Abstract Book

Dermato-Onco2024

The European Congress on

Dermato-Oncology

Bioevents
Sharing Biomed Knowledge

P-01

Adjuvant and Neoadjuvant Treatment

In vitro Evaluation of the Efficacy of Rose Bengal Photodynamic Therapy in Human Melanoma

Marie BOILEAU, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France
Smail MARHFOR, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France, LETI, Univ. Grenoble Alpes, CEA, France
Anthony LEFEBVRE, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France
Olivier MORALES, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France, UMR9020-U1277 - CANTHER – Cancer Heterogeneity Plasticity and Resistance to Therapies, CNRS, Inserm, France
Nadira DELHEM, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France
Laurent MORTIER, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France

Background: Photo-dynamic therapy (PDT) involves illumination of previously photosensitized tumor cells by a pharmacological agent (PS). In the presence of oxygen and light, PS generates reactive oxygen species (ROS), responsible for the death, combined with an immunological response to enhance the anti-tumor effect. Rose Bengal (RB), a molecule known for its antibacterial, antitumor and immunoactivating properties, is a green-light-regulating PS. RB has been evaluated for its cytotoxic properties at high doses in melanoma, but photosensitivity was described as a limiting side effect.

Objective: In this study we evaluate the ability of PDT-RB to induce tumor cell death (CD) in melanoma cells.

Materials and methods: Two human melanoma cell lines (HBL and LND) were used. We assessed RB incorporation by confocal microscopy and by measuring intracellular fluorescence. Effect of PDT treatment with RB was assessed on cell viability. Cells were treated or not with RB and illuminated with a 550 nm LED. Mitochondrial metabolism was measured at 24h. RB cytotoxicity was evaluated with lactate dehydrogenase (LDH) levels.

Results: We observed increasing incorporation of RB with increased concentration and incubation time. We observed a decrease in viability of melanoma cells by 50% at 25µM and 50µM respectively. RB showed cytotoxicity at 400µM and above. A decrease in viability linked to combination of RB and light, i.e. a PDT reaction. The study of apoptotic or necrotic death showed a predominantly necrotic death dependent on RB concentration. In the absence of illumination, RB alone does not induce necrosis below 100µM, at which dose an impact on cell viability is observed.

Conclusion: PDT-RB was capable of inducing CD, predominantly necrotic death, in melanoma cells at lower doses for which RB alone. Knowing that necrosis is an immunogenic CD and that RB is also known to be immunostimulant following tumor CD at high concentration, it would be interesting to the ability of PDT-RB to induce activation of the immun response. PDT-RB could be considered as an adjuvant treatment in the management of melanoma

P-02

Adjuvant and Neoadjuvant Treatment

Comparative Outcomes of Nodal Dissection Versus Observation in Stage-III Melanoma Patients with Positive Sentinel Lymph-node Biopsy: A Real-life Study Using Inverse Probability of Treatment Weighting

Gabriele Roccuzzo, Department of Medical Sciences, Section of Dermatology, University of Turin, Italy, Department of Dermatology, Lausanne University Hospital (CHUV) and Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland
Nicole Macagno, Department of Medical Sciences, Section of Dermatology, University of Turin, Italy
Pietro Grignani, Department of Medical Sciences, Section of Dermatology, University of Turin, Italy
Chiara Astrua, Department of Medical Sciences, Section of Dermatology, University of Turin, Italy
Matteo Brizio, Department of Medical Sciences, Section of Dermatology, University of Turin, Italy
Giovanni Cavaliere, Department of Medical Sciences, Section of Dermatology, University of Turin, Italy
Franco Picciotto, Department of Surgery, Dermatologic Surgery Section, Azienda Ospedaliera Universitaria (AOU) Città della Salute e della Scienza, Turin, Italy
Virginia Caliendo, Department of Surgery, Dermatologic Surgery Section, Azienda Ospedaliera Universitaria (AOU) Città della Salute e della Scienza, Turin, Italy
Enrico Fruttero, Department of Surgery, Dermatologic Surgery Section, Azienda Ospedaliera Universitaria (AOU) Città della Salute e della Scienza, Turin, Italy
Simone Ribero, Department of Medical Sciences, Section of Dermatology, University of Turin, Italy
Paolo Fava, Department of Medical Sciences, Section of Dermatology, University of Turin, Italy
Pietro Quaglino, Department of Medical Sciences, Section of Dermatology, University of Turin, Italy

Background: Advancements in managing stage III melanoma have involved the implementation of adjuvant therapies alongside a simultaneous decrease in the utilization of completion lymph node dissection (CLND) following positive sentinel node biopsy (SLNB).
Objectives: To investigate the role of CLND after a positive SNLB and its association with adjuvant therapy in a cohort of real-life patients (N=157) treated at the University of Turin, Italy, between Jan. 2016 and Jan. 2024.
Methods: Using an inverse-probability-of-treatment weights (IPTW) approach, we computed the propensity scores for CLND to estimate the marginal Hazard Ratios (HR) for CLND and marginal survival curves in terms of relapse-free (RFS) and overall survivals (OS).
Results: At a median FU of 36 months, patients without CLND (N=69) had a median RFS of 49 months (95% CI 42-NA), while CLND recipients (N=88) showed 51 months (95% CI 31-NA) (p = 0.139). The 48-month OS for non-CLND patients was 79.8% (95% CI 58.2-91.0) versus 79.2% (95% CI 67.5-87.0) for CLND recipients (p = 0.463). Adjusted HRs through IPTW revealed the impact of CLND to be insignificant on RFS (aHR 0.90, 95% CI 0.37-2.22) and marginal on OS (aHR 0.41, 95% CI 0.13-1.21). Conversely, adjuvant therapy, be it anti-PD1 (nivolumab/pembrolizumab) or dabrafenib+trametinib, significantly reduced the risk of relapse (aHR: 0.46, 95% CI 0.25-0.84), irrespective of CLND.
Conclusion: This real-life study corroborates the growing evidence that CLND after positive SLNB does not enhance RFS or OS, while emphasizes the crucial role of adjuvant therapy in reducing the risk of relapse in such patients.

P-03

Adjuvant and Neoadjuvant Treatment

Vulvar Melanoma with Vaginal Recurrence: A Case Study

Kristin Walker, Radiation Oncology, University of Virginia, USA
Daniel Leach, Radiation Oncology, University of Virginia, USA
Yhana Chavis, Radiation Oncology, University of Virginia, USA
Kari Ring, Gynecologic Oncology, University of Virginia
Elizabeth Gaughan, Medical Oncology, University of Virginia
Einsley Janowski, Radiation Oncology, University of Virginia, USA
Kara Romano, Radiation Oncology, University of Virginia, USA

Background:

Vulvovaginal melanomas represent a rare subgroup of melanoma. Surgery remains the primary treatment modality for localized disease with or without systemic therapy for higher risk cases. The role of radiotherapy remains unclear.

Case Presentation:

A 69-year-old woman presented with a large, discolored vulvar macule. Biopsy demonstrated a c-kit mutated ulcerated malignant melanoma with Breslow depth of 2.1 mm, staged as pT3b. PET-CT showed vulvar-confined disease. However, resection would require pelvic exenteration due to the extent. Given the significant morbidity, neoadjuvant systemic therapy was recommended.

The patient received ipilimumab/nivolumab, then relatlimab due to clinical disease progression. Interval PET-CT demonstrated FDG avidity in vulva and vagina, and exam confirmed nodular lesions in the vulva and posterior vaginal wall. Multi-disciplinary team recommended definitive radiotherapy with concurrent immunotherapy. She received 50 Gray in 25 fractions to the vulva, vagina, and regional at-risk nodal basins with a 4 Gray in 2 fraction boost. End-of-treatment MRI showed significantly decreased tumor volume, and she received an additional boost of 9.6 Gray in 6 fractions BID to the residual disease.

3-month post-treatment MRI revealed a complete response with no evidence of locoregional disease.

