Table II. Base transection subanalysis

Base transection factor and number of cases	Number	Location, clinical scenario	Invasive on initial biopsy?	Upgrade on wide local excision?	Operator intent
Partial biopsy of large lesion	3	Chest	Yes	No	Partial
		Neck (1) - IEC intermixed	Yes	No	Partial
		Arm	No	yes	Partial
Biopsy only intent — superficial shave performed, not intending to achieve deeper excision	8	Arm (amelanotic)	Yes	yes	Partial
		Neck (2) (amelanotic)	No	yes	Partial
		Shoulder (amelanotic)	Yes	No	Partial
		Leg	Yes	No	Partial
		Nose	No	No	Partial
		Cheek	Yes	No	Partial
		Infraorbital	No	No	Partial
		Jaw	No	Yes	Partial
Insufficient depth of intended shave excision	1	Scalp	Yes	No	Complete excision

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Age and sex differences for malignant melanoma in the pediatric population—childhood versus adolescence: analysis of current nationwide data from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program

To the Editor: Continuing efforts are warranted to better understand malignant melanoma (MM) in children and adolescent populations. The aim of this study was to report overall pediatric MM trends and differences when stratified by age and sex for both children and adolescents.

The SEER database (2000-2015) was used to extract data for patients 0 to 19 years with a diagnosis of MM (International Classification of Childhood Cancer codes: 8720-8780, 8790). Only cases with known age and malignant behavior (excluding in situ cases) were selected for analysis. Data were then stratified by age (children: 0 to 9 years and adolescents: 10 to 19 years) and by sex male/female. Incidence rates (IRs), IR trends (as annual percentage change [APC]), and 5-year cause-specific survival, were calculated. SEER*Stat software[1] was used for data extraction and analyses.

Of 1,891 pediatric MM patients, 236 (12%) were children, 1,655 (88%) were adolescents; 1,088 (57.5%) were female (children: 12.6%; adolescents: 87.4%); and 803 (42.5%) were male (children: 12.3%; adolescents: 87.7%).

Overall, the age-adjusted IR was 5.0 (95% confidence interval [CI], 4.8-5.2) per million persons (IR, 1.3 for children and 8.6 per million for adolescents). Stratified by sex, females had a significantly higher IR than males for both populations (children, 1.5 vs 1.1; adolescents: 10.1 vs 7.1; $P < .05$). Although pediatric MM, overall, had a decreasing IR trend (APC, −3.7%; 95% CI, −5.3, −2.0), the IR trend was significantly decreased for adolescents (APC, −4.4%; 95% CI, −5.9, −2.8), but not for children.

Five-year survival rate was not significantly different between children and adolescents (93.9% vs 95.3%, respectively). When stratified by sex, the 5-year survival rate for adolescents was significantly higher for females than males 97.0% (95% CI, 95.5%-98.0%) and 92.9% (95% CI, 90.4%-94.7%), respectively. No significant difference by sex was detected for children (92.4% for males and 95.0% for females).

Table I. Malignant melanoma histologic subtype frequency stratified by age and sex

	Female				Male			
	Childhood		Adolescence		Childhood		Adolescence	
	Count (n = 137)	%	Count (n = 951)	%	Count (n = 99)	%	Count (n = 704)	%
Malignant melanoma, NOS	90	65.7	504	53	62	62.6	392	55.7
Nodular Melanoma	12	8.8	49	5.2	8	8.1	43	6.1
Malignant melanoma, regressing	0	0	1	0.1	0	0	1	0.1
Malignant melanoma in magnocellular nevus (ocular)	0	0	1	0.1	0	0	0	0
Amelanotic melanoma	1	0.%	3	0.%	0	0	1	0.1
MM in junctional nevus	0	0	12	1.3	0	0	4	0.6
MM in precancerous melanosis	1	0.7	0	0	1	1	0	0
Lentigo maligna melanoma	0	0	0	0	0	0	3	0.4
Superficial spreading melanoma	12	8.8	332	34.9	7	7.1	201	28.6
Acral lentiginous melanoma, malignant	0	0	5	0.5	0	0	4	0.6
Desmoplastic melanoma, malignant	0	0	1	0.1	1	1	1	0.1
Mucosal lentiginous melanoma	0	0	1	0.1	0	0	0	0
MM in giant pigmented nevus	5	3.6	12	1.3	7	7.1	17	2.4
Mixed epithelioid and spindle cell melanoma	13	9.5	14	1.5	10	10.1	16	2.3
Epithelioid cell melanoma	1	0.7	4	0.4	2	2	7	1
Spindle cell melanoma, NOS	1	0.7	10	1.1	1	1	11	1.6
Spindle cell melanoma, type B	0	0	2	0.2	0	0	1	0.1
Blue nevus, malignant	1	0.7	0	0	0	0	2	0.3

NOS, Not otherwise specified.

