

BIODERMA

CONGRESS REPORTS

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Reports written by Dr Oriol Yélamos (Dermatologist, Spain)

Non-melanoma skin cancer: what's new

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speaker: Dr Alexander Stratigos

The newest 2026 EADO guidelines on squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) have been submitted.

What's new on SCC?

Speaker: Dr Alexander Stratigos

There's been numerous changes in the management of SCC in the recent years, from the management of local disease (mainly surgery), to disseminated disease with the advent of immunotherapy and biomarkers.

Regarding epidemiology, there's been rising incidence of cases as well as an increase in the complexity → **8% of all SCC are locally advanced.**

One of the main issues we encounter is the difficulty in distinguishing low risk vs high risk cases. We have been using different classification systems (AJCC; BWH) but all systems are not perfect, but they complement each other.

Also, some factors are relevant and not necessarily taken into account in some of these classifications:

- Lymphovascular invasion
- Immunosuppression
- Perineural invasion, tumor differentiation and depth of invasion

Since these systems are complex, there are several calculators and scores that help us predict prognostic information.

Additionally, there are different gene expression profiling (GEP) tests that can be run on the primary tumor that help predict prognosis in SCC. However, GEP are relatively new in SCC and are lacking robust prospective trials.

Regarding management, surgery is still the cornerstone of treatment of local disease, being Mohs surgery or other micrographic approaches the ideal methods, with robust studies showcasing its importance.

Regarding radiotherapy, there have been some news too in SCC, mainly 3 modalities:

- Flash radiotherapy: millisecond of doses
- Image-guided superficial radiotherapy
- Ppt

Regarding advanced SCC the revolution has been immunotherapy. There's a new agent on the metastatic setting, cosibelimab (anti-PD-L1), showing good efficacy with lower rates of grade ≥ 3 adverse events compared to other agents.

An issue is PD-1 refractory cases, in which we have to combine treatments especially EGFR inhibition with other drugs:

- AliCe trial: combination of cetuximab and avelumab showing activity in refractory SCC
- iTACKLE trial: intratumoral IL-12 plasmid combined with pembrolizumab, enhancing immune responses

And what about adjuvant treatment? Cemiplimab has significant benefit in the adjuvant setting with a 68% reduction of relapse rate compared to placebo in high risk SCC. However, these results are due to a good selection of cases:

- T4 tumours
- Relapsing tumors
- Perineural invasion, positive margins, or nodal disease

Also there's a lot of excitement regarding perioperative immunotherapy. A study by Gross et al. showed 64% complete or major pathological response and 92% overall survival using neoadjuvant cemiplimab.

Additionally, a study published in Nature Medicine demonstrated that neoadjuvant ipilimumab plus nivolumab achieves high pathological response rates and improves outcomes.

As a result, neoadjuvant therapy is now included in NCCN and European guidelines for SCC management.

What about basal cell carcinoma news?

Speaker: Dr Alexander Stratigos

Not many news recently. Maybe the most important one is that adding RT with hedgehog inhibitors is synergistic.

Combination strategies such as sonidegib plus cemiplimab are being explored, based on the rationale that hedgehog inhibition increases tumor immunogenicity.

Intratumoral therapies are also gaining interest. The NeoBCC trial evaluated intralesional T-VEC in the neoadjuvant setting, showing good responses and, importantly, downstaging of surgical procedures (conversion from complex to simpler surgeries).

Summary of intralesional ttx ppt :

- T-VEC
- RP-1: oncolytic HSV with immune activation, showing promising results in BCC
- Intralesional cemiplimab
- IL-2: ~81% complete response
- Daromun (IL2/TNF): promising preliminary data

What about Merkel cell carcinoma (MCC)?

Speaker: Dr Alexander Stratigos

Survival rates are improving significantly due to the introduction of immune checkpoint inhibitors, which provide more durable responses compared to chemotherapy.

A new agent, retifanlimab, has been approved by the FDA and EMA, with promising early results, although data remain limited.

What about prevention?

Speaker: Dr Alexander Stratigos

Yes, we have a lot of treatments, but prevention continues being crucial in NMSC.

Nicotinamide was studied in 2015 to prevent NSMC, and recently in 2025 Breglio showed again a reduction in NSMC with nicotinamide but in NON immunosuppressed patients, and has recently been added into the European guidelines in the management of NMSC.

Photoprotection is also essential, although confusion persists regarding SPF interpretation. EADO has addressed this issue in a recent publication led by Dr Forsea.

AI and overdiagnosis of melanoma

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speaker: Dr Susan Swetter

In 2021 there was a paper released mentioning that there's been a steep increase in the melanoma cases but the mortality isn't increasing, suggesting a melanoma overdiagnosis.

What is melanoma overdiagnosis?

Melanoma overdiagnosis is defined as the diagnosis of melanomas that would not have caused symptoms or death during a patient's lifetime.

Dysplastic nevi and even melanoma in situ (Mis) are not obligate precursors of invasive melanoma (even Mis! 30% of progression in some models). Thus, melanoma overdiagnosis is a worldwide problem.

There is ongoing discussion about redefining melanoma in situ terminology (e.g., "melanocytic intraepidermal neoplasia") to better reflect its biological behavior.

If screening campaigns worked, then mortality would go down and this is not really happening (or at least not happening clearly).

AI has been proposed as a solution. In 2017, Esteva et al. showed AI could match dermatologists in diagnostic accuracy. However, real-world (in vivo) performance has been less impressive due to multiple biases:

- Dataset bias (overrepresentation of lighter skin types)
- Spectrum bias
- Verification bias
- Lack of clinical context

One of the biases is the lack of images in darker skin tones, and that's why new datasets are being created to include all skin types, and that these datasets be open to train algorithms.

A crucial concept is that dermatologic diagnosis is multimodal, integrating clinical data, dermoscopy, and patient history.

A Stanford prospective real-world multimodal study confirmed that current AI models underperform compared to clinicians, often misclassifying cancers as inflammatory conditions.

The issue regarding melanoma overdiagnosis is that what we see, clinically or histologically, is a morphologic image and we do not know how that lesion is going to behave, so there's a disconnect between morphology and biology.

The SkinVision app experience in the Netherlands showed increased biopsy rates when AI is used, leading to higher costs and potential harm. Increasing sensitivity inevitably reduces specificity, especially in low-risk populations.

