

 #WCD2019

# AEDV

## HIGHLIGHTS

24<sup>th</sup> World Congress of Dermatology (WCD)

10-15  
JUNIO  
2019

*Milán*



Patrocina:

janssen  Immunology  
PHARMACEUTICAL COMPANIES OF 

Organiza:



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## Advances in the treatment of melanoma

**Dr. Garbe**

**Dra. Robert**

**Dra. Simeone**

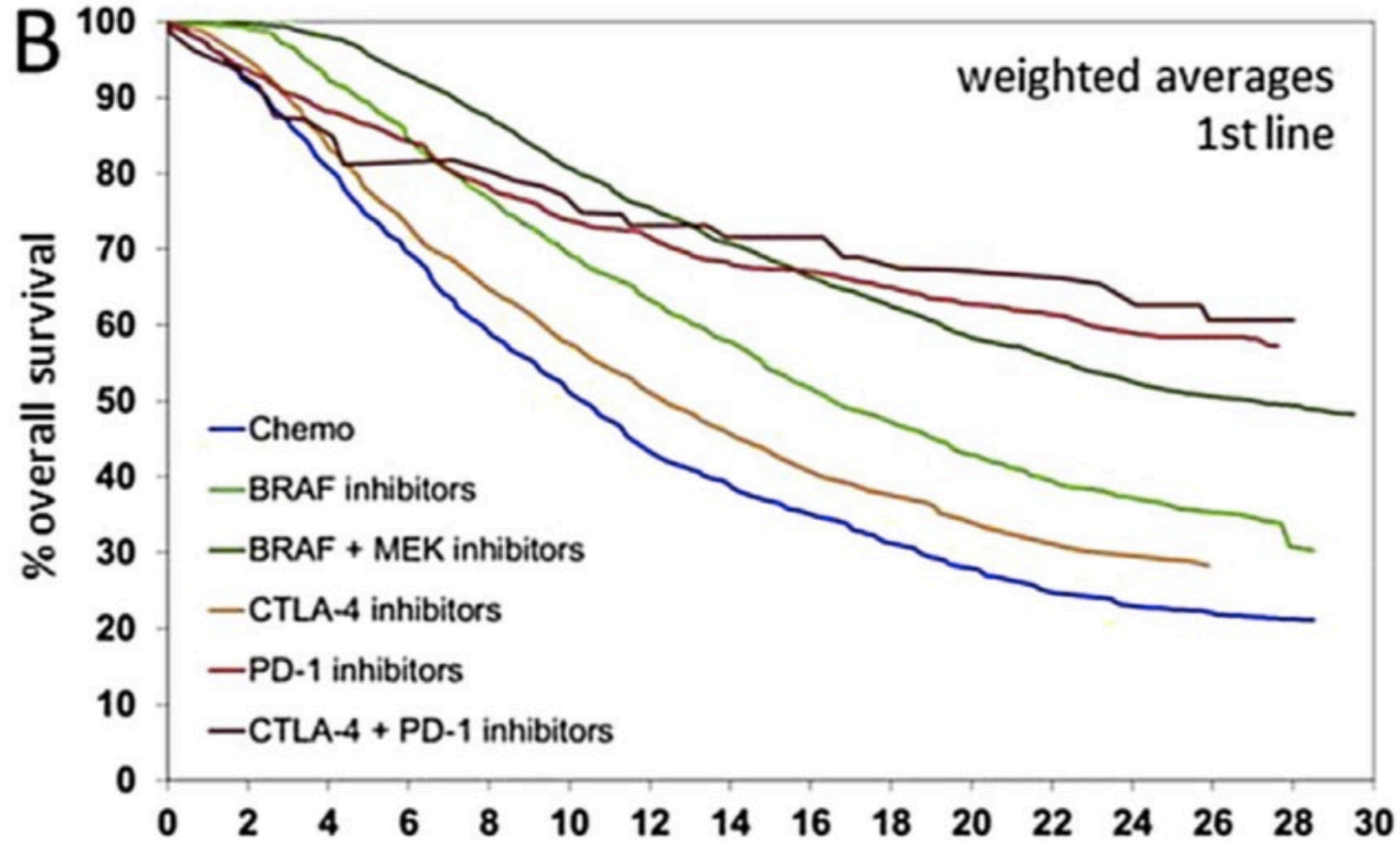
Patrocina:



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## Advances in the treatment of melanoma

