SUPPLEMENTARY MATERIALS to the original article

Immune checkpoint inhibition therapy for advanced skin cancer in patients with concomitant hematologic malignancy: a retrospective multicenter DeCOG study of 84 patients

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TABLE S1. Comparison of characteristics in patients with concomitant hematologic malignancy

	MM N (%)	cSCC N (%)	MCC N (%)	P-value
Total	52 (100%)	15 (100%)	17 (100%)	
Gender				0.78
male	37 (71.2%)	12 (80%)	12 (70.6%)	
female	15 (28.8%)	3 (20%)	5 (29.4%)	
Age at diagnosis of skin cancer				0.28
Median (IQR)	72.5 years (59.0;76.0)	76.0 years (70.0;78.0)	70.0 years (63.0;78.5)	
Primary site of skin cancer				0.006
head and neck	13 (23.1%)	13 (86.7%)	5 (29.4%)	
trunk	21 (40.4%)	2 (13.3%)	4 (23.5%)	
extremities	12 (23.1%)	0 (0.0%)	7 (41.2%)	
mucosa	2 (3.8%)	0 (0.0%)	0 (0.0%)	
unknown primary	4 (7.6%)	0 (0.0%)	1 (5.9%)	
Hematologic malignancy				0.30
CLL	16 (30.2%)	8 (53.3%)	8 (47.1%)	
NHL	28 (53.8%)	5 (33.3%)	5 (29.4%)	
other	8 (15.4%)	2 (13.3%)	4 (23.5%)	
Age at diagnosis of hematologic malignancy				0.81
Median (IQR)	68.0 years (58.7;76.0)	66.0 years (59.2;73.0)	68.0 years (46.7;73.0)	

Characteristics of the total n=84 patient cohort. Percentages are given per column. MM, malignant melanoma; cSCC, cutaneous squamous cell carcinoma; MCC, Merkel cell carcinoma. Hematologic malignancies were categorized as chronic lymphocytic leukemia (CLL), other non-Hodgkin lymphoma (NHL), and other (comprising all other entities not belonging to the previous two categories). IQR, inter-quartile range.

Table S2: Treatment of hematologic malignancy

	CLL N (%)	NHL N (%)	Other N (%)	P-value
Total	32 (100%)	38 (100%)	14 (100%)	
Treatment of hematologic malignacy				0.008
no	23 (71.9%)	16 (42.1%)	4 (28.6%)	
yes	9 (28.1%)	22 (57.9%)	10 (71.4%)	
Number of therapy lines				0.16
0	23 (71.9%)	16 (42.1%)	4 (28.6%)	
1-3	9 (29.1%)	16 (42.1%)	10 (71.4%)	
4-7	0 (0.0%)	6 (15.7%)	0 (0.0%)	
Chemotherapy				0.047
no	23 (71.9%)	14 (36.8%)	7 (50.0%)	
yes	8 (25.0%)	21 (55.7%)	7 (50.0%)	
unknown	1 (3.1%)	3 (7.9%)	0 (0.0%)	
Corticosteroids				0.044
no	28 (87.5%)	21 (55.3%)	11 (78.6%)	
yes	3 (9.4%)	14 (36.8%)	3 (21.4%)	
unknown	1 (3.1%)	3 (7.9%)	0 (0.0%)	
Rituximab				<0.001
no	27 (84.4%)	18 (47.4%)	14 (100.0%)	
yes	4 (12.5%)	17 (44.7%)	0 (0.0%)	
unknown	1 (3.1%)	3 (7.9%)	0 (0.0%)	
Radiotherapy				0.095
no	30 (94.1%)	27 (71.1%)	13 (92.5%)	
yes	1 (3.1%)	8 (21.1%)	1 (7.1%)	
unknown	1 (3.1%)	3 (7.9%)	0 (0.0%)	
Cell transplantation				0.35
no	31 (94.1%)	32 (84.2%)	13 (92.5%)	
yes	0 (0.0%)	3 (7.9%)	1 (7.1%)	
unknown	1 (3.1%)	3 (7.9%)	0 (0.0%)	
Ongoing treatment at start of ICI therapy				0.19
no	31 (96.9%)	37 (97.4%)	12 (85.7%)	
yes	1 (3.1%)	1 (2.6%)	2 (14.3%)	

Presented are all disease-specific therapies given to the total of n=84 studied patients for hematologic malignancy until the start of ICI treatment for skin cancer. Hematologic malignancies were categorized as chronic lymphocytic leukemia (CLL), other non-Hodgkin lymphoma (NHL), and other (comprising all other entities not belonging to the previous two categories). Percentages are given per column. More than one treatment per patient is possible, therefore numbers do not necessarily add up to 100%. ICI, immune checkpoint inhibition.

