Oncology and surgery
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Dermatologic adverse events of oncologic drugs
Grading of Dermatologic Adverse Events (ver 5.0)

- 5 grades: mild, moderate, severe, life-threatening and death
Chemotherapy rashes (Dr. Kwong)

- **Capecitabine:**
  - AK inflammation
    - (Lewis KG et al Arch Dermatol 204)

- **Citarabin/Idarubicin**
  - Toxic erythema of chemotherapy (not palms and soles) (specially intertriginous areas and back)

- **Docetaxel**
  - Blistering painful rash dorsum of hands and feet (PATEO) : taxene therapy related periarticular thenar erythema with onycholysis
Target therapies rashes (Dr. Kwong)

- **EGFR**
  - Papulopustular eruption
  - Avoid monotherapies
  - Avoid topical steroids on the face
  - Avoid overuse of antibiotic
    - Increase secondary infections
    - In press: from 122 patients, 71 + culture + 58% resistant tetracycline and clindamycin (MARS)
  - More use of antiseptics: benzoyl peroxide and diluted bleach socks.
  - Topical invermectin excellent results
Ipilimumab cutaneous side effects (Dr. Kwong)

- Morbilliform dermatitis
  - 24.3% incidence
  - Median time to onset 3-4 weeks (until 17 weeks)
  - +/- pruritus, eosinophilia
  - Histology nonspecific
- Vitiligo-like melanoma associated hypopigmentation
  - Possibly portends prognostic favorability
- Pruritus
  - 30% incidence
  - Corcosteroids, antihistamins, gabapentin, pregabalin, mirtazapine, aprepitant

Lacouture M et al. JAAD 2014;71:161-9
Anti PD-1/PDL1 cutaneous side effects (Dr. Kwong)

- **Lichenoid dermatitis**
  - 75% with pruritus
  - Variable time of onset (mean 4 months)
  - Variable clinical presentation
  - Histology lichenoid infiltrate with more spongiosis and epidermal necrosis than LP
  - Topical steroids

- **Autoimmune blistering disease**
  - Similar to bullous pemphigoid
  - Doxycycline, steroids, Mtx, tocilizumab, omalizumab.

Anti PD-1/PDL1 cutaneous side effects (Dr. Kwong)

- Psoriasiform dermatitis (+- arthritis)
  - Management topical drugs, phototherapy and apremilast or Mtx.
- Severe cutaneous and neurologic toxicity


Severe cutaneous and neurologic toxicity in melanoma patients during vemurafenib administration following anti-PD-1 therapy

Douglas B. Johnson¹, Erika K. Wallender¹, Daniel N. Cohen¹, Sunaina S. Likhari¹, Jeffrey P. Zwerner¹, Jennifer G. Powers¹, Lisa Shinn¹, Mark C. Kelley¹, Richard W. Joseph², and Jeffrey A. Sosman¹

Figure 2.
Diffuse erythematous papules covering the back and upper extremities (A and inset) with histologic evidence of superficial perivascular dermatitis with occasional eosinophils (B H&E, 20 × orig. obj. mag., C H&E 100× orig. obj. mag.)

acute inflammatory demyelinating polyneuropathy
Non-surgical treatments for skin cancer
5-fluorouracil chemowraps for Bowen diseases in legs

- 20 gr 5-FU/week
- Zn oxide impregnated Unnaboot
- Cotton bandage
- Wrap is in place for 7 days.
- Duration: 4-20 weeks
- Contraindications:
  - Moderate severe artery disease
  - Venous ulcers

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**Chemowraps as an adjuvant to surgery for patients with diffuse squamous cell carcinoma of the extremities.**

Mann M¹, Berk DR, Petersen J.
Basal cell carcinoma treatment (Dr. Epstein)

• “Not only oncologist should prescribe HH inhibitors”
• Problem: abandon the treatment for side effects
  • Cramps
  • Alopecia 50% after 6 meses
  • Ageusia 50% a los 2 meses
  • Weightloss

• Find a HHi molecule without the Aes: Itraconazol??
  • Itraconazol new formula in clinical trials more safe and more uptake by the tumor.