Therefore, AI should be used cautiously, and advanced imaging techniques (LC-OCT, RCM, OCT) may be more appropriate in high-risk patients.

Vaccines for skin cancer: a glorious future?

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speaker: Dr Georgina Long

Approximately 40% of advanced melanoma patients are cured with anti-PD-1 therapy, and a bit less than one-third with combination immunotherapy (antiPD1 + antiLAG3 or antiCTLA4). However, one-third remain non-responders, representing an unmet need.

Vaccines are particularly promising in this “third space” of non-responders. Ideally, biomarkers would identify these patients, but such tools are not yet available.

Vaccines seem an ideal approach to treat this third space, meaning the patients who are non-responders.

CD8+ T cells can be effective against cancer due to several factors:

- Antigen density
- Antigen quality
- Co-stimulation
- Strong TCR signal

Key determinants of vaccine efficacy include:

- MHC expression
- Tumor mutational burden (TMB)
- Tumor microenvironment (T-cell infiltration, IFN- γ signaling)

Vaccines can target:

- Neoantigens
- Tumor-associated antigens
- Cancer-testis antigens (e.g., PRAME, NY-ESO-1)

Also, there are several vaccine delivery platforms:

- mRNA /LNP
- Peptides
- Viral vectors
- DNA plasmids
- Dendritic cells
- Nanoparticles :
 - Only 3 platforms are important in melanoma: mRNA, peptides and nanoparticles

Previous combination trials (epacadostat, T-VEC, bempegaldesleukin) failed to reach statistical significance probably because patients were not selected correctly, or more importantly, the tumor was not selected correctly. These trials included naïve patients and vaccines probably perform better in PD1 resistant patients. But since these trials included all patients (they were naïve patients) we have to break down the data to see the potential efficacy of vaccines in melanoma.

Neoantigens :

- Pembrolizumab vs Pembrolizumab + Intismeran autogene (mrna 4157) ppt
 - Although the results are not statistically significant, if you break down the types of tumor included, there was more benefit in the tumors that were potentially worse from a biomarker standpoint (low TMB)
- Pembrolizumab + cevumeran
 - Also no differences in PFS, but when you look at the antigens that get a T-cell response, but it seems to work better when TMB low → this can be promising in PD1-refractory patients
- Peptide vaccine EVX-001
 - Similar results to mRNA
 - In PD-L1 negative patients, peptide vaccines seem to work better

IDO inhibition is also a strategy that may increase the anticancer immune response, and although trials didn't show great results, IDO inhibition may also work with peptide vaccines since the effect is synergistic.

BNT111 vaccines did reach its primary endpoint ppt. The difference of this trial is that the patients were PD1 refractory patients.

So, when do we use vaccines in melanoma? Ideally, we need to use them in patients who will not respond to antiPD1 or antiPD1 combined treatments (so, the third space patients). How do we do it? How do we predict who is going to be a non-responder?

- Patients who do not achieve major pathological response in the neoadjuvant setting
- In stage IV patients with tumors with low TMB
- In stage I/II patients with poor prognostic information with nomograms, GEP testing, ctDNA testing

To sum up, vaccines will likely require biomarker-driven patient selection and combination strategies and will probably be more useful in patients with bad melanomas, especially PD1 refractory tumors.

Cell-based therapies beyond TILs

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speakers: Dr Sapna Patel and Dr Schadendorf

Engineered T Cell Therapy for Cancer

Speaker: Dr Sapna Patel

Targetable antigens in cancer include viral, differentiation antigens, neoantigens and cancer-testis antigens.

TIL therapy involves harvesting tumor-infiltrating lymphocytes, expanding them ex vivo, and reinfusing them with IL-2 support. Typically IL2 works to fuel the immune response.

TIL therapy is FDA approved in 2024.

PRAME-targeted therapy (Anzu-cel) represents a promising engineered TCR approach with early clinical activity.

CAR-T treatment

Speaker: Dr Schadendorf

CAR-T treatments were initially designed for hematological malignancies, later have been used for autoimmune diseases and more recently they are being studied in solid tumors, including melanoma.

Tumor heterogeneity and microenvironment

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speakers: Dr Lukas Sommer, Dr Amaya Virós and Dr Ines Pires da Silva

Tumor-Associated Glia: Key Drivers of Skin Tumor Formation

Speaker: Dr Lukas Sommer

There are parallelisms between tumors and wounds.

In skin wounds, glia in peripheral nerves de-differentiate and form a regenerative niche that orchestrates skin repair.

Tumor-Associated Glia (TAG) are important in SCC since dedifferentiated peripheral glia are found in the stroma of SCC. These TAG detach from the nerves and go to the tumor stroma.

Hence, TAG are important in tumors and in particular in SCC.

What's the role of TAG in tumorigenesis? TAG promote tumorigenesis by enhancing tumor cell proliferation and interacting with macrophages. Their depletion reduces tumor growth and impairs pro-tumor macrophage polarization.

In other words, TAG interact with macrophages, and in fact loss of TAG impairs macrophage polarization toward a pro-tumorigenic phenotype in vivo.

To sum up, in SCC and also AKs, TAGs promote the SCC development.

Stromal, Site-Specific Lipid Cues Dictate Skin Cancer Metastasis, Tropism and Immunity

Speaker: Dr Amaya Virós

Some organs are less prone to melanoma metastases.

Metastatic patterns vary by organ and time. Lipid availability plays a major role.

Also there are temporal differences: brain metastases occur in younger patients (55 year old) whereas hepatic metastases occur later (78 year old). Some of these differences may be due to differences in lipids.

Age influences lipid composition:

- Young tissues: lipid-rich environment supporting tumor growth
- Aged tissues: reduced lipid availability

Also, there are questions regarding why some SCC do not metastasize. It can be due to different lipidomics:

- Lipid poor environment → exposed SCC to lipid-competent fibroblasts
→ this accelerates invasion

Brain metastases also show a different age pattern. This may be due to vascular differences in the brain but mostly differences in the composition of brain lipids → lipid availability decreases with age.

