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Irish Melanoma Forum – 12th Annual Scientific Meeting 2024

Abstracts

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Clinico-Pathologic and Molecular Analysis of Small (T1) Uveal Melanomas Treated by Enucleation

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Abstract

Background

Uveal melanoma (UM) is the most common type of eye cancer, originating in the uveal tract of the eye. UM accounts for 3-5% of melanomas and has a 50% rate of metastasis and early death. Tumour size is known to be related to the risk of metastatic disease and mortality in UM and other cancers. Large UM tumours are considered more aggressive and to have high-risk genetic factors.

Tumour size is categorised by the Union for International *Cancer* Control (UICC) Tumour Node Metastasis (TNM) staging system. Pathological stage (T1) tumours are classified by dimensions of maximum 12mm diameter and 3mm depth (if 12-9mm in diameter) / 6mm depth (if less than 9mm in diameter). The main treatment route for UM patients is removing the eye (enucleation) if the tumour is large, or radioactive plaque therapy if small. However, as it can be difficult to distinguish melanoma from a benign naevus clinically, they are often followed over time to demonstrate growth before they are treated with plaque radiotherapy or surgical eye enucleation.There is a significant gap in the literature on the behaviour of T1 tumours due to their rarity and the lack of histological material available if treated with a radioactive plaque, the more popular approach in recent times. The available studies imply that T1 tumours metastasise significantly less frequently than larger tumours, potentially due to less accumulation of secondary mutations.

Aim

Identify a cohort of patients with T1 enucleated tumours to determine their disease-free and overall survival.

Correlate this with known molecular markers of adverse survival such as BAP1 status, monosomy chromosome 3, and gain of chromosome 8.

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Methods

A search of the National Ophthalmic Pathology Laboratory (NOPL) database from 1970-2023 was performed.

Clinical information was obtained from hospital records and the National Death Registry. Histologic characteristics, immunohistochemical studies and FISH study reports were compiled from histology reports.

DNA exome sequencing on formalin-fixed-paraffin-embedded tumour tissues was undertaken on twenty patients, eleven of whom had blood samples taken for comparative analysis of normal tissue DNA exome sequencing. Additional DNA exome sequencing is currently being undertaken at present. The Institutional Ethics Committee awarded Ethical Approval to this study. This study was under the tenets of the Declaration of Helsinki.

Results

Seventy-six uveal melanoma enucleation patients were identified. (Total n=76). Sixty-nine patients, the primary treatment was enucleation (pT1). Seven patients were treated primarily with plaque radiotherapy. Due to recurrence, they underwent enucleation. The tumour dimensions for both cohorts were measured through macroscopic and microscopic examination, confirming their T1 status.

Forty-eight (48) were male (63%), and twenty-eight (28) were female (37%). The patient age ranged from 11 to 86, the mean age 57 years, and the median age 61 years. Histology showed spindle cell type in forty-one (54%), epithelioid cell type in seven (9%) and mixed cell type in twenty-eight (37%). The main area of tumour growth was the choroid (83%), followed by the ciliary body (8%), ciliochoroidal (3%), and iris (2%).

Twenty patients (26%) metastasised to distant systemic sites. Three (3) were alive at the time this review was conducted (December 2023). Thirty-five (35) patients died (46%). Eighteen (18) died of metastatic disease (52%), and seventeen (17) died of other causes (48%). Kaplan-Meier Survival estimates for five years is 79.8%; for ten years, 65.7%; and 46.3% at twenty years.

Bap1 immunostaining results were available for fifty-one patients. Thirty-four (34) were Bap1 positive and seventeen (17) were Bap1 negative. FISH results for chromosomes 3 (monosomy 3) and 8 (8qG) were reported for twenty-four patients. Four (4) patients were identified as monosomy 3, only one of which has metastasized to the liver. Five (5) patients were identified as having chromosome 8q gains, two having metastasized to the liver and bowel.

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DNA exome sequencing available for twenty of these patients is undergoing analysis for potentially pathogenic genetic variants from this cohort, and further sequencing on archival samples from this database is underway. Table 1 shows a summary of the current interesting findings from the young patients in our cohort:

TABLE 1: GENETIC EVALUATION OF YOUNG COHORT OF T1 ENUCLEATION PATIENTS

Gender and Age	Status	TMB	MSI Status	Germline driver mutations	Germline VUS	Germline variant biomarker	Somatic VUS	Somatic MSI mutations
M11	DOD	108.24	MSS	PRSS1	n=24, inc: PALB2, MSH2, APC	SH2B3		NONE
M12	NED	3.88	MSS	PRSS1, SLX4, GPC3, PH0X2B	RAD51B, TP53, ECC1, PRSS1	SH2B3, TP53	RECK	NONE
M23	NED	96.41	MSS	N=54, INC: MSH2, MLH1,	MUTYH	TP53	MTOR	NONE
F24	NED	74.62	MSI	MSH2, SDHB, MSH2, MSH6	BARD1, BAP1	TP53, SH2B3, VHL	NONE	NONE
F25	NED	245.79	MSI	NONE	NONE	NONE	BAP1	MSH3, MSH2,
M26	NED	108.24	MSI	n=8, inc: NF1, CTC1,	MSH2, MSH6,	SH2B3, TP53,	CDKN2A	POLE, POLD1

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M28	DOD	2.2	MSS	NONE	n=17, inc: BAP1, POLE	NONE	NONE	NONE

Conclusion

The most striking and novel findings are that:

- In comparison to published literature on T1 UM (Shields et al. 2013), our cohort presented a higher metastatic rate at 5, 10, and 20 years.
- Patients under 40 years of age had a much better prognosis than those over 40 years at presentation.
- UM typically occurs over the age of 60 years. We speculate that there is a cohort of younger patients whose oncogenic drivers may differ from typical UM patients who have a better prognosis, and who may potentially respond to immunotherapy.
- Although limited, molecular genetic data is available in younger patients. The usual driver mutations of UM (GNAQ/GNA11) are not seen. We have identified MSI in some of these patients.
- Monosomy 3 and BAP1 status - known to be highly prognostic in UM, (including in a large retrospective study from our institution, AJSP 2024) is not as important a prognostic factor in the young cohort.

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Validation of Predictive Nomograms for Sentinel Node Positivity in Malignant Melanoma: Insights from an Irish Cohort

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Abstract

Aim

Nomograms have emerged as valuable tools for estimating the likelihood of sentinel lymph node involvement in melanoma patients. Three widely recognised models have gained prominence: the Memorial Sloan Kettering (MSK), Melanoma Institute of Australia (MIA), and Lifemath nomograms. This study aims to validate the predictive accuracy of these nomograms in a cohort of Irish melanoma patients. Validation in this context is imperative to ascertain their applicability within this distinct population.

Methods

Patients diagnosed with malignant melanoma who underwent sentinel lymph node biopsy (SLNB) at the Mater Misericordiae Hospital, Dublin between 2010 to 2023 were included. The predictive performance of each model was assessed using discrimination, analysed by calculating the area under (AUC) the receiver operating curve (ROC), and calibration, assessed using calibration plots. The sensitivity, specificity, negative predictive value (NPV), error rate and potential SLNB reduction rates were calculated to assess clinical relevance of nomograms at various risk thresholds.

Results

177 patients met the inclusion criteria, 30 had a positive sentinel node, representing a SLNB positivity rate of 16.9%. The following table represents the predictive and clinical performance of the three nomograms when applied to our cohort taking 5% as the risk value quoted by the latest

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2023 NCCN guidelines on the management of malignant melanoma.

	MSK	Lifemath	MIA
AUC	0.722 (95% CI 0.619-0.825)	0.708 (95% CI 0.610-0.805)	0.682 (95% CI 0.579-0.784)
Calibration Co-efficient	1.13 (95% CI 0.94-1.32)	0.46 (95% CI -0.21-1.13)	1.22 (95% CI 0.68-1.75).
NPV	97.44%	88.24%	92.31%
Sensitivity	96%	93.33	96.55%
Specificity	30.4%	10.20	8.16%
Error rate	0.67%	1.13%	0.57%
SLNB reduction rate	26%	9.60%	7.39%

Discussion

The MSK and MIA nomograms are valid and accurate at predicting SLNB positivity in Irish patients with melanoma. The MSK nomogram appears to perform better in our population than the MIA nomogram and represents a clinically useful tool with acceptably low error rate, high NPV and the ability to significantly reduce the number of SLNB performed.

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Detection, quantification, and characterisation of circulating tumour DNA in uveal melanoma

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Abstract

Aim

Uveal melanoma (UM) is the most common intraocular malignancy in adults. Most deaths from UM occur due to the development of metastasis in ~50% of patients. After detection of metastasis, median overall survival is less than 1 year. Therefore, more effective biomarkers for early detection of metastasis are urgently needed. Circulating tumour DNA (ctDNA), DNA shed by tumour cells into the bloodstream, has potential as a minimally invasive biomarker for detection and monitoring of disease progression, recurrence, and treatment response. The aim of this study is to establish proof of principle that we can analyse, quantify, and characterise ctDNA as a biomarker for prognosis and surveillance in UM.

Methods

We obtained ethical approval to collect blood samples from UM patients at three Irish hospitals. All patients provided informed consent. Total cell-free DNA was isolated from 4 healthy donors, 4 patients with primary UM (PUM), and 12 patients with metastatic UM (MUM), using the MagMAX Cell-Free DNA isolation kit. DNA was quantified using a Qubit 2.0 fluorometer. The presence of the common UM-associated mutations *GNAQ* Q209P and *GNAQ* Q209L in the cell-free DNA was investigated using quantitative PCR (qPCR) and digital PCR

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(dPCR).

Results

Cell-free DNA was detectable in all 20 samples included in the study, at concentrations ranging from 0.18-23.8 ng/µl. qPCR analysis identified a *GNAQ* Q209P mutation in 1/12 MUM patient samples and a *GNAQ* Q209L mutation in 1/12 MUM patient samples. No *GNAQ* Q209P or Q209L mutations were detected in the PUM or healthy donor samples. We are currently optimising a protocol for ctDNA analysis using dPCR, which will allow for more sensitive, absolute quantification.

Conclusion

We were able to successfully isolate cell-free DNA from all samples. In 2 patients, we identified UM-associated mutations in the cell-free DNA, indicating the presence of ctDNA. Our next step will be to use dPCR to investigate these mutations in a larger cohort of patient samples. This study provides preliminary evidence that UM-associated mutations can be detected in ctDNA from patient blood samples, suggesting that ctDNA has potential as an early, minimally invasive prognostic biomarker in UM.

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Collision of Spitz naevus (with distinctive morphology and genetic pattern of MYO5A::NTRK3 fusion) and dermal naevus (with BRAF V600E mutation)

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Abstract

Aim

To present an interesting case of a Spitz naevus.

Background

A 29-year-old female was referred to St James' Hospital's Dermatology service by her general practitioner for a multi-coloured nodular lesion located on her right upper back showing recent worrisome changes, which was clinically suspicious for melanoma. There was a reported history of childhood sunburns and sunbed use as an adult. The lesion was excised with a 2mm clinical margin. Microscopy showed an asymmetrical spindled and epithelioid compound melanocytic lesion with a pushing lower border. There was central upward ascent of melanocytes and effacement of the epidermis centrally. A single possible mitosis was noted. Immunohistochemistry for PRAME was negative and p16 showed diffuse strong positivity. The lesion was initially favoured to represent an atypical Spitz tumour, and following MDT review, the possibility of a melanocytic lesion of uncertain malignant potential (MELTUMP) was raised. The case was sent to Dr Arnaud De La Fouchardière, Lyon, for expert opinion and further assessment.

Results

Consult opinion was of a compound Spitz naevus demonstrating a pseudoschwannomatous spindled pattern colliding with a common naevus. Immunohistochemistry confirmed a Spitz naevus with positivity for pan-TRK suggesting a probable fusion involving MYO5A-NTRK3 gene, given the typical morphology of that fusion type, in collision with a dermal naevus with BRAF V600E mutation. A 1cm wide local excision was done one month later as per MDT recommendation which showed no residual melanocytic lesion.

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Conclusion

This was an interesting case causing diagnostic difficulty, of a poorly described morphological subtype of Spitz showing specific genetic fusion. There are only fourteen such cases reported showing MYO5A::NTRK3 fusion. Pseudoschwannomatous pattern may be a diagnostic clue to the presence of this fusion. Molecular confirmation would be required to definitively diagnose a Spitz naevus with MYO5A::NTRK3 fusion

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Neo adjuvant immunotherapy for advanced melanoma: a clinical audit of pathological response and toxicity

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Abstract

Background
Outcomes associated with stage III and above melanoma are poor. The SWOG S1801 trial compared neo adjuvant and adjuvant pembrolizumab in advanced melanoma and found better event-free survival in the former. The OpACIN-neo trial identified a dose of neo adjuvant ipilimumab/nivolumab which induced a response with acceptable adverse events. Our audit's aim was to assess the pathological response of patients in our centre who received neoadjuvant immunotherapy and any associated toxicity.

Methods
Patients with melanoma who received at least one neo adjuvant immunotherapy treatment for their disease were chosen. Data was collected by manually reviewing their medical health records, including both their paper file and electronic databases. Information collected included age, gender, ECOG status, subtype, primary site, mutation status, blood results, number of cycles received, adverse events, date of surgery, pathological response, and date of death.

Results
Data from 17 patients was collected: 13 with nodular melanoma and 4 with superficial spreading. Stages ranged from III to IV. Thirteen received pembrolizumab, and four received ipilimumab/nivolumab, with all patients receiving between 2-4 cycles. Adverse events included dermatitis, colitis, hepatitis, hyperthyroidism, arthritis and neurovasculitis. Fourteen patients underwent surgery, with three patients excluded due to progression of disease. Only one patient had a complete pathologic response, with five having pathological partial response while eight patients had pathological non-response.

