Neoadjuvant immunotherapy for Stage III Acral Melanoma

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Background

- ❑ Acral melanoma (AM) is a rare subtype of melanoma arising from soles, subungual and palmar surfaces.
- ❑ Characterised by a low tumour mutational burden, AM is biologically distinct from non-acral cutaneous melanoma and associated with poorer prognosis in retrospective studies of patients in the advanced & adjuvant setting [1,2]
- ❑ Neoadjuvant immunotherapy (NAI) is the standard of care for macroscopic stage III melanoma, however AM patients are under-represented in landmark clinical trials, therefore efficacy in this population is unclear.

Aim

- ❑ The aim of this study was to determine the efficacy of neoadjuvant immunotherapy in acral melanoma.

Methods

- ❑ We conducted a retrospective analysis of patients with resectable, macroscopic stage III AM who commenced NAI prior to Dec 2025.
- ❑ The primary endpoint was major pathological response (MPR) and event-free survival (EFS) as assessed according to International Neoadjuvant Melanoma Consortium Criteria [3]
- ❑ EFS was defined as time from commencement of NAI to progression to unresectable melanoma before surgery, disease recurrence, or death
- ❑ Recurrence free survival (RFS) was a secondary outcome, defined as time from surgery to first recurrence.

Results

- ❑ 53 patients over 15 sites in 7 countries

Table 1: Baseline Characteristics

Sex - no. (%)	
Male	31 (58.5)
Female	22 (41.5)
Median age (range) – yr	65.0 (23.0, 85.0)
Stage (AJCC 8th) - no. (%)	
Unknown	1 (1.9)
IIIB	13 (24.5)
IIIC	35 (66.0)
IIID	4 (7.5)
In-transit metastases- no. (%)	
Yes	10 (18.9)
No	43 (81.1)
Primary site - no. (%)	
Palmar	3 (5.7)
Plantar	35 (66.0)
Subungual (fingers)	4 (7.5)
Subungual (toes)	11 (20.8)
Mutation - no. (%)	
BRAF/NRAS/KIT wildtype	28 (52.8)
BRAF V600	11 (21.2)
NRAS	10 (19.2)
KIT	2 (3.8)
Not reported	2 (3.8)

Table 2: Neoadjuvant regimen

Neoadjuvant drug used - no. (%)	
Anti-PD1 monotherapy	18 (34.0)
Anti-PD1 + Anti-CTLA4	32 (60.4)
Ipilimumab 80mg + Nivolumab 240mg	9 (17.0)
Ipilimumab 1mg/kg + Nivolumab 3mg/kg	14 (26.4)
Ipilimumab 3mg/kg + Nivolumab 1mg/kg	8 (15.1)
Ipilimumab + Pembrolizumab	1 (1.9)
Anti-PD1 + Anti-LAG3	3 (5.7)

- ❑ Median follow up was 14.6 months
- ❑ Among patients proceeding to surgery (87%), 34/46 (74.0%) had therapeutic lymph node dissection (TLND), 7/46 (15.2%) underwent index lymph node resection and 2/46 (4.3%) underwent in-transit metastasis resection only
- ❑ MPR rates comparable between monotherapy & doublet (25% in both), without significant difference in EFS
- ❑ 18/46 recurred: 12 distantly, 6 locally. All who had local recurrence did so despite TLND
- ❑ Of the 4 who did not proceed to surgery due to favourable clinical response, no events (death or progression) occurred.

Safety

- ❑ Adverse events attributed to NAI occurred in 68% of patients. 11 (20.8%) experienced a ≥G3 adverse event attributed to NAI (most commonly rash & hepatitis)
- ❑ Surgery was delayed for 2 patients due to immune-related events (G3 hepatitis, G3 nephritis)