TABLE S3: Characteristics of skin cancer disease at start of ICI therapy

	MM N (%)	cSCC N (%)	MCC N (%)	P-value
Total	52 (100%)	15 (100%)	17 (100%)	
Stage of disease and tumor load				0.08
locally advanced, measurable disease	3 (5.8%)	4 (26.7%)	0 (0.0%)	
locally advanced, disease-free after surgery	0 (0.0%)	0 (0.0%)	1 (5.9%)	
metastatic, measurable disease	41 (78.8%)	11 (73.3%)	16 (94.1%)	
metastatic, disease-free after surgery	8 (15.4%)	0 (0.0%)	0 (0.0%)	
Indication of treatment				0.18
adjuvant	8 (15.4%)	0 (0.0%)	1 (5.9%)	
inoperable disease	44 (84.6%)	15 (100%)	16 (94.1%)	
Sites of measurable disease				0.002
skin	3 (5.8%)	3 (20.0%)	0 (0.0%)	
LN	3 (5.8%)	5 (33.3%)	7 (41.2%)	
visceral	38 (73.1%)	7 (46.7%)	9 (52.9%)	
none	8 (15.4%)	0 (0.0%)	1 (5.9%)	
LDH (serum)				0.28
normal (≤ULN)	34 (65.4%)	8 (53.3%)	7 (41.2%)	
elevated (>ULN)	16 (30.8%)	6 (40.0%)	10 (58.8%)	
unknown	2 (3.8%)	1 (6.7%)	0 (0.0%)	
Systemic pre-treatment of skin cancer				0.29
yes	6 (11.5%)	6 (40.0%)	3 (17.6%)	
no	46 (88.5%)	9 (60.0%)	14 (82.4%)	
Pre-treatment: chemotherapy				0.39
yes	3 (5.7%)	3 (20.0%)	3 (17.6%)	
no	49 (94.2%)	12 (80.0%)	14 (82.4%)	
Pre-treatment: targeted/other				0.3
yes	3 (5.7%)	3 (20.0%)	0 (0.0%)	
no	49 (94.2%)	12 (80.0%)	17 (100.0%)	
Lines of systemic pre-treatment				0.32
1	5 (9.6%)	4 (26.7%)	1 (5.9%)	
≥2	1 (1.9%)	2 (13.3%)	2 (11.8%)	
Pre-treatment: radiotherapy				0.031
yes	9 (17.0%)	8 (53.3%)	8 (47.1%)	
no	43 (82.7%)	7 (46.7%)	9 (52.9%)	
Ongoing treatment of hematologic malignancy				0.24
yes	1 (1.9%)	1 (6.7%)	2 (11.8%)	
no	51 (98.1%)	14 (93.3%)	15 (88.2%)	

The presented characteristics of skin cancer disease refer to the start of ICI therapy in the total cohort of n=84 patients. Percentages are given per column. ICI, immune checkpoint inhibition; MM, malignant melanoma; cSCC, cutaneous squamous cell carcinoma; MCC, Merkel cell carcinoma; LN, lymph node; LDH, lactate dehydrogenase; ULN, upper limit of normal.

Table S4: Staging of hematologic malignancy at start of ICI therapy

	CLL		NHL	
	Stage	**N (%)**	**Stage**	**N (%)**
All patients		30		32
Melanoma (MM)				
Total		**14 (100%)**		**23 (100%)**
	Binet A	5	Ann Arbor I	3
	Binet B	4	Ann Arbor II	1
	Binet C	4	Ann Arbor III	6
			Ann Arbor IV	2
Missing data		1		11
Cutaneous squamous cell carcinoma (cSCC)				
Total		**8 (100%)**		**5 (100%)**
	Binet A	2	Ann Arbor I	1
	Binet B	2	Ann Arbor II	0
	Binet C	3	Ann Arbor III	2
			Ann Arbor IV	0
Missing data		1		2
Merkel cell carcinoma (MCC)				
Total		**8 (100%)**		**4 (100%)**
	Binet A	2	Ann Arbor I	0
	Binet B	1	Ann Arbor II	0
	Binet C	5	Ann Arbor III	2
			Ann Arbor IV	1
Missing data		0		1

The stage of the concomitant hematologic malignancy at start of ICI therapy for non-resectable skin cancer is given as available from patient files. Staging is shown for the largest groups chronic lymphocytic leukemia (CLL), and other non-Hodgkin lymphoma (NHL).