Discussion
Our findings indicate higher numbers of non-response to treatment than either complete or partial responses, along with a broad range of toxicities. Further patient enrolment is needed to accurately assess the risk-benefit profile of neo adjuvant immunotherapy in melanoma management.

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Unveiling the Rarity and Severity: Diabetic Ketoacidosis as an Immunotherapy-Related Adverse Event

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Abstract

Background

Immune checkpoint inhibitors have altered the therapeutic paradigm of advanced cancers and are now an attractive treatment strategy in several malignancies.

However, the toxicities associated with them can range from mild to fatal. Approximately 10% of patients may experience endocrine adverse effects, most commonly thyroid disease and hypophysitis, and rarely diabetes mellitus. This case highlights diabetic ketoacidosis (DKA) as a rare yet severe adverse effect of immunotherapy.

Methods

An 86-year-old female with metastatic malignant melanoma to the liver presented to the hospital with a three-day history of reduced oral intake, due to decreased appetite and dry mouth. Her other medical history included hypertension. She had no personal or family history of any autoimmune conditions. She had undergone 22 cycles of immunotherapy with pembrolizumab, achieving an excellent response with minimal disease burden.

Results

Initial blood results showed a metabolic acidosis, with a pH of 7.21, glucose level of 33 mg/dL, HCO3 of 12.8 mmol/L, and presence of ketones. Despite no prior history of diabetes, she was diagnosed with DKA. Treatment with an insulin and dextrose infusion was started, which normalized her blood glucose levels. However, on the following day, the patient became unresponsive, and was diagnosed with an ischemic stroke affecting her basilar artery. Despite receiving thrombolysis, she ultimately passed away within days. Her fatal pro-thrombotic state was attributed to diabetic ketoacidosis induced by immunotherapy.

Conclusions

DKA has been found to affect 0.2-0.9% of patients undergoing immunotherapy. Despite its rarity, the importance of clinical suspicion and patient education on the condition cannot be understated, given its potentially fatality. This case highlights the importance of early recognition and management of immunotherapy-induced toxicities.

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Seeing Both Sides - Paediatric Uveal Melanoma Treated With Plaque Brachytherapy in Ireland: A Case Series

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Abstract

Background

Uveal melanoma, although a rare cancer, is the most common primary intra-ocular malignancy in adults, accounting for 5-10% of all cases of melanoma. In contrast, it is extremely rare in children, with <1% of all cases occurring in patients <20 years old[1]. The current first-line treatment for small/medium sized melanomas is radiotherapy, generally in the form of plaque brachytherapy. In Ireland, brachytherapy for choroidal melanoma is delivered in St. Luke's Hospital Rathgar, in collaboration with the Royal Victoria Eye and Ear Hospital. This national service started in 2010, over which time a total of 414 patients have been treated, with only two of them being under the age of 18 (0.5%). Here we present these two cases.

Methods

The patients' electronic medical records and treatment details were reviewed, and a literature search on choroidal melanoma was performed.

Results

Two teenage boys presented with acute onset of visual impairment. Ophthalmological assessment confirmed a diagnosis of choroidal melanoma, without evidence of extra-ocular spread. They both proceeded to receive plaque brachytherapy, one with Ru^{106} and the other with I^{125}, with a planned dose of ~85Gy to the tumour apex.

Discussion

Uveal melanoma is extremely rare in children. Radiotherapy is the first line treatment for small/medium lesions, with primary enucleation reserved for large or locally invasive tumours. Plaque brachytherapy is successful in preventing local recurrence in >90% of cases[2], however approximately 50% of patients will go on to develop distant metastatic disease, most commonly to the liver. Brachytherapy is generally well tolerated, however late toxicity can lead to visual impairment and pain in some patients, necessitating secondary enucleation in a minority of cases.

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A new member of the panel: the use of PRAME in melanocytic lesions

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Abstract

Background

PRAME is a novel antibody against preferentially expressed antigen of melanoma that supports the diagnosis of melanoma in ambiguous cases. Its overexpression results in inhibition of cell differentiation and apoptosis, facilitating the malignant phenotype. It is recognised by cytotoxic T lymphocytes and therefore and thus, it has been discussed as a promising target for personalised treatment. It has a specificity of 0.91 (high PPV) and a sensitivity of 0.71 (lower NPV). We aim to assess the use of PRAME stain as part of an ancillary panel during the first year of use at University Hospital Waterford.

Methods

We performed a retrospective analysis to include all the cases where PRAME was used, and excluded all cases where PRAME was not used for diagnosis of melanocytic lesions during 2023. From the included cases, we extracted the following data: type of lesion, PRAME result, and other stains used for interpretation.

Results

We found PRAME to be used in 102 cases: 22 cases of invasive melanoma, 28 cases of in situ lesions, 48 cases of difficult diagnosis, and 4 cases of non-skin specimens to rule out or confirm metastasis. This is only 13% of all melanocytic lesions. All cases of invasive malignancy had some degree of positivity, but it was considered negative in 2 cases where it was only focal. All these cases were MelanA, HMB45, sox10/S100 and P16 positive with clear invasion. When diagnosing melanoma in situ, 21 of the cases were positive and 9 were negative for PRAME. All of the last were HMB45, MelanA and sox10 positive with no dermal staining. Finally, difficult cases were finally diagnosed as follows: 27 dysplastic naevi, 6 spitz naevi, 5 other benign cases including blue, acral, halo and deep penetrating naevi, 2 Wide Local Excision of a melanoma scar and 2 non-melanocytic lesions. Of all these cases, only 3 of the dysplastic naevi were PRAME positive, but the atypia was so mild that the histology prevailed when making a diagnosis.

Discussion

PRAME was used in only a minority of cases, meaning H&E is still the base of diagnosis. It was

mostly used as part of a panel to confirm or rule out invasion and metastasis, and to support the diagnosis of benign lesions in difficult cases. Its result must be interpreted in a context. Of a total of 8 consultants, only 2 used PRAME.

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KSR proteins: scaffolders or master builders of oncogenic signalling pathways in malignant melanoma?

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Abstract

Background

KSR proteins play a critical role in transducing oncogenic signalling via the ERK pathway. Originally described as scaffolds that bind the RAF-MEK-ERK pathway, they also modulate the pathway through allosteric effects. Although KSR1/2 have different functions, either of them seems required for RAS and BRAF mediated oncogenic transformation, which together contribute to ~40% of human cancers. However, it is unknown which KSR1/2 functions are essential for transformation and whether they could lend themselves as drug targets.

Methods

Here, we addressed this question by testing the hypothesis that KSR1/2 control a small subset of interacting proteins and ERK substrates critical for transformation. For this, we applied CRISPR gene editing and generated KSR-deficient BRAF- or NRAS-driven cutaneous melanoma cells. Cells were then subjected to multi-OMICS analysis including (phospho)-proteomics, RNA- seq, and interaction proteomics.

Results

The subsequent bioinformatics analysis and data integration indeed suggest novel crosstalk critical for transformation. Furthermore, we established a novel ERK-substrate-omics pipeline that suggests that KSR orchestrates signalling via subsets of highly specific ERK substrates. While depletion of KSR1 in BRAF driven melanomas results in upregulation of several tumour suppressors and reduced cell invasion, KSR1 in oncogenic NRAS signalling rather supports

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metabolic adaptations and reactivation of oxidative phosphorylation.

Discussion

Importantly, using this novel understanding of KSR signalling complexes in combination with structural data, we developed cell penetrable biotherapeutics and small molecule inhibitors to disrupt the KSR signalling complexes in therapy resistant malignant melanoma.

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Oestrogen Stimulation and Melanoma

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Abstract

Aim

This study explores the impact of 17β-estradiol stimulation on a HER4-expressing cutaneous melanoma (CM) cell line (SKMEL24). HER4 is a tyrosine kinase receptor of the Human Epidermal Growth Factor/HER/ErbB-family with a complex biology: four isoforms JM-a/b, CYT- 1/2, and tissue specific oncogenic/tumour suppressor roles. There is very little known about HER4 function in CM, despite CM showing the highest HER4 genomic alteration frequency (17.34%) across different cancers (cBioPortal). Due to the interplay between oestrogen and HER4 in estrogen receptor positive (ER+) breast cancer (BC), and given the observed tendency for female melanoma patients to have better outcomes than males, this investigation elucidates potential mechanisms that could influence tumour progression/suppression or immune modulation in CM.

Methods

SKMEL24 was serum starved for 4h prior to stimulation with a range of 17β-estradiol. PDL1 and HLA-ABC expression were investigated at 24h using the Guava Flow Cytometer (Luminex). RNA was extracted at 24h using TRIzol, followed by qRT-PCR to assess the expression of HER4 isoforms (JM-a/b, CYT-1/2), the hormone receptors estrogen receptor 1 (ESR1), estrogen receptor 2 (ESR2), progesterone receptor (PGR), G protein-coupled estrogen receptor 1 (GPER1) and the nuclear receptors retinoic acid receptor α/β/γ (RAR-A/B/G), and retinoid X receptor α/β/γ (RXR-A/B/G). Cell proliferation and caspase3/7 apoptosis assays were performed at 24/48/72h by using the IncuCyte Instrument (Sartorius). SN-38 (150nM) was used as positive control for apoptosis.

Results

SKMEL24 was negative for PDL1, while HLA-ABC expression decresed upon 17β-estradiol stimulation. Stimulation of SKMEL24 with 17β-estradiol showed a statistically significant increase in JM-a and CYT-1 HER4 isoforms, GPER1, and a dose-dependent increase in RARA and

RXRG, in the absence of ESR1, ESR2 and PGR. SKMEL24 stimulated with 17β-estradiol showed a decrease in proliferation, but no caspase3/7 apoptosis induction was found.

Discussion

These findings suggest a potential interplay between oestrogen and melanoma that could influence tumour progression/suppression or immune modulation in CM. Further studies are needed to clarify the specific receptor interactions and pathways involved.

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Targeting Uveal Melanoma with a Potent Cannabinoid: Insights from Cells, OPDX, and Patient Biopsy

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Abstract

Aim

This research evaluates the relevance of cannabinoid receptors in uveal melanoma (UM) and the therapeutic potential of synthetic cannabinoids in UM cell lines, in *ex vivo* orthotopic patient-derived xenografts (OPDX), and UM patients' biopsy. UM is the most common intraocular malignancy in adults with approximately 50% of patients progressing to liver metastases and overall survival ranging from 4-15 months.

Methods

Cannabinoid receptor gene expression in 80 primary UM samples within The Cancer Genome Atlas was analysed for association with survival. CB1 receptor expression was examined by

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Immunoblotting. In vitro assays utilised Mel285 and OMM2.5 human UM cell lines derived from tumours of the eye and a liver metastasis, respectively; and normal human epidermal-derived melanocytes (HEM). Cell viability was examined by measuring metabolic activity. Colony formation assays assessed long-term cell proliferation. Label-free real-time Live-Cell imaging and caspase 3/7 activation by fluorescence was detected by IncuCyte. Multiplex ELISA quantified secreted levels of inflammatory factors in cells, OPDX and patients' samples. Proteomic profiling of OMM2.5 and patients samples treated with 20 µM HU-210 was performed by mass spectrometry and confirmed by Immunoblotting.

Results

Kaplan-Meier curves demonstrate a significant correlation between high CB1 expression and lower disease-free survival or high CB2 expression and lower overall survival in UM patients. CB1 expression was confirmed in both UM cell lines and OPDX. 20 µM HU-210, a CB1 /CB2 agonist, significantly reduces cell viability in HEM or in Mel285 cells, respectively. However, HU-210 shows a selective effect in OMM2.5 where concentrations ranging 100 fM to 20 µM significantly reduce cell viability and proliferation. 20
µM HU-210 induces apoptosis in OMM2.5, significantly reduces long-term proliferation of Mel285 and OMM2.5 cells and significantly alters secretion of 17 out of 54 inflammatory factors analysed in OMM2.5 cells, 1 in OPDX and 3 in patient samples. Proteome profiling of OMM2.5 cells treated with 20 µM HU- 210 identified 55, 41 and 193 proteins significantly differentially expressed after 4, 8 or 24 hours treatment, respectively. Proteomic profiling of patient's samples is ongoing.

Conclusion

The potent cannabinoid HU-210 reduces viability and clone proliferation of UM cell lines, induces apoptosis and significantly alters the secretion of inflammatory factors in OMM2.5, *ex vivo* and patients biopsy. Future directions will evaluate the molecular mechanisms of HU-210 action in UM cells and its translational potential in pre-clinical in vivo study.

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Ferroptosis and Extracellular Vesicles as Potential Biomarkers for Uveal Melanoma Prognostication

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Abstract

Background

Uveal melanoma (UM) is an ocular cancer, with propensity for fatal liver metastases. Efficacious treatments and better prognostication approaches for MUM are urgently needed. We previously identified putative biomarkers of UM progression and therapeutic response. Now, we are additionally analysing extracellular vesicles (EVs) isolated from plasma of healthy subjects, primary UM and metastatic UM patients to discover potential therapeutic response or prognostic UM biomarkers.

Methods

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Association between expression of candidate biomarkers and UM-patient survival was investigated by analysing the RNA data from surgically removed UM tumors and deposited in the Tissue Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GEO). EVs were isolated from plasma of 6 healthy donors, 8 primary UM and 5 MUM patients using sucrose cushion ultracentrifugation and their proteomes profiled by mass spectrometry (MS). Western blot and transmission electron microscopy validated EV hallmarks.

