Decision Making on Adjuvant Anti-PD1 Treatment in Stage IIB/IIC Melanoma in Europe -DECIDE-II-

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BACKGROUND

- Stage IIB/IIC melanoma bears a significant risk of recurrence despite complete surgical resection. Adjuvant anti-PD1 treatment has been shown to improve recurrence-free survival in clinical trials leading to approval for routine use.
- Real-world data to understand treatment acceptance and patient characteristics are lacking.

OBJECTIVES

- Primary objectives were to describe adjuvant anti-PD1 treatment rates, factors influencing physician or tumor board recommendations, and patient motivations for declining recommended/offered adjuvant therapy.
- Secondary objectives were to examine patient-related (e.g., age, comorbidities, ECOG), socioeconomic (e.g., financial burden, travel effort), and disease-specific factors (e.g., tumor risk profile, recurrence risk) associated with treatment recommendations and decisions.

METHODS

- **Study population:** This multinational, prospective, observational, registry-based study included 502 patients in Europe with completely resected stage IIB/IIC cutaneous melanoma in routine clinical practice.
- Patients were classified into **three cohorts** according to treatment decision: **A)** accepted, **B)** declined, or **C)** were not recommended adjuvant anti-PD1 therapy (**Figure 1**).
- Patient demographics and data influencing treatment decisions were assessed using the EQ-5D-5L, SDM-Q-9, DECLINE and NOTOFFER questionnaires at baseline prior to treatment.

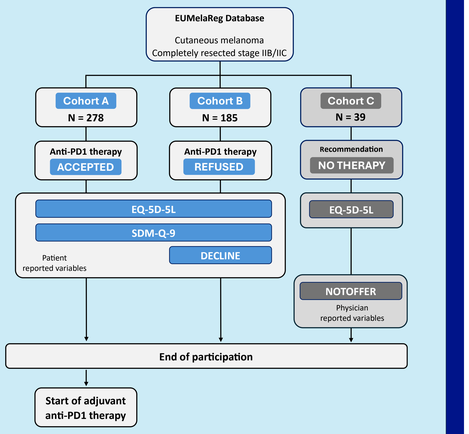


Figure 1: Graphical illustration of the study design using patient from the EUMelaReg database. N, number of patients; DECLINE, questionnaire was completed by patients in cohort B who decline therapy; NOTOFFER, questionnaire was completed by physicians who did not offer therapy to patients in Cohort C.

RESULTS

- 502 patients were included in this analysis, of whom 463 (92.2%) patients were offered adjuvant anti-PD1 therapy.
- The overall treatment rate was 55.4%, of the total study population. Among 463 patients offered therapy, acceptance rate was equal in stage IIB (59.4%; n=167) and stage IIC (61.0%; n=111).
- 39 (7.8%) patients included in cohort C were not offered adjuvant treatment by physicians.

Table 1: Treatment rate for adjuvant anti-PD1 therapy

	Stage IIB N = 303	Stage IIC N = 199
Patients offered treatment (A, B)	n = 281 (92.8%)	n = 182 (91.5%)
Treatment accepted (cohort A)	167 (59.4%)	111 (61.0%)
Treatment declined (cohort B)	114 (40.6%)	71 (39.0%)
Treatment not offered (C)	n = 22 (7.3%)	n = 17 (8.5%)
Treatment rate overall	55.4% (n = 278)	

- Treated patients were younger (median age: 66 vs. 79 years), had a higher percentage of ECOG performance status (PS) of 0 (84.2% vs. 65.9%) and exhibited fewer comorbidities (CCI: 2.5 vs. 3.8).
- Patients with stage IIB had lower rates of ECOG PS >1 (20.8% vs. 29.7%), comorbidities (66.3% vs. 76.9%), and comedications (46.2% vs. 57.3%) than those with stage IIC.

