

37-P: First-line BRAF/MEK-inhibitors versus anti-PD-1 monotherapy in BRAF^{V600}-mutant advanced melanoma patients: a propensity-matched survival analysis

van Breeschoten J., Wouters M.W.J.M., Hilarius D.L., Haanen J.B., Blank C.U., Aarts M.J.B., van den Berkmoortel F.W.P.J., de Groot J.W.B., Hospers G.A.P., Kapiteijn E., Piersma D., van Rijn R.S., Suijkerbuijk K.P.M., Blokk W.A.M., ten Tije A.J., van der Veldt A.A.M., Vreugdenhil G., Boers M.J., van den Eertwegh A.J.M.

Background

Anti-PD-1 antibodies and BRAF/MEK inhibitors are the two main groups of systemic therapy in the treatment of BRAF^{V600}-mutant advanced melanoma. Until now, data is inconclusive on which therapy to use as first-line treatment.

Objective

The aim of this study was to use propensity score matching to compare first-line anti-PD-1 monotherapy vs. BRAF/MEK inhibitors in advanced BRAF^{V600}-mutant melanoma patients.

Patients and methods

Design: Retrospective analysis of a prospective national cohort study
Inclusion:

- Patients diagnosed with unresectable stage IIIc or IV melanoma and registered in the Dutch Melanoma Treatment Registry (DMTR) with a known BRAF^{V600} mutation who received first-line systemic therapy of BRAF/MEK inhibitors or anti-PD-1 monotherapy

Exclusion: Mucosal and uveal melanoma

Primary outcome: Overall Survival (OS)

Analysis:

- Multivariable logistic regression to estimate propensity scores. Multivariable Cox proportional-hazards model to assess factors associated with OS. Patients were matched based on their propensity scores using the nearest neighbour and the optimal matching method.

Results

Cohort: 330 first-line BRAF/MEK inhibitors and 254 first-line anti-PD-1 antibodies (**Figure 1**)

Matched cohort: 155 BRAF/MEK inhibitors and 155 first-line anti-PD-1 antibodies (**Figure 2**)

Table 1. Comparison of baseline characteristics of patients receiving BRAF/MEK inhibitors or anti-PD-1 as a first-line treatment in the original sample and the matched sample

Baseline variable	Original sample			Nearest neighbour matched sample		
	BRAF/MEK (N = 330)	Anti-PD-1 (N = 254)	p-value	BRAF/MEK (N = 155)	Anti-PD-1 (N = 155)	SMD
Age, median (range)	59 (19-91)	62 (22-87)	0.177	62 (19-91)	62 (25-87)	0.027
Gender						
Male	178 (53.9)	145 (57.1)	0.500	81 (52.3)	81 (52.3)	<0.001
ECOG performance status						
0-1	254 (77.0)	232 (91.3)	<0.001	144 (92.9)	144 (92.9)	<0.001
≥2	76 (23.0)	22 (8.7)		11 (7.1)	11 (7.1)	
LDH						
Not determined/Normal	164 (49.7)	197 (77.6)	<0.001	108 (69.7)	108 (69.7)	<0.001
250-500 U/L	108 (32.7)	55 (21.7)		45 (29.0)	45 (29.0)	
>500 U/L	58 (17.6)	2 (0.8)		2 (1.3)	2 (1.3)	
Stage (7 th edition AJCC)						
Unresectable IIc	15 (4.5)	14 (5.5)	<0.001	10 (6.5)	10 (6.5)	<0.001
IV-M1a	13 (3.9)	29 (11.4)		13 (8.4)	13 (8.4)	
IV-M1b	13 (3.9)	40 (15.7)		12 (7.7)	12 (7.7)	
IV-M1c	289 (87.6)	171 (67.3)		120 (77.4)	120 (77.4)	
Brain metastases						
No	192 (58.2)	207 (81.5)	<0.001	120 (77.4)	120 (77.4)	<0.001
Yes, asymptomatic	42 (12.7)	24 (9.4)		15 (9.7)	15 (9.7)	
Yes, symptomatic	96 (29.1)	23 (9.1)		20 (12.9)	20 (12.9)	
Liver metastases						
Yes	112 (33.9)	54 (21.3)	<0.001	34 (21.9)	34 (21.9)	
Organ sites						
0-2	134 (40.6)	146 (57.5)	0.001	86 (55.5)	83 (53.5)	<0.001
≥3	196 (59.4)	108 (42.5)		69 (44.5)	72 (46.5)	
Immunomodulating agents						
≥1	88 (26.7)	30 (11.8)	<0.001	21 (13.5)	21 (13.5)	<0.001

Second-line therapy

Table 2. Subsequent therapies after receiving first-line BRAF/MEK inhibitors or anti-PD-1, therapies mutually exclude each other.