Results

TCGA and GSE84976 databases analysis showed high levels of transcripts modulating ferroptosis, e.g. SCL7A11, to correlate with reduced overall and disease-free-survival in UM patients. In addition, by using the data included in these two datasets, we iteratively identified a gene signature which predicts with high accuracy (AUC of 0.94) which patients will develop metastatic disease. Preliminary data from the initial cohort of EVs identified differentially expressed proteins between healthy, UM and metastatic (MUM) subjects.

Discussion

TCGA and GSE84976 data reveal that altered expression levels of ferroptosis-related genes correlates with UM prognosis. By analysing these two databases we generated a gene signature which can predict which patients will develop MUM, with higher accuracy compared to monosomy 3 alone. Currently we are expanding the cohort of UM patients analysed for differentially expressed EV proteins between healthy, UM and MUM subjects. These studies can provide relevant candidate prognostic or therapeutic response biomarkers for UM.

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Development of 2D and 3D pre-clinical tumour-derived models for in vitro analysis of personalised therapies in uveal melanoma

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Abstract

Background

Uveal melanoma (UM) is a rare tumour, but it is the most common primary intraocular malignancy in adults. Despite effective local treatments, approximately 50% of patients will develop metastasis, resulting in poor survival rates. The lack of representative in vitro patient tumour models limits the understanding of UM biology and hinders the development and testing of potential therapeutic combinations.

Methods

Primary enucleation UM tissue was digested and plated in 2D and 3D culture conditions. In silico transcriptomic and genomic data from TCGA dataset was used to assess actionable targets associated with overall survival and/or disease-free survival. Combinational drug viability assays were performed and synergy was determined using Combenefit, Loewe model. Drug response mechanistic assays were determined using qPCR and proteomic techniques.

Results

Three 2D primary cell lines and seven 3D patient-derived organoids (PDO) derived from primary UM tumours were successfully cultures for >6 months. These models retained the morphology, and the genomics of the matched primary tumour. Targeting the GNAQ/GNA11 downstream signalling pathway with PTK2/FAK1 (Defactinib) and PKCs inhibitors (Sotrastaurin and Darovasertib) in combination resulted in additive to synergistic effect in the cell lines. The combination of Defactinib+Sotrastaurin resulted in a mean synergy score of 14.25, while Defactinib+Darovasertib was also effective (mean synergy score, 13.5). Additionally, actionable targets in the DNA Damage Repair (DDR) pathways PARP1 (Talazoparib) and DNA- PKC (Nedisertib) inhibitors in combination

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with Temozolomide resulted in high synergy for the combination Talazoparib+Temozolomide in all the cell lines tested (mean synergy score, 29), while an overall additive effect was observed for the combination Nedisertib+Temozolomide.

Discussion

Successful establishment of 2D cell lines and novel 3D PDOs resulted in laboratory models capable of recapitulating the different genomic background sub-types of UM. Targeting specific aberrant pathways in UM revealed additive-synergistic combinations representing potential novel treatments for UM patients.

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Melanin presence in Melanoma cells & Normal Melanocytes modulates Apoptosis Activation, Caspase 8/9 expression and Cell migratory capacity

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Abstract

Background

Melanocytes have been considered resistant to apoptosis in human skin, in contrast to neighboring keratinocytes. Dysregulation of apoptosis constitutes a barrier to melanoma treatment. Moreover, pigmented melanoma cells are less metastasizing in nude mice compared to amelanotic melanoma cells. Here we studied the in vitro expression of apoptosis regulators in human epidermal melanocytes (HEM) and compared this with melanoma cells of distinct melanin content.

Methods

Light & dark human skin epidermal melanocytes (HEM) and melanoma cell lines of distinct melanin content were assessed for effector caspase 3/7 activity. Apoptotic markers were assessed in these cells using antibody arrays (43 markers) and Western blot. Cell migration capacity was assessed by scratch-wound healing assays.

Results

To explore the involvement of altered caspase expression in melanoma we examined the To explore the involvement of altered caspase expression we examined initiator caspases 8 & 9 and the apoptotic response to staurosporine in pigmented/amelanotic melanoma cells and primary HEM of distinct melanin content. Caspases 8 & 9 protein expression was downregulated in highly-melanized

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pigment cells incl. SK-Mel-23, FM55M, MNT1 melanoma and in HEM derived from SPT-IV & -V skin. By contrast, amelanotic cell lines (FM3, FM55P, A375, WM1366) and primary HEM from SPT I & II expressed higher levels of caspases 8 & 9 and were more responsive to staurosporine-induced apoptosis. Amelanotic melanoma cell lines (FM3, FM55P, A375) displayed higher migration capacity compared with melanotic cells (SKMEL23, FM55M & HEM SPT-IV).

Discussion

Our results suggest that melanogenesis-capacity and/or absolute melanin amount may regulate apoptosis activation and limit the migratory capacity of both melanoma and primary melanocytes. Reduction/loss of pigmentation capacity during melanoma-genesis may play a role in melanoma progression.

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Multi-disciplinary approach shows that the Hippo pathway core kinases MST2 and LATS1 have tumour suppressor roles in melanoma

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Abstract

Background

Metastatic melanoma is the most lethal skin cancer type with rising incidence rate. Treatment of the disease has been substantially improved with the discovery of BRAF inhibitors, however most patients develop resistance to these treatments. Meanwhile, no targeted therapy options have been developed for the 20% of the patients with an NRAS driver mutation. Increasing evidence from our group and others has shown an involvement of the pro-apoptotic Hippo pathway in melanoma development and in particular LATS1. While mutations in the Hippo pathway are rare, our work has shown that loss of pro-apoptotic signal mediated by the Hippo pathway is mediated by mutant BRAF and is associated with acquisition of resistance to BRAF inhibitors. Here we systematically characterise pathophysiological mechanisms associated with deregulation of the RAS RAF-Hippo network in melanoma using a zebrafish melanoma model and human clinical data.

Methods

Using CRISPR/Cas9 technology the expression of the hippo core kinase LATS1 was knocked- out in zebrafish which lack the expression melanocytes. A MiniCoopR plasmid harbouring the oncogene of interest downstream the mitfa promoter was injected at the single cell stage embryo to reinduce the expression of melanocytes carrying the BRAFV600E or NRASQ61L mutations. Monitoring of tumour onset and number of tumours per fish were used to generate survival and progression data. Histological analysis of the zebrafish was done using haematoxylin and eosin staining. Additionally, we were able to isolate the tumours and perform proteomics, phospho-proteomics and transcriptomics datasets from matching samples. The multi omics datasets are being integrated to reconstruct molecular networks and functional analysis identified deregulated modules associated with loss of function of the Hippo pathway. Publicly available databases for human melanoma samples were used to validate zebrafish findings in clinically relevant patients.

Results

We were able to observe that LATS1 has a significant protective effect when it comes to tumour

onset and tumour free survival for zebrafish developing BRAFV600E driven melanoma. We also observed differential disease progression in the NRASQ61L melanoma samples dependent on the status of LATS1 expression. Thickness of the zebrafish skin was found to be influenced by LATS1 proficiency both in BRAF and NRAS driven melanoma. Finally, our multi-omics data analyses identified key signalling modules that are differentially regulated between both types of driver mutations. We also found differentially enriched pathways dependent on the presence or absence of LATS1 within each subtype. Remarkably, several of these pathways were also found to be deregulated in patient samples with similar genetic backgrounds.

Discussion

We have established a melanoma zebrafish model that recapitulates the properties of human cutaneous melanoma. Our work has highlighted the role of the hippo pathway in melanoma onset and progression. Future work will be aimed at utilising the multi-omics data generated to reconstruct the signalling network of the different types of tumours.

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Scalp hair follicle dermal sheath fibroblasts from a patient with Recessive Dystrophic Epidermolysis Bullosa (RDEB) express an anti-melanoma gene signature

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Abstract

Background

RDEB patients with loss of collagen VIIA1 production/function present with skin blistering on body sites, and with high risk of aggressive squamous cell carcinoma. Remarkably, RDEB patient scalp is spared of blistering, and can indeed show luxuriant hair growth.

Methods

Hair follicle dermal sheath fibroblasts (DS) were cultured from scalp biopsies of an Irish RDEB (generalized intermediate type) donor and from two healthy donors. RNA-seq was performed (Illumina 2000) with data analysis (DRAGEN RNA pipeline) enhanced with Ingenuity Pathway Analysis (IPA).

Results

IPA (z-score) based on differential expression of RNA-seq data from RDEB DS fibroblasts (compared to healthy donor cells), showed pathway inhibition (z-score of ≤ -2) for: *Tumor tissue* (z-score= -2.33 and p-value = 3.59e-03), and *Occurrence of tumor* (z-score= -2.65, p- value = 2.07e-02). Additionally, pathway signaling downregulation (z-score of ≥ -2 but < -1) was found for *Advanced melanoma* (z-score= -1.51, p-value = 2.07e-02); *Skin hyperpigmentation* (z-score = -1.51, p-value = 1.41e-03); *Progressive solid tumor* (z-score = -1.73, p-value = 7.19e-05) and *Progressive malignant solid tumor* (z-score = -1.39, p-value= 1.6e-04).

The basis of potential inhibition of melanoma pathway signaling in RDEB DS fibroblasts (compared to healthy DS cells) may be related to inhibition of the following: Aryl hydrocarbon receptor (z-score = -2.18, p-value = 5.72e-03) and Interferon gamma signaling (z-score= - 3.54, p-

value= 7.97e-04). Additionally, pathway signaling downregulation in RDEB was associated with: WNT/beta-catenin (z-score =-1.48, p-value= 4.37e-06), IL1 (z-score= -1.51, p-value = 2.52e-03), Acute phase response (z-score= -1.71, p-value = 5.73e-03), IL17 (z- score =-1.18, p-value = 6.8e-03), Sonic Hedgehog (z-score= -1.41, p-value = 2.89e-03), IL- 6 (z-score =-1.52, p-value =1.31e-02).

Discussion

RDEB donor DS fibroblasts may exhibit enhanced anti-melanoma properties compared to similar cells in healthy donors. Loss of functional collagen VIIA1 protein may be associated with some protection against melanoma development in scalp skin.

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Dermal Fibroblast and Cancer-Associated Fibroblast Secretome Effects on Human Melanoma Cell Migration and Proliferation *in vitro*

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Abstract

Background

Melanoma is a cancer of melanocytes accounting for most skin cancer-related deaths. There is growing interest in the role of the tumour microenvironment (TME), including the dermal fibroblast (HDF) component, on melanoma progression. However, how paracrine signalling between HDFs and melanoma cells changes during the switch from the normal skin microenvironment to the TME remains unclear.

Methods

A melanoma-derived cancer-associated fibroblast (CAF) primary cell line and HDF derived from healthy skin were used to analyse the effect of HDF and CAF secretomes on melanoma cell outcomes *in vitro*. Conditioned media (CM) (72 hrs in serum-free DMEM) were produced from reticular, papillary and total (reticular & papillary) healthy HDFs, and from CAFs. CMs were assessed for impacts on melanoma cell migration [scratch wound healing (SWH) assays], and proliferation/metabolism (MTT assay).

Results

Melanoma cell lines derived from metastatic melanoma (FM-55-M, SK-MEL-2) appeared to be more sensitive than melanoma cells derived from primary tumours (FM-55-P, WM1366) to different CM, and then more affected by healthy HDF versus CAF-derived CM. Moreover, mesenchymal-type melanoma cells (FM-55-P, FM-55-M) were more responsive to HDF paracrine signalling than were epithelioid melanoma cells (WM1366, SK-MEL-2). HDF CM also stimulated metabolic and/or proliferative activity of melanoma cells derived from metastatic melanoma to a great extent than CAF CM.

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Discussion

The impact of fibroblast-derived secretome on melanoma cell behaviour may relate to melanoma cell status (i.e. derived from primary versus metastatic tumor), and whether melanoma cells had undergone epithelial-mesenchymal transformation. HDF secretome may influence metabolic activity of metastatic melanomas, which subsequently may increase migration and proliferation capacity.

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Investigating the Therapeutic Potential of Drug Combinations in Pre-Clinical Models of Metastatic Uveal Melanoma

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Abstract

Background

This project investigates the individual and combined drug efficacy of darovasertib, crizotinib and quininib analogues in pre-clinical models of metastatic uveal melanoma (MUM). Uveal melanoma (UM) is the most common primary intraocular tumours in adults with metastasis occurring in up to 50% of patients. The median survival after metastasis is 6-12 months, with only two currently FDA approved therapies for MUM, tebentafusp-tebn (KIMMTRAK) and melphalan (HEPZATO). However, these drugs are not effective in all patients highlighting the great need for better MUM treatments. A darovasertib and crizotinib combination recently received FDA orphan-drug status for MUM and is currently in phase 2 clinical trials. Meanwhile, CysLT1 antagonists, including 1,4-dihydroxy-quininib (Q7) significantly inhibit the hallmarks of MUM. The CysLT1 antagonists tested in UM cell lines include Q7 and the novel analogue PRZ6, which was identified via a virtual screening campaign.

Methods

In vitro assays utilised the OMM2.5 human UM cell line derived from liver metastasis. Cell viability was examined by measuring metabolic activity with MTT assays or Incucyte S3 live- cell imaging. OMM2.5 cells were treated with a range of concentrations from 0.08-20 µM darovasertib and 0.08-20 µM crizotinib alone, 6.25 µM-100 µM Q7 or 3.13 µM-50 µM PZR6 for 96 hours. Incucyte was set to take live cell images every 3-6 hours at 10x magnification. Data analysis is carried out on the live cell images using the Incucyte S3 system, data analysis results are exported from the Incucyte

system. The MTT results were analysed using GraphPad Prism 8 software.

