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Abstract Book

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Giant infected lipoma evolving over more than 30 years: case report and literature review

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Background: Giant lipomas, defined as benign tumours that measure more than 10 cm or weigh more than 1000 g, are rare. Secondary infection is exceptional, particularly in long-standing cases.

Methods: We report a case of a giant lipoma with secondary infection after three decades of evolution.

Results: Our 73-year-old patient, a 40-pack-year smoker, presented with a right periscapular mass evolving over 30 years, complicated one year earlier by spontaneous ulceration and infection. Clinical examination revealed a soft, mobile, painless subcutaneous mass measuring more than 10 cm in diameter. Vital signs were stable. Laboratory tests were normal, with no markers of inflammation or systemic infection.
Computed tomography showed a well-defined lesion with characteristic fatty density (-65 to -120 HU) measuring 16.3 cm, with no infiltration of adjacent structures. Complete surgical excision was performed. The surgical sample weighed 1050 g and measured 20 x 17 x 7 cm. Histology confirmed a remodeled fusiform lipoma without malignancy. Postoperative recovery was uneventful, with no recurrence at 6 months.

Discussion: Giant lipomas are a rare clinical form with prolonged growth, as shown in this case. The etiology of lipomas is unclear, smoking has been suggested but remains controversial. Rare secondary infections usually follow skin injury. Magnetic resonance imaging (MRI) is the imaging modality of choice for differentiating lipomas from well-differentiated liposarcomas. On computed tomography, lipomas appear as homogeneous hypodense masses with attenuation values characteristic of adipose tissue (-65 to -120 HU), often surrounded by a thin capsule.(table) Complete surgical

excision is the standard treatment. As antibiotics alone are insufficient for infection, in our case, dual antibiotics were used. Prognosis is excellent, with a 1–5% recurrence rate.

Conclusion: Infected giant lipomas are a rare clinical entity that requires a specialised diagnostic and therapeutic approach. complete excision remains the standard with excellent prognosis for benign lesions.

Targeted Hyperthermia Therapy Induces Immunogenic Cell Death to Enhance Immunotherapy Efficacy in Melanoma

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Background: Despite tremendous advances, immunotherapy for metastatic melanoma fails due to poor tumor immunogenicity, limited T cell infiltration, and an immunosuppressive microenvironment. Mild, tumor-focused hyperthermia triggers a heat shock response, releasing danger signals, enhancing antigen presentation, and promoting immune infiltration leading to immunogenic cell death (ICD).

Objective: We hypothesized that precisely delivered mild hyperthermia could reprogram the tumor microenvironment to overcome immunotherapy resistance.

Method: Precision hyperthermia using a Sona Targeted Hyperthermia Therapy (THT) System was administered via intra-tumoral injection of gold nanorods (SivaRods 2.0) engineered to absorb near-infrared (860 nm) light (SivaLum 2.0) producing hyperthermic conditions (42-48°C) in the tumor microenvironment. Preclinical murine melanoma models evaluated tumor growth, survival, and immune modulation. Mechanistic studies used flow cytometry, RNAseq, cytokine analysis, and TCR profiling.

Results: Tissue analysis demonstrated ICD and enhanced antigen presentation, marked by increased HSP70, calreticulin, and MHC-I expression, alongside dendritic cell and macrophage infiltration. Transcriptomics revealed heat shock activation, cytokine induction, complement upregulation, and TCR clonal expansion, consistent with robust immune activation. Effects were transient, with tumors reverting to an M2-dominant, immunosuppressive state within 96 h. Co-treatment with CSF1R blockade sustained M1 polarization and achieved durable regression. Adding checkpoint blockade or cytokine therapy further amplified T cell infiltration and tumor regression.

Conclusion: Sona THT System is a novel immunotherapy platform that precisely delivers mild hyperthermia to induce ICD and reprograms immunity, synergizing with immunotherapies to restore antitumor responses. Based on these findings, a first-in-human early feasibility trial in 10 patients with advanced melanoma refractory to immunotherapy is underway.

Quality of Life and Sexuality in Melanoma Patients Under Established Immuno- and Targeted Therapies: A Prospective Study

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Background: Immuno-oncological treatments for melanoma, such as PD-1 and BRAF/MEK inhibitors, have improved survival rates. However, their impact on patient's quality of life (QoL) and mental health, particularly sexual function and fertility remains insufficiently investigated.
Objectives: To evaluate QoL and mental health in younger melanoma patients receiving PD-1 or BRAF/MEK inhibitors, focusing on sexuality and reproductive health.

Methods: This prospective, non-randomized study at the National Center for Tumor Diseases Heidelberg includes males under 60 and females up to 43 years with cutaneous melanoma receiving PD-1 or BRAF/MEK inhibitors in the adjuvant setting. Quality of life and mental health were assessed via: EORTC QLQ-C30, GAD-7, PHQ-9. Male sexual function was evaluated with the IIEF-EF and a sexual function questionnaire for both sexes was included. Laboratory analyses included reproductive hormones (FSH, LH, AMH for women; testosterone for men) and WHO-standard semen analysis. Assessments were performed before therapy, every three months during treatment, and post-therapy.

Results: Between February 2019 and September 2025, 19 patients (13 females, 6 males; median age 33 and 45.5 years, respectively) were enrolled, with four still under treatment. Concerning endocrinological immune-related adverse events, no hypophysitis cases were observed; two females developed thyroiditis. Two patients discontinued adjuvant therapy due to progression, none for adverse events. So far, longitudinal analyses revealed no significant changes in QoL and fertility over time. Further detailed analyses are ongoing.

Conclusion: Despite increasing use of these therapies in younger melanoma patients, systematic data on fertility, sexuality and mental health are lacking. Closer attention to these aspects is essential to improve comprehensive patient counseling and informed decision-making.

Two Case-Reports on the Use of daromun for the Treatment of Locally Advanced Fully Resectable Stage III Melanoma from the Compassionate Use Program in Germany

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Background: Daromun is a neoadjuvant intralesional immunotherapy under development for locally advanced resectable stage III melanoma. It combines two antibody-cytokine conjugates, L19IL2 and L19TNF, which target the tumour while sparing healthy tissues.

Objectives: We present two cases from the German compassionate use program.

Methods: The compassionate use program collects data on the use of daromun in locally advanced resectable stage III melanoma patients with limited treatment options.

Results: The first case involves a patient with ulcerated secondary nodular melanoma on the left cheek, stage IIIC, with satellite metastasis in 2021. The patient also had Grover`s disease and basal cell carcinomas. Pre-therapy included R0 resection, adjuvant nivolumab and further excision with adjuvant radiotherapy. In 2025, the patient received four neoadjuvant daromun injections, experiencing lesion necrosis (grade 3) and injection site reaction (grade 1). Subsequently, the tumor was completely removed. The second patient had ulcerated malignant melanoma, stage IIIC, on the left mamilla in 2023 and multiple comorbidities. The patient experienced local recurrence and metastases after initial surgery. Adjuvant immunotherapy with pembrolizumab was discontinued after severe immune-mediated hepatitis and thyroiditis. Disease progression led to skin and nodal metastases. After a single nivolumab administration showed progression, treatment was switched to daromun in 2025. The patient received four injections, experiencing injection site reaction (grade 1), necrosis (grade 3), and mild flu-like symptoms. Subsequently, R0 resection was successfully performed.

Conclusions: These two cases underscore the challenges in managing locally advanced melanoma with immunotherapy and the potential role of daromun in addressing the unmet need.

Real-World Outcomes and Prognostic Indicators in Mycosis Fungoides Treated with Total Skin Electron Therapy: A Decade-Long Contemporary Experience from India

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Background: Mycosis fungoides (MF) accounts for 0.5% to 2% of all NHL in India. While Total Skin Electron Therapy (TSET) is an established treatment worldwide, it remains resource-intensive, with extreme paucity of real-world data from India.

Objectives: To assess the real-world efficacy, safety, and prognostic indicators of TSET in Indian patients with MF.

Methods: We conducted a retrospective analysis of 12 patients with MF treated with TSET (36 Gy over 9 weeks, Stanford technique) from April 2014 to April 2025. Treatment response was assessed at 3 months post-TSET and during follow-up.

Results: Median age was 40 years; 58.3% were male. Median symptom duration prior to diagnosis was 2.5 years. TNMB staging: IA (16.6%), IB (50%), IIB (16.7%), IIIB (16.7%). Most had classical MF (83.3%). CD30 was positive in 3 patients, Ki-67 25% in 4 (33.3%), and elevated LDH in 25%. Prior therapies included topical steroids (33.3%), PUVA (25%), nb-UVB (8.3%), ECP (8.3%), and methotrexate (25%). Median delay to TSET was 12 months. Common treatment-related toxicities were dermatitis (83.3%), alopecia (50%), epiphora (66.7%), mucositis (41.7%), nail pigmentation (41.7%), and blisters (25%).
At 3 months, 58.3% had complete response, 25% partial response, and 16.7% progression. At a median follow-up of 48 months, 58.4% were alive and disease-free. Poor outcomes correlated with advanced stage, CD30 positivity, high Ki-67, and elevated LDH.

Conclusion: TSET is effective and well-tolerated in Indian MF patients. This represents the largest contemporary single-center dataset from India. Early referral and recognition of high-risk features (CD30, Ki-67, LDH) are crucial for improving outcomes.