Table 2: Demographics and clinical characteristics stratified by cohort and stage

	Cohort A Accepted N = 278	Cohort B Refused N = 185	Cohort C Not offered N = 39	Stage IIB N = 303	Stage IIC N= 199
Age (years)					
Mean (SD)	65.1 (13.5)	76.6 (11.7)	80.1 (10.0)	69.7 (14.1)	71.6 (13.8)
Median (Min-Max)	66.0 (26-89)	79.0 (32-95)	83.0 (56-95)	72.0 (26-95)	74.0 (31-95)
Gender					
Male	166 (59.7%)	112 (60.5%)	28 (71.8%)	189 (62.4%)	117 (58.8%)
Female	112 (40.3%)	73 (39.5%)	11 (28.2%)	114 (37.6%)	82 (41.2%)
ECOG					
0	234 (84.2%)	122 (65.9%)	24 (61.5%)	240 (79.2%)	140 (70.3%)
1	38 (13.7%)	42 (22.7%)	9 (23.1%)	51 (16.8%)	38 (19.1%)
≥2	6 (2.1%)	21 (11.4%)	6 (15.4%)	12 (4.0%)	21 (10.6%)
BRAF mutation					
Wild type	84 (30.2%)	41 (22.2%)	8 (20.5%)	74 (24.4%)	59 (29.6%)
Positive	41 (14.7%)	17 (9.2%)	3 (7.7%)	30 (9.9%)	31 (15.6%)
Not tested	153 (55.1%)	127 (68.6%)	28 (71.8%)	199 (65.7%)	109 (54.8%)
AJCC stage					
Stage IIB	167 (60.1%)	114 (61.6%)	22 (56.4%)	303 (100%)	-
Stage IIC	111 (39.9%)	71 (38.4%)	17 (43.6%)	-	199 (100%)
Comorbidities					
Yes	178 (64.0%)	140 (75.7%)	36 (92.3%)	201 (66.3%)	153 (76.9%)
No	100 (36.0%)	45 (24.3%)	3 (7.7%)	102 (33.7%)	46 (23.1%)
CCS					
Mean (SD)	2.5 (1.6)	3.8 (1.7)	4.6 (1.8)	3.0 (1.8)	3.3 (1.9)
Median (Min-Max)	3.0 (0.0-9.0)	4.0 (0.0-9.0)	5.0 (1.0-10.0)	3.0 (0.0-10.0)	3.0 (0.0-9.0)
Comedication					
Yes	139 (50.0%)	96 (51.9%)	20 (51.3%)	141 (46.5%)	114 (57.3%)
No	139 (50.0%)	88 (47.6%)	19 (48.7%)	162 (53.5%)	84 (42.2%)
Unknown	-	1 (0.5%)	-	-	1 (0.5%)
Marital status					
Married	166 (59.7%)	103 (55.7%)	24 (61.5%)	176 (58.1%)	117 (58.8%)
In Partnership	11 (3.9%)	3 (1.6%)	-	10 (3.3%)	4 (2.0%)
Divorced	16 (5.8%)	4 (2.1%)	-	10 (3.3%)	10 (5.0%)
Widowed	15 (5.4%)	29 (15.7%)	11 (28.2%)	31 (10.2%)	24 (12.1%)
Single	33 (11.9%)	14 (7.6%)	-	30 (9.9%)	17 (8.5%)
Unknown	37 (13.3%)	32 (17.3%)	4 (10.3%)	46 (15.2%)	27 (13.6%)
Profession					
Active	133 (47.8%)	31 (16.8%)	5 (12.8%)	110 (36.3%)	59 (29.6%)
Worker	35 (12.6%)	4 (2.2%)	1 (2.6%)	25 (8.3%)	15 (7.5%)
Employee	75 (27.0%)	19 (10.3%)	1 (2.6%)	68 (22.4%)	27 (13.6%)
Self-Employed	14 (5.0%)	5 (2.7%)	3 (7.6%)	13 (4.3%)	9 (4.5%)
Unemployed	9 (3.2%)	3 (1.6%)	-	4 (1.3%)	8 (4.0%)
Former	145 (52.2%)	154 (83.2%)	34 (87.2%)	193 (63.7%)	140 (70.4%)
Retiree	117 (42.1%)	133 (71.9%)	25 (64.1%)	151 (49.8%)	124 (62.3%)
Pensioner	28 (10.1%)	21 (11.3%)	9 (23.1%)	42 (13.9%)	16 (8.1%)
Educational level					
Low education	167 (60.1%)	134 (72.4%)	28 (71.8%)	187 (61.7%)	142 (71.4%)
Mid education	45 (16.2%)	23 (12.4%)	10 (25.6%)	52 (17.2%)	26 (13.1%)
High education	66 (23.7%)	28 (15.2%)	1 (2.6%)	64 (21.1%)	31 (15.5%)

N, number of patients; SD, standard deviation; Min, minimum; Max, maximum; ECOG, Eastern Cooperative Oncology Group; AJCC, American Joint Committee on Cancer staging version 8; CCS, Charlson comorbidity score.