Results

5, 10 and 20 µM crizotinib or 20 µM darovasertib significantly ($p<0.01$) reduced cell viability (IC_{50} of crizotinib=1.95 µM, IC_{50} of darovasertib=0.33 µM) in OMM2.5 cells. Live imaging showed 10-20 µM crizotinib or 20 µM darovasertib reduced OMM2.5 cell viability three hours after drug treatment of OMM2.5 cells. 25 µM, 50 µM and 100 µM of Q7 reduced cell viability in OMM2.5. Live imaging showed that 25 µM Q7 began to reduce OMM2.5 cell viability 3 hours after drug treatment. 50 µM of PZR6 did induce a decrease in OMM2.5 cell viability, but not to the same extent as 50 µM Q7.

Discussion

Darovasertib, crizotinib, and Q7 alone reduce cell viability of a MUM cell line. Future directions will evaluate the effect of darovasertib, crizotinib and Q7 combinations in OMM2.5 cells and *ex vivo* orthotopic patient-derived xenograft (OPDX) models of MUM. The molecular mechanisms underlying the pharmacological effects will be assessed by biochemical and molecular approaches. This study has the potential to discover more effective treatments for MUM patients.

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Nail dystrophy induced by targeted treatment for metastatic melanoma

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Abstract

Background

Onycholysis, the separation of the nail plate from the underlying nail bed, has a range of potential causes, including medications. Encorafenib and binimetinib, inhibitors of protein kinases in the mitogen-activated protein kinase (MAPK) pathway, have been associated with nail changes including onycholysis. This occurrence is attributed to epidermal growth factor receptor (EGFR) inhibition in the nail matrix due to MEK inhibition. Despite the prevalence of nail toxicities, especially in targeted therapies, they are less commonly recognised compared with other chemotherapy and targeted therapy cutaneous side effects.

Case Report

A 44-year-old female with a history of metastatic melanoma presented with a one-year history of brittle nails. Due to progression of her melanoma, therapy had been switched from initial immune checkpoint inhibition to small molecule inhibition with binimetinib and encorafenib, due to her known BRAF-V600 point mutation. Follow-up dermatological examination revealed significant hapalonychia, leukonychia, and distal variable onycholysis in all ten fingernails, greatly impacting the patient's quality of life.

The psychosocial impact of cancer therapy-related alopecia is well-documented, but nail toxicities, despite their high prevalence, receive less attention. Fingernails, like hair, play a crucial role in self-esteem and body image, as well as in tactile sensitivity. Nail abnormalities can contribute to increased emotional distress, underscoring the complex impact of cancer and its therapies on overall well-being.

Discussion

With the expanding use of targeted therapies and improved survival rates in metastatic melanoma patients, broader acknowledgment of associated nail effects is warranted. Awareness

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and education regarding prevention and nail care practices can mitigate the impact on quality of life, potentially improving patient compliance and progression-free survival. Measures such as counselling patients and promoting preventive strategies, including avoidance of trauma and proper nail care, are essential in addressing this aspect of cancer therapy-induced side effects.

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To assess the attitudes of Irish patients attending a pigmented lesion clinic and healthcare staff employed in an academic hospital to biobanking, a quantitative study

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Abstract

Background

A Biobank is a collection of biospecimens or biological samples and corresponding patient data points which are used for the purposes of medical research. Patient participation and support is imperative to biobank research. We aim to quantitatively assess the attitudes of Irish patients attending a pigmented lesion clinic (PLC) in an Irish dermatology centre and staff working at an academic teaching hospital to biobanking.

Methods

A questionnaire was distributed to Healthcare staff working in an Academic Hospital and members of the Irish Association of Dermatology via their hospital email address. Patients who attended PLC between January and April 2023, and patients who had previously been diagnosed with melanoma between January 2019 and January 2021 rwere asked to complete the questionnaire. Respondents from a market research company, Bounce insights, was sent a modified questionnaire via a survey platform.

Results

In total there were 426 respondents of ages; <18 years=31 (7%), 18-35 years=105 (25%), 36 – 65 years=191 (45%) and > 65years=99 (23%). There were 166 (39%) males and 260 (61%) females. Of the 426 total respondents there were 180 (42%) previous healthcare workers. The number of total participants who were aware of biobanks was 130 (31%), no = 283 (66%), not sure = 13 (3%). Over 20% (84) of participants had donated a biospecimen previously. Healthcare workers reported a positive response in 84% (102) but only 46% (72) of the Bounce marketing respondents felt similarly (p=<0.001).

Over 60% of healthcare staff, 16% of all patients and 21% of the Bounce marketing group were aware of Biobanks.

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In total 83% (352) of all respondents were willing to donate a biospecimen following a medical procedure but 78% (331) were willing to donate an additional blood sample and that number fell to 57% (242) when asked if they would donate an additional tissue sample purely for the purposes of research. The number who would encourage a family member to donate a biospecimen was; yes = 241 (56.5%), no = 41 (9.6%), not sure = 144 (34%).

Interestingly age was related to individuals' initial impression of biobanks (X2 (6, N = 426) = 32, p = <0.001), to a willingness to donate a biospecimen (p=<0.039) and to a desire to be informed if their specimen was disposed of (p = <0.001).

Discussion

In Ireland, the majority of patients, healthcare workers and other members of the public are willing to donate biospecimens for the purposes of research.

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Acral lentiginous melanoma: A single centre retrospective review from 2011-2023

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Abstract

Background
Acral lentiginous melanoma (ALM) is an aggressive subtype of melanoma arising on acral skin. ALM is the rarest subtype of melanoma overall & is associated with poorer outcomes.
We collected data related to demographics, clinical presentation, tumour characteristics & disease course of patients with ALM.

Methods
We conducted a retrospective review of ALM diagnoses between 2012-22 in a centre in the mid-west of Ireland. Patients were identified by searching a dermatology clinical database.

Results
We identified 20 patients (11 females,9 males), all Caucasian, diagnosed with ALM from 2011- 2023. AThe median age at diagnosis was 63.5years (range 43-86) and median follow-up time was 36 months (range 4-110 months).

15 (75%) ALMs were on the foot & 5 on the hand.
Initial misdiagnosis was documented in 6 patients & included ulcer (n=2), trauma (n=2), fungal (n=1) & callus (n=1).

The median Breslow thickness (BT) was 2mm (range 0.4mm-19mm). 6 were amelanotic with higher BT (median 1.5mm pigmented vs 6.85mm amelanotic). 4 of 6 (67%) amelanotic lesions were initially misdiagnosed. 9 tumours were ulcerated (45%). 15 patients (75%) had stage 1B disease or greater. 14 of these had sentinel lymph node biopsies (SLNB) & one patient with clinical stage III disease (in-transit metastases). 2 of 14 (14.3%) SLNBs were positive.

Of 20 patients, 6 (30%) relapsed. Five had locoregional recurrences, two of these had distant metastases on imaging & one later progressed to metastatic disease. All relapses presented clinically with a median time to relapse of 42.5 months (range 7 – 108).

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Molecular status was available for four ALMs with Stage III & IV disease. None were BRAF/NRAS mutated. Two had c-kit mutations, both patients had brain metastases.
Overall, 30% (n=6) patients died during the study period & 83%(n=5) of these were melanoma-specific deaths. Of these five patients, the median time from diagnosis to death was 41.5 months (range 12-110).

Conclusion
In our small cohort over a 10 year period, 25%(n=5) of patients died from ALM, compared to 8% at 5-years & 14.2% at 10-years for all subtypes of melanoma nationally from 2014-18 (5 years) & 2010-14 (10 years). We plan to explore this further by looking at national data on ALM from the National Cancer Registry Ireland.

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The Sunbed Trend in Ireland

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Abstract

Background

Indoor tanning is a proven risk factor for the development of melanoma and non-melanoma skin cancer, and represents a major public health challenge. The *Public Health (Sunbeds) Act 2014*, introduced regulatory reform of commercial sunbeds in Ireland. Under this Act, sunbed businesses must notify the Health Service Executive of their intent to provide sunbeds for use, sale or hire. To our knowledge, no studies have reported on commercial sunbed distribution in Ireland to date.

Methods

Using data from the Environmental Health Information System, we analysed the number of sunbed business registrations in Ireland. A literature search was performed for international comparison of sunbed outlet prevalence.

Results

A total of 369 sunbed businesses were registered in Ireland in May 2023. According to the Irish census, the population in June 2022 was 5,123,536; extrapolating that there were approximately 0.7 sunbed premises listed per 10,000 inhabitants. County Westmeath had the highest number of sunbed outlets per capita at 1.4 per 10,000 inhabitants, followed by Longford (1.3), and Tipperary (1.1). Dublin had 0.5 sunbed outlets per 10,000 inhabitants. County Leitrim had the lowest rate (0.3). Additionally, a sunbed market exists on online forums. We found 38 sunbeds for sale (23 on Facebook Marketplace, 15 on DoneDeal) and 3 for hire (2 on Facebook Marketplace, 1 on DoneDeal) by private sellers. The total number of sunbed premises listed in Ireland has declined since the registry began. In 2015, there were 476 sunbed businesses listed, compared to 379 in 2023. This equates to a reduction of 20%.

Discussion

Ireland has seen a reduction in sunbed prevalence, due in part to the enactment of the Public Health (Sunbeds) Act 2014, and the success of public health campaigns. While considerable strides to reduce avoidable UV exposure have been made, the prevalence of sunbed outlets remains

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significant, and online marketplaces add to this concern given the potential for legislative avoidance. Interestingly, our data has shown that there is considerable variation between counties in Ireland. Future targeted interventions are needed to inform and discourage against indoor tanning. Our findings add to existing knowledge which can focus future public health initiatives.

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Early trends in neoadjuvant immunotherapy for melanoma – the stories of the first twelve cases treated in Cork and Kerry

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Abstract

Background

Melanoma is a malignant tumour arising from melanocytes. It is the fifth most common invasive cancer in Ireland and it's incidence is rising. It is treated surgically, with resection by wide local excision, in stage I and II disease. By contrast the standard of care for stage III and IV melanoma is combination surgical and adjuvant systemic therapy with immune checkpoint inhibitors or BRAF/MEK inhibitors. A series of recent studies have indicated that neoadjuvant systemic therapy may have an important role to play in stage III and resectable stage IV disease although the clinical implications remain unclear.

Aims

To assess the utility of perioperative therapy for clinically stage III and resectable stage IV melanoma. To identify broadly recurrent themes throughout cases and explore patient experience in order to generate hypotheses. To inform clinicians about this newly developing treatment. To characterise the patients who were suitable for neoadjuvant therapy and identify broadly recurrent themes throughout cases and to examine correlations between:

- Pathological response of melanoma cells
- CTCAE toxicity
- Patient survival and progression free survival.

Methods

Twelve participants were deemed eligible according to the following criteria.

Inclusion:

- Patients who were diagnosed with clinically stage III or IV resectable melanoma.
- Patients who received at least one dose of neoadjuvant immunotherapy with immune checkpoint inhibitors or BRAF therapy with the intention of surgical resection of the melanoma.
- Adults aged over 18 years old.
- Patients attending CUH, SIVUH or UHK between 2018 to 2022 and who commenced

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neoadjuvant therapy before September 2022

Exclusion:

- Children (<18 years old).
- Patients unable to provide consent.
- Patients with uveal melanoma.
- Patients who will not have undergone surgery by November 2022.

Results

A total of 12 patients underwent NST during the 18 month period. Ten underwent immunotherapy with immune checkpoint inhibitors and two underwent BRAF/MEK inhibition. Six (50%) achieved complete or near complete pathological responses. Of the patients who achieved near complete or complete pathological responses, none have relapsed to date. Three (25%) had partial or minimal pathological responses, all of whom required further treatment. Three (25%) had near complete or complete radiological responses and did not proceed to surgery. All later developed recurrences. Ten (85%) reported adverse immune responses in the neoadjuvant arm of treatment ranging from abdominal cramps, anorexia, diarrhoea and fatigue to anterior uveitis, dyspnoea, hypophysis and neutropenia. Three of the 10 who underwent immunotherapy experienced adverse effects which necessitated a change in neoadjuvant treatment regimen.

Discussion

NST for melanoma is a new and rapidly evolving field; with apparently favourable pathological responses and patient survival outcomes it is rapidly gaining traction in the Irish setting. Toxicity is common and the toxicity profile variable. There is no early indication of a corelation between toxicity and pathological response or overall survival however further research into this field is necessary. By contrast overall survival appears to relate to pathological response. It further appears radiological response alone is an insufficient indication of response and surgery may remain crucial to short term survival.

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MDT Safety Huddle

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Abstract

Background

Multidisciplinary Team Meeting (MDT) in skin oncology is described as the collaboration between differed healthcare professionals' involved in skin cancer care with the ultimate goal of improving patient care and treatment efficiency (Taberna *et al*., 2020). Beaumont Hospital Skin Oncology MDT incorporates the following healthcare professionals; plastic surgeons, dermatologists, medical oncologist, radiation oncologist, histopathologist, radiologist, advanced nurse practitioner, skin cancer nurse specialists, data manager, skin MDT coordinator and MDT scribe. The integration of these professionals allows continued support to skin cancer patients during diagnosis, treatment and follow-up periods (Taberna *et al*., 2020).

A safety huddle in healthcare is defined as a brief meeting including members of the MDT with a duration of no longer than 10-15 minutes. The aim of the safety huddle is to focus on patient safety, thereby facilitating team communication (Institute for Healthcare Improvement, 2019). The safe huddle technique enhances team communication in an effective and efficient manner, resulting in the delivery of safer patient care (Brady *et al.,* 2013).