Conclusion:

Vulvovaginal melanomas are rare tumors with high rates of recurrent disease even following definitive therapy. This case adds to the paucity of literature on vulvovaginal melanoma and highlights an important role for radiotherapy. As systemic therapy continues to evolves and outcomes improve, it is important to consider noninvasive local therapy such as radiotherapy when surgery would entail excessive morbidity.

P-04

Adverse Events Treating Skin Cancer

Acute Immuno-Induced Meningoradiculitis Leading to Patient Death

Juliette DEUZE, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France
Marie BOILEAU, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France
Bruno LEMARCHAND, Department of Neurology, Univ. Lille, CHU de Lille, France
Céline YELNIK, Department of Internal Medecin and Rares Disease, Univ. Lille, CHU de Lille, France
Eve DESMEDT, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France
Laurent MORTIER, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France

Introduction Neurological adverse reactions (NAR) to immunotherapy are mostly aspecific symptoms (headache, instability, dizziness). In less than 1% of cases, NTEs can be severe (grade 3).

Observations A 61-year-old patient with multi-metastatic melanoma with brain metastases was treated with ipilimumab 3mg/kg and nivolumab 1mg/kg. At the time of evaluation for the 3rd infusion, he had been presenting with hypophonia and mild swallowing difficulties for 5 days. Nasofibroscopic examination was unremarkable. At 24 hours, he presented with confusion and an increase in symptoms. Given the respiratory distress caused by probable inhalation, he was transferred to intensive care. The hypotheses put forward were cerebro-meningeal progression, paraneoplastic disease, infection or neurological toxicity. The electroneuromyogram showed neurogenic damage. Lumbar puncture revealed lymphocytic meningitis with no cells suspected of malignancy. Autoimmune and viral serologies were negative. Extension work-up using brain MRI and PET scans showed a virtually complete response after two infusions. We made the diagnosis of meningoradiculitis induced by immunotherapy on the basis of a compatible timeframe, clinical and laboratory findings. He was treated with corticosteroids (2 mg/kg) and antibiotics. Given the severity of the respiratory impairment, treatment with a monosuppressive agent was not started. The patient died a few days later of multi-visceral failure.

Discussion Immunotherapies represent a major advance in the treatment of melanoma. However, many NDEs have been described, including encephalitis, myelopathy, aspetic meningitis, meningoradiculitis, Guillain-Barré syndrome, peripheral neuropathy and myasthenic syndrome. Meningoradiculitis was suggested by multiple subacute cranial nerve involvement and the presence of lymphocytic meningitis on lumbar puncture. The severity of the neurological picture contrasts with the excellent therapeutic response. Most severe NDEs occurred within 6 to 12 weeks of the start of immunotherapy. Once differential diagnoses (infection, tumour invasion) have been ruled out, immunotherapy should be stopped and corticosteroids started. Plasmapheresis may be discussed.

Conclusion The aim of this poster is to remind us that a frustrating symptomatology may reveal severe neurological toxicity which may be life-threatening. Clinicians must remain vigilant. This case also raises the question of whether immunosuppressive treatment should be started quickly, as may be the case in immuno-induced myocarditis.

P-05

Dermatosurgery of Skin Cancer

The Definitive Treatment of Facial Lentigo Maligna with Tomotherapy-based Radiotherapy. The Experience of Centro di Riferimento Oncologico (CRO) di Aviano

Giuseppe Fanetti, Division of Radiation Oncology, Centro di Riferimento Oncologico di Aviano CRO IRCCS, Italy
Paola Corsetti, Division of Dermato-Oncology, Centro di Riferimento Oncologico di Aviano CRO IRCCS, Italy
Giuseppe Anastasio, Division of Medical Physics, Centro di Riferimento Oncologico di Aviano CRO IRCCS, Italy
Valentina Lupato, Division of Otolaryngology, General Hospital "S. Maria Degli Angeli", Italy
Paola Pase, Division of Radiation Oncology, Centro di Riferimento Oncologico di Aviano CRO IRCCS, Italy
Lisa Andreon, Division of Radiation Oncology, Centro di Riferimento Oncologico di Aviano CRO IRCCS, Italy
Federica Bertini, Division of Radiation Oncology, Centro di Riferimento Oncologico di Aviano CRO IRCCS, Italy
Manuele Roghi, Division of Radiation Oncology, Centro di Riferimento Oncologico di Aviano CRO IRCCS, Italy
Jerry Polesel, Unit of Cancer Epidemiology, Centro di Riferimento Oncologico di Aviano CRO IRCCS, Italy
Paola Chiovati, Division of Medical Physics, Centro di Riferimento Oncologico di Aviano CRO IRCCS, Italy
Vittorio Giacomarra, Division of Otolaryngology, General Hospital "S. Maria Degli Angeli", Italy
Maurizio Mascarin, Division of Radiation Oncology, Centro di Riferimento Oncologico di Aviano CRO IRCCS, Italy
Maria Antonietta Pizzichetta, Division of Dermato-Oncology, Centro di Riferimento Oncologico di Aviano CRO IRCCS, Italy

BACKGROUND

Lentigo maligna (LM) is in situ melanoma arising in sun-exposed areas. Radiotherapy can be used as treatment option when surgery is infeasible. Tomotherapy allows the treatment of skin areas with curvature.

OBJECTIVES

To report results of LM treatment with definitive Tomotherapy.

METHODS

A retrospective report of patients treated at CRO in 2022 was performed. Dermoscopy and reflectance-confocal-microscopy helped in biopsy site selection for histopathological diagnosis and to delineate subclinical LM margins. Radiotherapy was offered when surgery was contraindicated or according to patient preference. A metallic landmark was posed on the delineation area and a thermoplastic mask molded for radiotherapy simulation. Clinical Target Volume was defined by adding 5 mm to Gross Tumor Volume. Tomotherapy prescrition dose was 50 Gy in 20 daily fractions.

RESULTS

Five facial LM patients (median age 74 years) were treated. Median GTV and CTV volumes were 2,93 and 10,49 cm3, respectively. Maximum dose and mean dose were 55 and 51 Gy, respectively. Acute radiation dermatitis was G1 in 4 patients and G3 in 1 patient. Other toxicities included G1-2 conjunctivitis and oral mucositis. After a median of 5 months, complete response was obtained in all patients. One patient recurred after 18 months and underwent salvage surgery. After a median follow-up of 15 months, all patients are alive with no evidence of disease.

CONCLUSION

Tomotherapy response rate and toxicity profile are very favorable. To assure adequate and high precise Tomotherapy collaboration with dermato-oncologist and delineation of LM subclinical margins are mandatory.

P-06

Non-Melanoma Skin Cancer

PAGETEX Photodynamic Therapy Device for the Treatment of Extra Mammary Vulvar Paget`s Disease: Interim Analysis of Safety Data

Marie BOILEAU, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm
Anne Sophie DEWALLE, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm
Henry ABI RACHED, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France
Gregory BAERT, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm
Shirley BALIK, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm
Nadira DELHEM, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm
Cyril MAIRE, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, Dermatology, Centre Medical St Jean, France
Laurent MORTIER, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm

Introduction Extra mammary Paget`s disease (EMPD) is a rare superficial skin cancer that mainly affects the vulvar region (VPD) (76% of cases). The disease is characterised by chronic pruritus and burning, which have a lasting impact on patients` quality of life. Surgical excision is the preferred treatment, but recurrences are frequent (17 to 38%) despite healthy margins. Topical imiquimod, micrographic surgery, laser treatment and photodynamic therapy (PDT) are currently being researched. Most of these treatments are invasive and painful. A new device dedicated to PDT for VPD has been developed to improve treatment tolerance. A clinical trial (PAGETEX) has been initiated to evaluate this device. We present an interim analysis of the safety data on the 19 patients included to date.

