AEDV HIGHLIGHTS
27TH EADV CONGRESS
12-16 September 2018
PARIS, France
Oncologic Dermatology and Surgery

Dr. Antoni Bennassar
DERMATOSURGERY I
How to excise benign lesions (J. Kantor-US)

- Ideal outcome:
  - Preop: limit expectations, explain, explain and explain!
  - Intraop: low tension, undermine always, fascia plication, avoid foreign bodies, equal depth
  - Postop: follow up, early complications detection
How to excise benign lesions (J. Kantor-US)
The KISS principle (J. Paoli, Sweden):

- Set-back buried suture
The KISS principle (J. Paoli, Sweden):

- Pulley buried dermal suture: if tension +++
Laser resurfacing for improved scar cosmesis (J. Ostertag, Netherlands):

- **Skin Tension Lines**
  - Contraction
  - Wide
  - Stitch marks

- **Skin textural surface irregularities**
  - Thickness relief
  - Impingement trap door
  - Stitch marks dog ears pliability

- **Colour difference**
  - Hypertrophy / keloid

- **Depression**

- **Surgical scar revision**
  - Change direction
  - Z-plasty
  - Different closure

- **Ablative resurfacing classic / fractional**
  - Non ablative rejuvenation

- **Vascular lasers / IPL / pigment lasers**

- **Fillers hyaluronic acid / fat**
Dr. D. Moreno (Spain): The SLNB technique

- No OS benefit
- Importance of detecting lymph node mets to start an adjuvant therapy (Nivolumab, Pembrolizumab) in MM stage III
- Videos showing SLNB procedure
- Importance of keeping this surgery in the Dermatology department
Dr. D. Moreno (Spain): The SLNB technique

- SentiSim®: surgical model for SLNB training
DERMATOSURGERY II: videos
Reevaluation of the arterial blood supply of the auricle

Isaac Zilinsky, Detlev Erdmann, Oren Weissman, Niels Hammer, Mircea-Constantin Sora, Thilo L. Schenck and Sebastian Cotofana
The arterial blood supply of the helical rim and the earlobe-based advancement flap (ELBAF): A new strategy for reconstructions of helical rim defects

Isaac Zilinsky a,*, Sebastian Cotofana b,*, Niels Hammer c, Christine Feja c, Christine Ebel d, Demetris Stavrou d, Josef Haik d, Nimrod Farber d, Eyal Winkler d, Oren Weissman d
REVIEWS & UPDATES: BCC
Dr. E. Nagore (Spain): Non-surgical modalities for low-risk BCC

- Principles of treating BCC:
  - Complete removal of tumor>function>cosmetics

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High discordance between punch biopsy and excision in establishing basal cell carcinoma subtype: analysis of 500 cases

Table 2. BCC subtype at biopsy vs. excision. The percentage of corresponding subtype at excision in parenthesis.

<table>
<thead>
<tr>
<th>BCC subtype at biopsy</th>
<th>Histologically</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically Non-aggressive</td>
<td>175 (93.6%)</td>
</tr>
<tr>
<td>Clinically Aggressive</td>
<td>12 (6.4%)</td>
</tr>
</tbody>
</table>

- Infiltrative BCC
- Total within BCC

*Numbers do not add up to 100 due to percentages round off.
Dr. E. Nagore (Spain): Non-surgical modalities for low-risk BCC

- Principles of treating BCC:
  - Complete removal of tumor > function > cosmetics
- Non-surgical modalities:
  - Imiquimod
  - TFD
  - 5-Flu
  - CO2 laser
  - Ingemol mebutato
Five-Year Results of a Randomized Controlled Trial Comparing Effectiveness of Photodynamic Therapy, Topical Imiquimod, and Topical 5-Fluorouracil in Patients with Superficial Basal Cell Carcinoma

Table 3. Absolute differences and HRs with 95% CI of tumor-free survival at 5-year follow-up

<table>
<thead>
<tr>
<th></th>
<th>Intention-to-Treat Analysis</th>
<th>Per Protocol Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Difference, %</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Imiquimod versus MAL-PDT</td>
<td>17.8</td>
<td>0.48 (0.32–0.71)</td>
</tr>
<tr>
<td>5-fluorouracil versus MAL-PDT</td>
<td>7.3</td>
<td>0.74 (0.53–1.05)</td>
</tr>
<tr>
<td>Imiquimod versus 5-fluorouracil</td>
<td>10.5</td>
<td>0.65 (0.43–0.98)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HR, hazard ratio; MAL-PDT, methylaminolevulinate photodynamic therapy.

