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

Scan Me

Magdalena Walecki[1], Imke von Wasielewski[2], José Balsalobre Yago[3], Silvia Sequero López[4], Pablo Cerezuela-Fuentes[5], Shan Jiang[6], Ralf Gutzmer[7], Eggert Stockfleth[8], Stephan Grabbe[9], Dirk Schadendorf[10], Michael Weichenthal[11], DECIDE II Study Group*

[1]EUMelaReg Consortium, Berlin, Germany, [2]Skin Cancer Center Hannover, Department of Dermatology and Allergy, Hannover Medical School, Hannover, Germany, [3]Department of Medical Oncology, Santa Lucía University Hospital in Cartagena, Región de Murcia, Spain, [4]Hospital Universitario San Cecilio, [5]Servicio de Oncología Médica. Instituto Murciano de Investigación Biosanitaria (IMIB). Hospital Clínico Universitario "Virgen de la Arrixaca" Ciudad de Murcia. Spain, [6]Merck & Co., Inc., 126 East Lincoln Ave., Rahway, NJ 07065, USA, [7]Department of Dermatology, Johannes Wesling Medical Center, Ruhr University Bochum, Campus Minden, Germany, [8]Skin Cancer Center, Department of Dermatology, Venereology and Allergology, Ruhr-University Bochum, Bochum, Germany, [9]Department of Dermatology, University of Mainz Medical Center, Mainz, Germany, [10]Department of Dermatology, Venereology and Allergology, University Hospital Essen and German Cancer Consortium (DKTK) Partner Site Essen, and National Center for Tumor Diseases (NCT-West) Campus Essen, Essen, Germany, [11]Skin Cancer Center Kiel, University Hospital Schleswig-Holstein, Kiel, Germany.

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 is lacking.

OBJECTIVES

- Primary objectives are 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 are 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

- This multi-national prospective observational registry-based study recruits cutaneous melanoma patientswith stage IIB or IIC from the **European Melanoma Registry (EUMelaReg)** who have undergone complete resection and are theoretical candidates for an anti-PD1 adjuvant treatment.
- Data collection started in JUN 2024. The study plans to enroll 500 patients from participating centers in clinical routine setting in the following cohorts: A) those who accepted, B) those who refused, and C) those who were not recommended adjuvant anti-PD1 therapy (**Figure 1**).
- Study specific data are collected, including patient demographics, medical history, tumor characteristics, and demographic factors related to treatment decisions including the following questionnaires:
  - The **SDM-Q-9** (9-item Shared Decision Making) questionnaire measures the decision-making process from the patient's perspective, specifically assessing how involved they feel in treatment decisions. In this study, its use will help explore the relationship between patients' acceptance or refusal of adjuvant therapy and the education provided by study personnel (**Figure 3**).
  - Patients who decline adjuvant treatment are asked to complete the **DECLINE** questionnaire, which records their reasons for refusing therapy (**Table 3**).
  - In case a therapy is not offered to the patient, the physician must complete the **NOTOFFER** questionnaire. The aim is to identify the reasons why adjuvant therapy is refused or not offered, despite the potential benefit for the patient (**Figure 4**).
  - The **EQ-5D-5L** (Euro-QoL 5-Dimension 5-Level) questionnaire assesses patients' health-related quality of life (QoL) which is collected once from all study participants (**Figure 2**).