• Apply HHi topically drugs with just right percutananeous penetration, enough for anti HH/ anti-BCC efficacy but not enough to the systemic exposure that produces the adverse effects
  • Phase II clinical trials (Eepstein@Pellepharm.com)

• Clinical trial comparing PDT y vismo alternartion
Topical treatments for lentigo maligna

- **Imiquimod**
  - **Monotherapy**
    - Tio D et al. JEADV 2017;31:616-24: 78% clinical and 77 histological response
  - **6-7 applications/week, at least 60 applications**
  - Drug holiday when necessary
  - Recurrences in short time follow-up
  - **Combination**
    - Ablative laser or tazarotene
    - No better results and more side effects
Talimogene Laherparavec (T-VEC)

- Viral oncolytic immunotherapy (HSV tipo 1)
- Intrallesional injection (5 sessions in 8 weeks)
- Indication: cutaneous, in transit, nodal mets of melanoma
- Side effects (50% like a flu)
- CR: 10,8%
- ORR: 26,4%
- Videos on line how to inject it

Psoriasis therapies and risk of cutaneous malignancies

(Prof. M. Lebwohl)

*NMSC rates were 42% higher among individuals ever exposed to a biologic (aHR 1.42, 95% CI 1.12-1.80), largely driven by increased cutaneous squamous cell carcinoma risk (aHR 1.81, 95% CI 1.23-2.67).*

<table>
<thead>
<tr>
<th></th>
<th>Moderate psoriasis</th>
<th>Severe psoriasis</th>
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</thead>
<tbody>
<tr>
<td>Lymphoma</td>
<td>1.34 (95% CI, 1.18-1.51)</td>
<td>1.89 (95% CI, 1.25-2.86);</td>
</tr>
<tr>
<td>NMSK</td>
<td>1.09 (95% CI, 1.05-1.13)</td>
<td>1.61 (95% CI, 1.42-1.84);</td>
</tr>
<tr>
<td>Lung</td>
<td>1.12 (95% CI, 1.01-1.25)</td>
<td>1.62 (95% CI, 1.16-2.28)</td>
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</tbody>
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*Malignancy rates in a large cohort of patients with systemically treated psoriasis in a managed care population.*

*NMSC rates were 42% higher among individuals ever exposed to a biologic (aHR 1.42, 95% CI 1.12-1.80), largely driven by increased cutaneous squamous cell carcinoma risk (aHR 1.81, 95% CI 1.23-2.67).*
Psoriasis therapies and risk of skin cancer
(Prof. M. Lebwhohl)

- NB-UVB non increase
- PUVA increase
  - Specially genital cancer
  - Also melanoma
  - More than 15 year after treatment
- Methotrexate: *increase* SCC and x3 melanoma
- Cyclosporin: *increase* SCC and melanoma
- Acitretin: reduces SCC in ORT (only while taken)
Biologics therapies and risk of skin cancer (Prof. M. Lebwohl)

- TNF-a: increase
  - A lot of case reports of SCC, CBC, melanoma, Merkel cell carcinoma (1)
- Ustekinumab: non increase
- IL17 inhibitors: non increase
  - (in mice to block IL17 prevent from cancer)
- Apremilast (too soon)
  - Only 1 cases
  - Mechanism of action seems not be probable
- IL-17 and IL-23: too soon
- Patients with PUVA and anti-TNFa more risk of skin cancer
And..
POSTER: Paraneoplastic angiomatosis: a new entity

- 2 patients with lung carcinoma and melanoma
- Red violaceous indurated plaque
- Histopathology superficial dermal benign appearing vascular proliferation with associated edematous and fibrotic stroma, mild chronic inflammation and scattered eosinophils.
- CD4 and HHV8 negative
Adhesive skin sampling platform

- 15,000 melanoma and lymph node met
- NPV: 99% (no melanoma)
- Sensitivity: 91%
- Cost 249 dollars 72 hours
- No mucosa no soles and palms

Published in final edited form as:

**Development and validation of a noninvasive 2-gene molecular assay for cutaneous melanoma**

Pedram Gerami, MD, Zuxu Yao, PhD, David Polsky, MD, PhD, Burkhard Jansen, MD, Klaus Busam, MD, Jonhan Ho, MD, Mary Martini, MD, and Laura K. Ferris, MD, PhD
Algorithm for skin cancer detection
(Dr. Chren The state of (measuring) The Art of Dermatology)

• Computer – based diagnosis algorithm for skin cancer
• Database of 130,000 skin lesion images
• Trained the algorithm to detect cancer
• Performed as well as dermatologist

Esteva A et al. Nature 2017; Feb 2;542(7639):115-118
Thank your for your attention