Material and methods The aim of the prospective, phase II, single-centre clinical trial was to define whether PDT with the new device would enable a rate of disease control at 3 months (stability, partial response or total response) to be obtained in at least 30% of the patients included, with a reduction in pain during illumination sessions. After application of 5-aminolevulinic acid (Metvixia®) to the damaged areas, overlapping the margins by approximately 1 cm, and incubation for 30 minutes, the lesions were illuminated for 2.5 hours in order to deliver a light dose of 12J/cm2. Two sessions were carried out at D0 and D15, and were repeated after the visit at M3 and M6 in the event of persistent disease.ResultsTo date, 19 patients out of the 24 expected have benefited from PDT-PAGETEX.Two patients left the trial due to grade 3 adverse effects of erythema and swelling, which resolved within a few days with symptomatic treatment, and a third stopped due to travel related to the trial.The mean VAS during the sessions was 0.17. There was an improvement in the pain, which was observed at M3 and M6. There was an improvement in symptomatology, with a reduction in pruritus and pain, and a significant improvement in quality of life measured by the DLQI, which fell from 5.53 to 3.16 (p0.05) at 3 months and 3.33 (p0.05) at 6 months.

Discussion The device developed appears to be relevant to the treatment of PVM. PDT delivered with this device could be a non-invasive and conservative alternative in the treatment of non-operable, recurrent or extensive non-invasive VPD.

Conclusion Vulvar PDT with PAGETEX is well tolerated and improves patients` quality of life.

P-07

Non-Melanoma Skin Cancer

Primary Cutaneous B- cell Lymphoma: A Case Report

Sidita Borici, Dermatology, Tiare' Dermatology Clinic, Albania

Primary cutaneous B-cell lymphomas (CBCL) are a heterogeneous group of extranodal non- Hodgkin B-cell lymphomas without evidence of extracutaneous disease at the time of diagnosis. They present with non-specific clinical findings such as alopecia patches or erythematous nodules or papules. The aim of this case presentation is to emphasize the role of dermatologists as the primary physicians encountering the patients with such complaints and raising suspicion and diagnosing these rare entities.

The patient, a 44-year-old young woman, presented to the Dermatology clinic complaining of a slowly growing mass on the frontal region of the scalp that had been present for the last 6 months. Physical examination showed a painless, hairless erythematous nodule, 1 cm x 1 cm in diameter, nearly 0.5 cm raised from the background, firm and non-tender on palpation and a small erythematous alopecia patch next to it, which she was not aware of. She did not report any episodes of fever or night sweats. Dermoscopy showed background erythema with serpentine and also small arborising vessels. A punch biopsy was taken and the histopathological diagnosis resulted in lymphoid dermal infiltrates, not concerning the epidermis. The infiltrate was predominated by B lymphocytes with low proliferation index. CD 20 AND BCL 2 positivity was prominent on immunohistochemistry studies. In conclusion, the result was compatible with non-Hodgkin B- cell lymphoma.

Dermatologists should maintain a high level of suspicion for primary cutaneous B- cell lymphomas since they can mimick other conditions thus making biopsy crucial for accurate diagnosis.

P-08

Non-Melanoma Skin Cancer

Genomic Mechanisms of Aggressive and Metastatic Phenotypes in Non-Melanoma Skin Cancers

Andrey Yurchenko, Inserm U981, Gustave Roussy Cancer Campus, Université Paris Saclay,, France
Andrea Forschner, Department of Dermatology, University Hospital Tübingen, Germany
Fatemeh Rajabi, Inserm U981, Gustave Roussy Cancer Campus, Université Paris Saclay,, France
Oltin Pop, Institute of Immunobiology, Kantonsspital St. Gallen, Switzerland
Laurent Parmentier, Department of Dermatology, Hospital of Valais, Switzerland
Denis Salomon, Seujet Clinics of Dermatology, Seujet Clinics of Dermatology, Switzerland
Lukas Flatz, Department of Dermatology, University Hospital Tübingen, Germany
Sergey Nikolaev, Inserm U981, Gustave Roussy Cancer Campus, Université Paris Saclay,, France

Background/Objectives: Basal Cell Carcinoma (BCC) and cutaneous Squamous Cell Carcinoma (cSCC) are the most common human malignancies of keratinocyte origin with increasing incidence. Usually, these cancers can be effectively treated, but rarely, they can be aggressive or metastatic with very poor prognosis and still unknown genomic mechanisms.
Methods: We have assembled the largest to date cohorts of BCC (n=389) and cSCC (n=223) representing major histological subtypes, lymph node metastasis and distant metastasis. The samples were profiled with WES/WGS/RNA-seq and clinically annotated.
Results: The mutational profiles of BCC and cSCC were determined by UV-light exposure with high TMB (80 and 100 mt/mb respectively) and a median of six cancer driver alterations per sample. We found that loss of TP53 is typically the first driver event in keratinocyte carcinomas and is associated with a dramatic increase in successive driver mutation acquisition. Aggressive morpheaphorm BCC samples did not demonstrate specific genetic alterations but had fibrotic TME and increased activity of HIPPO-YAP pathway according to RNA-seq analysis and immunohistochemistry. Metastatic BCC were characterised by high genomic instability and aneuploidy not typical for this type of cancer. Metastatic cSCC tumours had an increased frequency of MAPK pathway alterations and high levels of aneuploidy and whole genome duplication events. These findings were confirmed by an independent cohort of the GENIE project. Lymph node metastasis of cSCC samples demonstrated lymphocyte-enriched TME favourable for immunotherapeutic treatment.
Conclusion: Genomic instability and transcriptional activation of HIPPO-YAP and MAPK pathways define the high-risk and metastatic potential of keratinocyte carcinomas.

P-09

Non-Melanoma Skin Cancer

Chondroitin Sulfate Proteoglycan 4 as a Driver of Malignancy in Aggressive Squamous Cell Carcinoma with a Focus on Epidermolysis Bullosa

Jasmine Mingjie Zhou, Ingham Institute for Applied Medical Research, University of New South Wales, Australia
Kathryn Chen, School of Medicine, Western Sydney University, Australia
Chen Wang, Ingham Institute for Applied Medical Research, University of New South Wales, Australia
Jessica Sydney Ramos, Ingham Institute for Applied Medical Research, University of New South Wales, Australia
Fiaz Chowdhury, Ingham Institute for Applied Medical Research, University of New South Wales, Australia
Verena Wally, Department of Dermatology and Allergology, University Hospital of the Paracelsus Medical University, Austria
Roland Zauner, Department of Dermatology and Allergology, University Hospital of the Paracelsus Medical University, Austria
Josefina Pinon Hofbauer, Department of Dermatology and Allergology, University Hospital of the Paracelsus Medical University, Austria
Kang Liang, Ingham Institute for Applied Medical Research, University of New South Wales, Australia
Kieran S Scott, Ingham Institute for Applied Medical Research, University of New South Wales, Australia, School of Medicine, Western Sydney University, Australia
Paul De Souza, Ingham Institute for Applied Medical Research, University of New South Wales, Australia, School of Medicine, University of Sydney, Australia
Fred Azimi, School of Medicine, University of Sydney, Australia
Albert S Mellick, Ingham Institute for Applied Medical Research, University of New South Wales, Australia, School of Medicine, University of Sydney, Australia

Introduction: Chondroitin sulfate proteoglycan 4 (CSPG4) is a cell surface protein that plays an important role in melanoma. Recent whole tissue RNA expression studies show a link between CSPG4 and malignancy in squamous cell carcinoma (SCCs). In this study, we have re-examined the role of CSPG4 in SCCs, focusing on patients with epidermolysis bullosa (EB). These patients present with mutations in collagen VII and have fragile skin. EB patients who survive childhood almost always develop an aggressive form of SCC that is almost always lethal.

Objective: We aim to confirm that CSPG4 is upregulated in SCCs and to develop a minimally invasive diagnostic protocol using CSPG4 as an additional biomarker for malignancy.

Methods: We examined CSPG4 protein levels in primary cell lines derived from SCC patients using next-generation anti-CSPG4 antibodies. Following characterisation, we will enrich circulating tumour cells (CTCs) from the blood using ScreenCell®.

Results: We have shown that CSPG4 is upregulated in more malignant SCCs, including those from patients with EB. Additionally, higher expression in mesenchymal cell lines also suggests a link between CSPG4 and the epithelial-to-mesenchymal transition in SCCs. Finally, putative CSPG4+ CTCs have been enriched and identified in the blood of late-stage cancer patients, providing further evidence of the role of CSPG4 in SCCs.