Table II. Frequency of anatomic site for pediatric malignant melanoma stratified by age and sex

	Female				Male			
	Childhood		Adolescence		Childhood		Adolescence	
	Count (n = 135)	%	Count (n = 912)	%	Count (n = 93)	%	Count (n = 676)	%
Skin of lip, NOS	0	0	1	0.1	1	1.1	1	0.1
Eyelid	1	0.7	3	0.3	1	1.1	1	0.1
External ear	4	3.0	23	2.5	9	9.7	27	4.0
Skin other/unspecified parts of face	13	9.6	63	6.9	12	12.9	74	10.9
Skin of scalp and neck	15	11.1	57	6.3	9	9.7	94	13.9
Skin of trunk	19	14.1	350	38.4	14	15.1	257	38.0
Skin of upper limb and shoulder	31	23.0	156	17.1	20	21.5	116	17.2
Skin of lower limb and hip	45	33.3	248	27.2	24	25.8	89	13.2
Overlapping lesion of skin	1	0.7	0	0	1	1.1	0	0
Skin, NOS	6	4.4	11	1.2	2	2.2	17	2.5

NOS, Not otherwise specified.

Data for histologic subtypes and anatomic locations are shown in Tables I and II.

These findings remain consistent with those of earlier reports[2,3] in that the IR for pediatric MM has continued to decrease, indicating a trend for decreasing IR of pediatric MM. Moreover, no significant change for childhood IR suggests that the decrease in IR is primarily attributed to adolescent MM IR reduction. Although pediatric MM may relate to genetics, increased surveillance and awareness of sunscreen use may also serve to explain the decrease in trends, especially for adolescents.

Unlike some prior reports,[4,5] our nationwide findings showed no significant age-related difference for 5-year survival between children and adolescents and showed the 5-year survival rate to be significantly worse for male adolescents but not for male children.

Major limitations of this study are nonadjustment for MM stage and race/ethnicity; thus, survival analysis may be biased.

These updated findings show that, for pediatric MM, distinct differences exist for age and sex that may represent underlying differences in pathogenesis for children versus adolescents. Moreover, these

findings point to the need for studies on sex and age differences in pediatric melanoma.

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De novo cutaneous connective tissue disease temporally associated with immune checkpoint inhibitor therapy: A retrospective analysis

To the Editor: With the success of immune checkpoint inhibitors (ICI) in cancer therapy, there is urgency to better characterize dermatologic immune-related adverse events (irAEs). De novo cutaneous connective tissue disease (CTD) has been associated with immunotherapy including reports of 2 cases of scleroderma, 7 cases of dermatomyositis, 6 cases of subacute cutaneous lupus erythematosus (SCLE), and 11 cases of eosinophilic fasciitis (EF).[1,2] In this study, we evaluated the frequency of immunotherapy-associated de novo cutaneous CTD among our institutions and reported clinical features and management.

In this retrospective cohort study, we queried electronic pharmacy and medical records to find the total number of adult patients treated with pembrolizumab, nivolumab, durvalumab, atezolizumab, tremilimumab, and/or ipilimumab at Dana-Farber Cancer Institute/Mass General Brigham between December 2013 and July 2019. Using institutional billing codes, diagnosis codes, and key word searches throughout notes and reports, we extensively reviewed medical records to identify patients with de novo cutaneous CTD (systemic sclerosis, dermatomyositis, cutaneous lupus [acute, subacute, chronic], systemic lupus erythematosus [SLE], EF, and morphea) up to 1 year after last ICI dose (Supplementary data available on Mendeley at https://doi.org/10.17632/8chdj89vhj.1). We excluded exacerbation(s) of pre-existing disease. In addition to diagnosis by the patient's dermatologist, 3 board-certified dermatologists reviewed cases and unanimously agreed with diagnoses.

A total of 4,487 patients received immunotherapy across our institutions. Among this cohort, 11 patients had immunotherapy-associated cutaneous CTD, for a frequency of 0.025%. Six (54.5%) were men. Median age was 59 years (53-69). Median time to onset was 8 months (0.5-26). There were 8 cases of SCLE (72.7%), 1 case of SLE (9.1%), 1 case of EF (9.1%), and 1 case of dermatomyositis (9.1%), with clinical and diagnostic features described in Table I. Among 9 patients tested, all had positive antinuclear antibodies (range, 1:80-1:5120). Among 7 patients with SCLE tested, 6 (85.7%) had positive anti-Ro(SSA) and 5 (71.4%) had positive anti-La(SSB) antibodies. Patients were treated with skin-directed (100%) and/or systemic therapies (36.3%). ICI was discontinued in 1 patient for dermatomyositis and held in 1 patient for SCLE.

Major findings include the rarity and striking lack of heterogeneity of immunotherapy-associated cutaneous CTD. We did not observe systemic sclerosis, morphea, or other types of cutaneous lupus beyond SCLE; we found only 1 case of SLE. There is 1 report of ipilimumab-associated lupus nephritis in the literature.[3] A possible mechanism for the disproportionate number of SCLE cases may be from immunologic recognition of previously immunologically tolerated drug antigens (all on longstanding, previously tolerated drugs reported to cause drug-induced SCLE), increased ultraviolet radiation