Young intracranial melanomas express programs of aggressive behavior. So young brains have more lipids and these lipids feed brain metastases. This explains why there are more brain metastases in younger patients and why they are more aggressive. In young patients tumors the fatty acids are reduced within the tumor since the tumor is using the lipids, as opposed to older patients.

Moreover, human melanoma brain metastases in young patients are larger and seed more diffusely than older individuals.

APOE plays a key role in tumor growth and immune regulation. APOE knockout reduces tumor growth but is difficult to target clinically due to its ubiquitous expression

To sum up, young brain lipids promote melanoma brain metastases growth and invasion. Young brain lipids are associated with immunosuppressive milieu. And interfering with lipid transport (ApoE) machinery of non-neuronal cells reduces tumor growth (and immunity).

Location Matters: How the Organ Microenvironment Shapes Immunotherapy Efficacy

Speaker: Dr Ines Pires da Silva

We have two main strategies to treat metastatic melanoma: targeted therapies (TT) and immunotherapy. Both have improved OS in melanoma, especially thanks to immunotherapy.

However, responses depend on the location of the metastases.

Liver metastases have a worse prognosis compared to all other sites in ipilimumab+antiPD1 treated patients. This doesn't happen with targeted therapies, where there's some degree of response with TT.

This leads to the hypothesis that liver M1 induces immunosuppression. This immunosuppression could be local but also systemic. So it has been studied what happens with patients with hepatic metastases and other mets and saw that there are no significant differences between liver mets and other location mets such as lung and subcutaneous mets, but not brain mets. So this data suggests that liver mets induce systemic immunosuppression.

What about lung mets?

Lung mets are a predictor of good response: they have high density of T cells, high expression of PDL1...

To sum up, liver metastases create a hypoxic, glycolytic immune-excluded niche which confers resistance to immunotherapy. Conversely, lung metastases show better T-cell infiltration and longer PFS.

How to manage Actinic Keratosis?

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speakers: Dr Nicole Kelleners-Smeets and Dr Markus Heppt

Biology of Actinic Keratosis: An Update

Speaker: Dr Nicole Kelleners-Smeets

Prevalence of AK keeps growing with rates around 15% of men and 5.9% have AKs, but this increases in Caucasian population over 70 (34% in men and 17% in women).

AK can evolve into 3 scenarios: remain stable, regress or progress into SCC. AK can regress spontaneously in immune-competent patients:

- 8% of patients
- More in the head and neck region

AK regression doesn't occur in immunosuppressed patients such as organ-transplant recipients.

Additionally, we know that invasive SCC is characterized by loss of e-cadherin, so e-cadherin enhancement could be a therapeutic strategy.

Another issue is the progression to SCC. A study in JID by Thomson et al showed that AKs already have the majority of genomic alterations present in SCC.

Also, another issue we sometimes see is the onset of SCC after field treatment for AK. We now know that this risk is 4%, being the risk highest in Olsen III lesions.

What about chemoprevention?

Weinstock showed that if you proactively treat patients with 5FU you can reduce the number of AKs, but after 2-3 years they come back. This suggests that we should retreat patients every 1-2 years to prevent SCC onset.

What about sunscreen?

If SPF is used, the number of AK reduces. Also, when sunscreen is used in combination with AK therapies, the effect is synergistic and reduces the onset of more AKs and of ultimately of SCC.

Hence, the ideal scenario would be to keep retreating patients + using sunscreen to decrease the AK progression.

Treatment of Actinic Keratosis in Specific Subsites

Speaker: Dr Markus Heppt

Some localizations are but harder to treat than the head and neck. We have 2 types of difficult to treat lesions outside the head and neck:

- Isolated thick lesions (for example on the dorsum of the hands)
- Widespread lesions (for example all over the arms)

It is true that for single lesions we tend to use destructive therapies (cryotherapy for example) but sometimes we need to combine treatments but we don't know which ones. Guidelines do not really help that much in selecting the best treatment in these scenarios.

The main issue is the lack of identifying which are the meaningful efficacy outcomes: complete clearance, partial clearance or lesional clearance.

Also, some classic treatments do not have many randomized clinical trials (RCT), and other treatment modalities have a lot of RCT (ie photodynamic therapy [PDT]) but this doesn't mean certain treatments don't work.

And more importantly, the majority of treatments have been studied in the head and neck, so we are extrapolating the results in other locations.

In these non-head and neck locations the treatment that has more evidence is PDT, especially red-light lamp PDT treating the dorsum of the hands. There's some evidence with daylight PDT but not much and even less in hyperkeratotic lesions which are the typical ones on the dorsum of the hands.

What do guidelines say about topicals?

Not much, maybe 5FU +/- salicylic acid is the one with more evidence. This treatment helps reduce the hyperkeratosis and it has a good mechanism of action, as well as it is in label for the extremities and for hyperkeratotic lesions.

There's some data from real world studies in Italy studying tirbanibulin in special sites with promising results. However, the label indicates its use in the head and neck region, something to explore and change.

5FU + calcipotriol 0.005% seems promising to treat extremities but it is off label. The combination works much better than 5FU alone.

Personalized neo-adjuvant therapy for melanoma

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speaker: Dr Blank

The management of resectable stage III melanoma patients has been revolutionized by the development of neoadjuvant studies. In this session, Dr Blank has made a quick overview of the trajectory of neoadjuvant treatments in melanoma.

Neoadjuvant therapy in melanoma started with a small trial, the OPACIN trial, as a proof of concept study in 2018. In resectable stage III patients it showed that patients receiving neoadjuvant immunotherapy with ipi + nivo had better outcomes than patients receiving these drugs in the adjuvant setting, even achieving almost flat Kaplan Meyer survival curves if complete pathological response was achieved.

However, in the OPACIN trial ipi+nivo was also administered in the adjuvant setting, thus leading to significant toxicity.

Hence, after the striking results of the OPACIN trial, further trials have been conducted in the neoadjuvant setting to maintain efficacy and reduce toxicity.

Later, other studies using nivolumab alone in the neoadjuvant setting showed that the responses were worse as opposed to ipilimumab + nivolumab but had less side effects with nivo alone.

