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

Dr. Antoni Bennassar
Dr. Läuchli (Zurich, Suiza): C. Mohs controversies

- Definition of different techniques: 100% evaluation margins
- 1 application criteria:

**Mohs micrographic surgery for basal cell carcinoma: evaluation of the indication criteria and predictive factors for extensive subclinical spread***

I. Hoorens,1 A. Batteauw,1 G. Van Maele,2 K. Lapiere,3 B. Boone1 and K. Ongenae1

1Department of Dermatology, University Hospital Ghent, Ghent, Belgium

*Correspondence: I. Hoorens, Department of Dermatology, University Hospital Ghent, Belgium.

www.esms-mohs.eu
Dr. Suzanne Olbricht (Maine, US):
- Mohs surgery in patients >80 years old:
- Use of the Barthel Index, activities of daily living, in dermatologic surgery in patients aged 80 years and older.
- (José C. Pascual, MD, Isabel Belinchón, PhD, and José M. Ramos, PhD)
- Characteristics of Surgical Procedures in the Spanish Mohs Surgery Registry (REGESMOHS) for 2013-2015.)

Dr. Suzanne Olbricht (Maine, US):

- Curettage prior to 1º stage: doesn’t affect nº of stages
- Curettage prior to Mohs’ Micrographic Surgery for Previously Biopsed Nonmelanoma Skin Cancers: What Are We Curetting? Retrospective, Prospective and Comparative Study
- Dermatologic Surgery. 31 (1):10-15, JAN 2005
Dr. JR Garcés (Barcelona): neoadjuvant treatment (Vismodegib) in the BCC locally advanced

- RC 33.8%, RP 32.9%, medium duration 22m
- **As neoadjuvant it reduces the area 27%:**
  - Symmetrical-Concentric? Asymmetrical?
  - C. Mohs rescue?

**Controversies regarding differentiated scammous areas:**
- Adjuvant RDT after C. Mohs
Original Investigation

Fast Evaluation of 69 Basal Cell Carcinomas With Ex Vivo Fluorescence Confocal Microscopy Criteria Description, Histopathological Correlation, and Interobserver Agreement

Antoni Bennàssar, MD; Cristina Carrera, MD; Susana Puig, MD, PhD; Antoni Vilalta, MD; Josep Malvehy, MD, PhD

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Ex vivo fluorescence confocal microscopy for fast evaluation of tumour margins during Mohs surgery

A. Bennàssar,¹ A. Vilata,¹ S. Puig¹,² and J. Malvehy¹,²

¹Melanoma Unit, Dermatology Department, Hospital Clínic & IDIBAPS (Institut d’Investigacions Biomèdiques Agustí Pi i Sunyer), Villarroel 170, 08036 Barcelona, Spain
²Investigación Biomédica en Red en Enfermedades Raras (CIBERER), Barcelona, Spain
Dr. M. Möhrle (Netherlands): Rapid Lump examination

Original Article

Diagnostic accuracy of a new ex vivo confocal laser scanning microscope (CLSM) compared to H&E-stained paraffin slides for micrographic surgery of basal cell carcinoma

Nina Peters, Melanie Schubert, Gisela Metzler, Jan-Philipp Geppert, Matthias Moehrle

Rapid Lump Examination as a New Aid to Speedup Mohs Micrographic Surgery: A Pilot Study

Veenstra, Marleen MD; Ostertag, Judith MD, PhD; Verhaegh, Marc MD, PhD; Nuessel, Nils BSc; Moehrle, Matthias MD, PhD
www.esms-mohs.eu

Dr. Ríos Buceta (Madrid):

- **Kinesiotape** (self-adhesive elastic band):
  - Prevents post IQ bruising
  - In areas and high risk patients
  - Economic and easy to use
www.esms-mohs.eu

Dr. E. Epstein (San Francisco, US): Founder of PellePharm

- **Patidegib (anti HH)**
- Formulated in a gel of external application
- FDA/EMA approved as orphan medication
- Proven anti BCC activity
- Phase 3 study for **preventive chemotherapy of BCC in patients with Sd Gorlin**
  (eepstein@pellepharm.org)
MELANOMA: GENETIC TESTING FOR RISK FACTORS