Conclusion: Our results show that CSPG4 is a driver of malignancy in SCC. In the future, we will use this information to develop a minimally invasive blood-based diagnostic protocol using CSPG4 as a marker.

P-10

Skin Cancer Diagnosis

Development of a Deep Learning Model for Histopathological Prognostication of Localised Melanoma

Tom Andrew, Translation and Clinical Research Institute, Newcastle University, United Kingdom
Grant Richardson, AMLo Biosciences, AMLo Biosciences, United Kingdom
Phil Sloan, Translation and Clinical Research Institute, Newcastle University, United Kingdom, AMLo Biosciences, AMLo Biosciences, United Kingdom
Marc Combalia, AMLo Biosciences, AMLo Biosciences, United Kingdom
Carlos Hernandez, AMLo Biosciences, AMLo Biosciences, United Kingdom
Aidan Rose, Translation and Clinical Research Institute, Newcastle University, United Kingdom
Penny Lovat, Translation and Clinical Research Institute, Newcastle University, United Kingdom, AMLo Biosciences, AMLo Biosciences, United Kingdom

Background
The combined expression of AMBRA1 and Loricrin is a prognostic biomarker able to classify clinical risk based on histological patterns in the epidermis overlying primary cutaneous melanoma (CM). However, Deep learning (DL) has emerged as a promising tool to aid histopathologist interpretation with the added benefit of improving workload efficiency.

Objectives
To develop deep learning models for the digital classification of epidermal AMBRA1 and Loricrin expression (AMBLor) for localised melanoma prognostication.

Methods
Histological images and clinical outcome data (minimum 10 years) were collected from 6 independent international training cohorts of non-ulcerated AJCC stage I/II cutaneous CM. Training data were acquired from US, Australian and 2 UK cohorts comprising over 1000 patients, with results tested on validation cohorts derived from Spain and Northern Ireland (500 patients). Histological images of hematoxylin/Eosin, AMBRA1 or Loricrin stained whole slide images were divided into 25,000 patches for image segmentation and feature extraction training and tested on 11,000 patches using several DL models.

Results
A U-Net/EfficientNet ensemble DL approach outperformed image segmentation and feature extraction of hematoxylin/Eosin, AMBRA1 and Loricrin stained whole slide images when compared to the validation of other models (p.05) with no difference in concordance when compared to expert pathologists. Kaplan-Meier analysis demonstrated two distinct digital classification groups with statistical differences in Disease-Free Survival (p.001).

Conclusion
These data reveal a novel deep learning model to confirm the prognostic performance of AMBLor expression with the potential to aid histopathological interpretation and histopathologist workload in supporting clinical decision making for patients with localised CMM.

P-11

Skin Cancer Diagnosis

Diagnosing and Guiding Non-Surgical Therapy of Basal Cell Carcinoma with Combined Optical Coherence Tomography/Reflectance Confocal Microscopy

Nicusor Iftimia, Biomedical Optics, Physical Sciences Inc, USA
Milind Rajadhyaksha, Deratology, Memorial Sloan Katering Cancer Center, USA
Aditi Sahu, Deratology, Memorial Sloan Katering Cancer Center, USA
Miguel Cordova, Deratology, Memorial Sloan Katering Cancer Center, USA
Gopi Maguluri, Biomedical Optics, Physical Sciences Inc, USA
John Grimble, Biomedical Optics, Physical Sciences Inc, USA
Cristopher Barker, Deratology, Memorial Sloan Katering Cancer Center, USA
Chih-Shan J. Chen, Deratology, Memorial Sloan Katering Cancer Center, USA

A novel technology for improved management of skin cancer based on combined Reflectance Confocal Microcopy/Optical Coherence Tomography (RCM/OCT) is presented. Recent studies show that the large majority of non-melanoma skin cancers (NMSCs) are nowadays detected at an early stage, when they are superficial and are posing low risk. This means that they may be treated non-surgically, at lower costs. Such treatments include curettage-and-electrodessication, topical drug therapy, cryotherapy, photodynamic therapy, radiotherapy, and lately laser ablation and/or coagulation. Due to the increasing incidence and prevalence of NMSCs, especially in an increasingly older population, and thus due the increase of the healthcare costs, the adoption of these alternative non-surgical treatments that can be less invasive and far less expensive is getting higher attention.

Unfortunately, the lack of adequate imaging tools that can be used in the clinics to assist physician-patient decision in treatment planning: biopsy vs. no biopsy, surgery vs. non-surgical therapy has negatively impacted the clinical spread of non-surgical methods. For example, in the case of RT, without adequate planning there is typically additional healthy skin irradiated than it is needed. Overtreatment, especially with RT, leads to side effects such as dermatitis, subcutaneous fibrosis, which can lead to poor cosmetic outcome, as well as secondary malignancies. Laser ablation, although very promising, has not gained large spread due to the absence of proper guidance techniques. Without guidance, laser therapy cannot be always effective since the laser fluence and the number of irradiation passes are not selected based on the accurate knowledge of the cancer margins. Therefore, laser ablation is not yet mentioned in the NCCN guidelines since more studies are needed to prove its effectiveness.

On a study on over 200 patients we show that RCM/OCT can reliably assess BCC margins and successfully guide laser ablation and radiotherapy. Improved cosmetic results and very low recurrence levels were recorded.

P-12

Skin Cancer Diagnosis

Reducing the Diagnostic Delay Between Tele-Expertise and Conventional Referral in the Management of Suspicious Lesions

Ines BELKASMI, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France
Selma AZIB, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France
Eve DESMEDT, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France
Sophie MAIEZZA, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France
Laurent MORTIER, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France
Marie BOILEAU, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France

Background: Tele-expertise has recently become widespread in the management of skin lesions. We set out to quantify the reduction in diagnostic delay for melanomas in our department, comparing those obtained by tele-expertise with those obtained by conventional stress analysis

Material and methods: Two groups were formed retrospectively on the basis of anatomopathological diagnoses of invasive melanomas, melanomas in situ and atypical nevi treated in our department between 12/2022 and 12/2023: patients referred via a tele-expertise platform with photographic cliché and/or endermoscopic examination for group 1 and patients referred via traditional referral, by e-mail or letter from a referring doctor, for group 2. Diagnostic times were measured in days, from the date of referral to the date of lesion removal. They were compared with the Mann-Whitney test (if non-parametric) and Test (if parametric) with an alpha risk of 5%.

Results: Seventy-five patients were analysed. Twenty-three patients were referred via tele-expertise (group 1), including 12 invasive melanomas, 7 in situ melanomas and 4 atypical nevi. Fifty-two patients were referred via conventional referral (group 2), including 29 invasive melanomas, 9 in situ melanomas and 14 atypical nevi. The difference in diagnostic time was 37 days for all lesions (p0.005), with an average diagnostic time of 21.08 days (±7.7) for patients referred via tele-expertise, compared with 58.9 days (±15.86) for patients referred via conventional referral. There was also a difference of 35 days on average for invasive melanomas (p0.005). No significant conclusions were drawn regarding the results for melanoma in situ and atypical nevi due to the limited number of samples. The Breslow was lower in group 1, but not statistically significantly.

Discussion: Despite the limitations of our study, such as the small sample size and the retrospective and monocentric nature of the study, we found that the tele-expertise solution led to a significant reduction in the time taken to treat suspicious lesions, particularly melanomas, in the Nord and Pas de Calais departments. Our results are in line with those reported in the literature, which show a reduction in the time taken to treat lesions ranging from 4 to 70 days.

Conclusion: The development of tele-expertise could be one of the solutions to the current epidemiological and demographic challenges, i.e. an increase in the number of skin cancers in the face of a limited number of dermatologists.