A Rare Case of Orbital Inflammatory Syndrome after Pembrolizumab in Metastatic Melanoma

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Background: Immune checkpoint inhibitors are the standard of care first-line treatment for unresectable stage III/IV melanoma internationally[1]. Rare cases have been reported of orbital or ocular toxicities from immune checkpoint inhibitors[2,3,4,5]. These cases have shown different possible mechanisms, such as a flare of thyroid eye disease[3], immune-mediated myositis of extra-ocular muscles, or a distinct inflammatory condition on its own[4]. As far as we are aware, acute inflammatory response has not been reported in patients with existing intraorbital metastases.

Clinical Case: We present a case of a 60-year-old woman with metastatic melanoma (to liver, bone, bilateral intraorbital lesions, subcutaneous and intramuscular lesions and widespread lymphadenopathy), who presented to the Emergency Department with bilateral periorbital oedema and right proptosis five days after her first dose of pembrolizumab. Computed tomography (CT) head demonstrated known orbital lesions, but no intracranial metastases.
Ophthalmology review showed restricted and painful eye movements with moderate periorbital oedema and conjunctival inflammation, without intraocular inflammation or optic nerve compromise. She received a course of oral dexamethasone (8mg/day, weaning dose by 2mg every two to three days) with marked improvement in her symptoms.
A second dose of pembrolizumab triggered a similar reaction, which also settled with dexamethasone.

Conclusions: This case demonstrated a rare complication of immune checkpoint inhibitors, with orbital inflammation secondary to pembrolizumab in a patient with known intraorbital metastases. Clinicians should be aware of the risk of orbital inflammation associated with checkpoint inhibitors and management strategies for this presentation.

References:

1. Cutaneous melanoma: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. (2024). Annals of Oncology, 36(1). https://www.annalsofoncology.org/action/showPdf?pii=S0923-7534%2824%2904912-3

2. Ang, T., Chaggar, V., Tong, J. Y., & Selva, D. (2024). Medication-associated orbital inflammation: A systematic review. Survey of Ophthalmology, 69(4), 622–631. https://doi.org/10.1016/j.survophthal.2024.03.003

3. Madala, S., Parikh, A., Hong, K., & Burnstine, M. (2025). Case Report: Development of severe inflammatory orbitopathy after immune checkpoint inhibitor initiation. Frontiers in Ophthalmology, 5. https://doi.org/10.3389/fopht.2025.1574643

4. Sheldon, C. A., Kharlip, J., & Tamhankar, M. A. (2015). Inflammatory orbitopathy associated with ipilimumab. Ophthalmic Plastic and Reconstructive Surgery, 33(3S), S155–S158. https://doi.org/10.1097/iop.0000000000000509

5. Nardin, C., Borot, S., Beaudoin, M., Cattin, F., Puzenat, E., Gauthier, A., Schillo, F., Borg, C., & Aubin, F. (2018). Long-term adverse event: inflammatory orbitopathy induced by pembrolizumab in a patient with metastatic melanoma. Investigational New Drugs, 37(2), 375–377. https://doi.org/10.1007/s10637-018-0659-9

Association Between Drug-Related Cutaneous Adverse Events and Survival Outcomes in Patients Treated with Enfortumab Vedotin

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Aim of the study: The antibody-drug conjugate enfortumab vedotin (EV) received approval in patients with metastatic urothelial carcinoma (mUC). EV-related cutaneous toxicities are frequently reported, whether EV-related AEs association with survival may exist is still unknown. We aim to report the association between cutaneous toxicities and survival in patients receiving EV.

Methods: This retrospective study enrolled patients treated with monotherapy EV from two oncology centers, followed up for at least 3-months, and data collection demographics, treatments, toxicities, and outcomes. The primary endpoint was progression-free survival (PFS) in patients experiencing cutaneous toxicities or not. Overall survival (OS) was the secondary endpoint.

Results: Data from 63 patients treated with EV from July 19, 2019, to March 12, 2024, were collected. Among them, the 18 (28.6 %) patients experiencing any-grade cutaneous toxicities during EV treatment showed significantly longer median PFS (mPFS: 9.2 vs. 4.7 months, hazard ratio [HR] 0.35; p =0.0041) and OS (mOS: not reached vs. 8.4 months, HR 0.38; p =0.0253). The multivariate analysis showed a significant association of cutaneous toxicities with improved PFS (HR 0.40, p =0.0319), and did not demonstrate significant association with OS even if tendency was kept (HR 0.41, p =0.067).

Conclusion: These results support that patients experiencing any-grade cutaneous toxicity (skin rash) had a prolonged PFS. With the recent expansion of combined treatment using EV plus pembrolizumab in first-line in mUC patients, cutaneous toxicities need to be carefully monitored and optimized dedicated management provided, considering that cutaneous toxicity may be predictive of patient outcome.

Successful Treatment of Immune-Mediated Generalized Cutaneous Sclerosis using Extracorporal Photopheresis

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Immunecheckpoint inhibitor therapies are standard of care for patients with advanced melanoma. However, they associate the risk of severe, and often therapy-refractory immune-related adverse events.
Whereas common adverse events can be managed with esthablished treatment algorithms, the management of rare events is challenging.
We report on a 66-year-old female with a BRAF-mutant nodular melanoma of the tigh and concomitant lymphnode macrometastasis (AJCC stage IIIC) at first diagnosis February 2023. She received adjuvant systemic nivolumab-therapy along with lymphnode dissection. Unfortunately she repeatedly progressed with cutaneous, lymphonodal and brain metastases upon 2nd line BRAF+ MEK-inhibitors and 3rd line ipilimumab+nivolumab combination and was stable under the triple combination BRAF+MEK+Pembrolizumab by July 2024.
However in October 2024 the patient presented with rapidly progressive generalized edema followed by disabling pansclerotic modifications resulting in severely impaired mobility. Subsequently, dyspnea with restrictive ventilarory impairment was observed along with detection of Pm-Scl autoantibodies.
After exclusion of other potential causes (concomitant medication, radiation, paraneoplastic), the generalized scleroderma was diagnosed as a very rare immune-mediated adverse event of immune checkpoint inhibiton.
Oncologic therapy was resumed and high-dose oral glucocorticoids were initiated. Despite initial response, a steroid-dependency of 40mg/day or more prednisolon developed. Steroid-sparing methotrexate and UVA therapy were not efficient.
Due to progressive fibrosis extracorporal photoperesis was started. Within six cycles, skin sklerosis regressed and immunosuppression was fully discontinued.
Extracorporal photophoresis should be considered as an efficient, non-immunosuppressive therapy for severe refractory immune-mediated adverse events.

The Positive Impact of a Dedicated Immunotherapy Toxicity MDT in the Early Intervention and Guidance of Patients Presenting with Dermatological irAEs

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Background: With increased use of immune checkpoint inhibitors (ICIs) in oncology, incidences of immune-related adverse events (irAEs) are rising. Skin toxicities are the most common type, often presenting heterogeneously. While steroids remain the recommended treatment, establishment of an immunotherapy toxicity MDT for severe refractory irAEs may improve outcomes.

Objectives: We evaluated the impact of an immunotherapy toxicity MDT at St George's University Hospital on management and outcomes of severe skin toxicities.

Methods: Data were collected from patients presenting with Grades 2-4 skin toxicities, January 2021-March 2025. Patients were divided into pre-MDT (n=10) and post-MDT (n=27) establishment cohorts. Baseline characteristics, treatment approaches, and outcomes were compared.

Results: Baseline characteristics remained similar between cohorts, including ICI cycle preceding toxicity (pre-MDT: 4.9[1–17], post-MDT: 5.8[1–27], p=0.541). Skin toxicities were reported earlier and initially treated with topical steroids in the post-MDT cohort, with systemic steroids introduced later after symptom onset (pre-MDT: 4.2[0–28], post-MDT: 27.9[0–182] days, p=0.002). Steroid administration routes and treatment durations were comparable (pre-MDT: 34.4[7–127], post-MDT: 59.4[7–192] days, p=0.751). Dermatology involvement increased by 55% and ICIs were 40% more likely to be discontinued post-MDT (RR, p0.001 each). One post-MDT patient died due to SJS/TEN. Eight patients post-MDT had concurrent irAEs, and four had recurrent skin toxicities. Despite increased discontinuation post-MDT, complete resolution rates were high in both cohorts (pre-MDT: 90%, post-MDT: 83%).

Conclusion: Establishment of an immunotherapy toxicity MDT was associated with earlier reporting and greater specialist input, optimising recognition, management and resolution of severe skin toxicities.

Asymptomatic Troponin T Elevation and Differential Diagnosis of ICI-Myocarditis in Skin Cancer Patients

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Background: Immune checkpoint inhibitor (ICI)-induced myocarditis is a rare but fatal immune-related adverse event associated with high mortality. While Troponin T (TnT) is a widely used sensitive but unspecific biomarker for cardiac monitoring during ICI therapy, asymptomatic TnT elevations without cardiac abnormalities represent diagnostic challenges.

Objectives: We investigated the prevalence and mechanisms of elevated TnT levels in skin cancer patients undergoing ICI therapy, hypothesizing that non-cardiac TnT elevations correlate with tumor progression and may arise from ectopic expression in metastases.