REMCO VAN DOORN (HOLANDA)
Melanoma: genetic testing for risk factors

- Europe: 0.5-2% risk of melanoma main population (20% M1)
- 22,000 deaths/year for MM
- MM → mutations:
  - Inherited (“genes”) + environmental (“lifestyle”) + replication errors (“bad luck”)
  - Occasional MM (90%) vs familiar (10%):

![Pie chart showing the distribution of mutations related to melanoma. CDKN2A is the most common mutation at 40%. Other mutations include CDK4, MITF, BAP1, TERT, and POT1. Polygenic and environmental factors are also mentioned.]

- CDKN2A > CDK4, MITF, BAP1 > TERT, POT1......50%
WHEN SHOULD WE DO GENETIC TESTING?

CDKN2A

- Family with 2 first-degree relatives with invasive melanoma, diagnosed in at least one patient before the age of 40
- Family with 2 first-degree relatives with invasive melanoma and a relative with pancreatic cancer
- Patient with 3 or more melanomas
- Patient with melanoma diagnosed before the age of 18
WHEN SHOULD WE DO GENETIC TESTING?

III. Suspicion of other hereditary tumor syndrome:

**BAP1**-associated tumor syndrome:
- Family history of melanoma + uveal melanoma, mesothelioma, renal cancer, cholangiocarcinoma
- Patient with 2 or more MBDTs

**POT1**-associated tumor syndrome:
- Family history of melanoma + glioma, CLL

**MITF**-associated tumor syndrome:
- Family history of melanoma + renal, pancreatic cancer
Melanoma: genetic testing for risk factors

WHICH GENETIC TEST?

- CDKN2A, CDK4
- BAP1, POT1, TERT, ACD, TERF2IP, MITF
- POLH, PTEN, BRCA2, BRIP1, POLE, OCA2, PRKN, RAD51B, EBF3, GOLM1
- MC1R, ASIP, TYR, IRF4, MTAP, ATM, MX2, CASP8, TERT, SLC45A2, AGR3, CCND1, PLA2G6, ARNT, PARP1, CDKAL1, TMEM38B, OCA2, OBFC1, FTO, CYP1B1

FOLLOW UP?

- DERMATOLOGIC EXPLORATION 2/YEAR
- CDKN2A: PANCREAS
- BAP1: FONDO OJO (MM UVEAL), TX-ABD (MESOTELIOMA-RENAL)
MOLECULAR TESTING FOR TARGETED MELANOMA

SUSANA PUIG (BARCELONA)
Molecular testing for targeted melanoma

- Somatic mutations in melanoma:

- In MM associated to nevus: BRAF/RAS also in patients in nevus: same origin UV

MCR: modulator of the ones before
Molecular testing for targeted melanoma

**TARGET TREATMENTS:**
- BRAF-inh: Vemurefenib, Dabrafenib
- MEK-inh: Trametinib, Cobimetinib

Better OS/DFS + less side effects

---

*Prognostic value of BRAF mutations in localized cutaneous melanoma.*

Nagore E, Requena C, Traves V, Guillen C, Hayward NK, Whiteman DC, Hacker E.
PMID: 24388723

*Survival of patients with advanced metastatic melanoma: the impact of novel therapies-update 2017.*

PMID: 28756457
Molecular testing for targeted melanoma

Mutation detection:
- More commercial kit for BRAF
- Immunohistochemistry
- **NGS**: multiple genes: genetic profiles for every MM → diagnosis, treatment implications
- “Liquid” biopsy: circulating tumor cells’ DNA (OCR)
  - Copies: the more tumor burden
  - Correlation with OS
  - It could identify patients who are candidates or refractory for target treatments
  - It could be elevated prior to relapse (can we advance treatment?)
  - It can monitor treatment
  - It could be positive for healthy patients: prevention?
SCC: MUTATIONS AND CLINICAL IMPLICATIONS

DANNY NASSAR
Clinical oncology: genetics, environment and clinical implications

- SCC
- Kinetocor gene mutations (KNSTRN), NOTCH1, Rras2....
- Multistep process: same mutations already present in QA → gradually adding more copies, amplifications, deletions...