P-13

Skin Cancer Diagnosis

Desmoplastic Melanoma as a Clinical and Therapeutic Challenge

Sidita Borici, Dermatology, Tiare' Dermatology Clinic, Albania

Desmoplastic melanoma is a rare and clinically challenging subtype of melanoma that poses unique diagnostic and therapeutic dilemmas. This abstract aims to summarize the clinical characteristics, diagnostic difficulties, and therapeutic considerations associated with desmoplastic melanoma.

It is characterized by the presence of densely collagenous stroma, which often results in a paucity of classic melanocytic features. This histopathological peculiarity makes accurate diagnosis challenging, frequently leading to misdiagnosis or delayed recognition. Furthermore, the absence of typical melanoma-associated features, such as pigment or a visible primary lesion, contributes to the difficulty in identifying desmoplastic melanoma at an early stage.

Immunohistochemical markers, such as S100, Melan-A, and HMB-45, are commonly utilized to aid in the diagnosis of desmoplastic melanoma. In addition, the infiltrative growth pattern and frequent lack of surface ulceration may lead to inadequate sampling during biopsies, resulting in false-negative results and delayed diagnosis.

Therapeutically, desmoplastic melanoma presents additional challenges. Traditional treatment approaches, including surgery, radiation therapy, and chemotherapy, have shown limited efficacy in controlling local disease progression and preventing distant metastases. The role of targeted therapies and immunotherapies remains unclear, as desmoplastic melanoma exhibits a unique immunoprofile and molecular landscape, potentially influencing treatment responses.

The rarity of desmoplastic melanoma also limits the availability of large-scale clinical trials and evidence-based guidelines for its management. Consequently, treatment decisions often rely on extrapolation from studies conducted on other melanoma subtypes, further complicating clinical management.

In conclusion, desmoplastic melanoma presents a substantial clinical challenge due to its elusive histopathological features, diagnostic pitfalls, and limited treatment options.

P-14

Skin Cancer Epidemiology

Ultraviolet Radiation and Skin Melanoma in Iceland and the Faroe Islands

Astrid Coste, Department Prevention Cancer Environment, Centre Léon Bérard, France, UMR 1296 Radiations Defence, Health, Environment, INSERM, France
Brian Koster, Cancer Prevention & Information, Danish Cancer Society, Denmark
Jean-François Doré, UMR 1296 Radiations : Defence, Health, Environment, INSERM, France
Philippe Autier, International Prevention Research Institute (i-PRI), International Prevention Research Institute (i-PRI), France

Background: Following substantial exposure to sunbeds, the incidence of skin melanoma has steeply increased in Iceland. High sunbed exposure has also been reported in the Faroe Islands.

Objectives: To analyse melanoma incidence and mortality trends in Iceland and the Faroe Islands.

Methods: Age standardized incidence rates were computed using the NORDCAN data and compared with Norway. Updated data on sunbed use and travels were searched.

Results: In Iceland, 25% of subjects aged 12-15 years in 2004 used sunbeds in the last year. Similar observations were done in the Faroe Islands. In contrast, travels to sunny areas were mainly prevalent among older subjects. After 1980, 5 to 10-fold increases in melanoma incidence occurred, mainly among females, with peak incidence rates of same magnitude in Iceland (2003), and the Faroe Islands (2006), after which incidence rates levelled off when restriction policies were introduced. In both countries, a 4.8-fold increase in numbers of melanoma deaths has been observed since 1985-89 for 1.8-fold increase in Norway. Mortality increases were mostly observed among males aged ≥60 years, and were simultaneous to increases in incidence. The sharp increase in melanoma incidence among females contrasted with the mortality predominance in males. Epidemiological observations cannot be explained by changes in dermatology services.

Conclusion: Comparable episodes of melanoma epidemic have affected Iceland and the Faroe Islands following massive exposure to sunbeds starting at young ages. The type of UV (UVA for sunbeds and UVB for travels) and age-sex-related factors could explain the mortality increase among older males.

P-15

Skin Cancer Epidemiology

Skin Cancer Risk in over 200.000 Patients with Hematologic Malignancies in 30 Years; a Nationwide, Population-based Study in the Netherlands

Celeste Eggermont, Department of Dermatology, Erasmus MC Cancer Institute, Netherlands
Andrya Hollatz, Department of Dermatology, Erasmus MC Cancer Institute, Netherlands
Marlies Wakkee, Department of Dermatology, Erasmus MC Cancer Institute, Netherlands
Marieke Louwman, Department of Research and Development, Netherlands Comprehensive Cancer Organization (IKNL), Netherlands
Avinash Dinmohamed, Department of Research and Development, Netherlands Comprehensive Cancer Organization (IKNL), Netherlands, Department of Public Health, Erasmus MC, Netherlands, Department of Hematology, Amsterdam University Medical Center, Netherlands
Eduardus Posthuma, Department of Research and Development, Netherlands Comprehensive Cancer Organization (IKNL), Netherlands, Department of Internal Medicine, Reinier the Graaf Hostpital, Netherlands, Department of Hematology, Leiden University Medical Center, Netherlands
Tamar Nijsten, Department of Dermatology, Erasmus MC Cancer Institute, Netherlands
Loes Hollestein, Department of Dermatology, Erasmus MC Cancer Institute, Netherlands

Background

Patients with hematologic malignancies are at higher risk of developing skin cancer and tend to experience worse outcomes. However, comprehensive, long-term, nationwide data on the risk of different skin cancers across all hematologic malignancies is lacking.

Objectives

To assess population-based risk estimates of developing cutaneous squamous cell carcinoma (CSCC), malignant melanoma (MM), Merkel cell carcinoma (MCC), and basal cell carcinoma (BCC) among patients with hematologic malignancies.

Methods

This nationwide cohort study analyzed data on 218,456 patients diagnosed with a hematologic malignancy between 1989 and 2020 from the Netherlands Cancer Registry (NCR). Data on the first histopathologically confirmed skin cancer were also retrieved. Patients with prior skin cancers were excluded. Cumulative incidences, standardized incidence ratio's (SIRs), and absolute excess risks for all skin cancers were calculated, stratified by hematologic malignancy, age, sex, follow-up, and treatment.

Results

The 10-year cumulative incidences for a first skin cancer were 2.6% for CSCC, 0.5% for MM, 0.05% for MCC, and 4.8% for BCC. Most hematologic malignancy subgroups had more than a twofold increased risk for each skin cancer compared to the general population. Chronic lymphocytic leukemia (CLL) patients showed the highest risks, with SIRs of 4.5 for CSCC, 2.8 for MM, 9.4 for MCC, and 2.9 for BCC. These increased risks persisted for over 30 years post diagnosis.

Conclusion

Patients with all types of hematologic malignancies, especially CLL, have an increased lifetime risk of skin cancers. These findings highlight the need for increased awareness, sun-protective measures, and regular skin self-examinations in this high-risk group.

P-16

Skin Cancer Epidemiology

Clinical Use of the i31-GEP for SLNB for T1-T2a Cutaneous Melanoma Significantly and Safely Reduces Unnecessary Procedures

Timothy Beard, Surgery / Clinical Research, Summit Medical Group, USA
Stanley P. Leong, Center for Melanoma Research and Treatment, California Pacific Medical Center and Research Institute
Rajan P. Kulkarni, School of Medicine, Oregon Health and Science University
Brian Martin, Research & Development, Castle Biosciences, Inc.
Kelli Ahmed, Research & Development, Castle Biosciences, Inc.
Andrew Ward, Nursing, University of Tennessee Medical Center
J. Michael Guenther, Surgical Oncology, Marshfield Clinic
Shawn Young, Surgical Oncology, Cancer Centers of Colorado (SLC Health)

Background: Accurate identification of cutaneous melanoma patients at low risk (5%) of sentinel lymph node (SLN) positivity can help patients avoid SLN biopsy (SLNB), reducing unnecessary surgery, complications, and healthcare costs. The integrated 31-gene expression profile (i31-GEP) test integrates the 31-GEP with Breslow thickness, ulceration status, mitotic rate, and age to provide a more precise estimate of SLN positivity than using clinicopathologic features alone.

Objective: Prospectively validate performance of the i31-GEP for SLNB risk prediction.