Second-line systemic treatment	BRAF/MEK inhibitors	Anti-PD-1	BRAF/MEK inhibitors	Anti-PD-1	p-value
Total (N = (%))	173 (52.4)	141 (52.5)	80 (51.6)	87 (56.1)	<0.001
Anti-PD-1	76 (43.9)	0 (0.0)	32 (40.0)	0 (0.0)	
BRAF/MEK inhibitors	1 (0.6)	105 (74.5)	0 (0.0)	64 (63.1)	
BRAF-inhibitors	0 (0.0)	14 (9.9)	0 (0.0)	9 (11.9)	
Ipilimumab	8 (4.6)	15 (10.6)	6 (7.5)	10 (11.9)	
Ipilimumab + nivolumab	80 (46.2)	1 (0.7)	39 (48.8)	1 (1.2)	
Other treatment	8 (4.6)	3 (2.1)	3 (3.8)	2 (3.6)	
Trial medication	0 (0.6)	3 (2.1)	0 (0.0)	2 (7.1)	

More information?

Contact to first author: J.vanbreeschoten@dica.nl

The first author, J. van Breeschoten, does not have any conflict of interest to declare

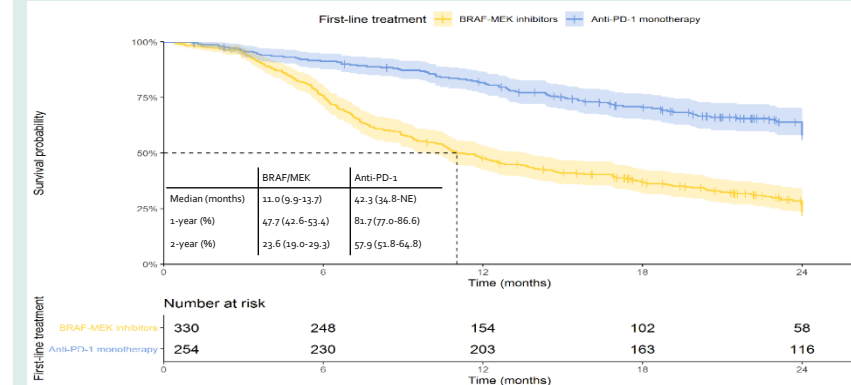


Figure 1. Kaplan-Meier estimates of OS of 1st line BRAF/MEK inhibitors vs. anti-PD-1. Confidence interval is displayed by the shadow of both curves.

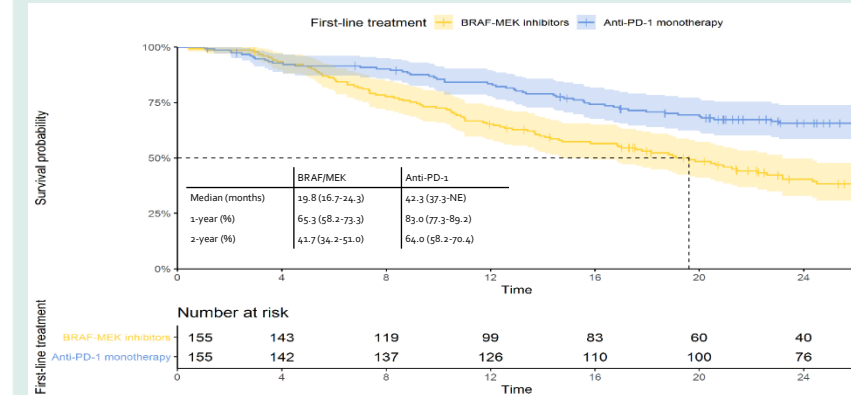


Figure 2. Kaplan-Meier estimates of OS for the nearest neighbour matched cohort. Confidence interval is displayed by the shadow of both curves.

Conclusion

Our data suggest that in the matched BRAF^{V600}-mutant advanced melanoma patients, anti-PD-1 monotherapy is the preferred first-line treatment in patients with relatively favourable patient and tumour characteristics.