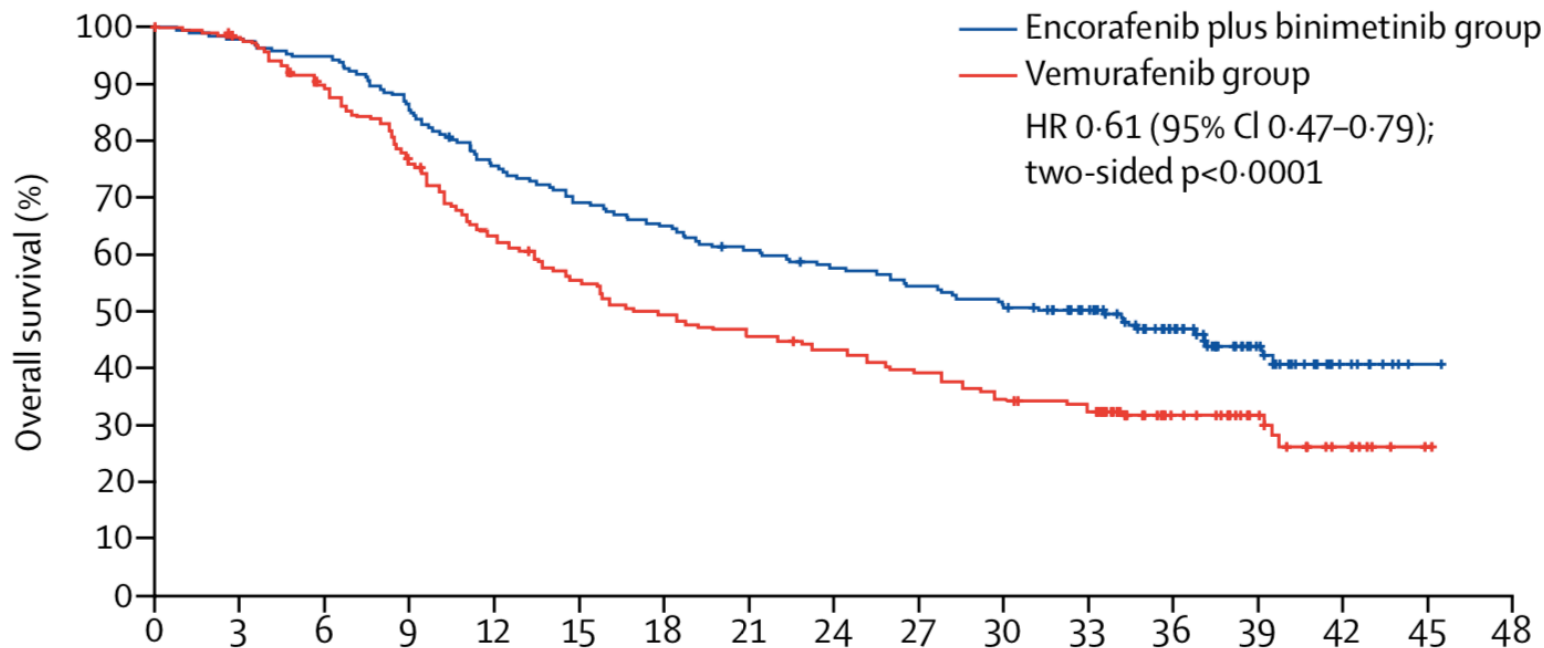


# Advances in the treatment of melanoma

- New anti-BRAF + anti-MEK combination
- Better results comparing to vemurafenib

Overall survival in patients with BRAF-mutant melanoma receiving encorafenib plus binimetinib versus vemurafenib or encorafenib (COLUMBUS): a multicentre, open-label, randomised, phase 3 trial

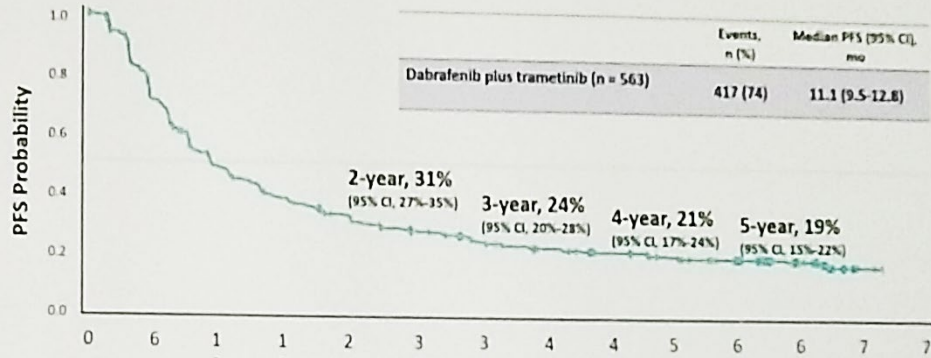
*Reinhard Dummer\*, Paolo A Ascierto\*, Helen J Gogas, Ana Arance, Mario Mandala, Gabriella Liskay, Claus Garbe, Dirk Schadendorf, Ivana Krajsova, Ralf Gutzmer, Vanna Chiarion Sileni, Caroline Dutriaux, Jan Willem B de Groot, Naoya Yamazaki, Carmen Loquai, Laure A Moutouh-de Parseval, Michael D Pickard, Victor Sandor, Caroline Robert†, Keith T Flaherty†*





