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Neoadjuvant immunotherapy for stage III melanoma – The cohort study of a large swiss hospital

Clinical solid tumor oncology

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Background and Objective

The OpACIN-neo[1] and PRADO[2] trials showed excellent outcomes for stage III melanoma treated with neoadjuvant immunotherapy. The superiority of the neoadjuvant approach was confirmed later on in the phase III NADINA trial[3]. The results of the OpACIN-neo and PRADO trials led us to adopt the neoadjuvant immunotherapy for stage III melanoma since summer 2022.

Methods

All patients showing macroscopic lymph nodes metastases clinically or on staging PET-CT were treated with two neoadjuvant cycles of ipilimumab 1mg/kg and nivolumab 3mg/kg followed by either the resection of the involved node(s) only or a complete lymph node dissection. Patients showing a major pathological response (MPR, ≤ 10% vital tumour cells) on histology didn't receive any further adjuvant treatment. Patients lacking a MPR received an adjuvant treatment, either dabrafenib and trametinib for BRAF mutated melanoma or nivolumab for BRAF wildtype tumors for the duration of one year. Patients who had only the involved lymph node resected and were lacking a major pathological response were strongly recommended to proceed to a complete lymph node dissection.

Results

Our cohort encompasses 8 patients so far with a median age of 66.5 years (range 56-86). On pathological examination of the resected node 4 patients showed a complete response (CR), 1 patient a near complete response nearCR), 1 patient a partial response and 2 patients no response. 4 CR and 1 nearCR account for a MPR rate of 5/8 = 62.5%. None of the patients with MPR relapsed so far (median time to follow-up 24.2 months, range 4.6 -33.6). Two out of three patients lacking an adequate response (MPR) on neoadjuvant immunotherapy relapsed, one of the two with distant metastases at restaging between neoadjuvant treatment and lymph node dissection. Immune-related adverse events seem to correlate with an optimal response on neoadjuvant immunotherapy.

Patient	Age	Sex	ir Adverse Events	Path Response	Adjuvant treatment	Time to recur (mo)	Follow-up NED (mo)
#1	57	F		CR		-	24.2
#2	81	F	Hypophysitis G3	CR		-	33.6
#3	56	F	Vitiligo G1, Hypothyroidism G2	CR		-	24.4
#4	81	F		NR	refused	6.1	† at 14.5
#5	59	M	Hepatitis G4	CR		-	14.8
#6	59	M		NR	Dabra/Tram	-	10.3
#7	86	F	Myocarditis G3	nearCR (5%)		-	4.6
#8	74	M	Diarrhea G2	PR (50%)	NA	M1 on preop PET	Dabra/Tram palliative

Conclusion

Our results are in line with the published data on neoadjuvant immunotherapy for stage III melanoma. This approach is more effective and ressource-sparing than the adjuvant treatment, thus has to be adopted as a standard of care. More effective salvage strategies are needed for patients failing neoadjuvant immunotherapy.

References

[1]OpACIN-neo, Rozeman, Lancet Oncol 2019

[2]PRADO, Reijers, Nat Medicine 2022

[3]NADINA, Blank, NEJM 2024

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