EE158

Characterization Of Recurrence Patterns and Healthcare Resource Utilization for Patients with Stage II Cutaneous Melanoma in Spain: METHEOR study

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INTRODUCTION AND OBJECTIVES

- Cutaneous melanoma (CM) rates have been rising rapidly over the past decades[1]. In 2023, more than 7,000 cases of CM were diagnosed in Spain, of those 15% were diagnosed at stage II. Additionally, more than 1,000 deaths are reported annually due to CM[2].
- Although stage II CM is a localized disease, it is observed that stages IIB-C may be associated with a worse prognosis than stages IIIA and IIIB[3]. Moreover, stage II is also associated with a greater number of deaths due to its higher incidence.
- Surveillance guidelines and several therapy options have been established for stage III CM. However, More studies are needed to obtain information about adjuvant treatment and surveillance of patients with stages IIB and IIC melanoma, as well as to identify biomarkers that will guide clinicians in the treatment of each patient. Additionally, a consensus for the monitoring of stage II CM patients is lacking, and there is a need for the characterization and understanding of the recurrence patterns of stage II patients.
- The **METHEOR study** aimed to describe recurrence patterns, healthcare resource utilization (HCRU), and costs associated with pathological stage II primary CM in the real-world clinical setting in Spain.

METHODS

- This is an observational, multicenter, retrospective, study conducted at 11 Spanish hospitals.
- Eligible patients were aged ≥18 years diagnosed with primary stage II CM (as per AJCC 8th edition)[4] between January 2013 and December 2017, with a minimum follow-up of 5 years for alive patients.
- The primary endpoint was RFS, measured from the primary tumour excision (index date) to the first disease recurrence or death due to any cause. Secondary endpoints included overall survival (OS) and health care resource utilization (HCRU).

RESULTS

Patient characteristics

A total of 324 patients were included in the study. The median age (IQR) was 64 (51.0-73.0) years, and most patients were male (169; 52.2%). A total of 144 (44.4%) patients were classified as IIA, 115 (35.5%) as IIB, and 65 (20.1%) as IIC (Table 1)

Table 1. Patient charactersitics

Characteristics	Value
Age (years), median (IQR)	64 (51.0-73.0)
Male, n (%)	169 (52.2)
Caucasian ethnicity, n (%)	323 (99.7)
Location of tumour(s), n (%)	
Trunk	128 (39.5)
Lower extremities	61 (18.8)
Head and neck	55 (17.0)
Upper extremities	48 (14.8)
Acral	32 (9.9)
Breslow depth (<4.0 mm), n (%)	229 (70.7)
Mitoses per mm² (≤5), n (%)	218 (67.3)
Ulceration (present), n (%)	194 (59.9)
Signs of regresion, n (%)	39 (12.0)
Tumour-infiltrating lymphocytes, n (%)	206 (63.6)
CM II sub-stages (AJCC 8th), n (%)	
IIA	144 (44.4)
IIB	115 (35.5)
IIC	65 (20.1)
Histology (>5%), n (%)	
Nodular	134 (41.4)
Superficial spreading	108 (33.3)
Acral lentiginous	29 (9.0)
Charlson Comorbidity index (<6), n (%)	293 (90.4)
Primary CM treatment (in addition to surgery), n (%)	
Radiotherapy	3 (0.9)
Pharmacological	28 (8.6)

AJCC, American Joint Commission on Cancer; CM, cutaneous melanoma; IQR, interquartile range.

Disease recurrence

After a median follow-up of 69 months, a total of 90 patients (27.8%) experienced at least one recurrence. Of these, 37 (41.1%) were lymphatic, 31 (34.4%) hematogenous and 18 (20.0%) presented both types of dissemination. Of patients, almost half of them experienced a second recurrence (41, 45.6 %) (**Table 2**).

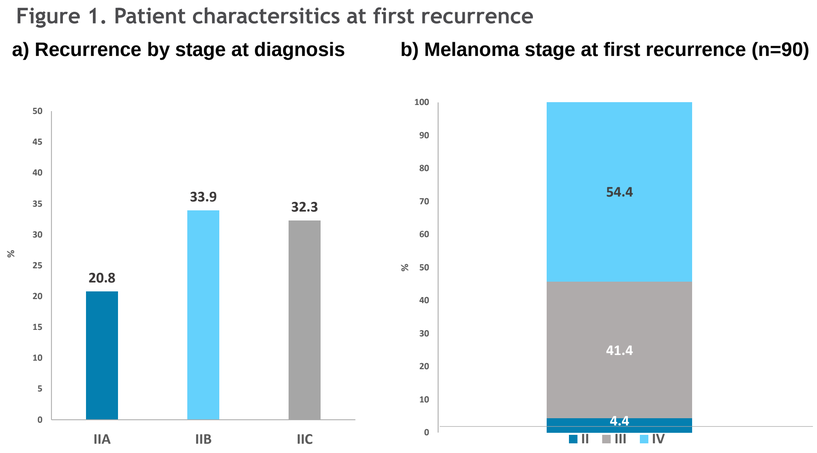
Table 2. Disease characteristics at first recurrence