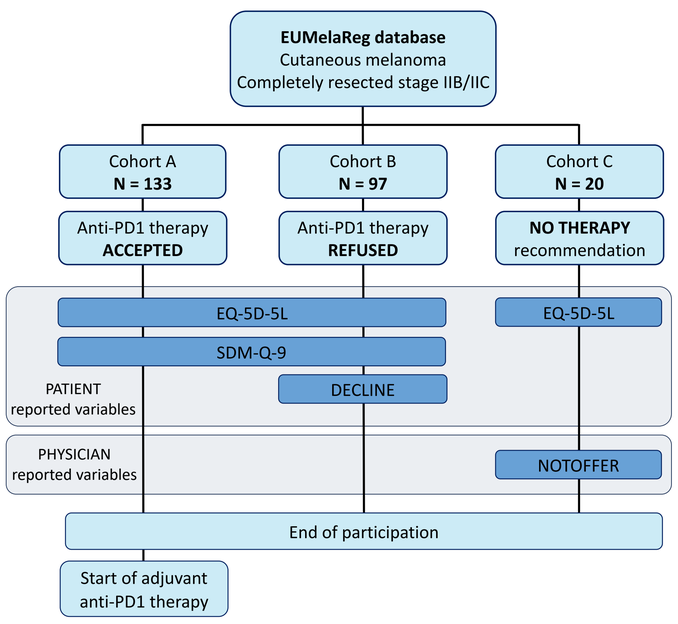

Figure 1: Graphical illustration of the study design using patient from the EUMelaReg database. N, number of patients; DECLINE, questionnaire is completed by patients in cohort B who decline therapy; NOTOFFER, questionnaire is completed by physicians who do not offer therapy to patients in cohort C.

CONCLUSIONS

- DECIDE-II provides preliminary results, showing that adjuvant anti-PD1 treatment acceptance in stage IIB/C tends to be lower due to patient's higher age and comorbidity rate than in the registrational trials.
- Likewise, the baseline real-world QoL was different from the patients enrolled in clinical trials due to many reasons including higher age at baseline which may also play a role in treatment decision.

RESULTS

- 250 patients with stage IIB (60.4%) and IIC (39.6%) were included in this interim analysis. The overall treatment rate was 57.8%: of the 230 patients (92%) offered adjuvant anti-PD1 therapy, over half accepted, with higher proportion in stage IIB (54.3%) compared to stage IIC (51.5%) (**Table 1**).
- Treated patients were younger (median age: 64y vs. 78y), had a higher percentage of ECOG performance status (PS) of 0 (86.5% vs. 68.0%) and exhibited fewer comorbidities (CCI: 2.3 vs. 3.7) (**Table 2**).
- Patients in stage IIB were slightly younger (median age: 72y vs. 73y), had higher proportion of ECOG PS 0 (79.5% vs 70.7%) compared to those with stage IIC (**Table 2**).

	Stage IIB N=151	Stage IIC N=99
Treatment offered to cohort A, B	92% (n=230)	
Treatment accepted by cohort A	54.3%	51.5%
Treatment declined by cohort B	39.7%	37.4%
Treatment not offered to cohort C	6.0%	11.1%
Treatment rate	54.3%	51.5%

Table 1: Treatment rate for adjuvant anti-PD1 therapy stratified by stage IIB/IIC.

- Median EQ-5D VAS scores were significantly decreasing over the three cohorts (A > B > C) and were higher (more favorable) in stage IIB patients (78 vs 70) compared to those with stage IIC.

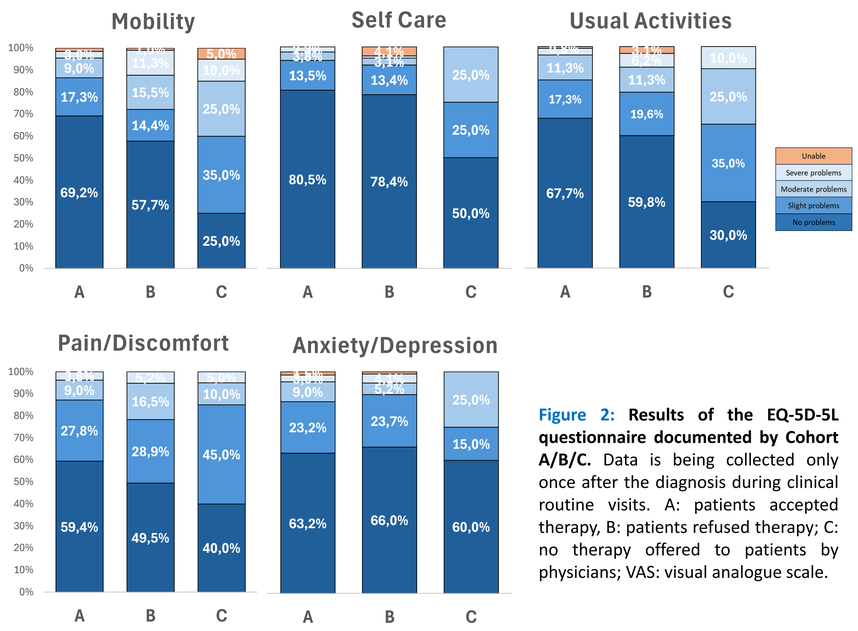

Figure 2: Results of the EQ-5D-5L questionnaire documented by Cohort A/B/C. Data is being collected only once after the diagnosis during clinical routine visits. A: patients accepted therapy, B: patients refused therapy; C: no therapy offered to patients by physicians; VAS: visual analogue scale.