Methods: Patients enrolled in the prospective DECIDE study were evaluated using the i31-GEP as part of SLNB decision-making. T1a with at least one high-risk factor, T1b or T2a tumors were included in the current analysis (n=471). SLNB utility was compared using 1:1 matched cohorts of patients from the DECIDE study and an independent population published by Whitman et al. 2021, for whom the i31-GEP was not considered in the SLNB decision-making process.

Results: In the DECIDE study, 221/471 patients (46.9%) underwent SLNB. Of these, the i31-GEP classified 58 patients as having 5% risk of SLN positivity, none of which (0%) had a positive node. The positivity rate in those predicted to have ≥5% risk was 9.8% (16/163). Compared to the matched Whitman cohort 25% fewer SLNBs were performed among patients in DECIDE, in which the i31-GEP was included in clinical decision-making (p0.001).

Discussion: The i31-GEP for SLNB accurately identified patients with 5% risk of SLN positivity who can safely forego SLNB, sparing patients from SLNB-associated morbidity and reducing healthcare costs.

P-17

Skin Cancer Diagnosis

The Possibilities of Electrophoton Emission Analysis in the Medical Examination of dysplastic nevi

Stanislav Panov, Intensive care department with extracorporeal detoxification and hemodialysis room, Military Clinical Hospital of the Ministry of Defense of the Republic of Kazakhstan, Kazakhstan
Nurlan Baltabekov, Department of Oncology, International Institute of Postgraduate Education in Medicine, Kazakhstan
Daut Makanov, Department of Oncology, Nano integrative personalized pharmacy, Kazakhstan

Background: The potential of electrophoton emission analysis in the medical dispensary management of dysplastic nevi

Purpose: primarily to evaluate and detect energetic or bioelectrical abnormalities in skin tissue that may indicate pathologic changes.

Methods: 2 groups of patients (n=100) with dysplastic nevi, one of whom received sodium nucleate for immune enhancement. Every 3 months they underwent EORTC questionnaire (QLQ-C30), assays for neutrophil-to-lymphocyte ratio (NLR), SD4/SD8, lactate dehydrogenase levels, dermatoscopy and electrophoton imaging using artificial intelligence (AI EPI).

Results: During dermatoscopy, it is not always possible to make a decision to remove a suspicious nevus as soon as possible. The combination of dermatoscopy deterioration with AI EPS signal amplification as an additional decision point in favor of surgical intervention during histological examination reliably confirms aplastic processes in the nevus.

Conclusion: Monitoring of the nevus condition in dynamics by dermatoscopy and AI EPS allows to accurately determine the necessity of nevus resection. Application of prophylactic immunotherapy with sodium nucleinate allowed to reduce the number of nevi to be monitored by dermatoscopy, which was combined with improvement of immunity indices. The most pronounced result was achieved in patients with secondary immunodeficiency.

Skin Cancer D

Circultating Tumor DNA (ctDNA) in Stage-III BRAF+ Patients: a Real-life Study in the Adjuvant Setting

Gabriele Roccuzzo, Department of Medical Sciences, Section of Dermatology, University of Turin, Turin, Italy, Service of Dermatology, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland
Sara Marchisio, Department of Medical Sciences, Laboratory of Immunogenetics, University of Turin, Turin, Italy
Alessia Andrea Ricci, Oncology, Pathology, University of Turin
Eleonora Bongiovanni, Department of Medical Sciences, Section of Dermatology, University of Turin, Turin, Italy
Erika Ortolan, Department of Medical Sciences, Laboratory of Immunogenetics, University of Turin, Turin, Italy
Luca Bertero, Department of Medical Sciences, Pathology, University of Turin, Italy, Pathology Unit, Candiolo Cancer Institute, FPO - IRCCS, 10060, Candiolo, Turin, Italy.
Enrico Berrino, Pathology Unit, Candiolo Cancer Institute, FPO - IRCCS, 10060, Candiolo, Turin, Italy
Valentina Pala, Department of Medical Sciences, Section of Dermatology, University of Turin, Turin, Italy
Renata Ponti, Department of Medical Sciences, Section of Dermatology, University of Turin, Turin, Italy
Paolo Fava, Department of Medical Sciences, Section of Dermatology, University of Turin, Turin, Italy
Simona Osella Abate, Department of Medical Sciences, Pathology, University of Turin, Italy
Silvia Deaglio, Department of Medical Sciences, University of Turin, Turin, Italy
Caterina Marchiò, Pathology Unit, Candiolo Cancer Institute, FPO - IRCCS, 10060, Candiolo, Turin, Italy
Anna Sapino, Pathology Unit, Candiolo Cancer Institute, FPO - IRCCS, 10060, Candiolo, Turin, Italy
Rebecca Senetta, Oncology, Pathology, University of Turin
Ada Funaro, Department of Medical Sciences, Laboratory of Immunogenetics, University of Turin, Turin, Italy
Simone Ribero, Department of Medical Sciences, Section of Dermatology, University of Turin, Turin, Italy
Paola Cassoni, Department of Medical Sciences, Pathology, University of Turin, Italy
Pietro Quaglino, Department of Medical Sciences, Section of Dermatology, University of Turin, Turin, Italy

Background: Circulating tumor DNA (ctDNA) has emerged as a promising candidate in monitoring melanoma patients, yet in the adjuvant setting only a limited number of exploratory analyses have been conducted so far.

Objectives: To assess the ctDNA dynamics in a cohort of resected stage III BRAF+ melanoma patients (n=32) undergoing adjuvant therapy with targeted therapy or anti-PD1.

Methods: Blood sample collection was performed before the start of adjuvant therapy (baseline) and monthly until the end of therapy or relapse whichever occurred first. CtDNA quantification was carried out through QX200 Droplet Digital PCR (ddPCR) system (Bio-Rad, Hercules, CA, USA), targeting the specific BRAF mutations V600E/K/R with the ddPCR BRAF V600 Screening Kit.

Results: At 36 months, individuals with negative basal ctDNA exhibited a significantly higher 36-month RFS of 75% (95% CI 50%-89%) compared to 36.4% (95% CI 11%-63%) in the positive group (p=0.014). Cox univariate analysis for RFS identified positive basal ctDNA status (HR 3.79, 95% CI 1.2-12.0, p=0.023) as a significant negative prognostic factor. This finding was confirmed in terms of 36-month OS, with a

significant difference observed between the negative basal ctDNA (95.0%, 95% CI 69.5-99.3) and the positive (54.6%, 95% CI 22.9-77.9) groups (p=0.004). Cox univariate analysis for OS identified positive basal ctDNA (HR 7.92, 95% CI 1.56-40.36, p=0.013) as a significant negative prognostic factor. Remarkably, stage showed no correlation with basal ctDNA status (p=0.324) nor LDH levels (p=0.540).

Conclusion: Basal ctDNA status proves to be an effective tool for predicting relapse and survival in stage-III melanoma patients, integrating the prognostic role of clinical stage and basal LDH values.

Skin Cancer Predisposition

Genomic Analysis of Skin Cancers from Xeroderma Pigmentosum Subgroups Revealed New Mechanisms of UV Mutagenesis

Sergey Nikolaev, U981, Gustave Roussy Cancer Campus, France
Andrey Yurchenko, U981, Gustave Roussy Cancer Campus, France
Fatemeh Rajabi, U981, Gustave Roussy Cancer Campus, France
Tirzah Lajus, Departamento de Biologia Celular e Genética, Universidade Federal do Rio Grande do Norte, Brazil
Hiva Fassihi, Department of Photodermatology, St John's Institute of Dermatology, United Kingdom
Konstantin Gunbin, U981, Gustave Roussy Cancer Campus, France
Ismael Padioleau, U981, Gustave Roussy Cancer Campus, France
Chikako Nishigori, Department of Internal Related, Kobe University Graduate School of Medicine, Japan
Patricia Kannouche, CNRS UMR9019, Gustave Roussy Cancer Campus, Czech Republic
Carlos Menck, Department of Microbiology, Institute of Biomedical Sciences, United Kingdom
Alain Lehmann, Genome Damage and Stability Centre, University of Sussex, United Kingdom
Alain Sarasin, CNRS UMR9019, Gustave Roussy Cancer Campus, Czech Republic

Rare autosomal syndrome Xeroderma Pigmentosum (XP) is characterised by 1000 times increased risk of skin cancer due to the impaired Nucleotide Excision Repair (NER) pathway or translesion synthesis (polymerase eta). We assembled a unique collection of skin tumours (n=39) from five most frequent and cancer-prone XP subgroups (XP-A, XP-C, XP-D, XP-E, XP-V) and performed whole genome sequencing to characterise in detail their genomic mutational landscapes comparing with tumour type-matched sporadic cancers (n=139).