TABLE S5: Characteristics of skin cancer disease at start of ICI therapy

	MM		cSCC		MCC	
	Hematologic Malignancy N (%)	**No Hematologic Malignancy** N (%)	**Hematologic Malignancy** N (%)	**No Hematologic Malignancy** N (%)	**Hematologic Malignancy** N (%)	**No Hematologic Malignancy** N (%)
Total	52 (100%)	257 (100%)	15 (100%)	59 (100%)	17 (100%)	76 (100%)
Stage of disease and tumor load						
locally advanced, measurable disease	3 (5.8%)	36 (14%)	4 (26.7%)	23 (39.0%)	0 (0.0%)	0 (0.0%)
locally advanced, disease-free after surgery	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)
metastatic, measurable disease	41 (78.8%)	221 (86%)	11 (73.3%)	36 (51.%)	16 (94.1%)	76 (100%)
metastatic, disease-free after surgery	8 (15.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Indication of treatment						
adjuvant	8 (15.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)
inoperable disease	44 (84.6%)	257 (100%)	15 (100%)	59 (100%)	16 (94.1%)	76 (100%)
Sites of measurable disease						
skin	3 (5.8%)	nr	3 (20.0%)	23 (39.0%)	0 (0.0%)	7 (9.2%)
LN	3 (5.8%)	nr	5 (33.3%)	32 (54.2%)	7 (41.2%)	31 (40.7)
visceral	38 (73.1%)	nr	7 (46.7%)	4 (6.8%)	9 (52.9%)	38 (50.0%)
none	8 (15.4%)	nr	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)
LDH (serum)						
normal (≤ULN)	34 (65.4%)	226 (87.9%)	8 (53.3%)	44 (74.6%)	7 (41.2%)	31 (40.8%)
elevated (>ULN)	16 (30.8%)	31 (12.1%)	6 (40.0%)	13 (22.0%)	10 (58.8%)	42 (55.3%)
unknown	2 (3.8%)	0 (0.0%)	1 (6.7%)	2 (3.4%)	0 (0.0%)	3 (3.9%)
Systemic pre-treatment of skin cancer						
yes	6 (11.5%)	0 (0.0%)	6 (40.0%)	18 (30.5%)	3 (17.6%)	25 (32.9%)
no	46 (88.5%)	257 (100%)	9 (60.0%)	41 (69.5%)	14 (82.4%)	51 (67.1%)
Pre-treatment: chemotherapy						
yes	3 (5.7%)	0 (0.0%)	3 (20.0%)	18 (30.5%)	3 (17.6%)	25 (32.9%)
no	49 (94.2%)	257 (100%)	12 (80.0%)	41 (69.5%)	14 (82.4%)	51 (67.1%)
Pre-treatment: targeted/other						
yes	3 (5.7%)	0 (0.0%)	3 (20.0%)	8 (13.6.%)	0 (0.0%)	4 (5.3%)
no	49 (94.2%)	257 (100%)	12 (80.0%)	51 (86.4%)	17 (100.0%)	72 (94.7%)
Pre-treatment: radiotherapy						
yes	9 (17.0%)	9 (3.5%)	8 (53.3%)	23 (39.0%)	8 (47.1%)	42 (55.3%)
no	43 (82.7%)	248 (96.5%)	7 (46.7%)	36 (61.0%)	9 (52.9%)	34 (44.7%)

The presented characteristics of skin cancer disease refer to the start of ICI therapy in the cohort of n=84 patients with concomitant hematologic malignancy as well as n=392 patients without concomitant hematologic malignancy. Percentages are given per column. ICI, immune checkpoint inhibition; MM, malignant melanoma; cSCC, cutaneous squamous cell carcinoma; MCC, Merkel cell carcinoma; LN, lymph node; LDH, lactate dehydrogenase; ULN, upper limit of normal; nr, not reported.