The OPACIN-neo trial compared different dosing strategies of ipilimumab + nivolumab, showing that low dose ipi (1mg) was good enough in the neoadjuvant setting compared to high dose ipi (3mg). Additionally, in this trial, after neoadjuvant ipi+nivo LND was performed but no further immunotherapy was given. This was disruptive since in patients achieving major pathological response there's always the doubt on whether adjuvant therapy is necessary. The PRADO also studied this issue. In this study patients received 2 cycles of 1mg ipi + 3mg nivo before surgery, got the index lymph node excised and histologically analyzed and if major pathological response was achieved, no lymph node dissection (LND) and no adjuvant treatment were performed. If partial pathological response was achieved then lymph node dissection was performed but adjuvant therapy was NOT administered, and only in cases of no pathological response LND + adjuvant therapy were performed.

If we then look into the data of the PRADO study we can see that if major PR was achieved, LFN omission did not affect survival outcomes. In this sense, to better understand the impact of not performing LND, 2 more trials, the OMIT and the MSLTIII trials, are ongoing and will provide very relevant information.

But what revolutionized the neoadjuvant setting has been the release of results of the SWOG1801 and NADINA trials.

The SWOG1801 trial studied a perioperative scheme administering pembrolizumab in the neoadjuvant and also in the adjuvant setting. NADINA studied the use of ipi+nivo in the neoadjuvant setting and confirmed what was observed in the OPACIN and PRADO trials, that if major pathological response the survival data improved dramatically. Also, it showed that in patients with partial PR, adjuvant therapy improves outcomes.

If we continue to look at the NADINA data, we see that the majority of the metastasis after neoadjuvant treatment come from patients without pathological response → non-responders. Therefore, we need to improve the outcomes in non-responders. What can we do in these non-responders?

- Escalate adjuvant treatment
 - o Results from the NCT04013854 trial seems that escalating adjuvant treatment (post-surgery) does not work
- Use alternative drugs such as vaccines, intralesional treatments

Additionally, some patients will do very well and sometimes we may need to de-escalate treatments to minimize toxicity. If we compare the NADINA with SWOG scheme we see that NADINA does better but has more toxicity, and sometimes some patients will be fine just with the SWOG scheme. So, we need tools to select patients to see which treatmentx scheme they need, in which ones we need to escalate and which ones de-escalate.

And in this sense biomarkers are crucial to select patients:

- IFN gamma seems the best tool: more objective to quantify
- PDL1: can be confusing since the threshold is 1% but there's subjectivity in the PDL1 immunostain (immunostain can be read differently among pathologists, sometimes the test doesn't work well...)
- TMB

Maybe in the future we will use AI to identify biomarkers and responders.

- The ALETTA trial is a new study that will assess a fully personalized neoadjuvant checkpoint inhibition in stage III macroscopic melanoma by deciding the doses and the drugs according to different biomarkers such as IFN gamma.

To summarize:

- neoadjuvant immunotherapy with ipi + nivo is the new standard of care for macroscopic stage III melanoma, with a subgroup of patients that can be de-escalated to neoadjuvant anti-PD1 alone
- adjuvant consolidation may not be necessary in cases of pathological response
- it is questionable if we should pursue perioperative schemes
- upfront identification of patients harboring unfavorable tumors and/or are less immune activatable is needed
- baseline IFN gamma signature is currently the most robust biomarker
- trials de-escalating in IFN gamma high signature patients and escalating in IFN signature low patients are warranted

GEP for melanoma and keratinocyte carcinomas

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speaker: Dr Teresa Amaral

We know melanoma can behave very differently. Some melanomas are clearly high risk and others are low risk.

What is a low risk melanoma?

In theory, stage I or II melanomas, but since there are so many melanomas in this group, although the % of melanomas that progress in this group is little, the absolute numbers of metastatic melanomas come from these I and II groups. So we need to identify these patients who are in the third space, the ones that behave aggressively but in theory should be more indolent.

Also, it is possible there are some limitations with current staging strategies such as sentinel lymph node biopsy (SLNB). Therefore, It could also be due to the fact that SLNB is not enough or not good enough.

In this sense, gene expression profiling (GEP) tests can help increase sensitivity and specificity. GEP identifies certain genes upregulated and others downregulated and can help predict how the tumor is going to behave. This can potentially identify the patients in the third space (non-responders to immunotherapy).

Also, GEP can be used to predict SLNB positivity or other prognostic information.

There are several GEP tests available: Merlin test, Melagenix, Castle.

There are issues with these tests which also include high costs of the tests themselves and of the associated therapies and follow-up tests.

Ultimately, we want to use these tests to decide whether we will treat a patient or not. In this sense, we are all waiting to see the NIVO-MELA trial results. Also, GEP can be useful to select which patients to treat in stage IIA, IIB or IIC.

Satellite symposium 4: Perspectives on Early-stage Melanoma: Diagnosis, Staging, and Treatment

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speakers: Dr Axel Hauschild, Dr Sapna Patel, Dr Alexander van Akkooi

How Do We Identify the Appropriate Patients for Adjuvant Treatment?

Speaker: Dr Axel Hauschild

The majority of patients with melanoma are stage I and II. But the majority of events happen in these groups.

Since adjuvant treatment is approved after IIB stages, we may not need to perform SLNB, but this is something that need to be discussed in a tumor board since we know some patients in stage IIB will do fine and others won't, so we need to better select treatments.

So the question here is, are we overtreating patients?

Yes, definitely. To prevent a recurrence in stage IIC you need to treat 4 patients, whereas 20 if you treat stage IA.

What can be done to improve patient selection?

Nomograms can be used to predict recurrence and prognosis but there are different nomograms with different populations, with differences up to 10% using the exact same data from a given melanoma.

What about biomarkers?

IFN γ can help select responders: high TMB, high IFN and high PD1 expression patients do better.

GEP can also be useful as mentioned in the previous talk. In this sense there's a lot of hope with the NivoMela data which is still waiting to be released, hopefully next year.

Why do patients decline adjuvant treatment?

Age, comorbidities, stage IIIA...

Also, when patients are asked if they regret undergoing adjuvant treatment, the main reason is lack of efficacy. Therefore, we need to better select patients undergoing adjuvant treatment and value correctly number needed to harm vs number needed to treat.

