Real-world treatment patterns in metastatic melanoma: Comparison of data from the Central and South Eastern European Registry (CSEEREG) and the Danish Metastatic Melanoma Database (DAMMED)

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BACKGROUND

- Treatment of metastatic melanoma (MM) has made significant progress over the past decade.
- However, the reimbursement process across European countries remains unharmonized.
- We evaluated the association between access to novel melanoma therapies and survival outcomes by comparing data from the CSEEREG (patients from Bosnia-Herzegovinian, Croatian and Serbian melanoma centers) with the DAMMED (comprising all Danish melanoma patients) registry.

OBJECTIVES

- To assess the impact on overall survival (OS) of first line (1L) treatments in CSEEREG vs DAMMED.
- To compare demographic and prognostic differences of an advanced melanoma population in CSEEREG vs DAMMED.

METHODS

- We performed a retrospective analysis of patients with metastatic melanoma from the **CSEEREG** (Central and South Eastern European Registry) and the **DAMMED** (Danish Metastatic Melanoma Database) registries, stratified by two periods based on the initiation of 1L treatment for metastatic disease:
  - ❖ **Period 1:** 01.01.2017 to 31.12.2019
  - ❖ **Period 2:** 01.01.2020 to 31.12.2023
- Both registries are integral parts of the **European Melanoma Registry (EUMelaReg).**
- **Matching:** For adjustment of imbalances between both registries, a 1:1 inverse propensity score-based matching for age, sex, BRAF status, brain metastases, ECOG, LDH, AJCC stage, and adjuvant therapy was performed.

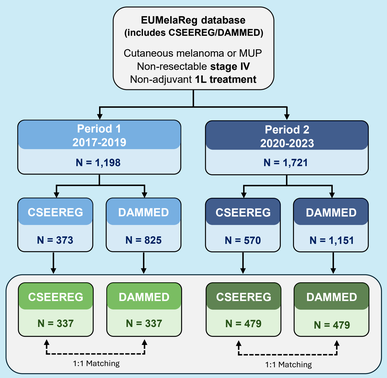


Figure 1: Flow chart illustrating the selected populations for analysis using real-world data from CSEEREG and DAMMED registry. N, number of patients; MUP, melanoma of unknown primary; CSEEREG, Central and South Eastern European Registry; DAMMED, Danish Metastatic Melanoma Database; 1L, first line. Matching was performed with an optimal matching algorithm using inverse propensity score matching.

RESULTS

- Baseline characteristics differed between registries, with a higher age and notably, a higher prevalence of brain metastases, among patients in DAMMED compared to patients in CSEEREG.
- Additionally, significantly more patients in DAMMED had been treated with adjuvant treatment prior to 1L therapy for metastatic disease, especially in Period 2.
- The proportion of missing LDH values was higher in CSEEREG compared to DAMMED.

Table 1. Baseline characteristics of the unmatched and matched populations at start of 1L treatment in Period 1 and 2