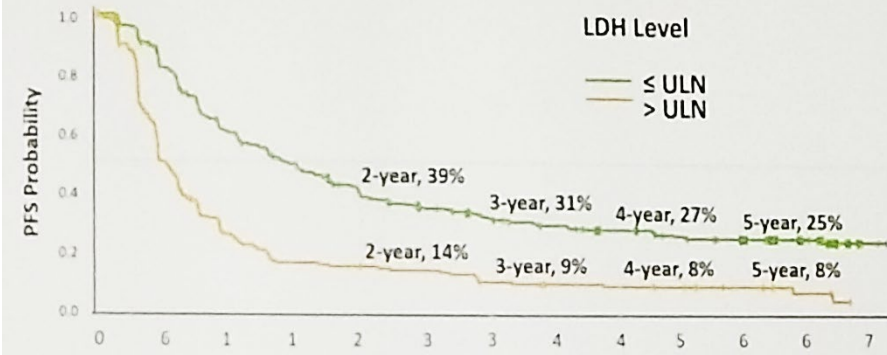
# Dabrafenib plus trametinib in advanced melanoma

## Dabrafenib Plus Trametinib: 5-Year PFS



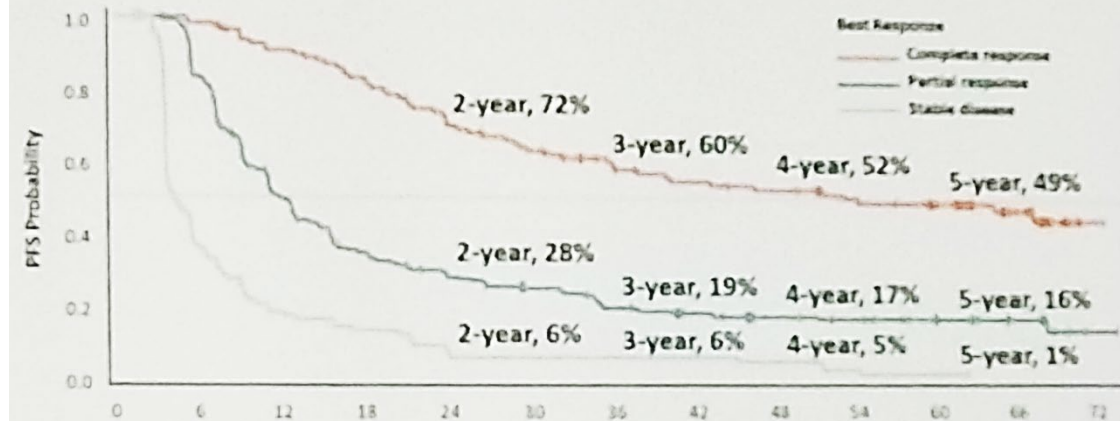
Available data at 5-year follow-up

## Dabrafenib Plus Trametinib: PFS by Baseline LDH Level



Better PFS in patients with lower LDH level

## Dabrafenib Plus Trametinib: PFS by Best Response



Increased PFS by Best response

## Advances in the treatment of melanoma

	COMBI-d/v	COLUMBUS	KEYNOTE-006	KEYNOTE-002	CheckMate-067
	<b>DABRAFENIB TRAMETINIB</b>	<b>ENCORAFENIB BINIMETINIB</b>	<b>PEMBROLIZUMAB</b>	<b>PEMBROLIZUMAB</b>	<b>NIVOLUMAB IPILIMUMAB</b>
Median PFS, months (95% CI)	11.1 (9.5-12.8)	14.9 (11-20.2)	8.4 (6.6-11.3)	4.2 (3.3-5.6)	11.5 (8.7-19.3)
4-year PFS rate %	21	25	23	15	37
5-year PFS rate %	19	-	-	-	-
Median OS months (95% CI)	26.2 (22.9-32)	33.6 (24.2-39.2)	32.7 (24.5-41.6)	14 (11.8-16.2)	NR (38.2-NR)
3-year OS rate %	44	47	48.1	30.3	58
4-year OS rate %	37	39	42.3	27.2	53
5-year OS rate %	34	-	38.7	-	-