Adjuvant Treatment Approaches for Early-stage Melanoma

Speaker: Dr Sapna Patel

We are facing some challenges in stage IIB/C melanoma:

- SLNB paradigm
- Overtreatment
- Treat now or later: the challenge of crossover designs
- Neoadjuvant treatment vs adjuvant treatment: is there going to be enough tumor to be identified by immunotherapy in primary tumors?
- Earlier disease stages with high risk of recurrences
- Mucosal and acral

When we look at the trials using adjuvant pembro or nivo in stage IIB/C, a significant amount of patients will have adverse events. They may not be grade III (which happens in 5% of case) but some grade I or II AE can be bothersome; for example, imagine having grade I arthralgia for all your life, this can really impair quality of life.

Which are the unmet needs and considerations for adjuvant therapy?

- Adjuvant pembro or nivo for stage IIB/C melanoma
- No targeted therapy or combination therapy approaches
- Who to treat? If recurrence is as high as nearly 40% and HR for adjuvant therapy is around 0.6
- Not everybody with stage IIB/C needs adjuvant therapy
- The impact of recurrent (metastatic) disease after adjuvant therapy is unknown
- Recurrence on adjuvant therapy vs after adjuvant therapy

Neoadjuvant or adjuvant therapies for stage II melanoma

Speaker: Dr Alexander van Akkooi

Although adjuvant therapy is approved in >IIB patients, SLNB still has a role since if these patients have a + SLNB, the prognosis goes down. Also, this helps better select the patients and do not harm patients unnecessarily.

Regarding neoadjuvant setting in stage IIB/C melanomas there are several trials ongoing without efficacy data yet

- Trial from Karakousis et al. using neoadjuvant pembrolizumab, which showed 14% grade 3 and 4 toxicities
- NeoReNi II trial, using nivo + rela in high risk stage II melanomas
- NEOPRIME using neoadj pembro in IIB/C melanoma patients
- MARIANE study: intradermal application of ipi + nivo

Cell-based Therapies: Not Only for Last-Line Treatment?

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speaker: Dr Inge Marie Svane

TIL therapy requires harvesting lymphocytes from the tumor, expanding them, and reinfusing them with IL2 that acts as a booster of the TIL therapy. This treatment was first described almost 40 years ago and recently has been getting more and more attention to treat mostly immunotherapy-refractory patients (the third space)

Several TIL treatments are now approved and commercially available but only in the USA.

TIL therapy can be used as monotherapy but also to enhance the response of immunotherapy. In this sense, there are several trials now ongoing using TILs's.

A trial using ipilimumab + TIL showed very good results, achieving RR 49% with ipi+TIL vs 29% with ipi alone.

Another trial to overcome immunotherapy resistance is using pembro + TIL.

We also know now that the order of the treatments impacts TIL therapy. For example, BRAF/MEKi can potentially reduce the efficacy of following TIL therapy. Hence, if we are thinking about using TIL therapy, we should NOT use BRAF/MEK inhibition before TIL therapy. Additionally, BRAF/MEK inhibition after TIL failure is equally effective as given after progression to antiPD1.

Interestingly, TILs seem to perform better in low TMB patients, which typically are the ones with worse outcomes in antiPD1 treatments.

To summarize:

- TIL therapy is more efficient in patients with low TMB, favoring early use of TIL in these patients
- Prior BRAF/MEKi is associated with lower efficacy of TIL therapy, while BRAF/MEKi efficacy is maintained if given after TIL therapy, favoring early use of TIL
- Despite all the favorable evidence of TIL therapy, it's not approved in Europe yet and it's only available via clinical trials

Lost in Translation: From Advanced Diagnostics to Everyday AK Care How to define treatment Success in AK?

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speaker: Dr Josep Malvehy

AK is a big problem since incidence is increasing due to sun exposure and population ageing. This leads to high costs and is resource consuming. So dermatologists alone cannot manage AK management.

So is AK treatment sustainable for healthcare systems?

We know that AK is a marker of carcinogenic damage, that there's a risk in SCC progression, that preventive care reduce cancer costs... However, the truth is that the number of AK patients is so big that it is impossible to treat them all. Also, since AK is a chronic condition, we need repeated treatments.

And do we have to treat all the AK?

The truth is that not all AK will progress into SCC and actually almost 10% of AK regress alone. But the problem is that we don't know which AKs will progress into SCC and which ones won't.

The issue is that dermatologists cannot be the only ones treating AKs because the numbers are huge. So we should also count on GPs for AK management. The problem is that dermatologists need to lead the training on AK diagnosis and treatment, since sometimes the lesions are difficult to treat. We may need to train GPs to better diagnose AK by training them in dermoscopy (identify Bowen's disease, SCC, distinguish AK from inflammatory diseases).

Teledermatology is very helpful too to teach them AK diagnosis, so we need to perform good answers in teledermatology.

But even dermatologists and using dermoscopy sometimes the AK diagnosis isn't that easy in some cases.

Monitoring patients with AK with photography seems an ideal situation even in our clinical practice, because it helps obtain more objective data. The problem is that many doctors don't have much time.

Additionally, we now have technologies that help us see the morphology of AKs in vivo. The most fascinating technology is LC-OCT that allow us to see whether an AK is proliferative, acantholytic... The problem is that these technologies are not widely available and they are expensive.

And how do we manage AKs?

The evidence shows that treating the field is the best, but it's true that not all patients need it. The problem is that it's impossible to standardize the treatments since the reimbursement systems are different, patient preferences may vary, drug access may be different in different settings (public vs private), regulatory issues with some drugs...

To sum up, we need to educate not only patients but also professionals (especially GPs) in AK management, focus on high-risk patients, using therapies that address field disease and integrate prevention and innovation.

How to define treatment Success in AK?

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speakers: Dr Claudio Conforti, Dr Carla Ferrándiz and Dr Laura Susok

Selectivity: "targetting what really matters"

Speaker: Dr Claudio Conforti

When we treat AK, complete clearance it may not be the ideal metric. Probably it will be better to calculate the reduction of lesions, mainly because AK is considered a chronic disease.

There are some classification systems that can also be used such as the AKASI, which ranges from 0 to 18, and it's a way to try to make a more objective evaluation.

Also, AKASI score is associated with a higher risk of SCC progression.

Why do we need to treat AKs? Because we don't know which AK will progress into SCC. There are two pathways of SCC: the classic one (that parallels the Olsen classification) and the one suggested by Fernandez-Figueras in which we know that some AK are more aggressive upfront (ie proliferative AKs).