	Cohort A N=133	Cohort B N=97	Cohort C N=20	Stage IIB N=151	Stage IIC N=99
EQ-5D VAS Score					
Mean (STD)	75.1 (18.4)	69.4 (18.1)	62.1 (18.0)	73.2 (19.4)	69.9 (17.2)
Median (Min-Max)	80.0 (20-100)	70.0 (15-100)	65.5 (24-90)	78.0 (15-100)	70.0 (24-100)
EQ-5D Index Value					
Mean (STD)	0.9 (0.2)	0.8 (0.2)	0.8 (0.2)	0.9 (0.2)	0.8 (0.2)
Median (Min-Max)	0.9 (0.0-1.0)	0.9 (-0.2-1.0)	0.9 (0.2-1.0)	0.9 (-0.2-1.0)	0.9 (0.2-1.0)

Table 2: Demographics and clinical characteristics stratified by cohort A/B/C and by stage IIB/IIC.

	Cohort A therapy accepted N=133	Cohort B therapy refused N=97	Cohort C no therapy offered N=20	Stage IIB N=151	Stage IIC N=99
Age (years) at index date					
Mean (STD)	64.4 (14.0)	75.9 (12.2)	79.7 (11.6)	69.5 (14.9)	71.0 (13.8)
Median (Min-Max)	64.0 (26.0-89.0)	78.0 (32.0-95.0)	84.0 (56.0-95.0)	72.0 (26.0-95.0)	73.0 (34.0-95.0)
Gender					
Male	75 (56.4%)	58 (59.8%)	13 (65.0%)	91 (60.3%)	55 (55.6%)
Female	58 (43.6%)	39 (40.2%)	7 (35.0%)	60 (39.7%)	44 (44.4%)
Marital status					
Married	83 (62.4%)	53 (54.6%)	12 (60.0%)	87 (57.6%)	61 (61.6%)
Single	17 (12.8%)	9 (9.3%)	-	18 (11.9%)	8 (8.1%)
Widowed	10 (7.5%)	15 (15.5%)	6 (30.0%)	16 (10.6%)	15 (15.2%)
Divorced	6 (4.5%)	1 (1.0%)	-	3 (2.0%)	4 (4.0%)
In partnership	3 (2.3%)	1 (1.0%)	-	3 (2.0%)	1 (1.0%)
Profession					
Active	67(50.4%)	19 (19.6%)	3 (15.0%)	57 (37.7%)	32 (32.3%)
Worker	9 (6.8%)	3 (3.1%)	-	8 (5.3%)	4 (4.0%)
Employee	44 (33.1%)	12 (12.4%)	-	40 (26.5%)	16 (16.2%)
Self-Employed	10 (7.5%)	3 (3.1%)	3 (15.0%)	7 (4.6%)	9 (9.1%)
Unemployed	4 (3.0%)	1 (1.0%)	-	2 (1.3%)	3 (3.0%)
Former	66 (49.6%)	78 (80.4%)	17 (85.0%)	94 (62.3%)	67 (67.7%)
Retiree	57 (42.9%)	65 (67.0%)	16 (80.0%)	77 (51.0%)	61 (61.6%)
Pensioner	9 (6.8%)	13 (13.4%)	1 (5.0%)	17 (11.3%)	6 (6.1%)