We found that heterogeneity of the mutation rates across skin cancer genomes is determined by the activity of NER, and that transcription-coupled NER extends beyond the gene boundaries reducing the intergenic mutation rate. The mutational profile in XP-V tumors revealed the role of polymerase η in the error-free bypass of (i) rare TpG and TpA DNA lesions, (ii) 3' nucleotides in pyrimidine dimers, and (iii) TpT photodimers. XP-V patients skin cancer mutational data are validated in-vitro. Specifically, we observed a 10-fold increase of mutagenesis in POLH-KO vs WT cells after treatment with UVA or UVC. Strikingly, mutations from TpG and TpA dinucleotides were most prevalent after UV-A exposure and were observed after UV-C exposure. However, they were undetectable following 8 weeks of cell culturing without treatment, or with Reactive Oxygen Species inducing Potassium Bromate treatment. Overall, our study unravels the genetic basis of skin cancer risk in XP and provides insights into the mechanisms reducing UV-induced mutagenesis in the general population.

P-20

Skin Cancer Prevention

cDNA Recombinant Proteins for Dermatological and Cosmetic Protection: Use of Synthetic Biology

Raul Cuero, Ph.D, N/A, Biocapital Holdings Llc, USA

Sunlight is known to cause sever sunburn and skin cancer. Despite using many UV-absorbent substances, the dermatological harm continues to be a health concern. Therefore, here is described a novel method to produce a metabolite from yeast plasmid for dermatological and cosmetic protection of skin against UV damage, using synthetic biology. Different DNA constructs were assembled containing genes encoding proteins with higher absorption-extinction coefficients, and/or DNA repairing capacity. These gene assemblages were cloned in yeast cells, and a lysate was extracted after culture growth. Different lysates containing the recombinant proteins were tested in vitro in mammalian skin cells and microbial cells. The UV-protectant lysate proteins were detected by using photonic, intense low mass ion, and ELISA methods. Results showed that the anti-UV lysate-metabolite is a protein with a valine and other amine tail. Microscopy results show that fibroblast cells were protected by the lysate protein (71% survival) after 1 hour of UV exposure, as compared to the 13% survival of untreated fibroblast cells. Nucleic acid assays confirm these results. Also, the number of elongated fibroblasts was higher in the lysate treated culture after exposure to UV radiation, as compared to the untreated cell culture, which had a lower number of elongated fibroblasts and more spherical fibroblasts, as an indication of the harmful effect of UV radiation. Similarly, microbial cells were protected by the lysate when exposed to UV radiation. These cDNA recombinant proteins also show great photo-protectant effect. This investigation demonstrated the benefit of this method for dermatological and cosmetic UV protection.

P-21

Skin Cancer Prevention

Selling Sunbeds

Amy Long, Dermatology Department, Beaumont Hospital, Ireland
Karen Eustace, Dermatology Department, Beaumont Hospital, Ireland

The sale of sunbeds from private sellers on online marketplaces in Ireland raises significant public health concerns, as it occurs outside the regulatory framework established by the Public Health (Sunbeds) Act 2014. This legislation, designed to mitigate the dangers of ultraviolet radiation, prohibits sunbed use by minors and misleading advertising claims, mandates prominent health warnings, and requires businesses to register with the Health Service Executive. Online marketplaces present nuanced challenges for ensuring public health and safety in the digital age.

A cross-sectional analysis of sunbed advertisements on Facebook Marketplace and DoneDeal was performed in July 2024.

There were 29 sunbed adverts listed by private sellers, with a total of 59 sunbeds for sale. Four advertisements mentioned that the sunbeds came from sunbed businesses. The language used in some advertisements was highly persuasive, describing a ‘perfect tan’, while also dangerously misinforming consumers on the safety of tanning, ‘the safe feeling of skin gentle tanning’. No advertisement included health warnings on sunbed usage.

The lack of regulatory oversight of sunbeds in a marketplace setting contrasts sharply with the strict controls imposed on traditional sunbed businesses, heightening the risk of harm to consumers, including minors. This study underscores the need for enhanced regulatory monitoring of online platforms, targeted consumer education on the risks associated with sunbed use, and possible incentives for the safe disposal of unwanted sunbeds. Strengthening collaboration between regulators and online marketplaces, while adapting regulatory frameworks to the evolving digital landscape, is essential for safeguarding public health.

Systemic Treatment of Advanced Skin Cancer

Therapy Sequencing in BRAF-Mutant Metastatic Melanoma, a Case Report

Luca Ambrus, Department of Oncodermatology, National Institute of Oncology, Hungary
Tímea Balatoni, Department of Oncodermatology, National Institute of Oncology, Hungary
Kata Czirbesz, Department of Oncodermatology, National Institute of Oncology, Hungary
Mihály Tamás Kispál, Department of Oncodermatology, National Institute of Oncology, Hungary

BACKGROUND: Melanoma, a highly aggressive skin cancer, is commonly associated with mutations in the BRAF gene, particularly the BRAF V600E mutation, which activates the MAPK/ERK signaling pathway and drives tumor proliferation.
OBJECTIVES: This case report details the clinical course of a 66-year-old male patient diagnosed with metastatic melanoma carrying the BRAF V600E mutation.
METHODS: The patient was initially treated with a combination of BRAF and MEK inhibitors, which led to significant tumor regression and clinical improvement. However, after 8 months, the disease progressed, prompting a switch to second-line therapy with immune checkpoint inhibitors (ICIs), specifically PD-1 blockade. Remarkably, the patient experienced a robust and sustained response to ICIs, with a marked reduction in tumor burden and stabilization of disease over the subsequent 17 months, when oligoprogression occured.
RESULTS: This case highlights the critical role of therapy sequencing in the management of BRAF-mutant melanoma. The initial response to targeted therapy provided rapid disease control, while subsequent immunotherapy offered durable long-term benefits, even after progression on targeted agents. This report underscores the importance of individualized treatment plans that consider the timing and sequencing of available therapies to maximize patient outcomes.
CONCLUSION: The findings contribute to the growing body of evidence supporting the strategy of combining and sequencing targeted therapies and ICIs in the treatment of advanced melanoma, particularly in BRAF-mutant cases, where resistance to targeted therapy remains a significant challenge. Further research is necessary to optimize sequencing strategies and to explore potential biomarkers that could predict response to subsequent therapies.

P-23

Systemic Treatment of Advanced Skin Cancer

Retrospective Real-life Evaluation of Outcome after Discontinuation of anti-PD1 Therapy for Complete Response Cutaneous Squamous Cell Carcinoma in Patients over 75 Years of Age

Julie LARDENOIS, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France
Marie BOILEAU, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France
Eve DESMEDT, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France
Marie BRIDOUX, Departement of Oncology, Univ. Lille, CHU de Lille, France
Sophie MAIEZZA, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France
Laurent MORTIER, Dermatology Department, Hôpital Claude Huriez, Univ. Lille, CHU de Lille, France, U1189 - ONCO-THAI - Assisted Laser Therapy and Immunotherapy for Oncology, Univ. Lille, Inserm, France

Background: The efficacy of anti-PD1 agents in locally advanced or metastatic cutaneous squamous cell carcinoma (CSC) has been demonstrated. The benefit-risk balance of continuing treatment after complete response (CR) is questionable.