There are some dermoscopic signs that help us predict a high risk AK, for example the presence of glomerular vessels in dermoscopy which are associated with basal proliferation.

There are numerous risk factors (immune suppression, HPV...) but a novel feature is the presence of basal proliferation. The more basal proliferation, the higher risk of SCC progression. This has been studied into the PRO classification: PRO I, II and III. The problem is that this classification is histological. How can we evaluate this in vivo? Using a new tool: LC-OCT. There's a very nice correlation between histology and LC-OCT in grading basal proliferation.

To better evaluate the basal layer, you can add a bit of water or a salicylic acid to remove the hyperkeratosis and improve imaging resolution.

Interestingly, tirbanibulin works also in PRO III AKs. Why? Tirbanibulin selectively affects cells with high proliferative profile with high mitotic rate, since it inhibits microtubules.

Building trust through Safety and tolerability

Speaker: Dr Carla Ferrándiz

AKs are not a one-time treatment disease, it's more a chronic disease. Hence, complete clearance is not realistic. Also, some treatments result in important local skin reactions (LSR) and since we will need to retreat AK patients, drugs with important LSR will be less likely to be repeated by the patient, and can eventually reduce the trust between the patient and the doctor.

Tirbanibulin has low LSR which results in high adherence. Also, when asking patients if they would be retreated with tirbanibulin, almost 90% of patients mentioned they may repeat the treatment. This was shown in the Tirbaskin trial recently published.

Another subset of patients are high-risk ones, such as OTR patients. In these patients no AK undergo spontaneous regression. Additionally, we need to treat these patients early and proactively to prevent SCC progression, as well as insist in primary prevention with photoprotection.

If we look into efficacy of tirbanibulin in OTR, the efficacy is a bit lower than immunocompetent ones but since the LSRs are better, we can retreat these patients easily.

Therefore, tirbanibulin has a balanced profile in terms of efficacy, safety, tolerability, and patient's satisfaction. This is very relevant since AK patients will have to repeat the treatment over time.

Simplicity counts for long-term disease control

Speaker: Dr Laura Susok

Skin cancer is an epidemic with a >500% increase in the last 30 years. This makes AK management impossible to do by dermatology alone. Therefore, we need to empower patients and GPs to improve AK management.

Teledermatology has numerous advantages:

- It improves access to care
- Time efficiency
- Convenience for patients
- Early detection and monitoring
- Reduces healthcare costs

Hence, we need simple treatments to treat AK patients.

Tirbanibulin is the shortest self-applied treatment for AK.

What about adherence?

We know that complex treatments result in lower adherence.

Are AK treatments available all year round?

Tirbanibulin yes, can be used all year round.

To sum up, patient satisfaction is key to improve adherence in the long term, teledermatology can help monitor patients, and the short course of tirbanibulin improves adherence.

Early Detection of Skin Cancer: new devices

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speakers: Dr Harald Kittler, Dr Lara Valeska Maul and Dr Josep Malvehy

3D Total Body Photography: The Austrian Experience

Speaker: Dr Harald Kittler

Total body photography (TBP) is recommended in high-risk patients. Now we have new 3D devices but we still don't know if these technologies are going to be better than previous 2D devices:

- Advantages
 - Provides additional information
 - Enables earlier detection
 - Provides reassurance both for the clinician and the patient
 - Facilitates storage, documentation, retrieval and telemedicine
 - Improves patient compliance → patients love it!
- Challenges
 - Does it really provide additional information?
 - Detecting melanoma earlier does have an impact in clinical practice?
 - Increased costs
 - Does not capture entire body (scalp, genitalia, soles)
 - Can provide wrong reassurance both for the clinician and the patient (false positives)
 - Potential concerns regarding data protection and confidentiality

We will have to perform more studies and see which is the real clinical impact of 3D TBP.

Synergy of Human and Artificial Intelligence in Melanoma Detection

Speaker: Dr Lara Valeska Maul

We already have numerous AI tools in melanoma detection. We know that AI outperforms dermatologists but only in artificial settings. Therefore, when AI is used with real daily data, it performs poorly if unsupervised. Therefore, AI should be used in a way to increase the physician's ability, in what is called augmented AI, in a synergistic manner. But what do we mean by synergy? That both AI and human brain complement each other, not that the combination will give us magical powers leading to $1+1 > 2$

We know now that the use of AI in the hands of experts isn't the best, and in fact the users who benefit the most of augmented intelligence (humans assisted with AI) are less experienced users/novices.

One of the main issues we encounter in current datasets is the lack of all skin types, especially from darker skin types.

What about consumer AI apps such as skin vision (unsupervised app-based AI)? They can be risky since they can have false positives or give potential false reassurance.

And what about the perception of the use of AI among patients? Patients love when AI is used. But the situation isn't the same among clinicians because many AI algorithms are a black box and clinicians want to know why a certain lesion is considered benign or malignant. In this sense, explainable AI may increase clinician confidence in AI.

Deep Imaging in Skin Cancer Diagnosis

Speaker: Dr Josep Malvehy

Integrating all the imaging tools we have can improve skin cancer management. There's been a lot of news since the advent of dermoscopy, with more and more technologies being used. We now have 3D TPB, digital dermoscopy, RCM, OCT, LC-OCT... and the integration of all these technologies with clinical data is crucial in a concept coined as dermatomics.

One of the main issues we face when using new imaging technologies is its difficult learning curve. However, AI can potentially help expedite this learning curve. As an example, LC-OCT incorporates 2 AI algorithms to detect BCC and AK. When this AI aid is activated, it can help less experienced navigate through a lesion, and gain 2 years of training. So, AI can potentially shorten the learning curve of some imaging technologies.

Finally, AI can also improve image acquisition, not only of full body images (such as Vectra or ATMB technologies), but also can improve dermoscopic acquisition with devices such as Deviskan from Dermavision which acquires dermoscopic images in an unsupervised manner. These images obtained with the device have been studied by Roses et al and published in JAMA Dermatology showing very good quality and correlation with manually-acquired dermoscopic images, minimizing the acquisition time.

How to manage cSCC (Cutaneous Squamous Cell Carcinoma)?