Methods: In a retrospective analysis over one year, 29 patients with advanced cutaneous malignancies and elevated TnT during ICI therapy were examined. Cardiological and laboratory parameters were compared between myocarditis and non-myocarditis patients. Immunohistochemistry and qPCR were used to detect TnT expression in metastases. 10x Genomics Single-nuclei sequencing was performed on myocardial tissue from ICI-myocarditis patients to identify disease-specific pathways.

Results: Three patients (10.3%) were diagnosed with ICI-associated myocarditis. No significant laboratory differences were found between groups. In the remaining 26 patients, elevated TnT was linked to cardiac disease or unexplained elevation. Those with unexplained elevations had lower peak TnT values (33.06 vs. 167.5 µg/L; p=0.01*) but demonstrated consistent tumor progression and elevated LDH. Non-myocarditis patients with other cardiac pathology were distinguished by lower LDH compared to the rest (218.4 vs. 334.7 U/L; p=0.0426*). Ectopic TnT expression was detected in 5/12 metastatic samples by immunohistochemistry. qPCR confirmed TnT expression irrespective of myocarditis status, showing highest values in a melanoma metastasis from a myocarditis patient.

Conclusion: TnT remains a key biomarker for ICI-myocarditis. Our data show that beyond cardiac injury, TnT elevation may reflect tumor progression and could be intensified via ectopic expression in metastases. LDH and peak TnT levels help differentiate causes, supporting combined cardiological and molecular assessment for accurate diagnosis and insights into disease mechanisms.

Synergizing ASOs unveil MAPK pathway associated vulnerabilities in drug resistant Melanoma

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Background: Synergistic drug combinations enhance therapeutic efficacy and reduce side effects, a key goal in cancer research. Dual treatments targeting the MAPK pathway are critical in melanoma therapy, often combining MEK (MEKi) and BRAF inhibition. However, resistance mechanisms frequently limit their efficacy. RNA-targeted therapies using Antisense Oligonucleotides (ASOs) effectively inhibit MAPK-dependent melanoma growth, but little is known about dual ASO treatments in treatment-naïve or drug-resistant MAPK-driven melanoma.

Objectives+Methods: This study explored dual ASO treatments targeting NRAS mRNA, T-RECS lncRNA, and MALAT1 lncRNA across melanoma cell lines with MAPK-hyperactivating mutations and mechanisms of MEKi-resistance, simulating various clinical conditions.

Results: In treatment-naïve and resistant cells not exposed to chronic MEK inhibition, combinations showed antagonistic or additive effects. However, in MEKi-resistant cells, dual ASO therapy combined with MEKi exposure produced synergistic responses. To understand these effects, we analyzed MAPK-pathway-associated kinase expression, and transcriptional interdependencies of NRAS, T-RECS, and MALAT1. MEKi-resistance profoundly altered MAPK-signaling activity and the transcriptional dynamics of NRAS, T-RECS, and MALAT1.

Conclusion: These findings reveal how resistance mechanisms reshape oncogenic lncRNA expression and identify patient groups who may benefit from dual ASO therapies targeting MAPK-pathway-associated RNA.

Giant infected lipoma evolving over more than 30 years: case report and literature review

Marwen Boughriba*[1]*, *Mohamed Rebei*[1]*, Hanen Bouattour*[1]*, Ahmed Ben Ayed*[1]*, Mouna Nasri*[1]*, Hala Alimi*[1]*, Hela Ben Jmeaa*[2]*, Zied Chaari*[1]*, Abdessalem Hentati*[1]
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Background: Giant lipomas, defined as benign tumours that measure more than 10 cm or weigh more than 1000 g, are rare. Secondary infection is exceptional, particularly in long-standing cases.

Methods: We report a case of a giant lipoma with secondary infection after three decades of evolution.

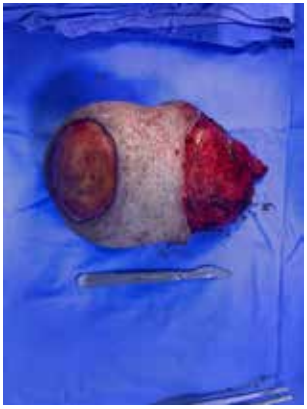
Results: Our 73-year-old patient, a 40-pack-year smoker, presented with a right periscapular mass evolving over 30 years, complicated one year earlier by spontaneous ulceration and infection. Clinical examination revealed a soft, mobile, painless subcutaneous mass measuring more than 10 cm in diameter. Vital signs were stable. Laboratory tests were normal, with no markers of inflammation or systemic infection.
Computed tomography showed a well-defined lesion with characteristic fatty density (-65 to -120 HU) measuring 16.3 cm, with no infiltration of adjacent structures. Complete surgical excision was performed. The surgical sample weighed 1050 g and measured 20 x 17 x 7 cm. Histology confirmed a remodeled fusiform lipoma without malignancy. Postoperative recovery was uneventful, with no recurrence at 6 months.

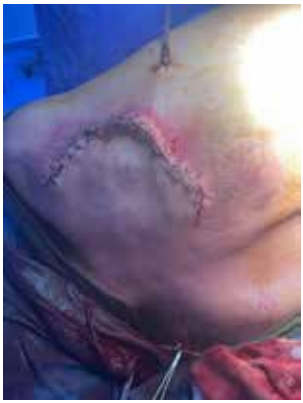
Discussion: Giant lipomas are a rare clinical form with prolonged growth, as shown in this case. The etiology of lipomas is unclear, smoking has been suggested but remains controversial. Rare secondary infections usually follow skin injury. Magnetic resonance imaging (MRI) is the imaging modality of choice for differentiating lipomas from well-differentiated liposarcomas. On computed tomography, lipomas appear as homogeneous hypodense masses with attenuation values characteristic of adipose tissue (-65 to -120 HU), often surrounded by a thin capsule.(table) Complete surgical excision is the standard treatment. As antibiotics alone are insufficient for

infection, in our case, dual antibiotics were used. Prognosis is excellent, with a 1–5% recurrence rate.

Conclusion: Infected giant lipomas are a rare clinical entity that requires a specialised diagnostic and therapeutic approach. complete excision remains the standard with excellent prognosis for benign lesions.

		Well-Differentiated Liposarcoma
Location	Subcutaneous (back, shoulders)	Deep (thigh, retroperitoneum)
Size	Usually 5 cm	Often 10 cm
Internal septa	Thin or absent	Thick, enhanced
Nodules	Absent	Present
MRI/CT	Homogeneous fatty density	Heterogeneous fatty component
Histology	No cellular atypia	Presence of lipoblasts, atypia





Lipomas of the chest wall: clinical-histological concordance and factors associated with recurrence

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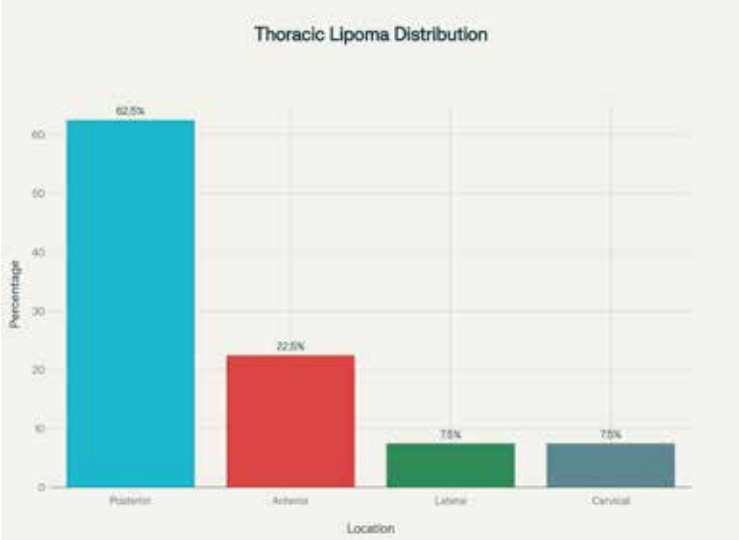
Background: Thoracic lipomas represent a diagnostic and therapeutic challenge due to occasional clinical-radiological-histological discordance.

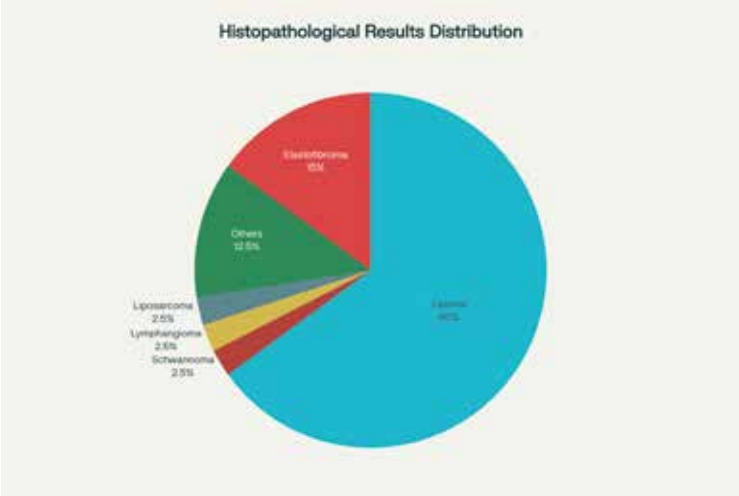
Objectives: This study aims to determine the epidemiological, clinical-radiological and anatomopathological characteristics, as well as the predictive factors for recurrence.

