIC	Nasal mucosa	12		
14	53	F	IIIC	Nasal mucosa	12	Local	
15	60	F	IIIA	Glans	5	Distance	Yes
16	78	F	IIIC	Anal	11	Local	
17	56	F	IIIC	Anal	4	Distance	Yes
18	74	M	IIIC	Anal	12		
19	79	F	IIIA	Vulva	12		
20	53	F	IIIC	Vulva	3	Local	
21	57	F	IIIC	Vulva	11		

Table 1: main characteristics of patients with mucosal melanoma

Materials and Methods

This retrospective multicenter study analyzed data from 23 patients referred to IMI (Italian Melanoma Intergroup) with stage III mucosal melanoma and undergoing adjuvant immunotherapy from January 2019 to December 2021. Two patients were on treatment at the time analysis and thus were excluded from the analyses.

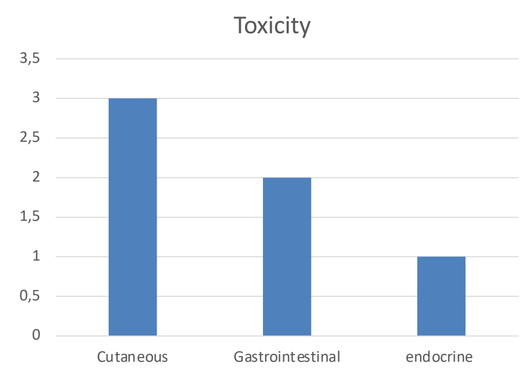

Table 2: toxicity during immunotherapy in mucosal melanoma patients

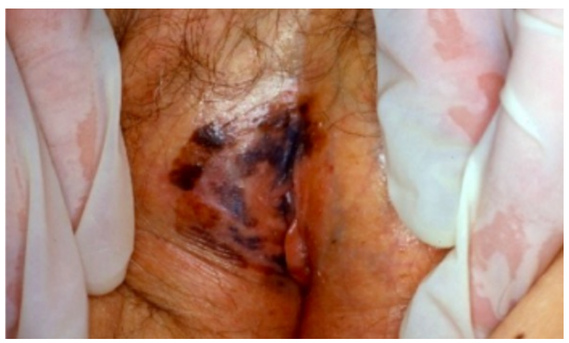

Figure 1:vulvar localization of melanoma

Results

We observed a prevalence of female gender with a F:M ratio 3:1. The mean age was 57 years (38-82 yrs). The sites involved were vulva (8), anal canal (6), glans (3), nasal mucosa (3), and 1 patient with conjunctival localization. According to the AJCC 8th edition 6 patients have a stage IIIA, 1 IIIB, 12 IIIC and 2 IIID. Twelve months adjuvant treatment was completed in 11 patients, while in 10 patients was interrupted early after a median time of 5 months (range 2-11 mo). The main cause of discontinuation was disease progression, while only two patients discontinued due to toxicity Overall, 3 patients had skin toxicity, 2 gastro-intestinal toxicity and 1 patient endocrine toxicity. Among patients who concluded the 12-mo adjuvant treatment, we observed a median PFS from the end of treatment of 5 months (range 2-11). Overall, 12 patients had a recurrence: 4 locally, 7 distant metastasis and 1 patient had a synchronous local and distant recurrence. Interestingly, of the 4 patients who continued anti PD-1 treatment after progression, none achieved a clinical response. 1 patient continues treatment with Ipilimumab, for two patients target therapy was used (Imatinib for a patient with c-Kit and Dabrafenib and Trametinib for a patient with BRAF mutation) achieving partial response. The other patients were switched to best supportive care.

Conclusion

MM has a very poor prognosis and significantly worse outcomes than cutaneous melanoma (CM). In fact, immunotherapy is less effective in MM than in CM, even for stage III disease in adjuvant setting. The high rates of progression suggest that MM deserves an early molecular characterization. Moreover, patients should be closely monitored to identify recurrences that could benefit from local-regional treatments.

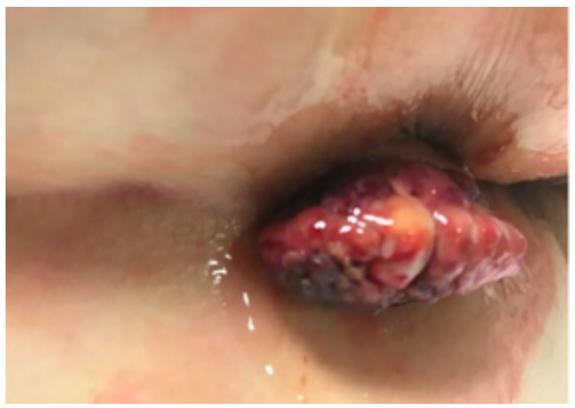

Figure 2:localization of melanoma in the anal canal