Results

Figure 1: Patient disposition & Pathological Response

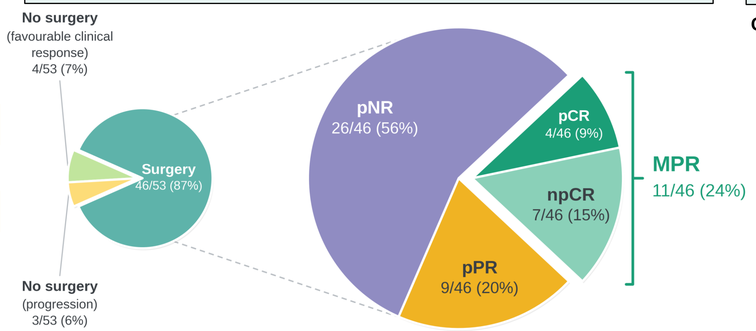
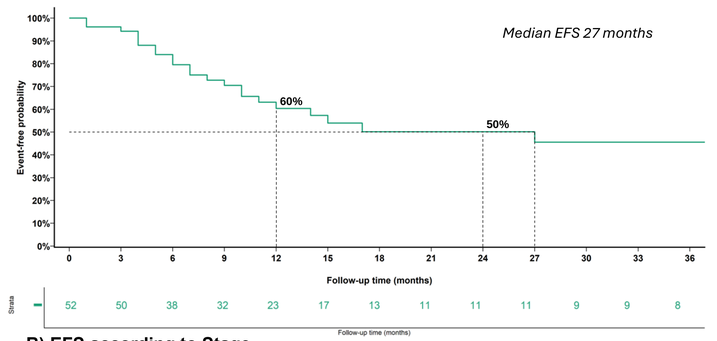


Figure 2: Event-free Survival

A) EFS among overall population



B) EFS according to Stage

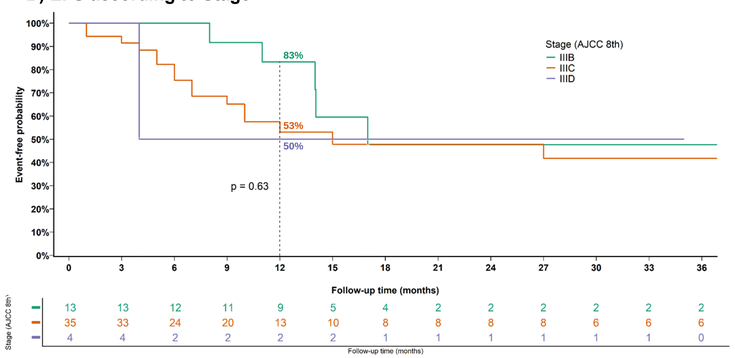


Figure 2: Event-free Survival (cont.d)

C) EFS according to Primary Site

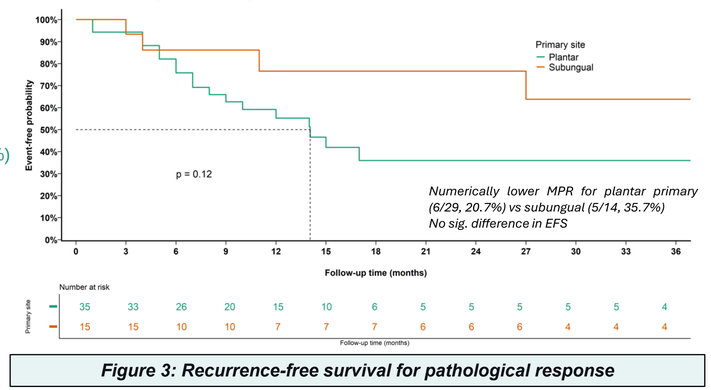
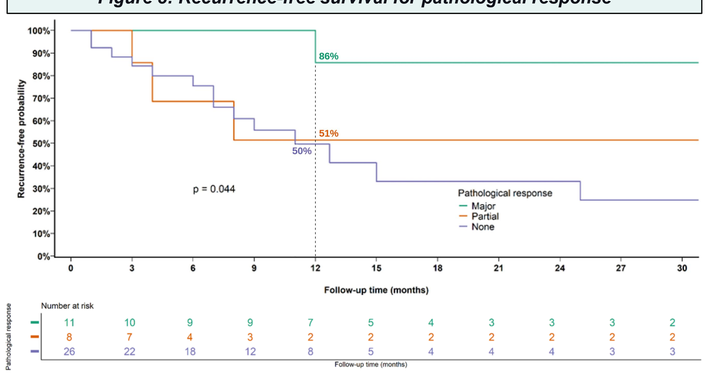


Figure 3: Recurrence-free survival for pathological response



Conclusions

Neoadjuvant immunotherapy demonstrates activity in acral melanoma, although response rates appear lower than those reported in non-acral cutaneous melanoma. Further studies are needed to define optimal neoadjuvant strategies for acral melanoma.

References

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The presenting author has no conflicts of interest to declare