Imiquimod > 5-fluorouracil > MAL-PDT

Pulsed CO₂ Laser Ablation of Superficial Basal Cell of Limbs and Trunk: A Comparative Randomized Clinical Trial With Cryotherapy and Surgical Ablation

Cristina Zane, MD,* Elena Facchinetti, MD,* Mariachiara Arisi, MD,* Bernhard Ortel, MD,† and Piergiacomo Calzavara-Pinton, MD*

Rationale: lack of controlled studies for laser treatment

Open-label, randomized clinical trial:
- Aim: to compare efficacy, safety, cosmetic outcome, time to would closure, and patient preference:
  - pulsed CO₂ laser ablation
  - cryotherapy
  - surgery
- Target: primary small (≤5 cm) superficial BCC of the trunk or extremities.
- Diagnosis: clinically/dermoscopy (biopsy if not unequivocal)
- Randomized 1:1:1 allocation ratio

Cryotherapy: liquid nitrogen unit (CRY-AC), two freeze-thaw cycles. Area frozen for 15-30 seconds, thawing period of 2-4 minutes (depending on size)

Pulsed CO₂ laser: under local anaesthesia. Single session of three laser passes until punctata dermal bleeding (charfree mode, 500 mJ pulses; 2.3 W, 50 Hz repetition rate); covering a 3-4 mm rim of clinically uninvolved surrounding skin

Surgery: under local anaesthesia, excision of the tumor with a 3-4 mm margin of clinically uninvolved surrounding skin

Dermatol Surg 2017;43:920–927
CLINICAL REPORT

Immunocryosurgery for Non-superficial Basal Cell Carcinoma: A Prospective, Open-label Phase III Study for Tumours ≤ 2 cm in Diameter
Georgios GAITANIS and Ioannis D. BASSUKAS

Cryotherapy applied day 14 of treatment with imiquimod (2 cycles of 15”)

JEAIV 2009, 23, 1427–1431

Immunocryosurgery for basal cell carcinoma: results of a pilot, prospective, open-label study of cryosurgery during continued imiquimod application
G. Gaitanis, K Nomikos, E. Vava, E. C. Alexopoulos, I. D. Bassukas

116/119 tumors
95% cure rate after one cycle

19/21 tumors
95% cure rate after one cycle
Successfully treated superficial basal cell carcinomas with ingenol mebutate 0.05% gel: Report of twenty cases

Dermatologic Therapy 2016

S. Izzé | P. Sorgi | P. Piemonte | A. Carbone | P. Frascione

- Efficacy and safety of ingenol mebutate 0.05%, o.i.d. x 2 consecutive days, 20 patients with superficial BCC
- Clinical and dermatoscopic clearance at 2 and 6 months
Dr. O. Cogrel (France): Surgical therapy for low-risk BCC

Review Article

Update on Keratinocyte Carcinomas
Kishwer S. Nehal, M.D., and Christopher K. Bichakjian, M.D.

A  Low risk Basal-Cell Carcinoma

- Risk Criteria
  - <2 cm on trunk and extremities
  - <1 cm on cheek, forehead, scalp, neck, shins (location independent of size may constitute high risk)
  - Well-defined borders
  - Primary tumor
  - Immunocompetent status
  - No prior radiation therapy
  - Nodular, superficial histologic pattern
  - No perineural invasion

- Standard excision with 4 mm margin

- Preferred Treatment Options
  - Standard excision
  - Electrodesiccation and curettage
  - Radiation therapy for nonsurgical candidates
  - Topical therapy or photodynamic therapy