Characteristics	Value
Lymphatic, n (%)	37 (41.1)
Haematic, n (%)	31 (34.4)
Lymphatic + haematic, n (%)	18 (20.0)
Missing, n (%)	4 (4.4)
Lymphatic localization, n (%)[a]	
Regional lymph nodes	34 (66.7)
Satellitosis/Metastasis in transit	24 (43.6)
Haematic location, n (%)[a]	
Lung	33 (67.3)
Central nervous system	14 (28.6)
Liver	12 (24.5)
Bone	7 (14.3)
Non regional lymph nodes	6 (12.2)
Number of metastatic sites, n (%)	
1	29 (59.2)
2-3	16 (32.7)
≥4	4 (8.2)
Patients with more than 1 recurrence, n (%)	
Second recurrence	41 (45.6)
Third recurrence	21 (23.3)
Fourth recurrence	3 (3.3)

[a]Multiple response.

Of patients diagnosed at stage IIA, IIB, and IIC, 20.8%, 33.9%, and 32.3%, respectively, experienced at least one recurrence (**Figure 1a**), with the majority (54,4%) progressing to stage IV (**Figure 1b**).
Among the patients with distant recurrence, 16 (32.7%) had metastases in 2-3 distinct sites, most commonly the lung (33; 67.3%), brain (14; 28.6%) and liver (12; 24.5%) (**Table 2**).

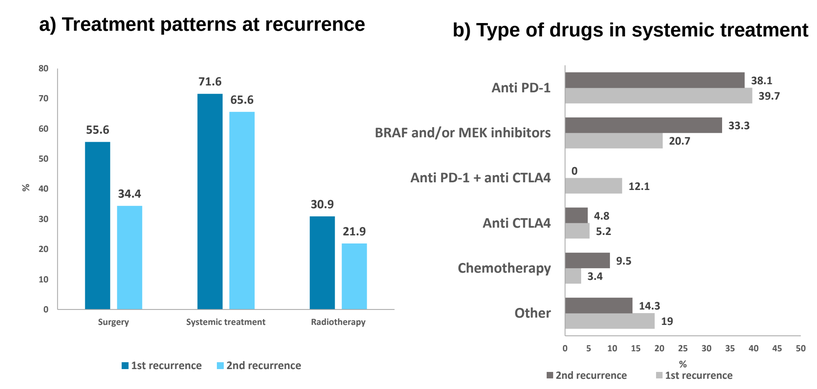
Figure 1. Patient charactersitics at first recurrence



A total of 81 patients with recurrence received treatment after the first recurrence of CM. Of these, 45 (55.6%) patients underwent surgery, 25 (30.9%) received radiotherapy and 58 (71.6%) received systemic treatment (**Figure 2a**), mainly anti-PD-1 (39.7%)(**Figure 2b**).

Treatment patterns for the 32 patients treated after the second relapse were similar to those in the first relapse, although fewer patients had surgery (**Figure 2a**).