- The **SDM-Q-9** (9-item Shared Decision Making-Questionaire) was used to explore the association between shared decision quality and the acceptance of adjuvant therapy.
- Major differences were observed in patients' education level between cohort A and B. Besides age, education level was also associated with treatment decision, with higher acceptance rate among patients with higher educational level.
- There was also a significant link to the shared decision-making process (**Figure 3**).

Figure 2: SDM-Q-9 questionnaire results stratified by education level of Cohort A (therapy accepted) and B (therapy refused). Low: primary/lower education; Mid: upper education; high: bachelor/master/doctoral/equivalent education. Data was being collected only once after the diagnosis during clinical routine visits. The SDM-Q-9 evaluates the shared decision-making process from the patient's perspective, focusing on their perceived involvement in treatment decisions.

- **SDM-Q-9 scores** were lower in patients who declined adjuvant anti-PD1 therapy, suggesting poorer shared decision process.

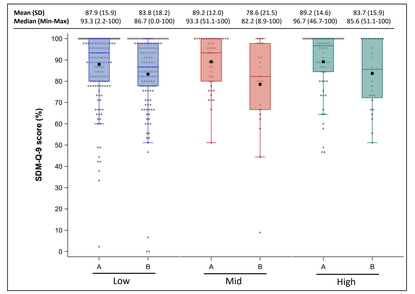
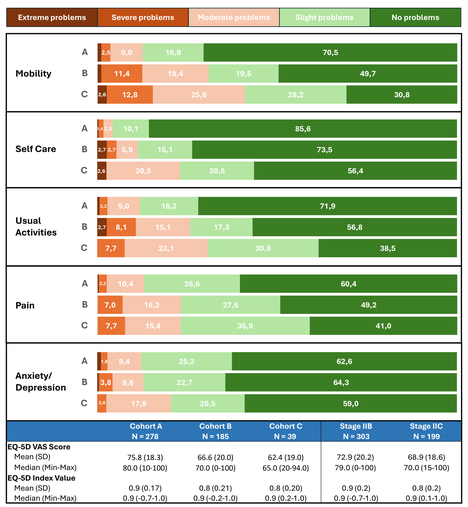


Figure 3: Box plot on the SDM-Q-9 across the education level of Cohort A and B. Low: primary/lower education; Mid: upper education; high: bachelor/master/doctoral/equivalent education. SD, standard deviation; Min, minimum; Max, maximum.

- The **EQ-5D-5L** (Euro-QoL 5-Dimension 5-Level) questionnaire assesses patients' health-related quality of life (QoL) which is collected once after the diagnosis at baseline prior to treatment from all study participants during clinical routine visits.
- Median EQ-5D VAS scores differed significantly across the three cohorts (A > B > C) and were higher (more favorable) in stage IIB patients (79 vs 70) compared to those with stage IIC.



	Cohort A N = 278	Cohort B N = 185	Cohort C N = 39	Stage IIB N = 303	Stage IIC N = 199
EQ-5D VAS Score					
Mean (SD)	75.8 (18.3)	66.6 (20.0)	62.4 (19.0)	72.9 (20.2)	68.9 (18.6)
Median (Min-Max)	80.0 (10-100)	70.0 (0-100)	65.0 (20-94.0)	79.0 (0-100)	70.0 (15-100)
EQ-5D Index Value					
Mean (SD)	0.9 (0.17)	0.8 (0.21)	0.8 (0.20)	0.9 (0.2)	0.8 (0.2)
Median (Min-Max)	0.9 (-0.7-1.0)	0.9 (-0.2-1.0)	0.9 (0.2-1.0)	0.9 (-0.7-1.0)	0.9 (0.1-1.0)

Figure 4: EQ-5D-5L questionnaire results completed by all cohorts. A: patients accepted therapy, B: patients refused therapy; C: no therapy offered to patients by physicians; VAS: visual analogue scale; SD, standard deviation; Min, minimum; Max, maximum.

- Patients in cohort B completed the **DECLINE** questionnaire, which documents the reason for declining adjuvant anti-PD1 therapy.
- The most important reasons for refusing therapy are concerns about possible side effects and the age of the patients.