Material and methods: We present a single-centre retrospective study of the outcome of patients 75 years of age treated with anti-PD1 for metastatic or locally advanced CEC between January 2019 and January 2024, for whom treatment was stopped for CR. Follow-up was performed until May 2024. Patients were identified using the prescription software.

Results: We identified 44 patients over 75 years of age treated, 14 of whom developed CR leading to discontinuation of anti-PD1 therapy. The median age was 83.5 years. The primary site was the head and neck in 92.8% of cases. It was a primary lesion in 6 patients and a relapse in 8. The lesion was localised in 57.1% of cases, with lymph node involvement in 28.6% and metastatic in 14.3%. Prior to treatment, none of the patients had received chemotherapy and 3 had received radiotherapy. The anti-PD1 agents received were pembrolizumab (64.3%), nivolumab (21.4%) and cemiplimab (14.3%), with responses shown in histograms (Figure 1). Five patients received concomitant radiotherapy. One third of patients had no adverse events (AEs) and only one case of grade 3 toxicity (pneumonitis) was reported. The most common AE was asthenia (35.7%), which was grade 1 only. The median duration of treatment before CR was 5.1 months. The median duration of continued treatment after CR was 1.3 months (Q1 0.5 -Q3 6.5). Median total follow-up was 22.5 months (Q1 19.1 - Q3 27.4). After stopping anti-PD1, median overall survival was 14.2 months (Q1 8.7 - Q3 20.8) and median progression-free survival was 10.5 months (Q1 5.9 - Q3 13.7). Only one patient experienced lymph node relapse 10 months after stopping anti-PD1. This was the only patient with a trunk positive and discontinuation of treatment for grade 3 pneumonitis. One death was reported, unrelated to the ECC or the treatment, 8 months after discontinuation of the anti-PD1.

Discussion: We observed that the efficacy of anti-PD1 was clear, with 31.8% of patients achieving CR after a short median treatment period, in line with the data in the literature. Tolerance was good, with mainly grade 1 toxicities (58%) and only one serious AE. This study is original in that it shows that early discontinuation of anti-PD1 after CR (median delay 1.3 months), or even after CR for some patients, does not lead to early recurrence of ECC. Immunotherapy treatment of symptomatic elderly subjects, even those who are already altered, is of interest given the rapid efficacy and good tolerability of anti-PD1.Early discontinuation of immunotherapy in this population is permissible if CR persists, in order to limit iatrogenicity and the inconvenience associated with treatment.

Conclusion: Anti-PD1 is effective and well tolerated in elderly subjects. CR can be obtained rapidly and be prolonged, despite early discontinuation. In this fragile population receiving palliative treatment for

symptomatic purposes, early discontinuation may be considered in order to avoid iatrogenicity. Further studies and prolonged follow-up are required.

1

P-24

Systemic Treatment of Advanced Skin Cancer

Neoadjuvant Atezolizumab in Patients with Surgically Resectable Advanced Cutaneous Squamous Cell Carcinoma

Vasu Divi, Department of Otolaryngology-Head and Neck Surgery, Stanford University, USA
Sumaira Aasi, Department of Dermatology, Stanford University, USA
Saad Khan, Department of Medicine - Oncology, Stanford University, USA
Lily Lam, Department of Otolaryngology-Head and Neck Surgery, Stanford University, USA
Luis Martinez Ramirez, Department of Otolaryngology-Head and Neck Surgery, Stanford University, USA
John Sunwoo, Department of Otolaryngology-Head and Neck Surgery, Stanford University, USA
Mobeen Rahman, Department of Pathology, Stanford University, USA
Yifei Ma, Department of Otolaryngology-Head and Neck Surgery, Stanford University, USA
Fred Baik, Department of Otolaryngology-Head and Neck Surgery, Stanford University, USA
Michelle Chen, Department of Otolaryngology-Head and Neck Surgery, Stanford University, USA
Andrey Finegersh, Department of Otolaryngology-Head and Neck Surgery, Stanford University, USA
Kelsey Hirotsu, Department of Dermatology, Stanford University, USA
Chris Holsinger, Department of Otolaryngology-Head and Neck Surgery, Stanford University, USA
Nour Kibbe, Department of Dermatology, Stanford University, USA
Davud Sirjani, Department of Otolaryngology-Head and Neck Surgery, Stanford University, USA
Nikita Bedi, Department of Otolaryngology-Head and Neck Surgery, Stanford University, USA
Harlan Pinto, Department of Medicine - Oncology, Stanford University, USA
Dimitrios Colevas, Department of Medicine - Oncology, Stanford University, USA

OBJECTIVE: To evaluate the feasibility of administering 3 doses of neoadjuvant atezolizumab prior to curative surgical resection in patients with advanced cutaneous squamous cell carcinoma.

METHODS: This single-arm phase 2 trial included patients with cutaneous squamous cell carcinoma of the head and neck with Stage III or IV disease, or Stage II lesions for which standard therapy would incur an unacceptable morbidity. Patients received up to 3 doses of atezolizumab at a fixed dose of 1200 mg every 21 days prior to undergoing surgical resection. The primary endpoint was the percentage of patients able to complete 3 doses of therapy and be eligible for surgical resection without discontinuation due to toxicity or progression. Secondary endpoints included unconfirmed RECIST 1.1 response rate, pathological response rate (major and complete pathological response), and safety and tolerability of atezolizumab.

RESULTS: 20 patients were enrolled and treated. 16 of 20 (80%) patients completed 3 doses of atezolizumab and all patients were eligible for surgical resection. A pathological complete response was seen in 7 (35%; 95% CI, 15.4%-59.2%) patients, and a major pathological response (10% viable tumor) was seen in 4 (20%; 95% CI, 5.7%-43.7%) patients. RECIST responses were seen in 8 (40%; 95% CI, 19.1%-64.0%) patients, and 1 (5%) patient progressed. Grade 3 or higher adverse events were seen in 1 (5%) patient who developed pneumonitis.

CONCLUSION: Neoadjuvant atezolizumab is feasible and well-tolerated in patients with advanced cutaneous squamous cell carcinoma and results in a high rate of major and complete pathological responses.

P-25

Systemic Treatment of Advanced Skin Cancer

A New Model of Dispensary, Rehabilitation and Immunosurveillance of Melanoma

Stanislav Panov, department of oncology, International Institute of Postgraduate Education (Clinic MIPO), Kazakhstan
Nurlan Baltabekov, department of oncology, International Institute of Postgraduate Education (Clinic MIPO), Kazakhstan

Background: the use of immunotherapy with immune checkpoint inhibitors (ICIs) in melanoma in half of the cases within a year leads to persistent immune-related adverse events (irAEs)

Objectives: improve the quality of life of patients with melanoma.

Methods: Patients with confirmed melanoma of the skin received pembrolizumab with sodium nucleate. every 3 months they did EORTC(QLQ-C30) questionnaire, analysis to determine Neutrophil-to-Lymphocyte ratio (NLR), SD4/SD8, neutrophil extracellular traps (NETs), functional assessment of phagocytosis quality, neutrophil mitochondrial dysfunction (NMD) and determined stress level, adaptive by artificial intelligence Electrophotonic imaging (AI EPI).

Results: Long-term therapy with pembrolizumab in combination with sodium nucleonate resulted in decreased quality of life in only 10% of patients. It appeared that on ICI, CD4/CD8=2.0+/-0.3 and NLR=2.2+/-0.5 progression of metastases may occur associated with spontaneous membrane damage due to high stress and decreased adaptation. Reduced adaptation was combined in 80% with NMD and reduced phagocytosis.

Conclusion: For Immunosurveillance, in addition to CD4/CD8 and NLR tracking, it is necessary to monitor the qualitative state of granulocytes, the proportion of NETs, the proportion of cells with active mitochondria and the stress level using AI EPI. This allows to see possible complications of ICIs at an early stage, as well as to select an adequate dose. increased stress causes damage to blood cell membranes, which reduces immunity and leads to the progression of metastases against the background of prolonged pembrolizumab administration. The combined use of sodium nucleonate with pembrolizumab and delays the moment of ICI patient`s arrest.