Methods: Retrospective study including 40 patients operated on between January 2010 and July 2025 at the Habib Bourguiba University Hospital in Sfax for a thoracic mass suspected of being a lipoma. Epidemiological, clinical, radiological, surgical and histopathological data were analysed.

Results: We included 40 patients with a mean age of 49.5 years and a sex ratio of 0.73. A personal history of lipoma was found in 5% of patients. The prevalence of smoking reached 35%.
The average duration of progression was 59 months. The location was mainly posterior, noted in 25 patients (62.5%). The average tumour size was 7.6 cm. On clinical examination, 52.5% of tumours were mobile, soft in 70% of cases, firm in 17.5% and hard in 7.5% of cases. Ultrasound was performed in 60% of patients, CT scan in 30% and MRI in 10%. All imaging tests were consistent with a lipoma. All patients in our series underwent conventional open surgery. No surgical complications were reported. Histological analysis confirmed the diagnosis of lipoma in only 65% of patients. The main other diagnoses included elastofibroma (15%) and liposarcoma (2.5%).
The overall recurrence rate was 5%. No recurrence was observed in the 24 lipomas with complete capsules, while the two recurrences occurred in the two patients with lipomas with incomplete capsules, representing a recurrence rate of 7.7% in this subgroup.

Conclusion: Thoracic lipoma can sometimes pose a differential diagnosis problem even in the presence of highly suggestive imaging, hence the importance of complete resection with preservation of capsular integrity if possible to ensure no recurrence.





Outcomes of patients with T1a primary melanoma close to critical anatomic structures treated with narrower excision of 5 mm instead of 10 mm

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Background: Melanoma guidelines recommend surgical excision with 10-mm margins for T1 cutaneous melanoma (Breslow thickness up to 1 mm). However, this procedure may be problematic at sites close to critical anatomic locations, such as scalp, face, external genitalia, acral, periumbilical, and perineal areas.
We retrospectively investigated whether a narrower (5-mm) excision margins may affect outcomes of patients with T1a melanoma near critical anatomic locations.

Material and methods: A total of 1179 consecutive patients ≥18 years old consecutively treated between 2001 and 2020 at the National Cancer Institute, Milan, Italy, were included in the study.

Results: Six hundred twenty-six patients (53.1%) received a wide excision, 434 (69.3%) with linear repair, 192 (30.7%) with flap or graft reconstruction; 553 (46.9%) patients received a narrow excision, 491 (88.8%) with linear repair, 62 (11.2%) with flap or graft reconstruction (P0.001). The weighted 10-year melanoma-specific mortality (95% confidence interval) was 1.8% (0.8-4.2%) in the wide and 4.2% (2.2-7.9%) in the narrow group; the weighted 10-year local recurrence rate was 5.7% (3.9-8.3%) in the wide and 6.7% (4.7-9.5%) in the narrow group. The weighted multivariable Fine-Gray model showed that Breslow thickness 0.4 mm (P0.001) and mitotic rate 1 (P 0.001) were prognostic factors for worse melanoma-specific mortality. Acral lentiginous melanoma, lentigo maligna melanoma, and increasing Breslow thickness were associated with a higher incidence of local recurrence.

Conclusions: Local excision with 5-mm margins, instead of 10 mm, for T1a melanoma was not associated with worse outcomes. These findings may be useful for future melanoma treatment guidelines.

High-Resolution Skin Ultrasound Mapping And Marking With Color Doppler Analysis For The Management Of Residual Squamous Cell Carcinoma In Situ: A Case Report

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Background: Skin cancer is the most frequently diagnosed malignancy worldwide. High-resolution ultrasonography is a noninvasive, versatile imaging modality whose use in dermatology—including the evaluation of cutaneous cancers—has expanded rapidly.

Objective: We present the case of a male patient with a history of multiple cutaneous squamous cell carcinomas in situ and comorbidities with physical disability that precluded surgery under general anesthesia or conventional Mohs micrographic surgery.

Methods: The study was performed using 18- and 22-MHz high-resolution transducers, with color Doppler analysis, and a FLIR E54 thermographic sensor with analysis in Thermofy software.

Results: The lesion had a depth of 1.4 mm, infiltrating the dermo-hypodermal junction, with a slight increase in echotexture at the dermo-hypodermal junction and superficial hypodermis, extending 13 mm in the lateral–lateral diameter and 15 mm in the cranio-caudal diameter. Margin marking was performed under ultrasound guidance. No nodular images suggesting satellitosis were identified within a 20 cm evaluation radius, and no preauricular lymphadenopathy was detected. Using that mapping, surgical excision of the lesion was performed, leaving the wound with a purse-string suture for secondary-intention healing. Histopathology using a staged ("slow") Mohs technique showed tumor-free (negative) margins.

Conclusion: Skin ultrasonography is a technique that facilitates detection and assessment of the extent of the primary tumor and its surgical planning, as well as locoregional staging.

The 31-Gene Expression Profile is an Independent Predictor of Poor 5-Year Outcomes and Identifies High-Risk Cutaneous Melanoma in Patients with a Negative Sentinel Lymph Node

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Background: Certain patients with cutaneous melanoma (CM) are at increased risk for recurrence despite a negative sentinel lymph node (SLN) biopsy. Accurate identification of these high-risk patients is necessary to improve management decisions and outcomes. The 31-gene expression profile (31-GEP) uses tumor biology to stratify risk of recurrence, metastasis, or death as low (Class 1A), intermediate (Class 1B/2A), or high (Class 2B).

Objective: Evaluate the independent prognostic contribution of the 31-GEP in SLN-negative patients and its ability to identify tumors at high risk of recurrence.

Methods: This multi-center, retrospective analysis included 31-GEP-tested, SLN-negative patients (2013-2018). Kaplan-Meier analysis was used to estimate 5-year recurrence-free survival (RFS) and the log-rank test compared differences between groups. Multivariable Cox regression was used to identify significant predictors of recurrence. Interaction terms determined whether the 31-GEP adds independent prognostic value for predicting recurrence beyond Breslow depth. Analysis of deviance assessed whether adding 31-GEP to AJCC staging improved recurrence prediction.

Results: Among patients with SLN-negative CM (n=810), including T1–T2 tumors (n=596), the 31-GEP significantly stratified 5-year RFS (All: Class 1A=93.1%, Class 1B/2A=83.8%, Class 2B=74.9%; p0.001 and T1–T2: Class 1A=94.4%, Class 1B/2A=84.7%, Class 2B=73.1%; p0.001). No significant interaction was detected between 31-GEP Class and Breslow depth (p0.05). Combining 31-GEP testing with AJCC staging significantly improved risk prediction compared with staging alone (p=0.02). Multivariable analysis identified Class 2B as a significant prognostic factor (HR=2.23, 95% CI=1.26–3.95).
Conclusion: The 31-GEP significantly and independently stratified recurrence risk in SLN-negative CM patients, allowing clinicians to make risk-aligned management decisions.

Importance of SPRED1 in cutaneous melanoma

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Background: Inactivating germline SPRED1 variants cause Legius syndrome, characterized by neurofibromatosis type 1 (NF1)- like pigmentation abnormalities. Spred1-/- mice exhibit hyperpigmentation, similar to Nf1 flox/flox mice, suggesting Spred1 loss affects melanocyte biology. NF1, frequently mutated in cutaneous melanoma (CM), encodes neurofibromin which interacts with SPRED1 to negatively regulate the RAS-MAPK pathway. SPRED1 is altered in 4% of CM and low SPRED1 expression correlates with poor prognosis and MAPK therapy resistance. However, the role of SPRED1 in CM remains understudied.

Objectives & Methods: To investigate Spred1 in melanogenesis, levels of melanin and melanin-producing melanocytes in the interfollicular epidermis of Spred1-/- and WT mice were quantified. Hyperpigmentation was further examined by inactivating Spred1 at postnatal day 23, 25 and 28 in TyrCre;Spred1 mice. To evaluate how Spred1 loss affects melanoma initiation, CM was induced in Braf;Ink4a, crossed with Spred1flox/flox mice (Braf;Ink4a;Spred1). Differential gene expression and enrichment analyses were performed on RNAseq data from Braf;Ink4a(;Spred1) tumours. CM progression and metastasis were assessed by immunohistochemistry and fluorescence microscopy.

Results & Conclusions: Tail skin hyperpigmentation in Spred1-/- mice was caused by significantly increased epidermal melanin and melanin-producing melanocytes. In TyrCre;Spred1 mice hyperpigmentation was absent, suggesting Spred1's importance during early melanogenesis and melanocyte development. The risk for CM development in Braf;Ink4a;Spred1 mice significantly increased to 87% with a latency of 3,3 months compared to 21% and 7 months in Braf;Ink4a mice, but without metastasis. Enrichment analysis showed significant upregulation of immune related Gene Ontology (GO) terms and significant downregulation of melanogenesis and skin development GO terms.

Metastatic Melanoma With Germline CDKN2A And BRAF V600E Mutations: A Fatal Case In A 46 Year Old Male

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Background: Approximately 9% of melanomas are melanomas of unknown primary (MUP). Familial melanoma accounts for 5-10% of cases and is associated with germline CDKN2A mutations. These mutations can cause melanoma-pancreatic cancer syndrome with autosomal dominant inheritance. Current NCCN guidelines recommend genetic counseling for patients with three or more invasive melanomas or specific family history patterns.