Aims

To create a safety huddle at the end of every skin oncology MDT meeting. The safety huddle will comprise of a plastic surgeon consultant (huddle leader), skin cancer nurse specialist, MDT coordinator and MDT scribe. The ultimate aim of implementing this safety huddle is to ensure that the verbalized MDT outcomes are correctly documented on the National Cancer Information System (NCIS).

Methods

Quarterly meetings with the Skin MDT group.

Results

Improved accuracy of MDT outcomes documented on NCIS.
Improved communication among MDT team.

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Improved delegation of tasks e.g. reg dictate consultation letters, intern order scans.
Improved the clarification of which patients needed to be relisted for MDT.

Discussion

In summary we implemented a safety huddle at the end of our weekly skin MDT in the same room where the MDT takes place. Our consultant leads the safety huddle which last approximately 10-15 minutes.

The safety huddle has a positive influence on the skin MDT as it reduces incorrect documentation of outcomes on NCIS.

To introduce pre MDT huddle. This would involve the CNS bringing forward the list of appointed patients for the following week skin MDT discussion. This would ensure patient are approximately listed.

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Incidence of malignant melanoma in adolescent and young adults aged 16-24 years, 1994-2020

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Abstract

Background

Melanoma is rare in children, but the risk of developing melanoma is increased in adolescents and young adults. It is the 3rd commonest cancer in this age group representing 8% of all cancers. In Ireland, strategies targeting improvement in sun protection measures have been in place for over 30 years [1]. In 2014, the provision of sunbed services to those aged under 18 years was banned. While the overall incidence of melanoma in children and adults is increasing in many countries, some countries are reporting decreasing incidence rates in adolescents and young adults in recent years (e.g. Australia, USA) [2].

Methods

Data on cases of malignant melanoma (ICCC group XId), aged 16-24 years were extracted from NCRI database for years 1994-2020. Joinpoint regression was used to identify significant trends in age-specific incidence rates over time.

Results

On average in the period 2011-2020 there were 13 cases of malignant melanoma diagnosed per year in 16-24 year olds, giving an age-specific incidence rate of 25.5/million population. 63% of cases were female and 37% were male. No significant trend in the age-specific incidence rate over time was identified in males, however a significant decreasing trend,17.3% (95% CI -27.9% to -5.1%) per year, was identified in females between 2014 and 2020.

Discussion

Changes in the incidence of melanoma over time, particularly in younger age-groups, have been reported in several countries, thought to be as a consequence of public health safe-sun messaging. Incidence rates in females aged 16-24 years decreased significantly in Ireland between 2014 and 2020, however rates in males showed no change over time.

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The 'Barbie Drug' - marketing and perceptions of Melanotan on social media

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Abstract

Background

Melanocyte stimulating hormone analogues such as Melanotan I & II are commonly used to promote tanning and appetite suppression. Melanotan has been branded on social media as a 'Barbie Drug', as expected effects are those of tanning and weight loss. The phenomenon raises public health concerns due to reported adverse effects, particularly an association with melanoma. The sale of Melanotan in Ireland is illegal, however it is widely available, and users of Melanotan are commonly encountered in daily practice.

Methods

In this observational study, the role of social media in the perception of Melanotan, its safety and accessibility, were subject to investigation. 400 Social media posts were selected using the search function across four social media platforms (Tiktok, Instagram, Facebook and X- formerly known as Twitter). Social media posts were interpreted and grouped by themes which were recorded on an excel spreadsheet.

Results

Thematic analysis demonstrated that Melanotan is commonly portrayed as protective against skin cancer (34.8% of posts mentioning skin cancer). Potential adverse effects and legal status received minimal attention (25.8%). Almost half (45.75%) of social media posts offered direct sale of Melanotan.

Discussion

This study provides an insight into the social media content that is likely to influence public perceptions regarding Melatotan and demonstrates the role of social media in the promotion and procurement of Melanotan. The posts subject to review in this study were selected from publicly available posts. As use of social media continues to increase, this study highlights a potential new role for physicians in utilising social media to improve health literacy and public access to evidence based medical information.

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Synchronous Melanoma: A retrospective study

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Abstract

Background

Synchronous melanoma (SM) is defined as ≥2 melanomas diagnosed at the same time, or within three months of diagnosing the first melanoma. Previous studies have shown that 0.5% of all patients with cutaneous melanoma have synchronous second primaries. A retrospective study of melanoma data in the South-East cancer centre of the Republic of Ireland was undertaken. We reviewed the demographics, risk factors and melanoma types in all the cases of SM discussed at the melanoma MDT meeting for the last 5 years.

Methods

Melanoma MDT lists, histopathology and clinical records were reviewed from July 2018 to July 2023 inclusive, for SMs. This study includes invasive malignant melanoma (MM), lentigo maligna (LM) and melanoma in situ (MIS).

Results

42 (3.8%) out of 1082 patients with cutaneous malignant melanoma had synchronous lesions. There were 26 males and 16 females. More than half of the patients (n=23) were above the age of 70. Nine (21.4%) cases had a previous history of melanoma, with four having previous SMs. A total of 91 SMs were identified, consisting of 26 (28.6%) invasive MM, 22 (24.2%) LMs and 43 (47.3%) MIS. Most lesions (33%, n=30) were located on the trunk followed by 26 on the head and neck region, 22 on the upper limbs and 13 on the lower limbs. 14 patients had SMs on same body sites. 27 (29.8%) lesions are located on non-visible body sites such as back (19) and posterior neck/scalp (8). 20 (47.6%) patients had synchronous in situ lesions, 20 patients had LM/MIS with an invasive melanoma (pathological stage 1A to 4B) and 2 (4.8%) patients had stage 1a with stage 1b melanoma. 92.8% of cases (n=39) attended Dermatology services for follow up.

Discussion

To the best of our knowledge, this is the largest case series to date of SM reporting a higher incidence compared to the literature (3.8% vs 0.5%). Special attention should be taken with high-risk patients who are male and elderly who have previous history of melanoma/SMs. Further, it

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highlights the importance of a total skin examination to avoid missing SMs located on non-visible body sites.

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Histological characteristics of lentigo maligna as predictors of progression to lentigo maligna melanoma

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Abstract

Background

The lifetime risk of progression from lentigo maligna (LM) to lentigo maligna melanoma (LMM) is estimated between 5-20% but cannot be reliably predicted. Most cases of LM are surgically excised. Certain histologic features are hypothesised to be associated with advanced LM and may correlate with the presence of invasion. This study aims to assess whether pagetoid spread, confluent growth, and nesting differ between cases of LM and LMM, and to determine if these features can predict upgrade from LM to LMM after wide local excision (WLE).

Methods

In this retrospective cross-sectional study, we analysed histologic slides from 58 randomly selected individuals diagnosed with either LM n=29 or LMM n=29 between 2016-2022. Nine of the LMM cases showed an upgrade to invasion on WLE not seen in initial biopsies. Demographic and clinical data were retrospectively obtained from patient records for each individual. Two independent evaluators, blinded to the final diagnoses, reviewed all slides and rated the degree of nesting, pagetoid spread, and confluence separately, as absent, mild or prominent. A consensus opinion was agreed in discrepant cases. After exclusions, 54 individuals remained in the final analysis (LM = 27, LMM = 27, 9 of which were upgraded on WLE).

Results

In multivariable logistic regression models, male sex was associated with higher odds of LMM compared to female sex (OR 4.57, 95% CI 1.25-16.66, p=0.021). Increasing pagetoid spread was associated with lower odds of LMM (OR 0.38, 95% CI 0.16-0.93, p=0.034), whereas increasing confluence was non-statistically significantly associated with higher odds of LMM (OR 2.50, 95% CI 0.96-6.51, p=0.062). No association was found between the degree of nesting and diagnosis of LM or LMM (OR 1.20, 95% CI 0.44- 3.24, p=0.723). There was no association between the three histological features assessed and upgrade from LM to LMM on WLE.

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Discussion

Our findings suggest that the degree of pagetoid spread (negative correlation) and confluence (positive correlation) differ between individuals with LM and LMM, however there was insufficient evidence that these histological features could be used to predict the upgrade of LM to LMM on WLE.

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Resection margins in cutaneous melanoma of the head and neck – a systematic review

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Abstract

Background

The World Health Organisation (WHO) recorded 324,635 new cases of melanoma, globally in 2020. Despite the introduction of targeted therapy options, surgical excision remains the first line treatment. Cutaneous melanoma of the head and neck exhibits poor prognosis and higher rates of recurrence. Furthermore the complex anatomical and aesthetic features of the head and neck can make wide local excision particularly difficult in this region.

Method

This systematic review was performed to identify studies that examined optimal excision margins in head and neck cutaneous melanoma between the year 2000 and 2022. Pubmed, Cochrane library and Embase were searched to identify relevant studies. Primary outcomes included rates of recurrence and overall survival (OS).

Results

Thirteen studies were included comprising 7738 patients. The cheek was the most common location for head and neck melanoma, with the highest rate loco-regional recurrences identified in scalp melanoma. Breslow thickness was consistently identified as a predictor of positive resection margins, increased risk of recurrence and reduced OS. 38.4% of studies reported no significant correlation between resection margin and survival.

Discussion

Our results reflect previous data in cutaneous melanoma which showed no significant prognostic effect of resection margins. Reduced margins may be applicable in selected patients to reduce morbidity and need for surgical reconstruction without negatively affecting recurrence rates or OS.

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Discrepancies in Imaging Surveillance Practices for Melanoma Patients: An Audit at Galway University Hospital

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Abstract

Background

Malignant melanoma, a highly aggressive form of skin cancer, has a propensity for rapid progression and metastasis. Its incidence has been increasing globally, making it a significant public health concern. However, over the last ten years there has been a dramatic improvement in the treatment of metastatic melanoma patients with the advent of targeted immunotherapies. With the corresponding increase in 5-year survival in metastatic melanoma patients' radiological surveillance is increasingly used to diagnose early locoregional and distant metastasis.

Methods

The audit focused on patients diagnosed with malignant melanoma in 2023, specifically those classified as stage IIC (pT4b N0 M0) and stage III (Any T node positive M0). Data was collated from our Skin Cancer Clinical Nurse Specialist database, our Evolve patient portal, and National Integrated Medical Imaging System (NIMIS). The primary evaluation parameters were the adherence to PET CT and US follow-up intervals as outlined in the 2021 local Galway University Hospital (GUH) Melanoma Imaging Guidelines.

Results

The audit encompassed 31 patients, including 14 with stage IIC and 17 with stage III melanoma (4 node-negative and 13 node-positive). In stage IIC, only 21.4% received staging PET CT, with none receiving a follow-up PET CT at 6 months. Conversely, 50% of these patients underwent CT TAP for staging and 42.9% of these patients received CT follow up at 6 months. Among stage III node-negative patients, 25% received staging PET CT while 75% of these patients received staging CT at diagnosis. In the stage III node-positive group, 23.1% had staging PET CT while 76.9% underwent staging CT. Follow-up imaging at 6 months was notably deficient, with less than 40% of all patients receiving PET CT/CT. Additionally, US follow-up compliance was suboptimal, with only 61.5% of Stage III patients receiving US at 4 months and 87.5% at 8 months.

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Discussion

The audit revealed a significant deviation from the established local imaging guidelines for melanoma surveillance. Less than a quarter of patients received PET CT for initial staging, contrary to recommendations. A preference for CT TAP over PET CT was observed, raising questions about resource availability and clinical decision-making processes. The low rate of follow-up imaging, particularly PET CT/CT at 6 months, highlights a critical gap in ongoing patient surveillance. The adherence to US follow-up protocols was relatively better but still below the expected standards. The audit underscores a substantial discrepancy between the recommended imaging surveillance protocols and actual clinical practice for melanoma patients at Galway University Hospital. These findings suggest a need for a comprehensive review of resource allocation, guideline awareness, and adherence strategies. With the impending introduction of the National Clinical Guidelines on staging and surveillance of patients with cutaneous melanoma, do we need to look at how feasible it is for every unit to access PET CT and other modalities of radiological surveillance in a timely manner.

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The detection of melanoma recurrence by an ultrasound surveillance scan

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Abstract

Background

There is a high incidence of melanoma reoccurring within the first 5 years after initial diagnosis. Regular surveillance imaging is key for the survival of these patients. As a result of recent research, ultrasound now plays a role in the detection of recurrence. The area specifically scrutinized by ultrasound is the lymphatic nodal basin near the previous primary site of cancer. Ultrasound has been proven to be more accurate in the detection of abnormal lymph nodes compared to other modalities.

A 56-year old man was diagnosed with stage IIIC melanoma. A wide local excision and sentinel node biopsy was performed which was positive. As a result, CT and ultrasound scans were performed at regular intervals after diagnosis and staging.

Results

The first ultrasound scan performed 4 months post-diagnosis was normal. However, 8 months post-diagnosis, an abnormal lymph node was detected on ultrasound. This lymph node had suspicious features indicating malignancy. CT identified this atypical lymph node also and showed prominent mesenteric lymph nodes concerning for metastasis. A biopsy was performed on the node detected by ultrasound which confirmed the return of metastatic malignant melanoma.

Discussion

Despite the excellent accuracy of ultrasound in detecting melanoma recurrence at the nodal basin, this service is only available in two hospitals in the Republic of Ireland. There are a number of barriers which inhibit its availability including the lack of specialised training and doubt regarding the need if regular cross-sectional imaging is performed.