# Advances in the treatment of melanoma

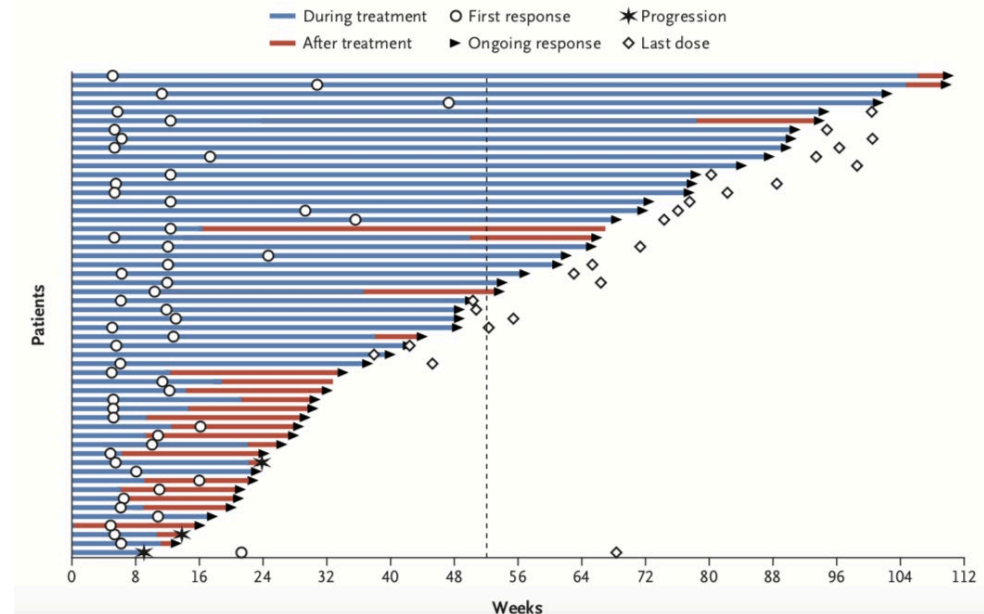
- Immunotherapy is more effective in asymptomatic brain metastases rather than symptomatic.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

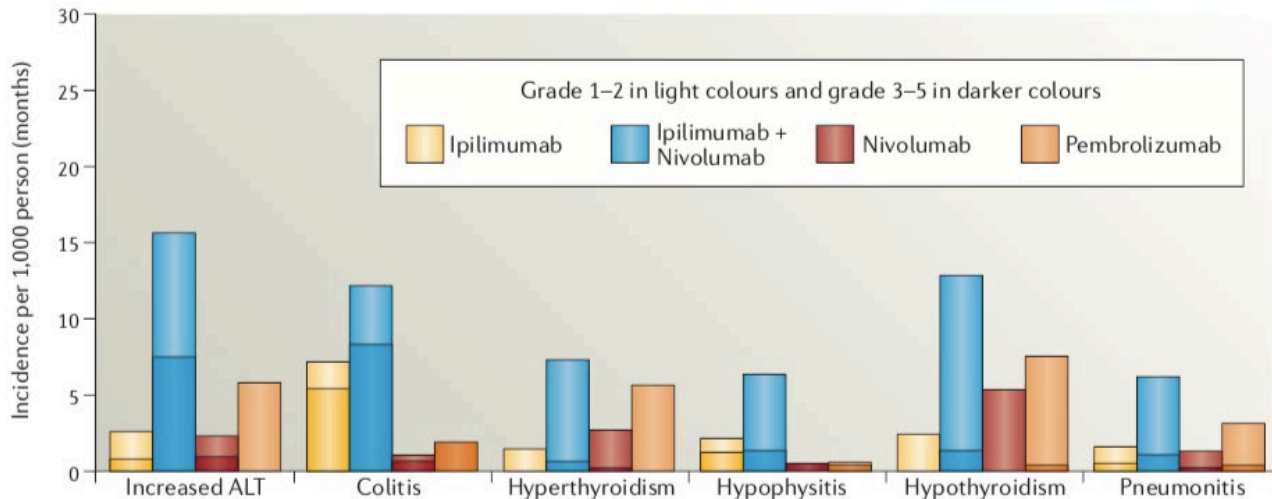
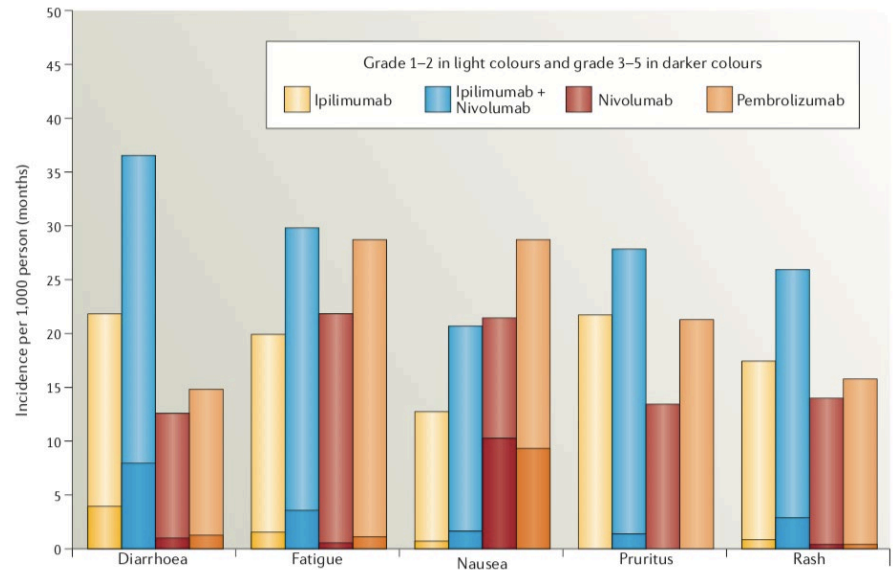
## Combined Nivolumab and Ipilimumab in Melanoma Metastatic to the Brain