Figure 2. Low-Risk versus High-Risk Basal-Cell Carcinomas
Dr. K. Peris (Italy): How to manage Gorlin syndrome

- BCC onset depends on cumulative UVR
- Palmar pitting: soak in water to make them more visible
- Treat each BBCC or group: depending on size, type, number, location,
- Combine therapies
PTCH MUTATION CARRIERS

BCC screening annually by age 10, with increased frequency after first BCC observed

Baseline echocardiogram in infancy, dental exams with jaw X-ray every 12 to 18 months beginning at age 8, and an ovarian ultrasound by age 18

Low risk of medulloblastoma ➤ no radiographic screening unless concerning neurologic exam, head circumference change, or other unusual signs or symptoms

If medulloblastoma ➤ radiation-sparing treatment given risk of radiation-induced skin cancers

SUFU MUTATION CARRIERS

Same as PTCH1 mutation carriers, with the exception of no jaw X-rays, as keratocysts have not been described

Additional medulloblastoma screening: consider every-4-month brain MRI through age 3 and then every-6-month brain MRI until the age of 5. Radiation-sparing treatments are again recommended if a brain tumor should occur

Foulkes WD et al. ClinCancer Res 2017
Inhibiting the Hedgehog Pathway in Patients with the Basal-Cell Nevus Syndrome

- Phase II, randomized, double-blind, placebo-controlled trial
- 41 BCNS patients: 26 vismodegib and 15 placebo (age: 35-75y)
- Treatment schedule: 150mg/day for at least 8 months (1-15 months)

↓ Number of new BCCs
↓ Diameter of existing BCCs

2 vs. 29 lesions per patient per year

mean -65% vs. -11% placebo
Vismodegib shows comparable efficacy and safety in patients with and without BCCNS

Safety and efficacy of vismodegib in patients with basal cell carcinoma nevus syndrome: pooled analysis of two trials

Anne Lynn T. Cheng, Sarah T. Aron, Michael R. Myriad, James A. Schumacher, Xiuwen Yao, Benjamin Doggett, Edward P. Michaels and Alexander Sabatini

Orphanet Journal of Rare Diseases (2016) 11:120

Table 3: Most common adverse events classified by BCCNS or non-BCCNS status

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>BCCNS (n = 100)</th>
<th>Non-BCCNS (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>22 (22)</td>
<td>16 (26)</td>
</tr>
<tr>
<td>Cauda 3-5 AE</td>
<td>9 (9)</td>
<td>10 (16)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>10 (10)</td>
<td>11 (18)</td>
</tr>
<tr>
<td>Muscle spasm</td>
<td>11 (11)</td>
<td>12 (20)</td>
</tr>
<tr>
<td>Weight decrease</td>
<td>9 (9)</td>
<td>11 (17)</td>
</tr>
<tr>
<td>Anemia</td>
<td>13 (13)</td>
<td>16 (26)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>11 (11)</td>
<td>14 (23)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>8 (8)</td>
<td>7 (11)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>7 (7)</td>
<td>5 (8)</td>
</tr>
</tbody>
</table>

Hay et al. 2016

Kunstfeld et al. Poster presentation at EADO 2016
New treatment option: Anti PD-1

Metastatic basal cell carcinoma with amplification of PD-L1: exceptional response to anti-PD1 therapy

Case Report

Responses of metastatic basal cell and cutaneous squamous cell carcinomas to anti-PD1 monoclonal antibody REGN2810

Baseline

Week 16

Baseline

Week 24
New treatment option

Anti PD-1 + SMO inhibitor

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Find Studies   About Clinical Studies   Submit Studies   Resources   About This Site

Recruiting: Pembrolizumab With or Without Vismodegib in Treating Metastatic or Unresectable Basal Cell Skin Cancer
Condition: Skin Basal Cell Carcinoma
Interventions: Other: Laboratory Biomarker Analysis; Biological: Pembrolizumab; Drug: Vismodegib
Topical Treatment of Basal Cell Carcinomas in Nevoid Basal Cell Carcinoma Syndrome with a Smoothened Inhibitor

Tumor response in nevoid basal cell carcinoma syndrome (NBCCS) patients after a 4-week treatment with 0.75% LDE225 cream.