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Conclusion

This case demonstrates how sensitive and specific ultrasound can be in identifying abnormal lymph nodes suspicious of metastatic melanoma recurrence. However, accuracy depends on the sonographer's skill. Hence, more training must be provided in order to make this service available at more clinical sites.

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Reducing the incidence of problematic seroma formation and skin necrosis post lymphadenectomy – TRIPLE ACTION Topical TXA, negative pressure wound therapy and prolonged drainage

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Abstract

Background

Axillary and inguinal lymph node dissections are commonly associated with complications, often requiring additional intervention.

Methods

Patients who underwent an axillary or inguinal lymphadenectomy using standard practice were compared to an intervention cohort of patients who underwent an axillary or inguinal lymphadenectomy with use of topical tranexamic acid (TXA) to the wound cavity, a PICO *(Smith&Nephew UK)* closed-incision negative pressure dressing and discharged early with a drain in-situ.

Results

Seventy-six patients in the control group (mean age 65.8, mean BMI 28.4) had an open lymphadenectomy with no topical TXA and a simple dressing. Seventy-eight patients were included in the intervention group (mean age 67.1, mean BMI 28.5).

Patients in the intervention group had an inpatient stay of mean 5.6 days fewer than those in the control group (CI 3.09-5.31;p<.0001), an estimated saving to the healthcare trust of £3046.40 (3723.61US$) per patient in "bed days". They had a longer drain duration (mean 15 days v 8.3 days) however they had a statistically significant lower risk of seroma formation requiring drainage (6.4% v 21%;p=.009), and skin necrosis (0% v 6.6%;p=.027). They also had a lower risk of infection (17% v 29%), wound dehiscence (15% v 25%) and readmission (7.7% v 14%), although not statistically significant.

Patients in the control group were more likely to receive antibiotics as inpatients (51% v

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7.7%;p<.00001) and on discharge (24% v 5%;p<.0011) than those in the intervention group.

Discussion

Topical TXA, PICO dressing and early discharge with a drain following lymphadenectomy results in a reduced rate of complications.

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The PENN Criteria: A Diagnostic Algorithm in the Detection of Acral Melanoma

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Abstract

Background

Acral melanoma (AM) is a rare low mutational burden sub-type of melanoma, prevalent in the palms, soles and nail matrix in non-Caucasians and is associated with poor prognosis. The aim of this study was to assess prevalence of this aggressive sub-type of melanoma in an Irish cohort and identify patterns of disease and treatment factors distinct to other sub types of melanoma.

Methods

We performed a retrospective review of consecutively presenting pa ents to a tertiary referral cancer centre for the management of melanoma. Pa ents diagnosed with melanoma treated between 2017 and 2023 at Beaumont Hospital, Dublin were identified from a prospectively maintained melanoma database. Patient medical records, pathology and radiology were reviewed for data extraction. Analysis of histopathological characteristics, treatment processes and outcomes was undertaken for pa ents with AM and then compared to non-acral melanomas (NAM). Descriptive statistics, data distribution and comparison between groups was performed using SPSS Version 28 software.

Results

A total of 33 AM and 350 NAM pa ents met the inclusion criteria. The majority of AM pa ents were acral lentiginous sub-type melanomas (63.64%) followed by nodular (18.18%). The average breslow's thickness of AM was 3.39mm (range 0.65mm to 8mm) compared with 2.74mm (range 0.5mm to 9.5mm) for NAM (p=0.038). T stage greater than or equal to 3 was noted in 72.72% of AM presentations. A positive sentinel lymph node biopsy was identified in 48.28% of AM compared with 15.80% NAM (p=0.01). Molecular mutation analysis was detected in 40% with BRAF being most prevalent (18.18%). Over 33% of the cohort presented 6 months a er the lesion was first detected.

Discussion

Diagnosis of AM is rare in Ireland and its atypical presentation on has led to diagnoses at more advanced stages. AM is more likely to require aggressive surgical management resulting in digital

amputations and adjuvant immunotherapy with significant morbidity. We developed the PENN criteria as distinct from the ABCDE of melanoma to help outline key characteristics to improve recognition of AM at earlier stages, PENN: Pigmented or non-pigmented, Enlarging, Non-healing lesions of the Nail-bed, palms or soles.

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Impact of the Provision of Sunscreen Dispensers at Outdoor Sport, Recreation and Tourism sites in Ireland

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Abstract

Background

Prolonged exposure to ultraviolet (UV) radiation puts participants in outdoor recreation at increased risk of developing skin cancer. The aim of this study was to investigate the effectiveness of sunscreen dispenser boards in raising awareness of the importance of skin protective behaviours and increasing sunscreen use amongst this group.

Methods

Participating organisations were recruited by sending an expression of interest request to all Healthy Club, Healthy County and Sláintecare Healthy Communities coordinators nationally who in turn sent it to community/voluntary groups involved in outdoor recreational activities in their areas. Interest exceeded availability and organisations were signed up on a first come, first served basis. 87 sunscreen dispenser boards which included a dispenser, mirror and UV index dial, were distributed amongst 48 outdoor sport, recreation and tourism groups nationally and left in situ for 12 weeks from June to August 2023. An invitation to scan a QR code and take the linked feedback survey was displayed alongside each. Participating organisations were also invited to nominate participants to take part in semi-structured interviews.

Results

The survey received 102 responses. The majority of respondents (73%) reported that they get most of their UV exposure while participating in outdoor recreation. 22% reported using the dispenser a few times per week, 18% once per week and 11% reported that they used it daily during the 12 week period. 91% stated that the presence of the sunscreen dispenser boards made them more likely to take skin protective measures. 100% of respondents stated that they will continue to apply sunscreen going forward.

Qualitative data were collected from semi-structured interviews with 6 participants. Common themes included that feedback from within organisations was largely positive, that the dispensers increased awareness and sunscreen use, and that there was an intention to

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continue to use them.

Discussion

Satisfaction with the dispensers within participating organisations was high, and results suggest that they were effective in raising awareness of the importance of skin protective behaviours and in increasing sunscreen use.

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Melanoma: Referral source and diagnostic query

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Abstract

Background

In 2014, Ireland's National Cancer Control Programme (NCCP) introduced an electronic referral form for general practitioners (GPs) to refer suspicious pigmented lesions to secondary care units. Ideally all patients diagnosed with melanoma should be referred using this pathway, with the query 'A likely melanoma.' A key performance indicator designated by the NCCP is that excision takes place within 6 weeks of receipt of referral.

This audit was performed to assess local uptake of the NCCP referral form and whether the route of referral of suspicious pigmented lesions aided accurate triage.

Methods

109 cases of invasive melanoma were diagnosed in our hospital in 2022, as identified from the local melanoma database. Source and route of referral, date of referral, referral query, and date of excision were extracted to compare accuracy in diagnosis across referral route and how the referral routes affect time to excision.

Results

Of the 109 patients diagnosed with melanoma, 84 were referred from primary care and were included in further analysis. The remaining 25 were diagnosed on follow-up or as incidental findings. 56/84 (66.7%) appropriately used the NCCP electronic referral pathway, 26/84 (30.9%) used standard GP referral pathway, and 2/84 (2.4%) used NCCP written referral forms.

Referral queries were separated by referral route and categorized by options on the NCCP E-Referral form with details outline in Table 1 below:

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	NCCP E-Referral (56)	GP Referral (26)
A likely melanoma	66.1% (37)	30.8% (8)
A changing mole	21.4% (12)	19.2% (5)
An ugly duckling sign	10.7% (6)	23.1% (6)
A benign mole	1.8% (1)	0
Other	0	11.5% (3)
N/A	0	15.4% (4)

Discussion

The majority (66.7%) of melanomas referred from primary care were referred using the preferred electronic NCCP referral form. This still falls short of the goal of 100%. In our experience the patients diagnosed with melanoma who were referred via electronic NCCP referral form were seen in a more timely fashion as more accurate information was provided at time of referral allowing more appropriate triage. We have highlighted the findings of this audit to the local GP community at the hospital GP liaison committee, in order to emphasise the importance of using the electronic NCCP referral form for suspicious pigmented lesions.

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An audit assessing measurement of Vitamin D levels at diagnosis in patients with melanoma

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Abstract

Background

Public sun protection campaigns underscore insufficient sun exposure as a significant public health issue, leading to inadequate vitamin D levels. Vitamin D3 and its active metabolites exhibit various anti-aging and photoprotective effects on the skin by modulating immunity and regulating keratinocyte activity. Recent research, including a significant cross-sectional study involving 498 adults in Finland by Kanasuo et al., suggests a potential link between regular vitamin D supplementation and reduced melanoma incidence compared to non-users[1]. Our audit was based on standards set by the National Institute for Health and Care Excellence (NICE) which state that Vitamin D levels should be measured at diagnosis in secondary care in all people with melano [3]. These standards also state that patients with suboptimal Vitamin D levels should be given advice for supplementation and monitoring in line with local policies. Our audit was completed in two cycles.The first cycle aimed to identify the proportion of patients with a new melanoma diagnosis from July 2023 to September 2023 who had vitamin D levels checked at diagnosis. Our intervention included an educational session outlining our results and subsequent plan of action to the plastic surgery and dermatology departments in our institution. Our second cycle included a re-audit of our new melanoma diagnoses, to show an improvement in our practice.

Methods

The audit's registration number is 487. Our initial cycle identified new melanoma cases from July to September 2023 via skin MDT records. Weblab review assessed vitamin D testing at diagnosis, excluding non-melanoma skin cancers and melanoma in situ. Data was collected securely on a departmental computer. Following our local educational session, we re-audited our new melanoma diagnoses between November 2023 and January 2023, to determine whether we had made an improvement in:

a) Measuring vitamin D levels at diagnosis;

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b) Educating patients on the importance of vitamin D Supplementation.

Results

In our initial cycle, out of 75 newly diagnosed melanoma patients, only 2 had documented vitamin D levels, both within the normal range. In the subsequent cycle with 10 patients, all had their vitamin D levels measured, all of which were normal. These results highlight the necessity for standardized protocols and enhanced documentation regarding vitamin D assessment in melanoma patients. Interestingly, all assessed serum vitamin D levels were normal, suggesting increased awareness among healthcare professionals and patients regarding vitamin D supplementation benefits for bone health and immune function.

Discussion

In conclusion, it's vital to implement a structured approach for assessing Vitamin D levels in newly diagnosed melanoma patients. Following NICE guidelines, initial steps should involve routine screening of Vitamin D levels through blood tests, supported by educational campaigns to reinforce awareness of melanoma and vitamin D
intake. Patient education on the correlation between Vitamin D levels and melanoma, along with guidance on sun protection measures, is crucial. For those with low Vitamin D levels, supplementation, and regular monitoring as
per local policies is advised. This comprehensive strategy aligns with best practices and empowers patients in managing their melanoma.

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≈1%

Audit of Sentinel Lymph Node Biopsy for Primary Melanoma in a Tertiary Centre: Rate of Metastasis Detection and Quality of Reporting over 10 Years

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Abstract

Background

Sentinel lymph node biopsy (SLNB) in patients with intermediate to thick 1° melanomas may identify patients for complete LN dissection and prolong disease free survival. NICE suggest SLNB in patients with risk factors for higher incidence of nodal disease.

In Beaumont, melanomas of pT1b (UICC 8th) or higher have SLNB. Current protocol is 3 H&E levels at intervals with 3 immunostains (S100, MelanA and HMB45), 1 at each level. A new reporting template was introduced in 2021.This audit aims to determine the percentage of SLNB in Beaumont Hospital, over 10 years, that are positive for metastatic disease to see if this meets targets set by the EORTC protocol endorsed by the RCPath (the standard of practice considered in this audit). It will also assess suggested reporting features to see how reports comply.

Methods

Searched Lab IT system for entries including "sentinel" under plastic surgery from 01/01/13 to 31/12/23. Not included: referred material. Included: identified as sentinel by surgeon and confirmed node by pathologist.

Results

Cases: 560, 1047 nodes
Positive: 109
Capsular naevi identified: 36
Cases with both melanoma and capsular naevi: 3
Positivity rate: 19.5%
Cases with either metastasis or naevi or both: 25%
Included size of largest metastasis: 93%
Included location of largest metastasis: 55%, *82% in 2023*

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Included presence/absence of extranodal extension: 77 %, *88% in 2023 Note: new reporting templates were introduced in 2021.*
Included presence of blue dye noted in only ≈1% of cases Included presence of matted nodes in less than 1% of cases

Discussions
Detection of metastases in SLNB for melanoma is just below the advised limit of 20% at 19.5% with the current protocol, modified from the EORTC. Reports are deemed sufficient (>90%) regarding size of largest metastases but not for location of largest metastases or presence/absence of extranodal extension. However, with the introduction of reporting templates in 2021, these figures have improved. Recommendations from the audit include discussion with consultants involved in reporting of the skin MDT regarding the alteration of the current protocol as well as the continued use of reporting templates.

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Variation in the practice of wide local excision for melanoma in Ireland and the United Kingdom: a questionnaire survey

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Abstract

Background

Wide local excision (WLE) is standard practice in the management of melanoma, but no national or international guidelines exist regarding its technique.

The aims of this study were to assess variation in the practice of WLE and to explore the effect of clinicians' specialty and grade on such variation.

Methods

This was an international, anonymized, cross-sectional study. An online questionnaire was distributed to the Irish Association of Dermatologists, British Association of Dermatologists, British Association of Plastic and Reconstructive and Aesthetic Surgeons, Melanoma Focus, and BioGenoMEL members.