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speakers: Dr Heather Shaw, London, United Kingdom and Dr Paolo Bossi, Brescia, Italy

Neoadjuvant and/or Adjuvant Treatment in High-Risk: How to Integrate these Approaches?

Speaker: Dr Heather Shaw, London, United Kingdom

The management of high-risk cutaneous squamous cell carcinoma (cSCC) is undergoing a paradigm shift with the incorporation of systemic immunotherapy into earlier stages of disease. While surgery, with or without adjuvant radiotherapy, has traditionally been the standard of care, immune checkpoint inhibitors are increasingly being integrated into perioperative strategies.

Neoadjuvant immunotherapy has demonstrated promising activity, with high rates of major pathological response in patients with resectable but high-risk tumors. This approach may reduce tumor burden, facilitate less extensive surgical procedures, and potentially improve long-term outcomes. Importantly, pathological response has emerged as a relevant surrogate marker for survival.

Adjuvant treatment with PD-1 inhibitors, particularly cemiplimab, has shown a significant reduction in recurrence risk in selected high-risk populations. These include patients with adverse pathological features such as deep invasion, perineural invasion, nodal involvement, or recurrent disease.

A central challenge remains the optimal integration of neoadjuvant and adjuvant approaches. Neoadjuvant therapy may be particularly advantageous in borderline resectable tumors or when surgical morbidity is expected to be high. In contrast, adjuvant therapy remains appropriate for patients with high-risk features identified postoperatively.

Multidisciplinary decision-making is essential, taking into account tumor characteristics, patient factors, and anticipated surgical outcomes. Ongoing studies will further define optimal sequencing and patient selection strategies.

New Frontiers in Treatment of Recurrent/Metastatic cSCC

Speaker: Dr Paolo Bossi, Brescia, Italy

The therapeutic landscape of recurrent and metastatic cSCC has been transformed by immune checkpoint inhibitors, which are now the standard first-line treatment and offer durable responses in a subset of patients.

Nevertheless, primary and acquired resistance to PD-1 blockade remains a major clinical challenge. Current research is focused on overcoming resistance through combination strategies and novel therapeutic approaches. What can be done to overcome resistance? Use of alternative systemic drugs (for example EGFR inhibitors alone or in combination with antiPD1) as well as the use of intralesional drugs.

Combinations of immunotherapy with EGFR inhibitors have shown encouraging activity, particularly in PD-1 refractory disease, by enhancing tumor immunogenicity and modulating the tumor microenvironment.

Intratumoral therapies are also being explored, aiming to induce both local tumor control and systemic immune activation.

These strategies may be particularly relevant in patients with accessible lesions and who show resistance to antiPD1 therapy. Intralesional drugs investigated include IL2, daromun (IL2/TNF conjugate), intralesional cemiplimab, among others.

Despite these advances, predictive biomarkers remain limited. PD-L1 expression and tumor mutational burden (TMB) have not consistently correlated with response, highlighting the need for more refined biomarkers, including immune microenvironment profiling.

Future directions include the development of next-generation immunotherapies, cytokine-based treatments, and oncolytic viral therapies, with the goal of improving outcomes in this difficult-to-treat population.

SYMPOSIUM ON SKIN CARE IN ORGAN TRANSPLANT PATIENTS EUROPE (SCOPE)

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speakers: Dr Ulrike Leiter and Dr Catherine Harwood

Immunotherapy in the Treatment of Post Transplant Skin Cancers in OTR

Speaker: Dr Ulrike Leiter

Solid organ transplant recipients (OTRs) represent a unique and challenging population due to their markedly increased risk of skin cancer, particularly cSCC, and their chronic immunosuppressed state.

The use of immune checkpoint inhibitors in OTRs is complex due to the risk of allograft rejection. While these therapies can achieve meaningful tumor responses, they are associated with a significant incidence of graft rejection, which can be severe and potentially fatal.

Reported rejection rates vary but can approach 40–50%, particularly in kidney transplant recipients. The risk appears to be influenced by factors such as the type of transplanted organ, baseline immunosuppressive regimen, and timing of immunotherapy.

Strategies to mitigate rejection risk include modification of immunosuppressive therapy, such as switching to mTOR inhibitors, and careful patient selection. However, robust prospective data are lacking.

Alternative administration routes of immunotherapy, such as the intralesional route, should also be considered. Intralesional cemiplimab shows good responses regardless of the doses. Regarding adverse effects, they were dependent on the physician performing the injection; if the injection was done in the subcutis there were more adverse events since injecting in the subcutis increases the systemic absorption.

Thus, treatment decisions must be individualized, balancing oncologic benefit against the risk of graft loss, and require close collaboration between dermatologists, oncologists, and transplant specialists.

Primary and Secondary Prevention of Skin Cancer in Solid Organ Transplant Recipients

Speaker: Dr Catherine Harwood

Prevention remains a cornerstone in the management of skin cancer in OTRs, given their substantially elevated lifetime risk. Primary prevention focuses on rigorous photoprotection, including the use of high-SPF sunscreens, protective clothing, and behavioral modifications to reduce UV exposure.

Secondary prevention involves regular skin surveillance and early detection strategies. Patient education and self-examination play a critical role, as early identification of lesions significantly improves outcomes.

However, there are no randomized clinical trials (RCT) in OTR regarding these primary and secondary strategies. In fact, the only RCT performed in prevention strategies include the use of acitretin and the switching of conventional immunosuppressants to mTORs. Therefore, there are no prospective RCT for photoprotection in organ transplant patients or for any of the drugs used for the treatment of actinic keratosis (AKS). This does not mean these strategies and treatments should not be used, but support the fact that RCT need to be performed in OTR patients.

When we assess in What about AK and field cancerization in OTR, there are some challenges that need to be taken into account: OTR have a higher burden of disease, accelerated progression to SCC, low or absent spontaneous AK regression, decreased treatment effectiveness, potential effects on allograft (for example with imiquimod)...

This also limits the inclusion of immunosuppressed patients in RCT therefore leading to a lack of meaningful data. Hence, most of the data available on AK treatment comes from RCT in immunocompetent patients.

When we look into the treatments available, 5-FU is the one that has shown higher cost-effectiveness but it has been studied in 2 RCT in immunocompetent patients (Jansen NEJM 2019, Weinstock JAMA Derm 2018).