Hussein A. Tawbi, M.D., Ph.D., Peter A. Forsyth, M.D., Alain Algazi, M.D., Omid Hamid, M.D., F. Stephen Hodi, M.D., Stergios J. Moschos, M.D., Nikhil I. Khushalani, M.D., Karl Lewis, M.D., Christopher D. Lao, M.D., M.P.H., Michael A. Postow, M.D., Michael B. Atkins, M.D., Marc S. Ernstoff, M.D., David A. Reardon, M.D., Igor Puzanov, M.D., Ragini R. Kudchadkar, M.D., Reena P. Thomas, M.D., Ph.D., Ahmad Tarhini, M.D., Ph.D., Anna C. Pavlick, D.O., Joel Jiang, Ph.D., Alexandre Avila, M.D., Ph.D., Sheena Demelo, M.D., and Kim Margolin, M.D.



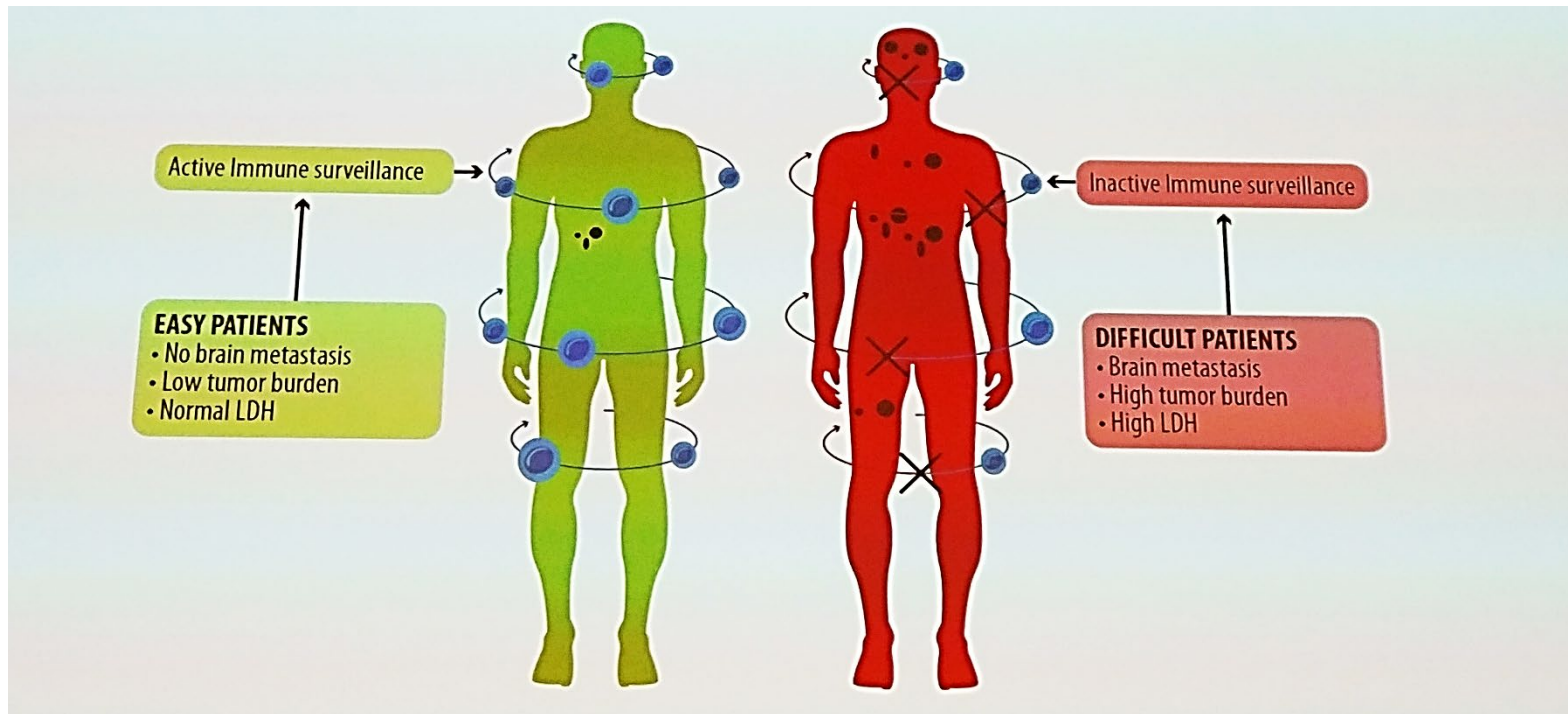
# Adverse events incidence according to the immunotherapy type

