Real-world data of relapse after adjuvant treatment (Tx) in high-risk melanoma.

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Background:

Adjuvant (adj) Tx with programmed cell death protein 1 (PD-1) inhibitors or targeted therapy (TT) for 1 year in patients (pts) with high-risk resected melanoma prolongs relapse-free survival (RFS). However, up to 1/3 of pts recur in the year after adj Tx and there are few data regarding patterns of relapse, management and outcomes. Our aim was to describe how adj Tx impacts the outcomes in melanoma pts in our center.

Methods:

Single-institution experience of 123 consecutive pts with melanoma resected in our center from 2014 to 2019 were retrospectively analyzed. Clinicopathological factors, adj Tx, timing and patterns of relapse, Tx at relapse and subsequent outcomes were examined.

Table 1. Descriptive Analysis.

Variable		n	%
Gender	Female	67	54.5
	Male	56	45.5
Comorbilities	yes	73	40.6
	no	50	59.4
Hystology	Cutaneous	114	92.7
	Mucose	9	7.3
BRAF	Mutant	29	37.7
	Wild type	48	62.3
Stage at diagnosed	IA-IB	15	10.1
	IIA-IIC	54	43.8
	IIIA	8	6.5
	IIIB	12	9.8
	IIIC	24	19.5
	IIID	1	0.8
	IV	1	0.8
	UNK	8	6.5

A total of 123 pts were identified. Median age 57y.
BRAF mt was found in 29 pts (38%)

Results:

Table 2. Descriptive Analysis of treatment.

	n	%
No adjuvant treatment	**74**	**60,16%**
Comorbidities	9	12,00%
Not indicated	14	18,92%
Patient rejects it	3	4,05%
Time to surgery	4	5,41%
UNK	44	59,46%
Adjuvant treatmente	**49**	**39,84%**
Grand Total	**123**	**100,00%**

	Nro pt	%
Metastatic Disease	**30**	**100,00%**
Prior Adjuvant Tx.	**16**	**53,33%**
Immunotherapy	10	62,50%
Immunotherapy_Target Therapy	1	6,25%
Interferon	1	6,25%
Interferon_Immunotherapy	3	18,75%
Radiotherapy	1	6,25%
No prior adjunvant Tx.	**14**	**46,67%**

A total of 49 pts received adj Tx: 3 pts (6%) TT, 8 pts (16%) IFN-α, and 38 pts (31%) immunotherapy (iTx) with anti-PD-1 and/or ipilimumab.

Table 3. Recurrence after first surgery

No prior adjuvant Tx.	74	60,16%	Prior adjuvant Tx.	49	39,84%
Recurrence	28	37,84%	No recurrence	37	75,51%
metastatic	9	32,14%	Recurrencia	12	24,49%
non resecable	4	44,44%	metastatic	5	41,67%
resecable	5	55,56%	non resecable	5	100,00%
locoregional	19	67,86%	locoregional	7	58,33%
No resecable	6	31,58%	non resecable	2	28,57%
Yes resecabl	13	68,42%	Yes resecable	5	71,43%

A total of 40 pts (32%) had relapse (65% locoregional and 35% distant), 8 pts (21%) had prior adj iTx with a median RFS of 21.5 months (m) (CI95% 17.4-NA).

24 pts (60%) were resected (6 pts with distant recurrent), 14 pts received adj Tx (12 pts iTx, 1 pt IFN-α and 1 pt TT), for 4-pts was the second adj Tx. A total of 31 of 123 pts (25%) developed metastatic melanoma (MM), of these 17 pts (55%) received adj Tx. PFS at 1st line of Tx of pts with prior adj-Tx vs no was similar (HR=1.01, p=0.98), mainly Tx were iTx (65%), TT (31%) and chemotherapy (4%). Remarkably, there was no worse response rate (complete response [CR] or partial response [PR]) in pts with prior adj Tx (68.8% vs 35.7%, p=0.14).

Table 4. Response to Tx at first line

Tx to Metastatic Disease	30		30
Prior Adjuvant Tx.	16	Interferon_Immunotherapy (adj)	2
1L Chemotherapy	1	PD	1
Interferon (adj)	1	RC	1
PD	1	Radiotherapy (adj)	1
1L Immunotherapy	9	RC	1
Immunotherapy (adj)	5	**1L target therapy**	4
PD	2	Immunotherapy (adj)	4
RC	2	RC	3
NA	1	RP	1
Immunotherapy_Target Therapy (adj)	1	No Tx	2
PD	1	Immunotherapy (adj)	1
		Interferon_Immunotherapy (adj)	1

Of 17 pts with prior adj-Tx (16 pts adj-iTx) who had MM, twelve (70.6%) received iTx at 1st line, 50% had response to iTx. Also, all 4 pts BRAF-mt with prior adj-iTx who received TT at 1st line had CR or PR. There was no correlation between treatment-free interval after adj TX and PFS at 1st line (p=0.66).

Conclusions

Our real-world data demonstrates that after a locoregional or distant relapse of melanoma, despite prior adj-Tx, Tx with iTx or TT can be active. But additional research is needed.