Objectives: To report a case of metastatic melanoma with CDKN2A and BRAF mutations and highlight the consequences of delayed genetic screening in families with hereditary cancer syndromes.

Methods: A 46 year old male presented with a left neck mass. We performed CT imaging, excisional biopsy with H&E staining and immunohistochemistry, CARIS molecular profiling, and genetic testing. Family members underwent genetic screening after diagnosis.

Results: CT showed extensive left supraclavicular, subcarinal, and left hilar adenopathy with osseous metastases. Biopsy confirmed malignant melanoma positive for MART1, S100, WT1, and BCL2. No primary cutaneous lesion was identified. Molecular profiling revealed BRAF V600E mutation. Genetic testing showed c.47_50del CDKN2A mutation. Family screening identified multiple carriers including mother, brother, and son. Several family members had died from melanoma without prior diagnosis. Patient received ipilimumab and nivolumab but developed grade 3 colitis after two cycles. He developed malignant pleural effusions requiring repeated thoracentesis and died three weeks after treatment discontinuation.

Conclusion: This case demonstrates fatal outcomes from delayed diagnosis of familial melanoma. Screening for CDKN2A mutations should be considered in patients with family history of melanoma or pancreatic cancer. Early detection could potentially improve survival outcomes in hereditary melanoma syndromes.

Implication of Alpha-Genus Papillomaviruses in Cutaneous Squamous Cell Carcinoma

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Background: Cutaneous squamous cell carcinoma (cSCC) is mainly driven by ultraviolet (UV) radiation, but β-human papillomavirus (HPV) types may contribute to its development. While α-HPV is a known cause of mucosal cancers, its role in cSCC remains unclear. This study investigates the presence and potential oncogenic role of α-HPV, particularly HPV16 integration, in cSCC.

Methods: We retrospectively analyzed 129 formalin-fixed paraffin-embedded cSCC samples collected from 2017 to 2022. α-HPV was detected using Anyplex™II HPV 28; 99 samples were additionally tested with INNO-LiPA. β- and γ-HPV were detected using a Luminex-based assay. HPV16 DNA integration was assessed via real-time PCR (E2/E6 ratio).

Results: Among 129 samples (99 invasive cSCC, 30 Bowen's disease), 58 patients were immunosuppressed. HPV was detected in 56.6% of cases, with 25 (19.4%) positive for α-HPV. All α-HPV-positive samples carried a single type, most commonly HPV16 (10/25, 40%). Integration of HPV16 DNA was confirmed in 8 of 9 assessable cases. Other types included HPV26, 33, 45, 51, 56, 66, 73, and 82. Healthy surrounding skin was HPV-negative in 10 of 11 tested cases.

Conclusion: The detection of high-risk α-HPV, particularly HPV16 with DNA integration, supports its potential role in cSCC pathogenesis. Unlike β-HPV, α-HPV may act as a direct carcinogen. These findings highlight the need for further research and suggest possible implications for vaccination, screening, and treatment, especially in immunosuppressed populations.

Intralesional interleukin-2 therapy is highly effective in treatment of cutaneous squamous cell carcinoma

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Background: Since 2017, we have treated 17 patients with cSCC using intralesional interleukin-2 (iIL2), drawing on our success with melanoma and its favorable efficacy–toxicity profile. Patients were generally poor surgical candidates or had tumors in cosmetically sensitive sites where intralesional therapy offered an alternative to extensive surgery.

Objective: Herein we report findings from our prospectively collected, non-randomized cSCC patient cohort treated with our iIL2-based immunotherapy regimen.

Methods: All patients had histologically confirmed cSCC. Informed consent outlining the experimental nature of this protocol and common expected side effects was obtained. iIL2 was administered at a concentration of 0.1mL/2mm2-clinically positive lesion (500,000 i.u./ 0.1ml). A maximum dose of 4,000,000 i.u. of iIL2 distributed into up to eight separate injection sites was administered during the first treatment.

Results: Between 2017 and 2024, 17 cSCC patients (mean age 78, median ASA 2) received iIL2; average number of treatments was 10, with a mean treatment duration of 12 months. Progression-free survival was 20 months, with a complete response rate of 82% (14/17). Only grade I/II adverse events were observed.

Conclusion: IL-2 based immunotherapy is extremely effective in the treatment of cSCC. We observed complete and durable responses in 14 of our 17 patient cSCC cohort. Treatment was very well tolerated with no grade III-IV toxicity observed in any patient and obviated the need for advanced and potentially mutilating surgical procedures in some patients. IL-2 should be considered as first line therapy in patients with significant co-morbidities and patients with cSCC in surgically sensitive areas.

Merkel Cell Carcinoma of Unknown Primary Presenting as Deep Vein Thrombosis: Salvage Dual Checkpoint Inhibition After Pembrolizumab Failure

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Background: Merkel cell carcinoma (MCC) is an aggressive neuroendocrine malignancy that rarely presents as venous thromboembolism. Although checkpoint inhibitors have transformed frontline therapy with impressive response rates, managing refractory disease remains a significant clinical challenge. Notably, about 4% of MCC cases lack an identifiable cutaneous primary site.

Objectives: To describe an atypical presentation of MCC manifesting as deep vein thrombosis (DVT) and report outcomes with combination checkpoint inhibition after pembrolizumab failure.

Methods: A gentleman in his 60s presented with progressive left leg swelling. Workup revealed extensive DVT caused by external compression from a bulky 10.1×5.2cm inguinal lymph node mass. Biopsy demonstrated poorly differentiated neuroendocrine carcinoma with unusual CK20-negative staining. Molecular profiling (Caris) was crucial, detecting Merkel cell polyomavirus and confirming MCC with 84% probability. Staging revealed Stage IV disease with osseous and mediastinal involvement.

Results: The patient started pembrolizumab. After 4 cycles, restaging showed significant progression - pelvic mass increased to 17.5×12.1cm and mediastinal disease progressed. Despite MCPyV-positivity, biomarkers were unfavorable: PD-L1 0%, TMB 3 mut/Mb, MSI-stable. Treatment was switched to ipilimumab/nivolumab. The patient developed hypercalcemia and obstructive uropathy requiring nephrostomy. Palliative radiation to the pelvic mass achieved local control, though unirradiated sites progressed.

Conclusion: This case demonstrates mechanical vascular compression as a presenting feature of occult MCC, highlights CK20-negative disease requiring molecular confirmation, and provides evidence that dual checkpoint inhibition can achieve responses in pembrolizumab-refractory patients with poor predictive biomarkers. The differential response between radiated and unirradiated sites suggests potential synergy worth exploring.

Trends of Non-Melanoma Skin Cancer Treatment as the Society Ages

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Background: As society ages, non-melanoma skin cancer (NMSC) cases have increased. Radiation therapy (RT) is effective for treating NMSC, particularly in elderly patients.
Objectives: This study was aimed at analyzing NMSC treatment changes in Jeju Province over the past five years and elucidating the role of RT.

Methods: We retrospectively analyzed the medical records of 376 patients diagnosed with facial NMSC between March 2018 and August 2023, and collected data regarding their age, sex, pathological disease type, tumor size and location, treatment, and recurrence.

Results: Of 237 patients treated, 141 and 96 underwent wide resection and RT, respectively. Histological examination revealed 137 and 115 cases of basal cell carcinoma and squamous cell carcinoma, respectively. The predominant tumor locations were the nose (n = 77), cheeks (n = 64), and periorbital area (n = 38). RT was used for 58 and 39 T1- and T2-stage tumors, respectively, while the corresponding surgery-associated numbers were 126 and 18. Treatment pattern analysis revealed that the RT rate increased and surgery rate decreased from 12.4% to 40.5% and from 87.6% to 59.5%, respectively. The mean patient ages at surgery and RT were 76.4 and 80.5 years, respectively ($p = 0.045$).

Conclusion: Compared with the 2010–2015 data, the March 2018–August 2023 data indicated a notable increase in the average patient age and a substantial increase in NMSC incidence. Furthermore, a treatment pattern change from surgery to RT was observed. The RT increase was closely correlated with the elderly population increase.

The Development of Patient Specific Immobilization Device for Non-Melanoma Nasal Skin Cancer

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Purpose: We developed the patient specific immobilization device related for radiotherapy with the facial non-melanoma skin cancer when the cancer is located on the nose.

Methods: The three main materials as the plastic zip, the ruler, and the nail tip were used to make the immobilization device. For the cavity and flexibility of the nose, the facial phantom was made by using the silicone rubber. The reference CT image of 2 mm thickness were obtained without bolus and immobilization. After then CT images were obtained for the facial phantom covered with bolus on the nose about with and, without applying the immobilization device. We evaluated the expansion of the nasal cavity compared with reference CT and the immobilization device applied CT. The gaps between the bolus and nose surface were measured at the specific locations through comparison between when the immobilization device was inserted and not.

Results: When the patient specific immobilization device was applied, it was confirmed that the geometric distance between the skin and the bolus. The nasal cavity was expanded about 2.0 mm. As a result of measuring the gap between skin and bolus at the same position in the same slice on CT, it was confirmed that the gap can be reduced to 1.2 mm to 2.4 mm.