Dermatoscopic images of a nodular ulcerated basal cell carcinoma (b, d) before (baseline) and (c, e) after treatment.

2011 H. Skvara et al. The Society for Investigative Dermatology
REVIEWS & UPDATES: SCC
Progressive acquisition of genetic and epigenetic alterations during the development of SCC


<table>
<thead>
<tr>
<th>CSD skin</th>
<th>AK / SCCIS</th>
<th>Invasive SCC</th>
<th>Metastatic SCC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequently mutated genes</strong></td>
<td><strong>Frequently mutated genes</strong></td>
<td><strong>Frequently mutated genes</strong></td>
<td><strong>Frequently mutated genes</strong></td>
</tr>
<tr>
<td>TP53, NOTCH1, NOTCH2</td>
<td>TP53, NOTCH1, NOTCH2</td>
<td>TP53, ATM, NOTCH1, NOTCH2</td>
<td>TP53, CDKN2A, NOTCH1, NOTCH2</td>
</tr>
<tr>
<td>CDKN2A, HRAS, XRNR, CARD11</td>
<td>CDKN2A, HRAS, EGFR, XRNR, CARD11</td>
<td>HKRAS, EGFR, RAF1, BRAF, WMNT, ESRB4, CASP8, RTCH1, FAT1, NF1, PARD3, TERT, RASA1, p300, KMT2D, PTPN, BRCA2, CARD11, MK67, NFKB</td>
<td>TP53, CDKN2A, NOTCH1, NOTCH2, PKR1, RAF1, HRAS, EGFR, BRAF, WMNT, ESRB4, CASP8, RTCH1, FAT1, NF1, PARD3, TERT, RASA1, p300, KMT2D, PTPN, BRCA2, CARD11, MK67, NFKB</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Differentially expressed miRNAs</th>
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<th>Differentially expressed miRNAs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upregulation of let-7a, miR-305, miR-9, miR-21, miR-223</td>
<td>Upregulation of miR-4286, miR-200b-3p, miR-148a-3p</td>
<td>Downregulation of miR-1225b, miR-34, miR-124, miR-483-3p, miR-193b-365a, miR-302*, miR-378, miR-145, miR-140-3p, miR-30a, miR-526, miRNA-125a, let-7a, let-7d, let-7e, let-7f, let-7g, let-7h, miR-99a, miR-99b, miR-100, miR-101 and miR-143</td>
<td>Downregulation of miR-1915-3p, miR-205-5p, miR-4516 and miR-150-5p</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cytogenetic alterations</th>
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<th>Cytogenetic alterations</th>
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</thead>
<tbody>
<tr>
<td>Gains of 3q, 7, 8q, 9q, 9p, 11q, 14, and 20</td>
<td>Gains of 3q, 7, 8q, 9q, 9p, 11q, 14, and 20</td>
<td>Gains of 3q, 7, 8q, 9q, 9p, 11q, 14, and 20</td>
<td>Gains of 3q, 7, 8q, 9q, 9p, 11q, 14, and 20</td>
</tr>
<tr>
<td>Loss of 2q, 3p, 4, 5q, 8p, 9p, 11, 13, 17p, 18, 19, and 21</td>
<td>Loss of 2q, 3p, 4, 5q, 8p, 9p, 11, 13, 17p, 18, 19, and 21</td>
<td>Loss of 2q, 3p, 4, 5q, 8p, 9p, 11, 13, 17p, 18, 19, and 21</td>
<td>Loss of 2q, 3p, 4, 5q, 8p, 9p, 11, 13, 17p, 18, 19, and 21</td>
</tr>
<tr>
<td>Allelic gain on 3q, 8q and 11q</td>
<td>Allelic gain on 3q, 8q and 11q</td>
<td>Allelic gain on 3q, 8q and 11q</td>
<td>Allelic gain on 3q, 8q and 11q</td>
</tr>
<tr>
<td>Isochromosomes 3q, 8q and 9q</td>
<td>Isochromosomes 3q, 8q and 9q</td>
<td>Isochromosomes 3q, 8q and 9q</td>
<td>Isochromosomes 3q, 8q and 9q</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Epigenetic changes</th>
<th>Epigenetic changes</th>
<th>Epigenetic changes</th>
<th>Epigenetic changes</th>
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</thead>
<tbody>
<tr>
<td>Methylation of DAPK1</td>
<td>Methylation of DAPK1</td>
<td>Methylation of CDH13, CDKN2A</td>
<td>Hypermethylation of 9p23, TFAP2C and ASC12</td>
</tr>
<tr>
<td>Telomere dysfunction*</td>
<td>Telomere dysfunction*</td>
<td>Telomere dysfunction*</td>
<td>Hypomethylation of ACTG2</td>
</tr>
</tbody>
</table>