Educational level					
Primary edu.	23 (17.3%)	32 (33.0%)	10 (50.0%)	37 (24.5%)	28 (28.3%)
Lower secondary edu.	61 (45.9%)	39 (40.2%)	6 (30.0%)	62 (41.1%)	44 (44.4%)
Upper secondary edu.	18 (13.5%)	11 (11.3%)	3 (15.0%)	22 (14.6%)	10 (10.1%)
Bachelor's or equivalent	11 (8.3%)	7 (7.2%)	1 (5.0%)	14 (9.3%)	5 (5.1%)
Master's or equivalent	17 (12.8%)	8 (8.2%)	-	14 (9.3%)	11 (11.1%)
Doctoral or equivalent	3 (2.3%)	-	-	2 (%)	1 (1.0%)
Melanoma subtype					
SSM	32 (24.1%)	20 (20.6%)	2 (10.0%)	30 (19.9%)	24 (24.2%)
NMM	61 (45.9%)	53 (54.6%)	12 (60.0%)	75 (49.7%)	51 (51.5%)
LMM	4 (3.0%)	1 (1.0%)	-	5 (3.3%)	-
ALM	6 (4.5%)	3 (3.1%)	3 (15.0%)	5 (3.3%)	7 (7.1%)
UCM	6 (4.5%)	3 (3.1%)	1 (5.0%)	6 (4.0%)	4 (4.0%)
Other/unspecified	24 (18.1%)	17 (17.5%)	2 (19%)	30 (20.9%)	13 (13.2%)
ECOG					
0	115 (86.5%)	66 (68.0%)	9 (45.0%)	120 (79.5%)	70 (70.7%)
1	15 (11.3%)	22 (22.7%)	7 (35.0%)	24 (15.9%)	20 (20.2%)
≥2	3 (2.3%)	8 (8.2%)	4 (20.0%)	7 (4.6%)	8 (8.1%)
BRAF mutation					
Wild type	42 (31.6%)	17 (17.5%)	3 (15.0%)	32 (21.2%)	30 (30.3%)
Positive	18 (13.5%)	10 (10.3%)	2 (10.0%)	12 (7.9%)	18 (18.2%)
Unknown/Not tested	73 (54.9%)	70 (72.1%)	15 (75.0%)	107 (70.9%)	51 (51.5%)
Stage					
Stage IIB	82 (61.7%)	60 (61.9%)	9 (45.0%)	151 (100%)	-
Stage IIC	51 (38.3%)	37 (38.1%)	11 (55.0%)	-	99 (100%)
Comorbidities					
Yes	79 (59.4%)	66 (68.0%)	17 (85.0%)	95 (62.9%)	67 (67.7%)
No	54 (40.6%)	31 (32.0%)	3 (15.0%)	56 (37.1%)	32 (32.3%)
Charlson comorbidity score					
Mean (STD)	2.3 (1.5)	3.7 (1.7)	4.2 (1.8)	2.88 (1.71)	3.19 (1.89)
Median (Min-Max)	2.0 (0.0-7.0)	4.0 (0.0-8.0)	4.0 (1.0-7.0)	3.00 (0.0-7.0)	3.00 (0.0-8.0)
Comedications					
Yes	67 (50.4%)	47 (48.5%)	9 (45.0%)	67 (44.4%)	56 (56.6%)
No	66 (49.6%)	49 (50.5%)	11 (55.0%)	84 (55.6%)	42 (42.4%)