Conclusion: In the case of facial non-melanoma skin cancer with tumors in the nose, the developed patient specific immobilization device can reduce air gap between the skin and bolus.

i31-SLNB for Cutaneous Melanoma Outperforms Clinicopathologic-Only MIA Nomogram at Identifying Patients at Low Risk of Having Positive Sentinel Lymph Node Biopsy: A Prospective, Multicenter Study

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Background: Up to 88% of sentinel lymph node biopsies (SLNB) for cutaneous melanoma (CM) are negative, while 15% of patients experience surgery-associated morbidities. Therefore, tools to decrease unnecessary SLNBs are needed. The Melanoma Institute Australia (MIA) developed a clinicopathologic-based nomogram to predict SLN positivity. The integrated 31-gene expression profile for SLNB (i31-SLNB), which combines the 31-GEP score with clinicopathologic factors, is validated to improve SLN positivity prediction over AJCC staging. Here we compared the accuracy of the i31-SLNB and the MIA nomogram in a prospective cohort.

Methods: This prospective, multicenter US-based study included 430 patients with T1–T4 tumors who underwent SLNB and had i31-SLNB. The i31-SLNB and MIA nomogram were compared using area under the receiver operating characteristic curve (AUC) and using DeLong's test. Decision curve analysis (DCA) compared clinical net benefit.

Results: In patients predicted to have 5% risk of SLN positivity by the i31-SLNB (n=114, 26.5%), SLNB positivity rate was 2.6%. Fewer patients were predicted to have 5% risk of SLN positivity by MIA (n=69, 16.1%) and these had a positivity rate of 5.8%. The i31-SLNB (AUC=0.74) performed significantly better than MIA nomogram (AUC=0.61; p=0.001). DCA demonstrated the superior clinical benefit of i31-SLNB versus MIA.

Discussion: The i31-SLNB more accurately identified patients at high and low risk of SLN positivity than the MIA nomogram. Utilizing i31-SLNB to aid SLNB decision-making can help low-risk patients safely avoid unnecessary SLNB, decreasing associated morbidities.

Palatal Relapse of Mycosis Fungoides After Total Skin Electron Therapy: Successful Salvage with Volumetric Modulated Arc Therapy

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Background: Oral involvement of Mycosis fungoides (MF) is rare, with fewer than 100 reported cases, most commonly affecting the tongue and palate. Total skin electron therapy (TSET) is effective in advanced-stage MF, but extranodal mucosal relapses are unusual and clinically challenging.

Objectives: To describe a rare case of MF relapse involving the hard palate post-TSET and its successful salvage using volumetric modulated arc therapy (VMAT).

Case Presentation: A 22-year-old male with stage cT4N0M0B0 MF received ECP and localized radiation for large cutaneous tumors, followed by TSET (36 Gy in 18 fractions) completed in November 2023. In January 2024, he developed a rapidly enlarging palatal lesion. PET-CT showed an FDG-avid mass (SUV 6.7) involving the proximal hard palate and alveolar bone. Biopsy confirmed CD8-positive T-cell lymphoma. He received CHP-BV chemotherapy with no response.

Results: In May 2024, the patient underwent VMAT-based re-irradiation to the palatal lesion (20 Gy in 5 fractions). He experienced rapid symptomatic relief and complete clinical regression. Remission was sustained at six-month follow-up.

Conclusions: This case highlights an unusual palatal relapse of MF post-TSET and the effectiveness of VMAT as a salvage modality. Palatal involvement significantly impacts quality of life due to pain and feeding difficulty. Re-irradiation with precision radiation techniques like VMAT can offer durable and meaningful local control in select cases.

High-Frequency Ultrasound in Merkel Cell Carcinoma: A Case-Based Narrative Review Highlighting Diagnostic, Prognostic and Follow-Up Relevance

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Background: Merkel cell carcinoma (MCC) is a rare and aggressive cutaneous neuroendocrine tumor with a rising incidence. Early diagnosis and accurate follow-up are critical but often delayed due to the tumor`s subtle clinical presentation. While histopathology remains the diagnostic gold standard, imaging—particularly high-frequency ultrasound (HFUS)—can offer meaningful support in clinical decision-making.

Objectives: To present a clinical case of MCC and to highlight the potential role of HFUS as an adjunctive tool for both diagnosis and longitudinal management.

Methods: We report the case of an elderly patient with a rapidly enlarging nodular lesion on the dorsal aspect of the third finger. A 22 MHz linear HFUS probe (Samsung V6, Hoskey Stick) was used. Sonographic examination revealed a hypoechoic, non-compressible solid mass with irregular margins, marked vascularization on color Doppler. These imaging findings raised clinical suspicion of malignancy and led to prompt surgical excision and histopathological evaluation.

Results: Histology confirmed MCC with positive surgical margins. HFUS was subsequently employed for serial follow-up to monitor for local recurrence and guide further treatment decisions. Sonographic findings correlated well with the

clinical course and proved particularly useful in detecting early subclinical changes during follow-up.

Conclusion: HFUS is a promising yet often overlooked imaging modality in the management of MCC. It provides real-time, non-invasive insight into lesion morphology and vascularity, supporting earlier diagnosis and safer surveillance, particularly in elderly or frail patients.

Evaluation of the Viscoelastic Properties of Skin Cancers by Non-Contact Palpation based on Surface Wave Propagation

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Background: Many pathologies involve structural changes in the multilayered structure of skin tissue, resulting in changes to its mechanical properties such as viscoelasticity. These changes are difficult to palpate, making it necessary to carry out additional medical tests, with quantifiable measurements, in order to obtain a complete understanding of the physical asperities.

Objectives: This study introduces a new method for characterizing the mechanical properties of tumoral and non-tumoral human skin ex vivo. It aims to aid dermatological diagnosis and create a database for artificial intelligence research.

Methods: A non-invasive, non-contact palpation method was developed. It mechanically generates airflow to create ripples on the skin surface. Analyzing this wave dispersion via Fourier transform and a skin-specific inversion model provides a detailed view of wave propagation in the subsurface. This offers new insights into the mechanical responses of basal cell carcinomas (BCC) and squamous cell carcinomas (SCC). The study analyzed over 150 BCC specimens, 50 SCC specimens, and 20 healthy skin samples. Line-field confocal optical coherence tomography (LC-OCT) characterized each specimen`s epidermal, dermal, and tumor thickness for correlation with mechanical data.

Results: The findings display the viscoelastic properties of the tumors compared to healthy skin for each layer, alongside a dermatologist`s tactile analysis.

Conclusion: Although dermatologists are able to feel and have a good overall assessment of what they palpate, they are so far unable to quantify it and indicate where firmness or softness comes from, which is necessary to make an accurate diagnosis, prognosis, treatment, future surgery and teledermatology.

Change in Cutaneous Melanoma Aggressiveness Over Time

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Background: After 1980, melanoma deaths is progressively decreasing among people under 60.

Objective: To examine if changes in the disease contribute to these decreases.

Methods: First, we looked at age-specific trends in melanoma deaths based on diagnosis years in Nordic countries. Next, we searched for studies that reported incidence trends of melanoma by stage or thickness over at least 10 years. Then, we explored studies that reported the risk of dying from melanoma based on the year of diagnosis, adjusting for survival factors such as age (mandatory factor), thickness (mandatory factor), ulceration or body site.

Results: From 1965 to 2022, melanoma death rates increased in older groups but decreased in younger ones. While deaths fell in those under 60, 13 studies from 1980 to 2021 showed stable or rising incidence rates of advanced-stage or thick melanomas in these individuals. In 17 studies from 1970 to 2007, the adjusted hazard ratio for melanoma survival decreased from earlier to more recent diagnosis years.

Discussion: Cutaneous melanomas are evolving into a less aggressive disease over time. This change coincides with reduced exposure to ultraviolet radiation in early life, moving away from the peak exposure period of 1920-1960. Due to decreased aggressiveness, metastatic melanomas tend to be rarer in younger individuals, whereas they tend to concentrate in older individuals when the age-related decline of the immune system can no longer resist the progression of melanomas with a metastatic phenotype.

Quality of Life in Colombian Patients with Cutaneous Malignant Neoplasms

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Background: The assessment of quality of life (QoL) has gained relevance comparable to mortality and morbidity endpoints in cancer. In Colombia or Latin America, no studies have been found that evaluate the impact of cutaneous malignant neoplasms on quality of life.

Objective: To evaluate the impact of cutaneous malignant neoplasms on QoL in Colombian patients.

Methods: This was a descriptive cross-sectional study that included patients older than 16 years whom were collected prospectively and retrospectively. Sociodemographic and clinical information was gathered. For quality-of-life assessment, we used the Colombian-validated version of the Skindex-29 and the Spanish version of the Dermatology Life Quality Index (DLQI).

Results: The prospective sample included 126 patients (mean age: 66.3 years) The retrospective sample included 111 patients(mean age: 58.6 years). The main diagnoses in both groups were basal cell carcinoma, squamous cell carcinoma, melanoma, and mycosis fungoides. Global Skindex-29 scores had medians of 12.9 and 17.2 for the prospective and retrospective groups. Higher scores were observed in women. Higher global scores were found for melanoma and mycosis fungoides in the prospective group, and for squamous cell carcinoma and mycosis fungoides in the retrospective group; however, the emotional domain was notably affected across all tumors. A strong correlation was found between the global Skindex-29 and DLQI scores.

Conclusion: This study confirms that skin cancer primarily impacts the emotional domain of health-related QoL, with women being the most affected. It is therefore important to identify any HRQoL impairment—preferably using the Skindex-29—in patients with skin cancer.