- Increased Grade 1-2 and grade 3-5 adverse events in ipilimumab plus nivolumab group
- More relevant adverse events in this group
  - Colitis
  - Increased ALT
  - Hypophysitis
  - Pneumonitis
  - Hyper- and Hypothyroidism





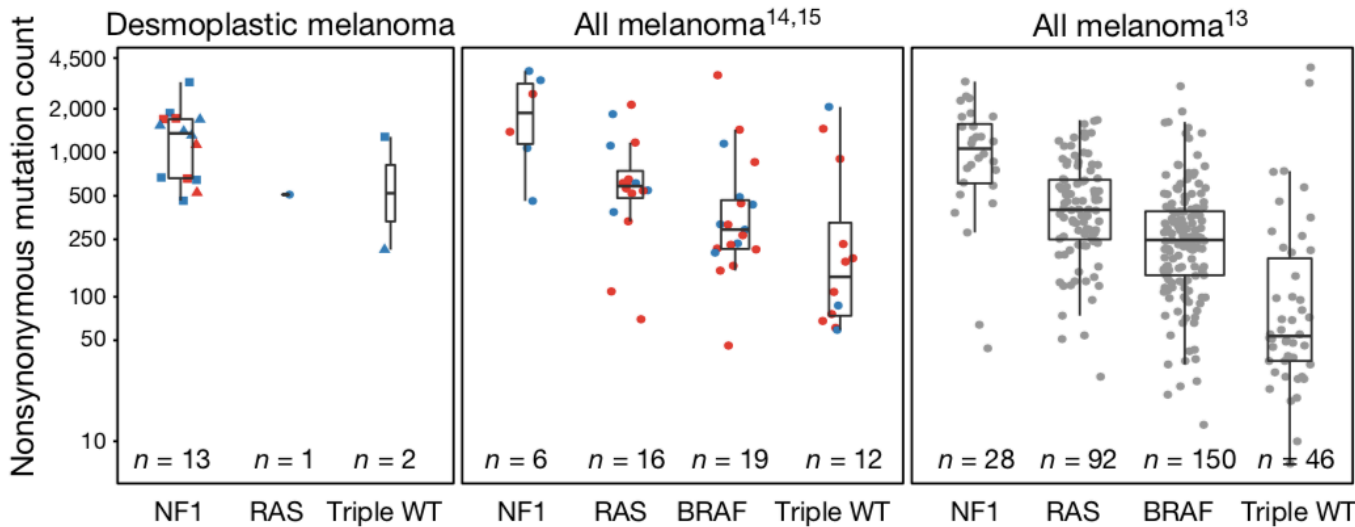
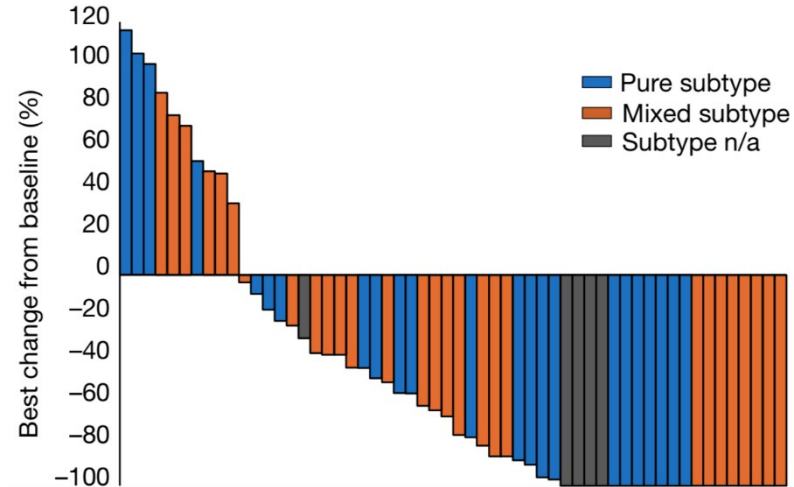
## Questions and answers about immunotherapy