Table S6: Best response to ICI therapy for non-resectable skin cancer

	CLL **N (%)**	**NHL** **N (%)**	**other** **N (%)**	**P-value**
All patients	30	32	13	
Melanoma (MM)				0.48
Total	**14 (100%)**	**23 (100%)**	**7 (100%)**	
CR	1 (7.1%)	1 (7.1%)	0 (0.0%)	
PR	3 (21.4%)	6 (21.4%)	3 (42.9%)	
SD	5 (35.7%)	4 (14.2%)	2 (28.6%)	
PD	5 (35.7%)	7 (35.7%)	2 (28.6%)	
NE	0 (0.0%)	5 (21.4%)	0 (0.0%)	
objective response (CR+PR)	4 (28.6%)	7 (28.6%)	3 (42.8%)	
disease control (CR+PR+SD)	9 (64.2%)	11 (42.8%)	5 (71.4%)	
Cutaneous squamous cell carcinoma (cSCC)				0.29
Total	**8 (100%)**	**5 (100%)**	**2 (100%)**	
CR	1 (12.5%)	0 (0.0%)	0 (0.0%)	
PR	1 (12.5%)	2 (40.0%)	0 (0.0%)	
SD	2 (25.0%)	1 (20.0%)	1 (50.0%)	
PD	4 (50.0%)	2 (40.0%)	1 (50.0%)	
NE	0 (0.0%)	0 (0.0%)	0 (0.0%)	
objective response (CR+PR)	2 (25.0%)	2 (40.0%)	0 (0.0%)	
disease control (CR+PR+SD)	4 (50.0%)	3 (60.0%)	1 (50.0%)	
Merkel cell carcinoma (MCC)				0.28
Total	**8 (100%)**	**4 (100%)**	**4 (100%)**	
CR	0 (0.0%)	0 (0.0%)	0 (0.0%)	
PR	1 (12.5%)	0 (0.0%)	2 (50.0)%	
SD	3 (37.5%)	1 (25.0%)	0 (0.0%)	
PD	4 (50.0%)	2 (50.0%)	2 (50.0%)	
NE	0 (0.0%)	1 (25.0%)	0 (0.0%)	
objective response (CR+PR)	1 (12.5%)	0 (0.0%)	2 (50.0%)	
disease control (CR+PR+SD)	4 (50.0%)	1 (25.0%)	2 (50.0%)	

Response to ICI therapy is presented for n=75 patients treated for non-resectable skin cancer disease, subdivided by skin cancer entity and categorized concomitant hematologic malignancy. Hematologic malignancies were categorized as chronic lymphocytic leukemia (CLL), other non-Hodgkin lymphoma (NHL), and other (comprising all other entities not belonging to the previous two categories). Treatment response is presented as best overall response recorded from start of ICI until disease progression. ICI, immune checkpoint inhibition; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; NE, not evaluable.

TABLE S7. Blood counts of skin cancer patients with concomitant hematologic malignancy at start of ICI therapy

	CLL N (%)	NHL N (%)	other N (%)	P-value
Total	30 (100%)	32 (100%)	13 (100%)	
Leukocytes				**0.003**
normal	15 (50.0%)	24 (75.0%)	5 (38.5%)	
elevated	14 (46.7%)	3 (9.4%)	7 (53.8%)	
decreased	1 (3.1%)	5 (15.6%)	1 (7.7%)	
Lymphocytes				**<0.0001**
normal	8 (26.7%)	12 (37.5%)	6 (46.2%)	
elevated	18 (60.0%)	5 (15.6%)	1 (7.7%)	
decreased	4 (13.3%)	15 (46.9%)	6 (46.2%)	
Thrombocytes				**0.01**
normal	20 (66.7%)	23 (71.8%)	6 (46.2%)	
elevated	1 (3.1%)	3 (9.4%)	6 (46.2%)	
decreased	9 (30.0%)	6 (18.7%)	1 (7.7%)	

Blood counts at baseline of immune checkpoint inhibition (ICI) therapy are provided for n=75 patients treated for non-resectable skin cancer disease.