The Role of Early Detection in Reducing Malignant Melanoma Mortality: A Systematic Review

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Background: Malignant melanoma is one of the most aggressive skin cancers, and prognosis depends on the stage at diagnosis. Patients with thin melanomas (≤1 mm) achieve more than 90% 10-year survival, underscoring the importance of early detection.

Objectives: To evaluate the impact of early detection strategies on stage at diagnosis and melanoma-specific mortality.

Methods: A systematic review was conducted using literature from PubMed, Google Scholar, Wiley Online Library, and ScienceDirect. Eligible studies included retrospective and prospective cohorts investigating early detection of melanoma. The primary outcome was reduction in melanoma-specific mortality. Study quality was assessed using Joanna Briggs Institute (JBI) tools.

Results: Five studies were included. Whole-body skin examination (WBSE) consistently identified melanomas at earlier stages and with thinner Breslow thickness. Population-based programs, such as the Schleswig-Holstein and SCREEN initiatives in Germany, demonstrated feasibility and effectiveness in large cohorts. Observational and case-control studies indicated that systematic WBSE may contribute to earlier diagnosis and potential mortality reduction. WBSE was also reported to be cost-effective, supporting its adoption in community-based health programs.

Conclusion: Early detection, particularly WBSE, improves prognosis and may reduce melanoma mortality. Structured screening programs could provide substantial clinical benefit and should be considered within public health policy, especially in regions with rising incidence.

Keywords: Malignant melanoma, early detection, screening, whole-body skin examination, mortality

Radiotherapy and Cutaneous Mastocytosis: A Rare Association?

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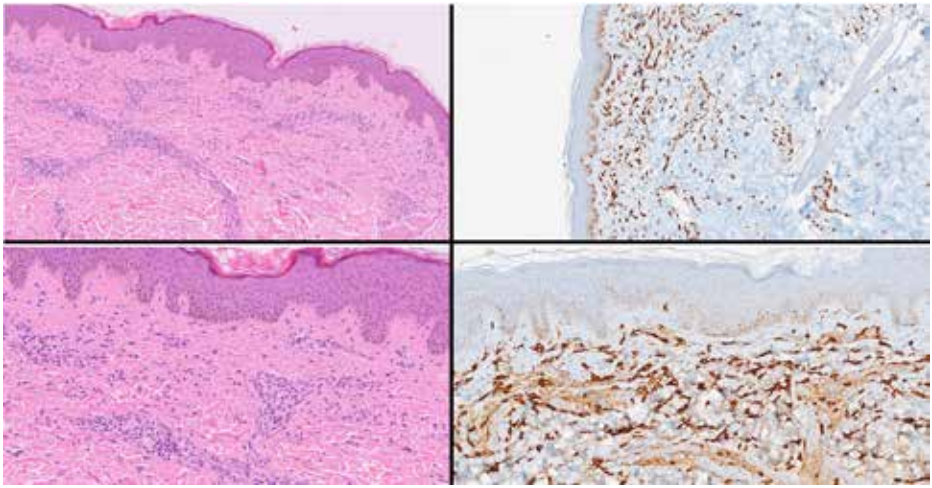
This case report describes two patients: a 52-year-old woman who received 50 Gy of radiotherapy to the right breast 16 years ago and has presented with skin lesions for the past 6 years, and another 55-year-old woman who underwent radioactive iodine treatment for papillary thyroid cancer 10 years ago and has been followed for cutaneous mastocytosis for 6 years. In the first case, a biopsy revealed mast cells and eosinophils in the papillary dermis with a lymphohistiocytic infiltrate, which was positive for tryptase and CD117, with elevated serum tryptase levels. Bone marrow analysis was not performed, and a provisional diagnosis of "cutaneous mastocytosis" (CM) was made, with close follow-up due to the potential of systemic mastocytosis (SM). In the second case, bone marrow biopsy did not meet the criteria for systemic mastocytosis, but the patient showed clinical improvement with treatment that included omalizumab and PUVA therapy. These two cases represent the first reported instances of radiotherapy-induced mastocytosis in Turkey, and they are among the rare examples found in the literature. To date, only 13 cases of radiotherapy-induced cutaneous and systemic mastocytosis have been reported, and the pathogenesis remains unclear. It is hypothesized that clonal mast cell proliferation is triggered in the irradiated area in association with the Koebner phenomenon. This case emphasizes the need for further investigation into the effects of radiotherapy on mast cells, the relationship between mast cells and malignancies, and the rare complications of radiotherapy.

Figure 1 A.B.C: *Red-brown macular rashes, 3-4 mm in diameter, observed on the right side of the body and chest.*

Figure 2: *Mast cells concentrated in the superficial dermis in perivascular areas (H&E stain). Mast cells were positive for CD117 (IHC), and positive reaction with tryptase (Triptase-IHC).*

Figure 3: *Red-brown macules and papules, 3-5 mm in diameter, on the back and upper trunk*



The Sun Balance Study: Tailoring Education about the Harms and Benefits of Sun Exposure

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Background: Exposing the skin to sunlight has both harms and benefits, and the balance is not the same for everybody. A new position statement has been developed which recognises the balance, but the information is complex and nuanced.

Objectives: We aimed to determine whether receiving tailored educational materials changes participants' knowledge, attitudes, and behaviours with respect to sun exposure and vitamin D.

Methods: We recruited Australians aged 18 years and over via email lists and social media. Participants completed an online questionnaire assessing sun exposure and vitamin D knowledge, attitudes, and behaviours. They were then provided with educational materials specific to their skin cancer risk profile and residential location, after which they completed a second questionnaire.

Results: 515 participants were included (average age 58 years; 73% female). Most participants were considered high risk (n=422; 82%).
The percentage of people who correctly identified the UV index above which sun protection is required increased from 45% to 95%. Knowledge of the time needed to maintain adequate vitamin D increased (e.g., with 35% skin exposed in summer: 36% to 69%), as did the intention to use sunscreen every day (face: 42% to 58%; hands/arms 15% to 37%). After education high-risk participants were more likely to be aware of the need to meet vitamin D requirements through supplementation (33% to 48%).

Conclusion: Tailored educational materials, stratified to skin cancer risk and location, lead to improved knowledge and attitudes regarding the harms and benefits of sun exposure, and to intentions to improve behaviour.

Risk Factors for Thick Melanoma and for Melanoma Death: Implications for Screening

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Background: The primary goal of skin screening is to avoid death caused by cutaneous melanoma. However, early detection efforts are currently guided by risk factors for melanoma occurrence, which may differ from risk factors for melanoma death. Few studies have examined determinants of thick melanoma or of melanoma death.

Objective: To perform a systematic review of the literature on genetic, phenotypic and lifestyle factors associated with an outcome encompassing pathological characteristics of aggressive melanoma (e.g., thickness), and melanoma death.

Methods: A systematic search of Medline was preformed for articles exploring relationships between any other risk factor and outcomes. To avoid false negatives, all articles having an outcome in their title or abstract were fully read, so that negative results on a risk factor not mentioned in abstracts was avoided.

Results: We found no evidence for an association between the following classic risk factors for melanoma occurrence and advanced melanoma or melanoma death, i.e., higher socio-economic status, light-skin complexion/hair colour/eye colour/freckles, poor tanning ability, history of sunburn, cumulated sun or sunbed exposure, increasing number of common or of atypical nevi, solar keratoses. In contrast, the following risk factors were associated with advanced melanoma or melanoma death, i.e., age, male sex, migration, lower socio-economic status, low education level, loneliness/living alone, being unmarried/divorced, bereavement, diabetes, obesity, current smoking, sleep disorders.

Conclusions: The perspective of skin screening should be modified towards greater involvement of subjects at higher risk of advanced melanoma and of melanoma death.

RECQL4 Overexpression Fosters Immune Escape and Anti-PD-1 Resistance in Melanoma

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Background: Immune checkpoint inhibitors (ICI) have improved survival in advanced melanoma, but resistance remains a major challenge. DNA repair pathways are increasingly recognized as modulators of immunotherapy response. RECQL4, a DNA helicase essential for genomic stability, has been associated with poor outcomes in several cancers, but its role in melanoma and ICI efficacy is underexplored.

Objective: To assess the impact of RECQL4 expression on survival and ICI response in melanoma patients.

Methods: Transcriptomic data were analysed from melanoma cohorts of untreated patients (n=471) and anti-PD-1–treated patients (n=212). Prognostic significance was evaluated with Kaplan–Meier and Cox regression models. RECQL4 expression was compared between responders (n=95) and non-responders (n=86) to anti-PD-1 therapy. Immune cell infiltration and pathway alterations were evaluated by RNAseq-based deconvolution and gene set enrichment analyses. Functional validation included RECQL4-engineered melanoma cell lines subjected to proteomic and mechanistic studies which complemented clinical observations.

Results: Elevated RECQL4 expression was linked to shorter survival in both untreated (DFS, p0.01; OS, p0.001) and anti-PD-1–treated patients (PFS, p=0.02; OS, p0.001). Multivariate analysis confirmed RECQL4 as an independent prognostic factor. Non-responders to anti-PD-1 therapy exhibited significantly higher RECQL4 levels (p=0.03). Tumours with high RECQL4 expression showed diminished infiltration by CD8+ and CD4+ T cells, and suppression of interferon responses and antigen presentation pathways. Mechanistic analyses confirmed that RECQL4 overexpression suppressed CIITA and MHC-II expression, fostering immune evasion.