- Can determine some clinical factors the currently immune status of patients? Seems to be...
- Can expression of PDL1 help to estimate the prognosis? No
- Can BRAF mutation status modify the response to immunotherapy? No

# Desmoplastic melanoma

- Response rate to immunotherapy: 70%



Response to anti-PD-1

- Response
- Progression
- NA

Desmoplastic subtype

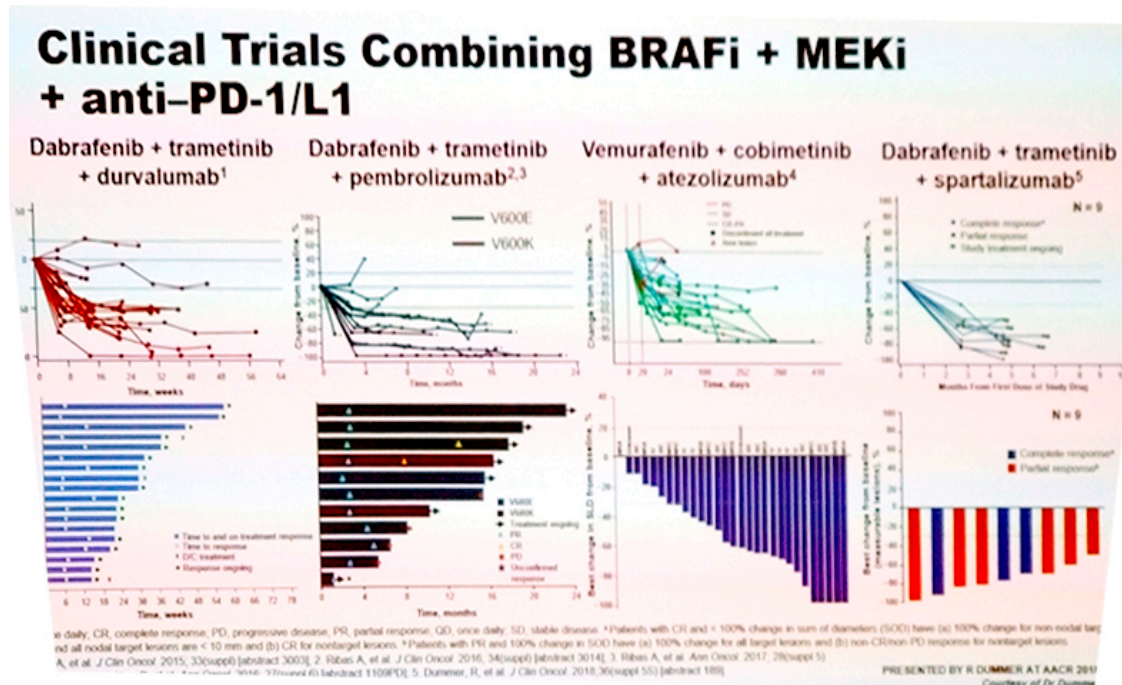
- Pure
- ▲ Mixed
- NA



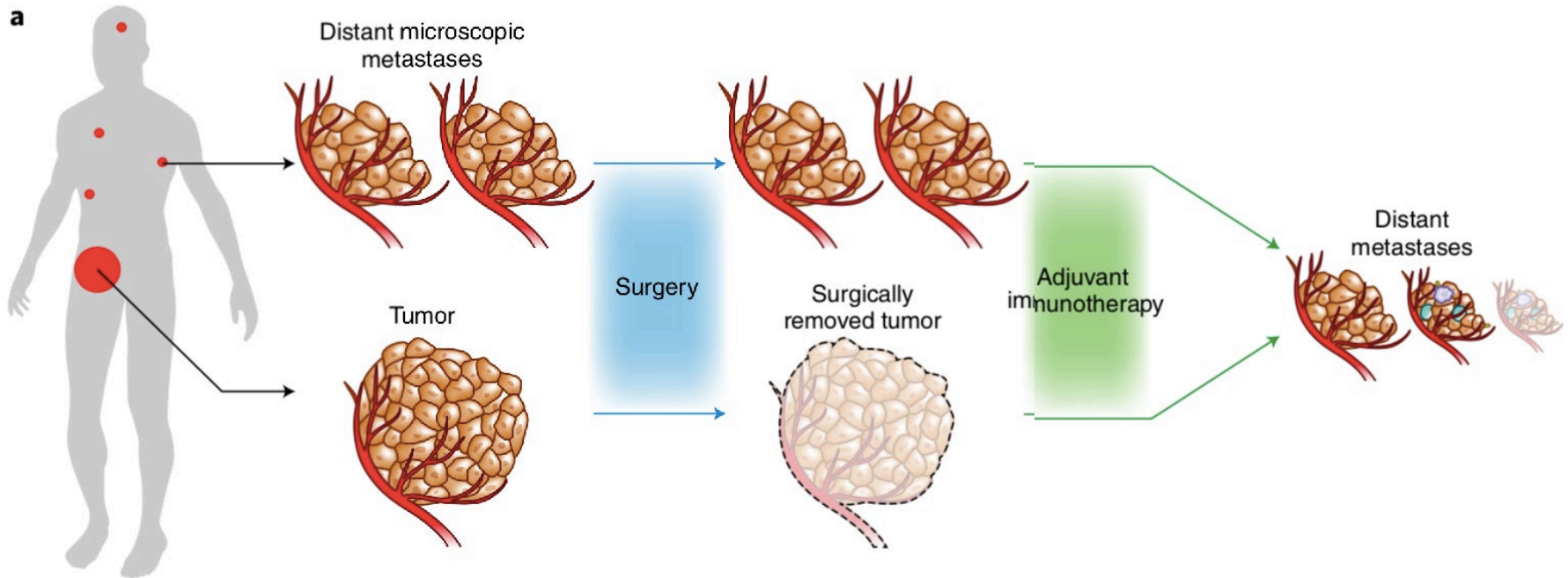
# Novel combination therapies in advanced melanoma