Figure 2. Treatment patterns at recurrence

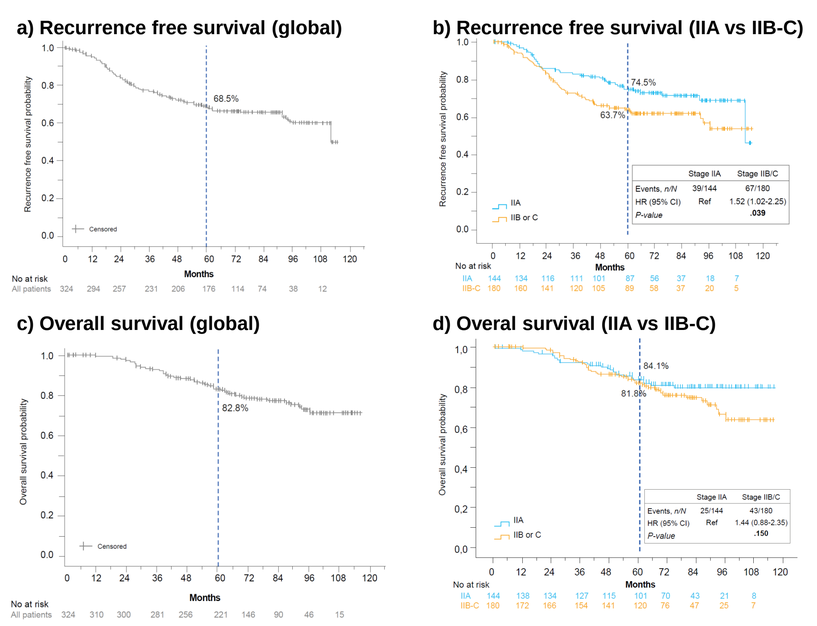


Survival outcomes: RFS and OS

The 5-year recurrence free survival (RFS) was 68.5% for the overall population (**Figure 3a**), 74.5% for stage IIA and 63.7% for stages IIB-C. The risk of recurrence was significantly higher for stages IIB/C than for stage IIA (HR=1.52; 95% CI: 1.02-2.25, P=0.039) (**Figure 3b**).

Five-year overall survival (OS) for all patients was 82.8% (**Figure 3c**), 84.1% for stage IIA and 81.8% for stages IIB-C (**Figure 3d**).
At the end of follow-up, 68 (21.0%) patients had died, 66.2% of them from melanoma.

Figure 3. Recurrence free survival and overall survival

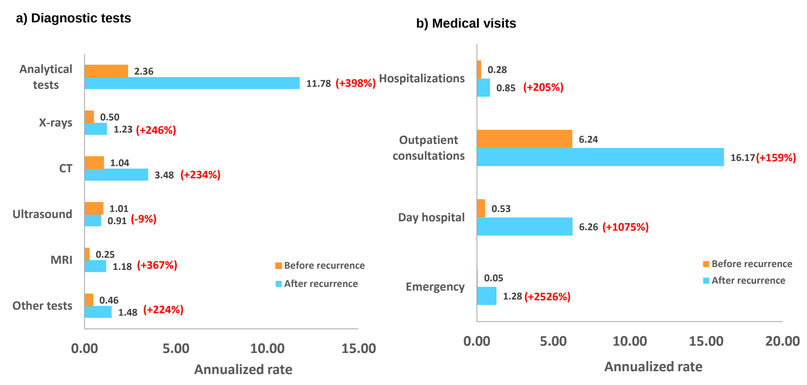


Use of healthcare resources and costs

After first recurrence, all diagnostic tests except ultrasound increased annually (**Figure 4a**). No significant differences were found between stage IIA and IIB/C patients (except for analytical tests and X-rays).

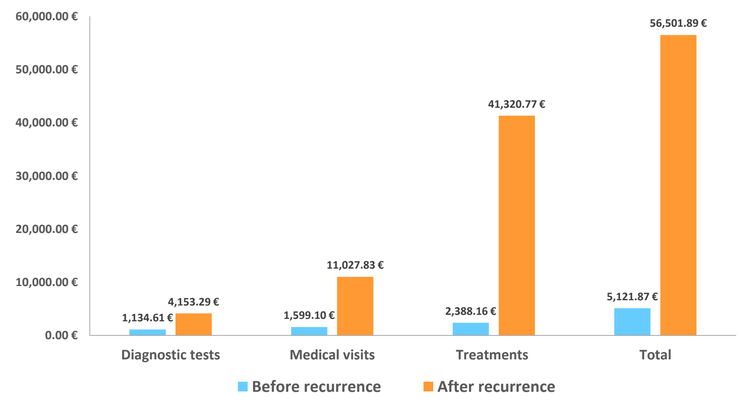
Overall, there was also an increase in the annualized rates of all medical visits after first relapse (**Figure 4b**), with the higher increase observed in emergency visits, day hospital and outpatient consultations.

Figure 4. Variation in annualized cost rate after recurrence



The annualized cost per patient per diagnostic test increased from €1,134.61 before recurrence to €4,153.29 after the first recurrence. Additionally, the annual cost per patient of medical visits increased from €1,599.10 to €11,027.83 after the first recurrences, and the cost of treatments increase from 2,388.16 € to 41,320.77 €. (**Figure 5**).

Figure 5. Variation in total annual costs after recurrence per patient



CONCLUSIONS

- Our study shows that aproximately one-third of patients diagnosed with stage II cutaneous melanoma experience at least one recurrence, regardless of the substage at diagnosis. Disease recurrence occurred more often in patients with stage IIB and IIC. Most of these patients progressed to stage IV. Moreover, more than 60% of the 64 patients who died were due to CM.
- After the first recurrence, diagnostic tests (except X-rays) and medical visits increased annually in both stage IIA and stage IIB/C patients. The total costs per patient after recurrence increased annually by 3,018.68 € in diagnostic tests, by 9,428.73 € in medical visits and by 38,932.62 € in treatments.
- These results highlight the need for better follow-up and treatment strategies to reduce the risk of recurrence in patients with stage II CM, especially in stages IIB-C.

References

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