Analysis of cancer-associated fibroblasts and the epithelial-mesenchymal transition in cutaneous basal cell carcinoma, squamous cell carcinoma and malignant melanoma.

Sasaki K¹, Sugai T², Ishida K³, Osakabe M³, Amano H⁴, Kimura H⁵, Sakuraba M⁵, Kashiwa K⁵, Kobayashi S⁵.
Dr. MT Fdez-Figueras (Spain): From early to late SCC

Classical pathway

AK I → AK II → AK III

Differentiated pathway
Dr. MT Fdez-Figueras (Spain): From early to late SCC

- Significant differences in E-cadherin, β-catenin, vimentin and Ki67
- No significant differences in podoplanin (D2-40), p16 and p53

### Treatment options for SCC in situ

<table>
<thead>
<tr>
<th>Lesion (small &lt; 2cm)</th>
<th>5-FU</th>
<th>imiquimod</th>
<th>Cryo.</th>
<th>Curettage</th>
<th>Excision</th>
<th>PDT</th>
<th>Radiotherapy</th>
<th>Laser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small, single/few, good healing</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Large, single, good healing</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Multiple, good healing</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Small, single/few, poor healing site</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Large, single, poor healing site</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td>6</td>
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<tr>
<td>Facial</td>
<td>3</td>
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<td>4</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>4</td>
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<tr>
<td>Digital</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>3</td>
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<tr>
<td>Nail-bed</td>
<td>-</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>2***</td>
<td>3</td>
<td>4</td>
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<tr>
<td>Penile</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>4***</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Immuno-compromised</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

1: Treatment of choice, 2: Good choice, 3: Fair choice, 4: Reasonable choice, usually not required, 5: Poor choice, 6: should not be used
Diagnosis and treatment of invasive squamous cell carcinoma of the skin: European consensus-based interdisciplinary guideline

Alexander Stratigos, Claus Garbe, Celeste Lebbe, Josep Malvehy, Veronique del Marmol, Hubert Pehamberger, Ketty Peris, Jürgen C. Becker, Iris Zalaudek, Philippe Saïag, Mark R. Middleton, Lars Bastholt, Alessandro Testori, Jean-Jacques Grob, On behalf of the European Dermatology Forum (EDF), the European Association of Dermato-Oncology (EADO), and the European Organization for Research and Treatment of Cancer (EORTC).

Surgical excision (at times in combination with plastic reconstruction) is the treatment of choice and by far the most convenient and effective means of achieving cure of any invasive cSCC, as it allows to confirm the tumour type and assess the tumour-free status of the resection margins. Surgery is rarely contra-indicated even in old debilitated patients, or in difficult tumour size and locations with potential functional and cosmetic consequences, if these patients are carefully managed in a day-care hospital setting.
Conclusions

Surgery is the treatment of choice for all early SCC

Standard excision with 5 mm margins is adequate for most early SCC

Mohs surgery is the optimal treatment with lowest recurrence rates and optimal tissue preservation

In the presence of field cancerisation, surgery should be combined with other destructive methods
• Advanced cSCC is a difficult-to-treat disease and usually need association of treatments to achieve the optimal outcome (mainly surgery with RT)

• Targeted therapies and immunotherapies are promising in disseminated disease Cetuximab (EGFR inhibitor)
  Pembrolizumab, Nivolumab (checkpoint inhibitors)