Conclusion: RECQL4 overexpression may identify melanoma patients resistant to ICIs. Assessing RECQL4 in clinical practice could refine patient stratification and guide novel therapeutic strategies.

Clinical Outcomes and Toxicity of Combined Ipilimumab and Nivolumab in Rare Melanomas – a Nationwide Population-Based Study

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Background: Immune checkpoint inhibitors (ICIs), especially combined anti-CTLA-4/ anti-PD-1 have improved outcomes for advanced cutaneous melanoma (CM).

Mucosal, uveal, and acral melanoma (MM, UM, and AM) seem less immunogenic than CM, and the benefit of anti-CTLA-4/anti-PD-1 treatment is unclear.

Objectives: This study assesses clinical outcomes and toxicity of combination of ipilimumab and nivolumab in advanced MM, UM, and AM using nationwide real-world data.

Methods: Patients with advanced MM, UM, and AM treated with first-line ipilimumab/nivolumab from 2016 to 2025 were included from the Dutch Melanoma Treatment Registry. Patient and tumor characteristics, as well as toxicity, were described, and overall response rates (ORR) were calculated. Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method.

Results: 124 Patients with MM, 28 patients with UM, and 45 AM were included. ORR was 37.8% for patients with MM, 22.2% for UM, and 39.0% for AM. Median PFS was 3.5 months (95%CI 3.0-5.5) for MM, 3.5 months (95%CI 2.8-6.6) for UM, and 3.0 months (95%CI 2.6-6.4) for AM. Median OS was 13.8 months (95%CI 9.7-19.9) for MM, 11.3 months (95%CI 8.2-23.7) for UM, and 15.4 months (95%CI 7.4-NA) for AM. Grade ≥3 toxicity occurred in 36.3% of MM, 39.3% of UM, and 31.1% of AM.

Conclusion: Our study indicates that patients with advanced rare melanomas treated with ipilimumab/nivolumab have a relatively poor prognosis. International collaboration and novel clinical trials are essential to improve outcomes for patients with advanced MM, UM, and AM.

The Role of Nucleotide Excision Repair (NER) in endogenous and exogenous mutagenicity

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Xeroderma Pigmentosum (XP) is caused by a deficiency in nucleotide excision repair (NER), leading to extreme sensitivity to UV damage and a greatly elevated risk of skin cancer. Beyond UV-induced lesions, XP patients-especially those with XPC deficiency-show increased internal cancer risks and a distinct mutagenesis related to purine residues. The mechanisms behind this remain unclear but may involve both endogenous and exogenous genotoxins such as acetaldehyde, formaldehyde, and benzo[a]pyrene.

This project investigates how impaired NER influences mutational burden and signatures upon chronic exposure to widespread genotoxic agents. Using whole-genome sequencing of single-cell derived clones, we aim to:

In vitro: Analyze mutational landscapes in isogenic XPC-/- and WT human cell lines exposed to genotoxins.

In vivo: Assess mutational consequences in hematopoietic stem cells and internal organs of XPC-/- and WT mice following .

Comparative analysis: Compare experimental data with mutational signatures from large-scale cancer genome datasets (PCAWG and HARTWIG) and with XPC-deficient leukemia profiles.

Methodologically, we apply chronic genotoxin treatments in cell lines and mouse models, followed by WGS and computational deconvolution of mutational signatures. The goal is to define the contribution of NER deficiency to mutagenesis, clarify environmental and endogenous drivers, and link them to mutation patterns observed in human cancers.

Whole-genome sequencing (WGS) analysis of cells treated with Cisplatin, KBrO3, and BPDE revealed an increased mutation rate along with partial emergence of Signature 8 (SBS8) in XPC-deficient cells. WGS of hematopoietic stem cells (mHSCs) isolated from untreated 4-month-old mice showed a higher mutation burden, with a prominent

presence of SBS8 in XPC-KO mice. This suggests that SBS8, a mutational pattern observed in internal tumors of XPC-deficient patients, may arise independently of cancer and could be linked to an endogenous mutagenic process.
Comparison of mutator phenotypes between 4- and 8-month-old mice demonstrated a significant increase in mutagenesis in the older cohort, with persistent detection of SBS8. Mice treated with Cisplatin, Benzo[a]pyrene (BaP), and KBrO3 displayed the Cisplatin mutational signature in both wild-type (WT) and XPC-KO mice, with a notably higher mutation load in XPC-KO animals.
Ongoing studies involving additional genotoxins aim to further clarify these effects. Comparative analyses of mutational profiles from in vitro and in vivo experiments are expected to elucidate the mutational processes induced by these genotoxins and their interplay with XPC deficiency.

Advanced BRAF-mutant Malignant Melanoma with Rare Abdominal Dissemination – Targeted Therapy and the Challenges of Complex Care

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Introduction: Modern treatment options have significantly improved the prognosis even for patients with advanced melanoma and high tumor burden. Targeted and immunotherapies enable rapid and effective tumor response, contributing to prolonged survival.

Case Presentation: In 2014, a pT2a melanoma was excised from the trunk of a 47-year-old woman. Sentinel biopsy showed micrometastasis, but axillary dissection was negative. She received adjuvant interferon and was followed until 2022.

In March 2025, she presented with abdominal distension and leg swelling. Imaging showed extensive retroperitoneal and peritoneal masses with ascites. Cytology confirmed metastatic melanoma with BRAF V600 mutation.

Given the high tumor burden, BRAF–MEK inhibitor therapy was started. Baseline CT scan showed extensive intra-abdominal dissemination, a right-sided pulmonary embolism and filling defects in both femoral and external iliac veins. During treatment, tumor lysis syndrome and severe anemia developed, due to intratumoral hemorrhage. CT angiography identified the primary bleeding source, which was successfully embolized.

The patient stabilized, therapy continued, and by July 2025 CT showed significant regression with ECOG improvement from 4 to 0. After 8 weeks, treatment was switched to ipilimumab–nivolumab for better long-term survival expectations.

Conclusion: Previously, extensive viseral metastases allowed only palliative attempts. In our case, initiation of targeted therapy resulted in a rapid and substantial tumor response. Following early, significant tumor mass reduction, we switched to immunotherapy to optimize therapy sequencing. With current therapeutic options and a multidisciplinary approach, long-term survival is achievable for patients with advanced melanoma, even in the presence of massive tumor burden and serious complications.

Cancer Genomics of Basal Cell Carcinoma: Origins and Progression

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Basal Cell Carcinoma (BCC) is the commonest type of skin cancer which has not been yet studied by whole genome sequencing (WGS). We have assembled a large BCC cohort representing major histological subtypes for genomic and transcriptomic analyses. Mutational profile in BCC is due to UV-light exposure, however it differs from melanoma by high fraction of COSMIC signature SBS7b mutations due to high contribution to mutagenesis of GC-rich early replicating regions, which in BCC are characterized by more condensed and difficult to repair chromatin. We report that loss of TP53 is the first driver event in BCC resulting in a dramatic increase of mutation rates. We discovered novel BCC driver genes outside the Hedgehog pathway (Hh) pathway. 65% of BCC harbor mutations in HIPPO-YAP and Contact Inhibition of Proliferation pathways: (FAT1 (30%), NF2 (9%), ARHGAP35 (18%), CREBBP (21%), PTPN14 (21%), LATS1 (9%)). We validated the role of these genes in BCC cell line by siRNA screening followed by migration and proliferation assays. HIPPO-YAP pathway is moderately activated in high-risk BCC versus low-risk BCC and is hyperactivated BCC with intrinsic resistance to Hh inhibitors. The tumor microenvironment (TME) of BCC is dominated by cancer-associated fibroblasts and CD4 T-cells. Immune component of TME in BCC is characterized by abundance of neutrophils as compared to the other cancer types from TCGA. This can contribute to previously observed limited response rate to immune checkpoint blockade despite very high TMB in these tumors.

Cost-Effectiveness of an AI-Based Smartphone App Compared to Usual Care for the Early Detection of Skin Cancer in Belgium: A Decision Tree Analysis

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AI-based apps for skin cancer detection are increasingly used and reimbursed by healthcare insurers, yet evidence on their cost-effectiveness within the Belgian healthcare system remains lacking. Therefore, the aim is to evaluate the incremental cost-effectiveness ratio of an AI-based smartphone app for the early detection of skin cancer in Belgium compared to the standard of care. Decision-tree models for melanoma, basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and benign skin lesions were conceptualized based on a study evaluating the diagnostic accuracy of the app. The analyses were performed from a healthcare sector perspective. One-way and probabilistic sensitivity analysis were used to assess parameter uncertainty. The smartphone app was less effective than the standard of care in detecting melanoma, BCC, SCC and benign skin lesions, while costs differences varied by type of skin cancer. For melanoma, the detection rate was lower with the app, 0.601 vs. 0.874 but so were the costs €419 vs. €536. For BCC, the detection rate was lower with the app, 0.585 vs. 0.912 and cost differences were minimal €143 vs. €145. The app detection rate for SCC was 0.706 vs. 0.922 and costs were €228 vs. €233. For benign skin lesions, the app incurred lower costs: €60 vs. €90 and a reduced detection rate of 0.820 vs. 0.937. In its current diagnostic performance, the AI-based smartphone app was associated with lower costs, but lower skin cancer detection rates. The app also led to unnecessary referrals for benign lesions, that could hamper the healthcare system.