Results

Of 128 respondents, 57% were dermatologists and 38% plastic surgeons. Most (80%) were consultants. Almost all clinicians learned their technique from colleagues (99%) "on the job", while 21% also used textbooks/media as part of WLE training. There was significant variation in planning and performing WLE: 59% considered margins already achieved, 71% marked margins with the skin relaxed. For 1 cm WLE, 84% delineated 1 cm from the scar edge; with plastic surgeons more likely to mark from the scar midpoint ($p < 0.05$). Most followed a longitudinal/oblique axis on the limbs for WLE (81%). Only 40% sent "dog ears" for histology. Most (71%) incised along the marked line, 27% incised outside it. Most (79%) excised to deep fascia, 19% to the next biological margin.

Discussion

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This study demonstrates significant variation among clinicians performing WLE, an essential component of melanoma management. We postulate that this could impact on patient outcomes. A consensus statement should be developed, to achieve more consistency in the practice of WLE.

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Sunbeds - What do Irish patients know?

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Abstract

Background

Dermatologists are familiar with the harmful effects of sunbed use, but how aware are patients? The National Skin Cancer Prevention Plan 2023-2026 recommends that the Irish population never use a sunbed. Furthermore, legislation was put in place in 2014 to prevent the use of sunbeds by minors. However, do patients' attitudes and behaviours reflect recent public health initiatives?

Aims

To establish current and past patient use of sunbeds in Ireland. To assess patients' attitudes towards sunbed use and understanding of its potential side effects.

Methods

The authors carried out a survey of general dermatology patients attending the outpatient clinic in a tertiary referral centre between February 2024 and March 2024.

Results

43 patients were surveyed with a variety of skin conditions ranging from inflammatory to potential skin cancers. Each survey was comprised of 13 questions. Of the 559 total questions, 547 questions were answered.

As this was an anonymous survey, no demographic details were collected. One question asked patients whether they were members of an ethnic community. 1 patient was a member of the Irish traveller community and 1 patient was of African ethnicity.

Of the total group surveyed, 67% of patients report some degree of knowledge about skin cancer, and 84% of patients are familiar with the term melanoma.

No patients currently use sunbeds. 46.5% of patients used sunbeds in the past. Of these, 35% reported using sunbeds before the age of 18. 60% used sunbeds less than 20 times, 15% used sunbeds less than 50 times, 15% used sunbeds up to 100 times, and 10% used sunbeds more than 100 times. No patients had a sunbed at home. 25% of patients reported using tanning salons.

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18% of patients commented on their reason for using sunbeds, varying from a desire to achieve a tanned appearance to self-treating skin conditions and acne. 87% of patients who never used sunbeds thought sunbeds cause harm compared to 80% patients of sunbeds users. 80% of patients who used sunbeds are aware that sunbeds cause skin aging and 100% know sunbed use is associated with skin cancer.

Discussions

While none of the patients currently use sunbeds, there is a significant proportion of patients who used them in the past and under the age of 18. Most sunbeds users did so for lower amounts of time (less than 20 sessions) and in salons. In terms of awareness, patients in this snapshot review appear to be cognisant that sunbeds cause harm, skin aging and skin cancer.

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POT1 Gene family case series: an important familial cancer syndrome in Dermatology

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Abstract

Background

Around one in ten cases of cutaneous malignant melanoma (CMM) are reported in a familial setting with approximately 40% of cases being accounted for by deleterious germline variants in CDKNA[1, 2]. Several other rare genetic variants exist including protection of the Telomere 1 Gene (POT-1), playing a role in telomere maintenance and protection. Mutations in the POT1 gene can lead to a condition known as POT1 tumour predisposition (POT1-TPD), which is associated with an increased risk of cutaneous melanomas as well as several other malignancies including chronic lymphocytic leukemia (CLL), sarcoma, angiosarcoma (particularly cardiac angiosarcomas), Hodgkin lymphoma, colon carcinoma and gliomas. Associated cancers have been described in less than one hundred families worldwide[3].

Method

A case series was collated of family members attending the Southern Health and Social Care Trust with POT1-TPD since 2018. The family has a history of multiple cutaneous melanomas, malignant myxofibrosarcoma and sarcoma.

Results

This case series also noted that the patients with POT1-TPD in this family were more likely to have dermatofibromas and atypical blue naevi than the general population. This suggests that these skin findings may be a marker for POT1-TPD and could be an indication for genetic testing when taking into account the patient's family and past medical history.

Discussion

The findings of this case series highlight the importance of genetic testing for POT1 mutations in families with a history of malignancies as specified previously. Early diagnosis, surveillance and treatment can help to improve the prognosis for patients with POT1-TPD.

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To develop and establish a National Health Service (NHS) Nurse Led Automated Total Body Mapping (ATBM) service in the Dermatology Unit, Ulster Hospital Northern Ireland.

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Abstract

Background

In Northern Ireland there has been a 30% increase in the incidence of malignant melanoma in the last decade. Malignant melanoma cases represented the 7th most common cancer type in Northern Ireland. In 2021 353 cases of malignant melanoma were diagnosed in Northern Ireland, a 5.4% increase from 2018-2019 figures. The projected incidence of malignant melanoma cases are expected to rise to approximately 533 per year by 2025 and 687 per year by 2035 (Northern Ireland Cancer Registry, 2021). The Nurse led Automated Total Body mapping service is an improvement project representing a unique partnership of a local charity- Cancer Focus Northern Ireland and the South Eastern Health and Social Care Trust (SEHSCT). This was funded by The Department of Health Cancer Charities Support Fund supporting a small clinical team to develop and implement this service. This service was not available in the NHS in Northern Ireland despite the increasing evidence to support the role of ATBM in the screening and early detection of malignant melanoma.

Aims

To detect malignant melanoma as early as possible in specific high-risk patients identified through agreed clinical referral criteria. To reduce the number of surgical excisions for non-melanoma lesions.

To identify patients with suspected malignant melanoma and refer for surgical excision.

To provide health education advice on skin cancer prevention and promotion of skin self-examination. To measure patient satisfaction with ATBM.

To reduce the Dermatology waitlist across the SEHSCT.

Referral criteria:

- Over 18 years old and have one or more of the below:
- Genetic diagnosis confirming high risk of malignant melanoma.
- 5 or more atypical naevi AND at least one of the following: Previous melanoma, first or second degree relative with history of melanoma or >50-100 melanocytic lesions or more

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atypical naevi in the patient AND a first degree relative with melanoma AND>50-100 moles.

- >50-100 moles and past history of MM. Patients with >2 primary melanoma.
- 50 moles or 5 or more atypical naevi or past history of Melanoma, AND immunocompromised. Single lesion of concern for short term monitoring.

Automated Total Body Mapping (ATBM) Melanoma Screening

Technologically enhanced screening interventions have been developed which have been noted to offer promise in earlier melanoma detection, including Total Body Photography (TBP); Sequential Digital Dermoscopic Imaging (SDDI); and computer assisted diagnosis using artificial intelligence.

ATBM Technology

Our ATBM service utilises the FotoFinder system using a two-step algorithm consisting of ATBM through TBP and SDDI whilst also incorporating an optional AI component. This system incorporates a digital camera and video dermoscopy camera with an attached computer trolley; including automatic camera positioning; integrated lesion analysis software using an AI option that provides an automated second opinion. This technology aims to identify new and changed moles faster and more precisely, with potentially reduced examination time. As noted, it also includes an artificial intelligence (AI) software component that has achieved 86.6% sensitivity and 82.5% specificity for the malignancy classification of dermoscopic images of melanocytic lesions, matching dermatologist performance in an experimental setting. High-resolution, polarised and RAW-processed photos and powerful image processing enable dermatoscopic structures to be visible in the clinical image. An integrated medicam 1000s hand held video dermatoscope is used for lesions that require further examination. This involves magnification of images up to 400 times, from the whole body to the cell body. A Mosaic View of moles can be developed, where the system visualises new and changed lesions from all total body images and organises them intelligently on one screen, sorted by new, changed and unchanged nevi (according to their relevance). This “Mosaic View” helps to identify suspicious lesions. These images are then reviewed and compared with new images taken when the patient is reviewed. Artificial Intelligence (AI) scoring technology is also available to assist the Clinician in prioritising further examination and follow up.

Following screening the images are reviewed by the Consultant Dermatologist and Skin Cancer CNS who then makes decisions on whether further referral for excision is required.The development and implementation of the service has been overseen by a Project Steering Group (SG) representing senior clinical and managerial staff from both organisations. This group is chaired by the Consultant Nurse for Skin Cancer (one of two Trust Co-Project Leads), the other being the Operations Manager of Cancer Services. Clinical Lead oversight is by a Consultant Dermatologist who is also pivotal to

this service.

Methods

To gather information on the overall structure of setting up a Nurse led Total body mapping service to include the impact on dermatology waiting time, and overall dermatology service demand.
To meet with the key stakeholders in service provision to include-dermatologists, nurse specialists, and allied health professionals. To provide training for the Skin Cancer Clinical Nurse Specialist by identifying opportunities for learning such as shadowing an existing Private Clinic in Belfast (currently offering similar MM services) as well as attendance at specific equipment training in London. To explore the education needs of patients and their families in preparation for ATBM To discuss the development of patient information in various formats, such as written and web-based to explain the screening process.To measuring outcomes- a Research & Development (R&D) Subgroup has been established to oversee the evaluation of the service. Overall, the development and implementation of the service required considerable resource and a cohesive and collaborative approach from each stakeholder to include administrative support.

Project Management Arrangements
Key aspects of developing and implementing the service have included:
Purchasing and set up of the ATBM FotoFinder equipment.
Recruitment, induction, and training of funded posts.
Establishing robust governance arrangements, including the development of clinical referral criteria and development of Trust Clinical Guidelines.
Development of data capture requirements, including Database design.
Ongoing review of literature to inform the development of the project
Planning service evaluation methods.
Refining Project Aims and Objectives to include additional elements not included in the original funding submission.
Engagement with Patient User Groups to develop patient information materials.
Development and roll out of a postal Patient Satisfaction Survey.
Development of a Volunteer clinic role.
Process Mapping of the MM Clinics from July-Sept.
Planning the formal launch of the service by the Minister for Health on 25th August 2022.
Establishment of a R&D subgroup overseeing ongoing service evaluation.

Results

Clinics commenced 14/07/2022.

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2 clinics per week, Wednesday and Friday. Capacity for 6 patients per clinic.
Up until 19/01/2024 there have been a total of 523 appointments of which 292 have been new referrals and 223 review appointments.
Excision number data-There have been 56 excisions to date

Lesion Type	Melanoma	Melanoma in situ	Lentigo Maligna	Dysplastic Naevus	Junctional Naevus	Compound Naevus	BCC	Other
	3	4	1	23	3	11	2	9

The 'other' category refers to other dermatological non-cancerous conditions such as lichenoid keratosis, cylindroma, Intradermal naevus, blue naevus and seborrhoiec keratosis. This high risk group of patients have highly evaluated the ATBM service as they feel it is reassuring to have their moles screened and review appointments if required. They have expressed great psychological benefits as they can be highly anxious when examining or photographing their own moles.

Reflections, Recommendations and Key Learning
It took 5 months to establish the ATBM service. This period was vital to address key areas including recruitment of the team; purchasing and set up of the ATBM equipment; training and induction of project staff; establishing the project management arrangements as well as ensuring the governance of the service through the development of clinical guidelines.
It would be suggested that recognition be given to the necessary “lead in” time required, for any future funding applications. ATBM screening appointments are not comparable with other Outpatient appointments and take on average 45-50mins. The initial clinics were process mapped to define the time frames required. The images for each patient are also reviewed separately outside clinic times by the Clinical Nurse Specialists and the Consultant Dermatologist. Initially one Skin Cancer Clinical Nurse Specialist (CNS) was trained to deliver the ATBM service. This created a level of risk to the service should the post holder be unavailable and another specialist nurse was trained to deliver the service and provide cover to maintain the service.

The importance of senior representation and support as part of the Project Steering Group from both organisations has required significant commitment from all members meeting initially on a minimum monthly basis. This has been instrumental in the successful launch of the pilot and demonstrates the considerable level of investment which is required when a new pilot is being developed. It is essential therefore that when planning joint initiatives there continues to be strong senior support across partner organisations to drive such projects. This pilot has created many opportunities for collaborative working however it is also important to note that when project posts are created which are recruited and managed by different employers there can

inevitably be challenges such as access to data from organisations outside of the hospital trust. This should be considered in the pre planning phase, with possible consideration being given to developing Honorary contracts as required.

Discussion

The ATBM service has been developed in Northern Ireland in partnership with Cancer Focus NI and the SEHSCT. This is a pilot project and we are currently working towards a fully commissioned service. It is a replicable service with relatively low costings required for equipment and staff training. It is a great example of a Nurse-led service where new technology, clinical skills and competencies have been extended to deliver this innovative service. Moving forward our Research and Development (R&D) Subgroup has been established, and will oversee detailed service evaluation. To date an ATBM database has been finalised and populated. A Patient Experience survey has been completed and more formal service evaluation and research projects are planned.

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Metastatic Melanoma to Axillary Lymph Nodes with Complete Regression of the Primary Lesion: a case report.

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Abstract

Metastatic melanoma presenting with complete regression of the primary lesion poses diagnostic, prognostic and treatment challenges. We report a case of metastatic melanoma initially presenting as axillary lymphadenopathy, without definitive evidence of a primary lesion. Initial lymph node biopsy revealed the presence of metastatic melanoma and subsequent careful clinical investigation, including total body examination, revealed a possible primary lesion candidate.