	UNMATCHED Cohort				MATCHED Cohort			
	Period 1: 2017-2019		Period 2: 2020-2023		Period 1: 2017-2019		Period 2: 2020-2023	
	CSEEREG N = 373	DAMMED N = 825	CSEEREG N = 570	DAMMED N = 1,151	CSEEREG N = 337	DAMMED N = 337	CSEEREG N = 479	DAMMED N = 479
Age								
Mean (SD)	60.1 (13.5)	66.4 (13.1)	63.3 (12.8)	68.7 (13.4)	60.1 (13.6)	61.7 (12.6)	63.7 (12.8)	65.2 (13.6)
Median (Min-Max)	62 (27-93)	69 (20-94)	65 (19-94)	72 (20-94)	62 (28-93)	62 (29-91)	66 (19-94)	66 (20-94)
Sex								
Female	129 (34.6%)	337 (40.9%)	213 (37.4%)	451 (39.2%)	117 (34.7%)	113 (33.5%)	170 (35.5%)	186 (38.8%)
Male	244 (65.4%)	488 (59.1%)	357 (62.6%)	700 (60.8%)	220 (65.3%)	224 (66.5%)	309 (64.5%)	293 (61.2%)
BRAF status								
Positive	223 (59.8%)	447 (54.2%)	285 (50.0%)	608 (52.8%)	207 (61.4%)	194 (57.6%)	266 (55.5%)	261 (54.5%)
Wild type	136 (36.5%)	378 (45.8%)	224 (39.3%)	542 (47.1%)	130 (38.6%)	143 (42.4%)	212 (44.3%)	217 (45.3%)
Missing/Unknown	14 (3.8%)	-	61 (10.7%)	1 (0.1%)	-	-	1 (0.2%)	1 (0.2%)
Brain metastases								
Yes	60 (16.1%)	174 (21.1%)	95 (16.7%)	279 (24.2%)	56 (16.6%)	51 (15.1%)	83 (17.3%)	79 (16.5%)
No	313 (83.9%)	651 (78.9%)	475 (83.3%)	872 (75.8%)	281 (83.4%)	286 (84.9%)	396 (82.7%)	400 (83.5%)
ECOG								
0	193 (51.7%)	422 (51.1%)	322 (56.5%)	615 (53.4%)	178 (52.8%)	189 (56.1%)	266 (55.5%)	286 (59.7%)
1	139 (37.3%)	272 (33.0%)	200 (35.1%)	354 (30.8%)	128 (38.0%)	127 (37.7%)	172 (35.9%)	151 (31.5%)
≥2	26 (7.0%)	128 (15.5%)	34 (6.0%)	163 (14.2%)	21 (6.2%)	18 (5.3%)	30 (6.3%)	30 (6.3%)
Missing/Unknown	15 (4.0%)	3 (0.4%)	14 (2.4%)	19 (1.6%)	10 (3.0%)	3 (0.9%)	11 (2.3%)	12 (2.5%)
LDH								
Normal	174 (46.7%)	484 (58.7%)	299 (52.5%)	678 (58.9%)	165 (49.0%)	163 (48.4%)	276 (57.6%)	256 (53.4%)
Elevated	137 (36.7%)	310 (37.6%)	186 (32.6%)	431 (37.5%)	132 (39.2%)	147 (43.6%)	164 (34.2%)	192 (40.1%)
Missing/Unknown	62 (16.6%)	31 (3.7%)	85 (14.9%)	42 (3.6%)	40 (11.9%)	27 (8.0%)	39 (8.1%)	31 (6.5%)
TNM								
M1a	70 (18.8%)	166 (20.1%)	117 (20.5%)	227 (19.7%)	61 (18.1%)	69 (20.5%)	91 (19.2%)	104 (21.7%)
M1b	63 (16.9%)	132 (16.0%)	129 (22.6%)	169 (14.7%)	55 (16.3%)	48 (14.2%)	112 (23.4%)	71 (14.8%)
M1c	180 (48.2%)	351 (42.6%)	229 (40.2%)	470 (40.8%)	165 (49.0%)	167 (49.6%)	193 (40.3%)	223 (46.6%)
M1d	60 (16.1%)	176 (21.3%)	95 (16.7%)	285 (24.7%)	56 (16.6%)	53 (15.7%)	83 (17.3%)	81 (16.9%)
Adjuvant therapy								
Yes	6 (1.6%)	48 (5.8%)	29 (5.1%)	269 (23.4%)	6 (1.8%)	6 (1.8%)	24 (5.0%)	23 (4.8%)
No	367 (98.4%)	777 (94.2%)	541 (94.9%)	882 (76.6%)	331 (98.2%)	331 (98.2%)	455 (95.0%)	456 (95.2%)

N, number of patients; CSEEREG, Central and South Eastern European Registry; DAMMED, Danish Metastatic Melanoma Database; SD, standard deviation; min, minimum; max, maximum; ECOG, Eastern Cooperative Oncology Group; LDH, Lactate dehydrogenase; 1L, first line.