N, number of patients; STD, standard deviation; ECOG, Eastern Cooperative Oncology Group; edu, education; SSM, superficial spreading melanoma; NMM, nodular malignant melanoma, LMM, lentigo malignant melanoma; ALM, acral lentiginous melanoma; UCM, unclassifiable melanoma.

- The SDM-Q-9 scores were similar between cohort A and B (86.8 vs 81.8), indicating no meaningful difference in perceived shared decision-making.

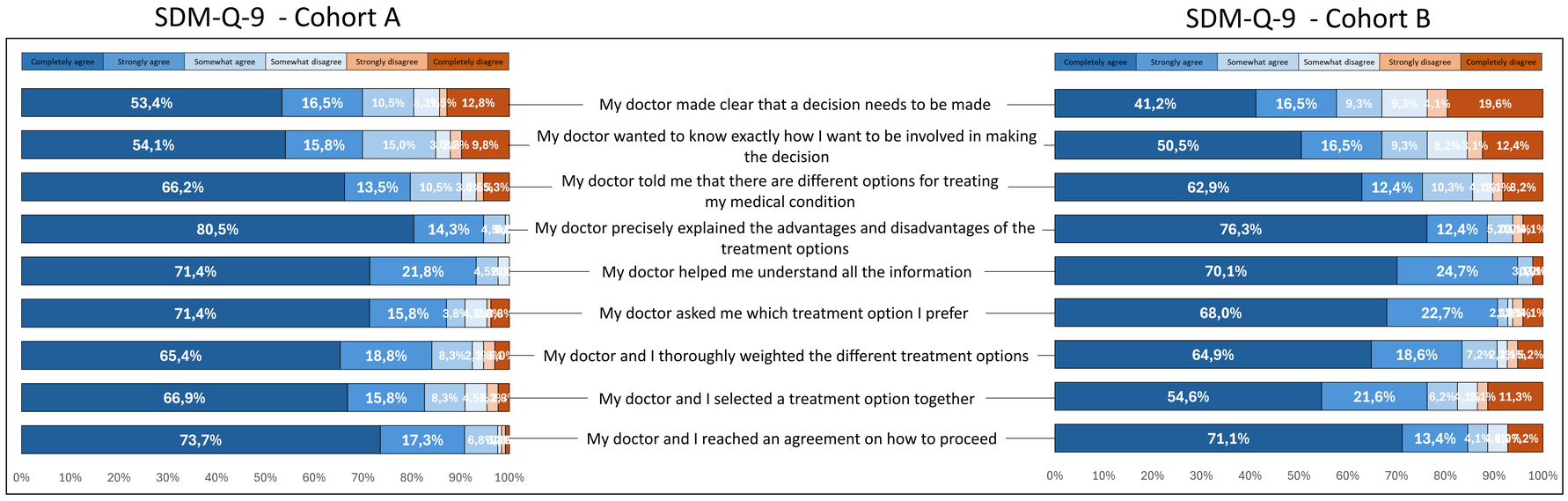

Figure 3: Results of the SDM-Q-9 questionnaire documented by A) cohort A (therapy accepted) and B) cohort B (therapy refused). Data is being collected only once after the diagnosis during clinical routine visits.

- Patients in cohort B are asked to complete 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.

Reasons for declining adjuvant therapy by Cohort B	N=97
Most important reason	
I do not want to suffer any possible side effects	34 (35.1%)
I feel too old for a therapy	23 (23.7%)
I am suffering from other diseases	11 (11.3%)
I believe that further treatment is not necessary after a successful operation	11 (11.3%)
I think that my quality of life could be affected	9 (9.3%)
I believe that the risk of the disease coming back is very low	5 (5.2%)
A therapy is too time-consuming for me	1 (1.0%)
A person I trust has advised me to do this	1 (1.0%)
Other reasons (multiple answers possible)	
I think that my quality of life could be affected	37 (38.1%)
I do not want to suffer any possible side effects	35 (36.1%)
I believe that further treatment is not necessary after a successful operation	18 (18.6%)
I believe that the risk of the disease coming back is very low	17 (17.5%)
A therapy is too time-consuming for me	17 (17.5%)
I feel too old for a therapy	15 (15.5%)
A person I trust has advised me to do this	14 (14.4%)
I am suffering from other diseases	12 (17.9%)
I would like to avoid possible costs that would be associated with the therapy	3 (3.1%)
Not answered	6 (6.2%)

Table 3: Reasons for declining adjuvant therapy by the patients in cohort B are documented by completing the DECLINE questionnaire.

- Patients in cohort C (n=20, 8.0%) had a median age of 84y, an ECOG PS >1 in 55.0% of cases, and a median EQ-5D VAS score of 65.5 (**Table 2, Figure 2**).
- Advanced age, concerns about side effects and comorbidities of the patients were key factors cited by physicians for not recommending adjuvant anti-PD1 treatment to cohort C.

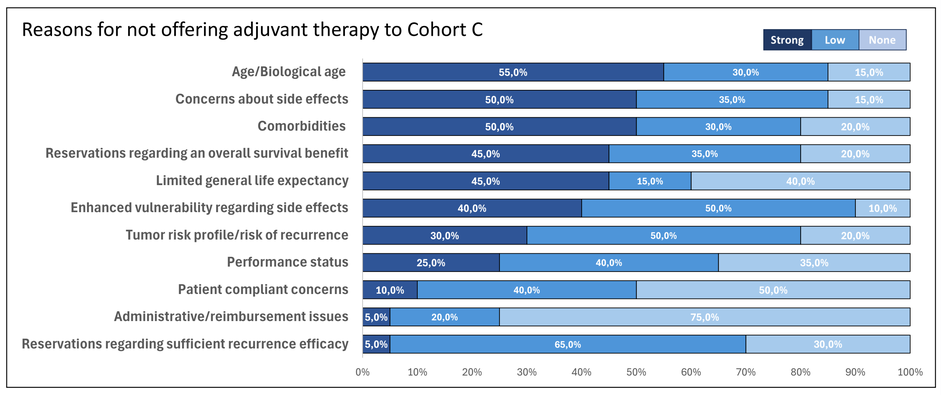

Figure 4: Results of the NOTOFFER questionnaire completed by the physicians for cohort C (no therapy offered).

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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.