Table 3: Reasons for declining adjuvant therapy by patients in Cohort B

Reasons for declining adjuvant therapy by Cohort B	N = 185
Most important reason	
I do not want to suffer any possible side effects	65 (35.1%)
I feel too old for a therapy	41 (22.2%)
I am suffering from other diseases	20 (10.8%)
I believe that further treatment is not necessary after a successful operation	19 (10.3%)
I think that my quality of life could be affected	17 (9.2%)
I believe that the risk of the disease coming back is very low	11 (5.9%)
A therapy is too time-consuming for me	8 (4.3%)
A person I trust has advised me to do this	3 (1.6%)
Other reasons (multiple answers were possible)	
I think that my quality of life could be affected	64 (34.6%)
I do not want to suffer any possible side effects	61 (33.0%)
I believe that further treatment is not necessary after a successful operation	31 (16.8%)
I feel too old for a therapy	29 (15.7%)
I believe that the risk of the disease coming back is very low	27 (14.6%)
A therapy is too time-consuming for me	26 (14.1%)
A person I trust has advised me to do this	22 (11.9%)
I am suffering from other diseases	22 (11.9%)
I would like to avoid possible costs that would be associated with the therapy	5 (2.7%)
Not answered	16 (8.6%)

- Patients in cohort C (n=39, 7.8%) had a median age of 83 years, an ECOG PS >1 in 38.5% of cases, and a median EQ-5D VAS score of 65.0.
- Comorbidities of the patients, advanced age, reservation about overall survival and concerns about side effects were key factors cited by physicians for not recommending adjuvant treatment to these patients.

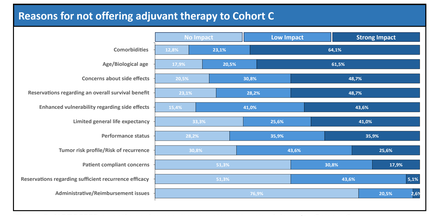


Figure 5: NOTOFFER questionnaire results completed by physicians for Cohort C

SUMMARY AND CONCLUSION

- Acceptance of adjuvant anti-PD1 in stage IIB/C melanoma is limited, driven primarily by higher age and comorbidities.
- Beside age as the main determinant, quality of the shared decision making seems crucial.
- These findings highlight a gap between clinical trial populations and real-world patients, underscoring the need for tailored benefit-risk communication in older patients.

ACKNOWLEDGEMENTS AND FUNDING

***DECIDE II Study Group: Bulgaria:** Aleksandar Tsvetanov Gerasimov (Sofia); Anita Hvarchilkova (Veliko Tarnovo); Teodora Sotirova Karanikolova (Sofia); Ivan Kazmukov (Burgas); Tsvetelina Kondzhova (Vratsa); Antoaneta Marcheva (Sofia); Aynuraa Syuleymanova Changalova (Panagyurishte). **Germany:** Nina Devereux (Hamburg); Edgar Dippel (Ludwigshafen); Thilo Gambichler (Unna); Christoffer Gebhardt (Hamburg); Jessica Hassel (Heidelberg); Markus Heppt (Erlangen); Silke Hofmann (Wuppertal); Florian Löhr (Oldenburg); Friedegund Meier (Dresden); Peter Mohr (Buxtehude); Florian Jothe (Duedilinburg); Susen Rode (Rostock); Michael Sachse (Bremerhaven); Jan Christoph Simon (Leipzig); Anca Sindrilaru (Ulm); Max Schlaak (Berlin); Gaston Schley (Schwerin); Eggert Stockfleth (Bochum); Silke Thies (Schwedt); Thomas Tüting (Magdeburg); Selma Ugurel (Bielefeld); Jochen Utikal (Mannheim); Amir Yazdi (Achen). **Spain:** Elisabet Bujons Buscarons (Girona); Pablo Cerezuela-Fuentes (Ciudad de Murcia); Silvia Sequero López (Granada); Berta Hernandez Marin (Madrid); Juan Francisco Rodriguez (Madrid); María Quindós Varela (A Coruña). **USA:** Cassidy Kenny (NJ).

COI of the presenting author: M.W. reports honoraria from BMS, MSD, Novartis, Takeda and Kyowa Kirin, advisory roles for Roche, Takeda, BMS, and Novartis, Takeda, grants or funds from BMS, Millennium, Roche, Novartis, Takeda, and conference travel support from Amgen, MSD, BMS, Pierre Fabre, Novartis, and Beyersdorf.

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Funding: The study was supported by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

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.