Following excision, histological analysis of this lesion showed mild but convincing features of regression, including lymphocytic infiltration, fibrosis and absence of melanoma cells, with some residual benign naevus elements. No evidence of tumoural melanosis was seen. Despite the absence of a definitive primary lesion, significant metastatic spread was evident in the axillary lymph node dissection. Staging PET-CT and MRI brain showed no evidence of further metastatic spread. Subsequent molecular testing of the metastases was negative for BRAF V600E. The case was discussed at the Plastic Surgery/Dermatology multidisciplinary team meeting and it was concluded that this lesion, due to the presence of features of regression and no alternative melanoma lesions, was highly likely to be a regressed primary melanoma. The final histological stage was pTX N3b, with a final clinical stage III-C. The patient subsequently started adjuvant immunotherapy and is currently continuing therapy with no clinical or radiological evidence of recurrence.

It is not possible to be entirely certain of the nature of melanocytic lesions which have regressed, but the presence of residual melanocytes can be assessed and used as evidence for what the likely underlying lesion most likely was prior to regression. In this case, the absence of tumoural melanosis and the presence of residual benign naevus elements may have led to a histologic diagnosis of a partially regressed naevus, however in the clinical context the features support complete regression of melanoma with some residual precursor naevus cells. This case highlights the importance of clinical-pathologic correlation with comprehensive clinical examination and histological assessment in cases of regressed melanocytic lesions.

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Checkpoint Inhibitor associated Autoimmune Vasculitis of the Central Nervous System: A Case Report

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Abstract

Presentation

A 60 year old man was diagnosed with locally advanced malignant melanoma involving axillary lymph nodes, with no primary identified. He was treated with neoadjuvant Ipilimumab and Nivolumab. He presented after 2 cycles with progressive rhythmic jerking affecting the right upper and lower limb and trunk.

Diagnosis

Routine blood tests were normal. CSF analysis showed elevated protein, negative gram stain and culture and negative cytology. Paraneoplastic screen was negative. MRI outruled metastatic disease. CT-angiogram showed diffuse contour irregularity of the intra-cranial arteries consistent with intracranial vasculitis. EEG confirmed intermittent dysfunction involving mainly the left fronto-temporal region. A diagnosis was made of autoimmune CNS vasculitis manifesting as epilepsy partialis continua triggered by Ipilimumab/Nivolumab.

Treatment

At initial presentation the patient was treated with PO Dexamethasone and Levatiracetam with resolution of symptoms. Ipilimumab was discontinued. Symptoms recurred on rechallenge with Nivolumab. IV methylprednislone 1mg/kg was initiated and anti-epileptics titrated with minimal clinical response. IV Immunoglobulin and Rituximab were added as further immunosuppressive agents. Anti-epileptics were titrated, ultimately requiring four drugs.

Seizure activity improved though the patient had persistent right thumb jerking. He developed progressive neurological symptoms with cognitive dysfunction and significant deconditioning requiring prolonged hospital admission. The melanoma progressed leading to death 6 months post presentation.

Discussion

CNS vasculitis is a rare but serious neurological complication of checkpoint inhibitors. The

majority of reported cases resolved with immunosuppressive treatment. This case highlights the difficulty managing treatment refractory immune related toxicities, especially in the neoadjuvant setting.

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Assessment of cutaneous toxicities in Irish oncology patients

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Abstract

Cancer incidence rates are on the rise globally, with Ireland experiencing an estimated 42,000 new cases annually[1]. As advancements in cancer treatment lead to increased survival rates, the use of systemic anti-cancer therapies, including chemotherapy, immunotherapy and targeted therapies, has also surged. Consequently, patients undergoing these treatments are encountering a spectrum of dermatological side effects[2–4]. Despite the prevalence of such issues and evidence that integrating dermatologic care into oncology practices can reduce cutaneous adverse events and toxicity-associated therapy interruption, Ireland has yet to develop a systematic record-keeping mechanism for cutaneous side effects of anti-cancer treatments[3,5]. In response to this, we established a dedicated on-demand dermatology consult service aimed at promptly addressing the dermatological needs of cancer patients and recording the data so we can further analyse associations of dermatological conditions with specific cancers and treatment.

We aim to assess the incidence and impact of these adverse events on patients. The services primary goals include early detection and management of cutaneous side effects to help minimise withholding of treatment for patients and also improving their quality of life. Additionally, the service seeks to establish clear pathways for addressing dermatological toxicities and develop a model of care tailored to the needs of oncology patients. As the incidence of cancer continues to rise, and with systemic therapies becoming increasingly prevalent, the establishment of an oncodermatology service holds promise in optimising patient care and addressing the evolving dermatologic challenges in oncology practice.

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Navigating Fertility and Parenthood in Melanoma Patients: Patient Perspectives.

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Abstract

Introduction

Melanoma poses a unique challenge in women of childbearing age, with one-third of cases occurring in this demographic and it being the most prevalent malignancy diagnosed during pregnancy[1].The landscape of melanoma treatment has evolved significantly, particularly with the introduction of immunotherapies. Immune checkpoint inhibitors have provided a significant improvement in recurrence-free survival[2,3]. As dermatologists, we are now treating patients who were once considered facing a fatal prognoses instead achieving prolonged disease-free survival. Within this context, it becomes imperative to address the intersection of fertility considerations and melanoma management, both from the perspective of patients and clinicians.

Patient perspectives

To highlight the journey of melanoma patients navigating fertility and pregnancy post-diagnosis and immunotherapy treatment, we present two patient narratives. They offer invaluable insights into the lived experiences of women who were diagnosed with melanoma before conceiving and subsequently had successful pregnancies following immunotherapy interventions. By sharing their experiences, we aim to foster greater awareness and understanding faced by melanoma patients of a childbearing age and ultimately enhancing patient-cantered care outcomes.

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The role of a sentinel node biopsy for patients with thick (>4mm,pT4) melanomas.

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Abstract

The object of this study is to evaluate the impact of Sentinel lymph node biopsy (SLNB) in patients with melanoma and primary tumours that have Breslow thickness >4mm (T4). We will review the number of patients with T4 melanoma who underwent SLNB, adjuvant therapy and or a complete lymph node dissection, and review their recurrence- free survival (RFS) and Melanoma Specific survival (MSS). SLNB plays a crucial role in assessing melanoma prognosis, as it is the strongest prognostic factor for melanoma-specific survival, as demonstrated in studies such as the Multicentre Selective Lymphadenectomy Trial (MSLT-I).

However, its role in T4 patients is controversial due to the significant risk of disease progression regardless of lymph node involvement. Moreover, if adjuvant treatment is offered regardless of SLNB status in T4 melanoma patients, the ongoing role of SLNB is debatable. Despite these controversies, SLNB continues to have an important role. Firstly it can provide risk stratification and prognostic information, secondly it can be important in determining patients suitable for adjuvant therapies and lastly SLNB can improve regional disease control. The value of SLNB in the management of T4 melanoma patients warrants careful consideration with special attention to the potential overall reduction of regional disease recurrence when combined with adjuvant therapy.

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Understanding the needs and experience of melanoma and skin cancer patients including educational knowledge which may assist in preventing the condition in the future.

L. Chanders

Abstract

Background

Research shows that protection from UV Rays may assist in reducing risks of melanoma and skin cancers. The Author experienced personal difficulties during treatment for the condition, including accessing suitable information and UPF/SPF products, leading to further research with other patients. The aim is to investigate the difficulties, needs and well-being of individuals with melanoma and skin cancer.

Method

Primary research was conducted in the form of a questionnaire and completed by respondents in their own time. The data was then collected and analysed, followed by interviews with Melanoma and skin cancer patients. The interviews were conducted in person. The age range was 29 to 72 years old, with 20% males and 80% females. Individuals were sourced through Cancer Societies and Active Age groups. Participants were offered the opportunity to opts out at any point, with a 100% response rate.

Results

Of 5 participants, the key findings show 0% of participants were aware of UPF in fabrics and clothes, with 100% indicating they would consider clothing as an option after being informed of the contents. 80% stated they would purchase such items/garments in local retailers and 20% through websites. When asked about the recommended rim length on protective head gear, 80% were unsure. 100% replied it was difficult to access information in simple understandable language, 80% indicated they would welcome and participate in regular information updates, conversations and interactions with other melanoma and skin cancer patients. 100% replies showed they were not aware of the necessity to use SPF while in shaded spaces. 80% advised how they remained indoors during and after treatments of topical medical interventions to protect from UV rays, causing further anxieties. 100% of replies indicated they did not use SPF when the UV index is low.

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Discussion

Further research is required into melanoma and skin cancer patient's needs, simple terms and education would greatly benefit UV protection with direct and easy access to SPF products, shields, garments and services. Public awareness of melanoma and skin cancer is necessary.

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Navigating Complexities: Successful BRAF/MEK Inhibition in a Renal Transplant Recipient with Metastatic Melanoma

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Abstract

Background

Renal transplant recipients (RTR) face a significant 4.9-fold increase in the risk of developing cutaneous malignant melanomas (1). Melanomas diagnosed in RTR often present at a higher disease stage and result in poorer melanoma-specific survival rates (2). The utilization of checkpoint inhibitor immunotherapy (ICI) in RTR with melanoma is complicated by the risk of transplant rejection, affecting approximately 40% of treated patients (3). Around 50% of cutaneous melanomas exhibit BRAF mutations (4), particularly the BRAF V600E mutation, as a consequence of alterations in the MAPK/ERK pathway (5). In response to this, combination BRAF/MEK inhibition such as Dabrafenib/Trametinib have emerged as effective treatments for melanomas carrying BRAF mutations (5,6).

Methods

A retrospective analysis was performed on medical records of a patient who attended University Hospital Waterford (UHW).

Results

Our patient is a 60-year-old male diagnosed with cutaneous melanoma stage 1B in 2020. Notably, he underwent a renal transplant in 1994, necessitating long-term immunosuppression and was on treatment for Parkinson's disease. In August 2023, the patient was admitted to UHW acutely unwell with subacute bowel obstruction. CT imaging confirmed diffuse metastatic deposits, and diffuse omental involvement with ascites and peritoneal carcinomatosis. A biopsy confirmed BRAF V600E-mutated metastatic melanoma. He declined ICI following a discussion of the risk of renal transplant rejection. Despite significant oral intake limitations due to near-complete disease-related bowel obstruction, oral treatment with Dabrafenib/Trametinib was commenced. At treatment initiation, a dose reduction was implemented due to drug interaction concerns, as well as

a reduction in immunosuppressive medication dosage after nephrology consultation. Within days his bowel obstruction improved and he was escalated to full dose therapy. He has an ongoing excellent response to treatment without deterioration in renal function or control of his Parkinson's disease.

Discussion

This case demonstrates a striking response to first-line combination BRAF/MEK inhibition in a RTR with metastatic melanoma. It highlights the complexity of cancer care in the setting of transplantation and the need for vigilant screening for melanoma in this high-risk population.

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Developing a Consensus Statement for the Implementation of Neoadjuvant Immunotherapy in Melanoma

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Abstract

Background

Immune checkpoint inhibitors (ICI) targeting PD-1 and CTLA-4, as well as targeted therapies such as BRAF/MEK inhibitors have transformed the landscape of advanced/unresectable mel- anoma. Multiple phase II trials have assessed the safety and efficacy of neoadjuvant ICI ther- apy in resectable stage III/IV melanoma, but there remains a lack of consensus regarding the decision points that need to be addressed, in order to optimize the implementation of periop- erative therapy in this setting. Herein, we aim to develop a consensus statement for the im- plementation of neoadjuvant immunotherapy in melanoma, to critically review the available evidence supporting this strategy, and consider the practical application in an Irish healthcare setting. The overall goal is to standardise the care of patients with locally advanced melanoma through multidisciplinary collaboration.

Methods

We developed a series of statements addressing the key decision points and options required to institute the use of neoadjuvant ICI for melanoma. Statements centred on key themes were developed based on published literature, addressing: diagnosis, staging, patient selection; neoadjuvant systemic therapy details; response assessment; operative considerations; and post-operative management. Draft statements were electronically circulated to panel members from specialists involved in the multidisciplinary management of patients with melanoma (Plas- tic Surgery, Dermatology, Radiology, Pathology, Medical Oncology, Radiation Oncology). A modified Delphi Consensus process was conducted wherein panel members from relevant specialties were invited

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to rate their level of agreement with the statements using a Likert score, with statements updated iteratively based on feedback from respondents.

Results

The results of 2-3 rounds of the above Delphi consensus statement review will be presented. A completed proposed pathway for the implementation of neoadjuvant immunotherapy will be presented.

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A Case of Acute Transplant Rejection due to Immunotherapy in Metastatic Melanoma

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Abstract

Background

Solid organ transplant recipients (SOTRs) require life-long immunosuppression to reduce the risk of transplant rejection. As a result, malignancy is twice as common in SOTRs compared to the normal population.[1] In those SOTRs who develop malignancy, immune checkpoint inhibitor (ICI) use can lead to acute transplant rejection, while the use of chronic immunosuppression can attenuate the anti-tumour response of ICIs.[2]

Case Presentation

We report the case of a gentleman with renal allograft for end-stage renal disease secondary to IgA vasculitis who, following diagnosis of advanced metastatic melanoma, was treated with Nivolumab and Ipilimumab. ICI administration quickly led to acute transplant rejection within 6 weeks with a subsequent haemodialysis dependency, though the patient achieved a complete and durable response to his disease.

Conclusion

Though the administration of ICIs in SOTRs is not a commonly encountered clinical scenario, the development of acute transplant rejection is a common side effect with ICI use in the cohort. This case demonstrates the durable responses that can be achieved with ICI use in these patients though highlights the devastating side effect of transplant rejection in a previously stable allograft. Trials exploring the use of ICIs in allograft recipients and methods to preserve grafts through pulsed immunosuppression are in their early stages.[3]

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