When 5FU is associated with calcipotriol, the response is superior to 5FU alone since calcipotriol acts as a local immunotherapy increasing the Th2 response thus reducing the number of AKs. Also, if a Th2 response is built, it is much less likely to be associated with graft rejection.

What about this combination in OTR?

There's a new promising trial using 5FU + calcipotriol + photoprotection currently running in the UK and Canada without data yet (the SPoTIT trial).

Photodynamic therapy has several RCT. What is interesting of these studies is that they include immunocompetent patients and also some OTR, although in small number. The results of PDT in OTR are good but results are mixed.

There are several cases reports and series with tirbanibulin and cryotherapy, with good reduction of AK but no data on the effect of SCC reduction.

Sirolimus showed a reduction of AK and SCC in situ, but no reduction in invasive SCC.

The best evidence in systemic chemoprevention in OTR comes from acitretin. The issue is that prices change from country to country, requires lab monitoring... but EADO guidelines recommend acitretin after the onset of the first SCC, especially at a low dose (10mg).

What about other chemopreventive agents?

Nicotinamide showed improvement of NMSC in immune competent patients in the ONTRAC trial, but did not work in OTR probably because the study in BJD was underpowered.

More recent papers are showing good results of nicotinamide in OTR, but a new trial ongoing in Canada (SPRINTR) will give more information about the use of nicotinamide in OTR.

Another crucial issue (and proven to reduce SCC in OTR) is to modify immunosuppression. Reducing or stopping azathioprine or mycophenolate, reducing immunosuppressant doses...all these strategies are beneficial to prevent SCC onset. However, the most relevant action is to change immunosuppressant medications to mTOR inhibitors such as everolimus or sirolimus.

HPV vaccination is another promising strategy. It creates cross-protective status that reduces the onset of SCC, including in immunosuppressed patients. The VAXAK study showed that HPV vaccination reduced AK numbers in immunocompetent patients, so it's a potential line of research in OTR patients.

To summarize, although many of the interventions for OTR make sense, they lack robust scientific evidence because of the lack of RCT.

ChatGPT and beyond

Report written by Dr Oriol Yélamos (Dermatologist, Spain)

Speakers: Dr Titus Brinker, Dr Lukas Flatz and Dr Alexander Zink

Explainable AI in Skin Cancer Screenings

Speaker: Dr Titus Brinker

Artificial intelligence (AI) has demonstrated significant potential in skin cancer screening; however, its widespread adoption is limited by concerns regarding transparency and trust. Explainable AI (XAI) aims to address these challenges by providing insight into how algorithms arrive at diagnostic decisions.

AI has been shown to be a very good tool to detect skin cancer detection in silico. However, they perform poorly with real images and the problem is that most the studies do not show why an image is a skin cancer or or not. To be able to understand AI we need explainable AI (XAI). XAI tools can identify and visualize the features or image regions that drive model predictions, thereby enhancing interpretability and facilitating clinician acceptance.

The problem with current XAI is that it highlights certain areas that do not correlate at what dermatologists look at. So there's been some attempts to develop XAI with what clinicians look at (Chanda et al study). How this has been done traditionally is with manual annotation but it's time consuming. In this sense, there are now numerous studies using eye-tracking correlating what doctors look at and what XAI is highlighting.

But why is XAI important? What do clinicians and patients want when using AI?

Of course doctors want diagnostic accuracy to be good, but also explainability, which is what patients want in first place. There are also some news on devices which have AI built in a handheld dermatoscope. These devices are now being studied and we will have results in the future.

Also, it is possible to use generative AI to better understand things. You can ask chatGPT or DeepSeek why a certain lesion is a melanoma or not, for example. This is potentially very useful for tumor boards in which we can ask generative AI why certain things are the way they are, which are the best treatment decisions.

AI is so important right now that even the US congress is discussing its use in medicine to legislate it with an ultimate goal to allow even AI to prescribe drugs. This can be potentially useful to save money in health systems.

There are several ethical questions regarding the use of AI. It is true that nowadays people may prefer the human touch, but it is true that AI is being used a lot for medical consultations since both patients and clinicians are using AI before the actual medical appointment. This can be tricky because we are feeding algorithms with confidential data.

To sum up, integration of multimodal data, including clinical metadata and patient history, is critical to improving performance and aligning AI systems with real-world clinical decision-making. Ultimately, XAI is expected to function as a decision-support tool, augmenting rather than replacing clinician expertise.

ChatGPT: A Doctor's Perspective on AI in Medicine

Speaker: Dr Lukas Flatz

Large language models such as ChatGPT are increasingly being explored for applications in clinical practice. These tools can assist with documentation, summarization of medical information, and patient communication.

From a physician's perspective, ChatGPT offers the potential to improve efficiency and reduce administrative burden. It may also enhance patient education by providing clear and accessible explanations.

However, limitations include the risk of generating inaccurate or misleading information, as well as the lack of true clinical reasoning. Therefore, outputs must be critically evaluated by healthcare professionals.

Ethical considerations, including data privacy, transparency, and accountability, are essential when integrating such tools into clinical workflows.

ChatGPT should be viewed as a supportive technology that complements, rather than replaces, clinical judgment.

Closing the Care Gap: Tele dermatology, Wearables & AI Triage for Population-Level Skin Health

Speaker: Dr Alexander Zink

Digital health technologies are playing an increasingly important role in addressing disparities in dermatologic care.

Tele dermatology has proven effective in expanding access to specialist care, particularly in underserved and remote areas. AI-based triage systems can further optimize resource allocation by prioritizing high-risk lesions.

However, the effectiveness of such systems depends on disease prevalence and the balance between sensitivity and specificity. In low-risk populations, increased sensitivity may lead to overdiagnosis and unnecessary interventions.

Wearable devices and mobile applications are emerging as tools for continuous monitoring and early detection of skin lesions, empowering patients and facilitating timely intervention. Examples of these devices include smart toilets that can perform urine and stool tests, useful even to monitor treatment response (we know we can monitor immunotherapy treatment response using stool analysis).

Successful implementation requires integration into healthcare systems, along with robust validation, data security, and consideration of cost-effectiveness.

At a population level, the combination of tele dermatology, AI, and digital monitoring has the potential to significantly improve early detection and reduce inequities in skin cancer care.