Differentiation degree:
- No mutation types differences
- Yes: metilation type differences already present in original cell
BCC: MUTATIONS AND CLINICAL IMPLICATIONS

Nicole Basset-Seguin (Francia)
Clinical oncology: genetics, environment and clinical implications

- 85% occasional BCC: PTCH>>>SMO>>SUFU
  - Many other mutations MYCN, PPP6C, SKT19, LATS1, ERBB2, NRAS, KRAS, .......
  - MYC y Hippo-YAP: worse prognosis??


**Genomic analysis identifies new drivers and progression pathways in skin basal cell carcinoma.**

Bonilla X1, Parmentier L2, King 3, Bezrukov F4,5, Kaya G6, Zoete V7, Seplyarskiy VB8,9,10, Sharpe HJ11, McKee T12, Letourneau A1, Ribaux PG1, Popadin

- Vismodegib /Sonidegib: inhibit via HH (SMO)
  - CBC locally advanced and/or metastatic
  - Intrinsic/acquired rare resistances:
    - Mutations/variants of SMO
    - Other downstream: SUFU, Gli....
    - Clonal selection not included by Vismodegib
ONCOGENIC MUTATIONS AND THE ENVIRONMENT

Julia Newton-Bishp (UK)
Clinical oncology: genetics, environment and clinical implications

- **UVR-MM RELATION:**
  - C Mutations $\rightarrow$ T signed by UVR
  - UVR causes MM in all locations
  - MM caused by exposing, causing burns
  - Not clear whether chronic exposure causes MM:
    - SVit D synthesis: antiinflammatory
    - Photoadaptive mechanisms
    - People with low phototype should choose between Jobs with no exposition
CHECKPOINT INHIBITORS

JJ GROB (FRANCIA)
**Checkpoint Inhibitors**

- **ANTI-PD1/PD-L1 (CTLA-4):**
  - Prognosis of patients with MM-IV has changed
  - First drugs to prove:
    - Chronic control of the metastatic disease
    - Control after stopping treatment
  - Better response if combined: PD1-CTLA-4
  - Independent response regarding BRAF stage
  - **Optimal response after 3-6 months**
  - +LDH=-response
  - **When to stop? Not clear, 1-2 years**
  - Response after new progression
  - Hopeful results in adjuvant stages III and IV
CHECKPOINT INHIBITORS: ACQUIRED RESISTANCE

A. ENK (Germany)
ACQUIRED RESISTANCE TO CHECKPOINTS INHIBITORS:

The MM inhibits immunity in a very specific way to protect itself against the immune system:

- Alters tumor antigens
- Loss of specific antigens
- Activates suppressive PD-L1 molecules
- Inactivates alters LT-reg
- Changes in phenotype
- Induces hypoxia
OTRAS INMUNOTERAPIAS
A. Reich (Poland)
Otras inmunoterapias

- **T-VEC: ONCOLOYTIC VIRUS**
  - Local + systemic effect
  - Only in “injection” injuries
IMMUNOTHERAPY SIDE EFFECTS

J. BOLOGNA (US)
Immunotherapy side effects

- Treatment for cutaneous cancers but also generally used for other tumors
- The dermatologist must know them and know how to use them, especially because they are drugs used for various months (treatment y adjunvancy)
- Potentially bad systemic: colitis, hepatitis, encephalitis, hypotoroidism, SR insufficiency, DM 1, myocarditis.....
- 50% of patients will use cutaneous type: morbilliform, PA, DRESS/SJS/NET, sarcoidosis, vitiligo, PLEVA.....
- Energically treat with GC

Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: American Society of Clinical Oncology Clinical Practice Guideline.

Brahmer JR¹, Lacchetti C¹, Schneider BJ¹, Atkins MB¹, Brassil KJ¹, Caterino JM¹, Chau I¹, Ernstoff MS¹, Gardner JM¹, Ginex P¹, Hallemeier S¹, Holter Chakrabarty J¹, Leigl NB¹, Mammen JS¹, McDermott DF¹, Naing A¹, Nastoupil LJ¹, Phillips T¹, Porter LD¹, Puzanov I¹, Reichner CA¹, Santomasso BD¹,