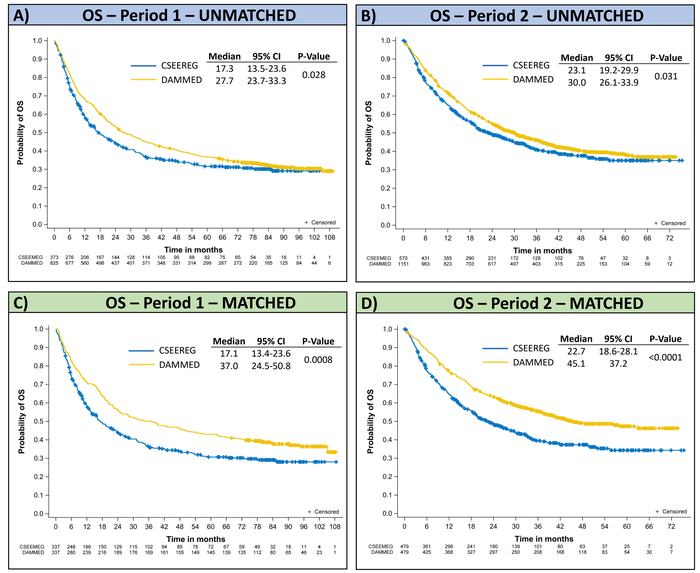


Figure 2: Kaplan-Meier curves of OS from start of 1L treatment for unmatched (A/B) and matched (C/D) cohorts from CSEEREG (blue line) or DAMMED (yellow line) registry during Period 1 (2017-2019) and Period 2 (2020-2023). OS, overall survival; 1L, first line; CI, confidence interval.

- Median OS was significantly longer in DAMMED than in CSEEREG in both periods in the unmatched cohort.
- After matching, Kaplan-Meier estimates still demonstrated longer OS in DAMMED in both time periods.
- Median OS improved over time in both registries in the unmatched (from 17.3 to 23.1 months in CSEEREG and 27.7 to 30.0 months in DAMMED) and matched (from 17.1 to 22.7 months in CSEEREG and 37.0 to 45.1 months in DAMMED) cohort.

Table 2. Type of 1L therapy of the unmatched and matched populations at start of 1L treatment in Period 1 and 2

	UNMATCHED Cohort				MATCHED Cohort			
	Period 1: 2017-2019		Period 2: 2020-2023		Period 1: 2017-2019		Period 2: 2020-2023	
	CSEEREG N = 373	DAMMED N = 825	CSEEREG N = 570	DAMMED N = 1,151	CSEEREG N = 337	DAMMED N = 337	CSEEREG N = 479	DAMMED N = 479
Type of 1L therapy								
Anti-PD1 monotherapy	174 (46.6%)	400 (48.5%)	352 (61.8%)	510 (44.2%)	161 (47.7%)	155 (46%)	293 (61.2%)	219 (45.7%)
Anti-PD1/Anti-CTLA4	2 (0.5%)	209 (25.3%)	16 (2.8%)	326 (28.3%)	2 (0.6%)	110 (32.6%)	15 (3.1%)	164 (34.2%)
Anti-CTLA4	-	13 (1.6%)	-	32 (2.8%)	-	1 (0.3%)	-	2 (0.4%)
BRAF/MEKi	128 (34.3%)	152 (18.4%)	182 (31.9%)	212 (18.4%)	114 (33.8%)	54 (16%)	153 (31.9%)	56 (11.7%)
BRAFi monotherapy	44 (11.8%)	3 (0.4%)	2 (0.3%)	1 (0.09%)	40 (11.9%)	1 (0.3)	2 (0.4%)	-
MEKi monotherapy	1 (0.3%)	-	-	-	1 (0.3%)	-	-	-
Chemotherapy	22 (6%)	3 (0.4%)	14 (2.5%)	2 (0.17%)	17 (5%)	3 (0.9%)	12 (2.5%)	-
Other	2 (0.5%)	45 (5.4%)	4 (0.5%)	68 (5.9%)	2 (0.6%)	13 (3.9%)	4 (0.8%)	38 (7.9%)

N, number of patients; CSEEREG, Central and South Eastern European Registry; DAMMED, Danish Metastatic Melanoma Database; 1L, first line.

- Significant differences in treatment patterns were observed between registries.
- **DAMMED** showed a higher proportion of patients initiating 1L treatment with anti-PD1/CTLA4 combination in both time periods.
- **CSEEREG** had a higher proportion of patients receiving BRAFi monotherapy or chemotherapy in Period 1, and more patients treated with BRAF/MEKi in both periods, compared with DAMMED.
- After matching, differences in treatment patterns persisted.

SUMMARY AND CONCLUSION

- To our knowledge, this is the first study showing significant differences in treatment patterns and OS between patients with metastatic melanoma in selected European countries.
- After matching for significant prognostic factors clear OS differences were observed, indicating that restricted access to therapies negatively affects survival outcomes.

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European Melanoma Registry (EUMelaReg; www.eumelareg.org): This registry is a multi-center database run by a cross-national consortium of academic groups in Europe collecting and evaluating real-world melanoma cases with non-resectable stage III or metastatic stage IV melanoma. Data has been captured since 2018 entered voluntarily into the system by participating centers.