- Multiple clinical trials combining **BRAF inhibitors** + **MEK inhibitors** + **Anti-PD1/L1**

- Dabrafenib + Trametinib + Durvalumab
- Dabrafenib + Trametinib + Pembrolizumab
- Dabrafenib + Trametinib + Spartalizumab
- Vemurafenib + Comimetinib + Atezolizumab



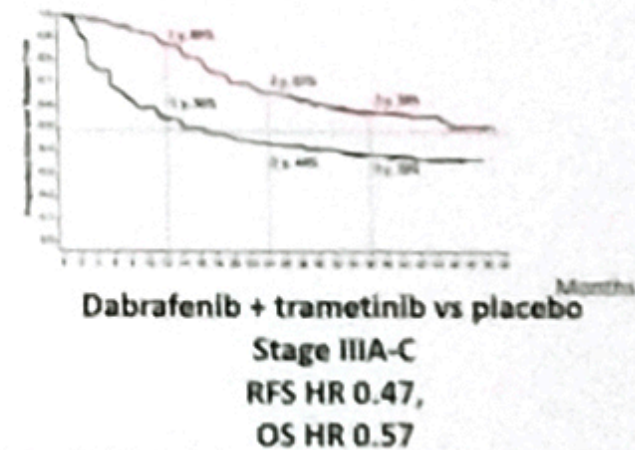
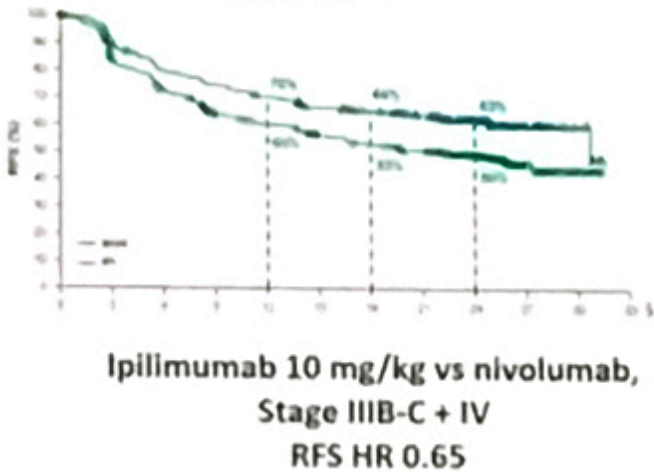
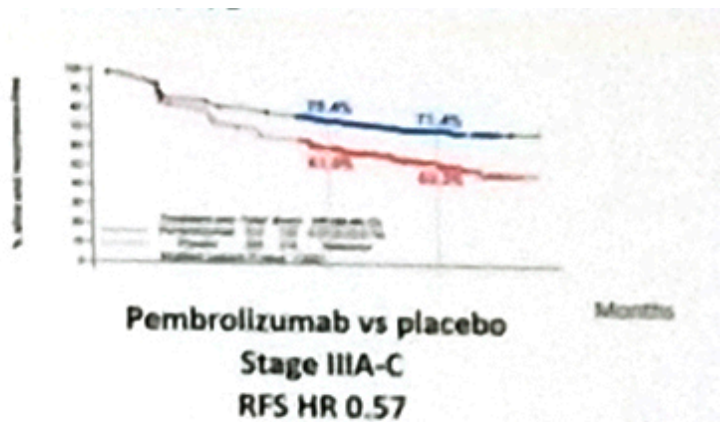
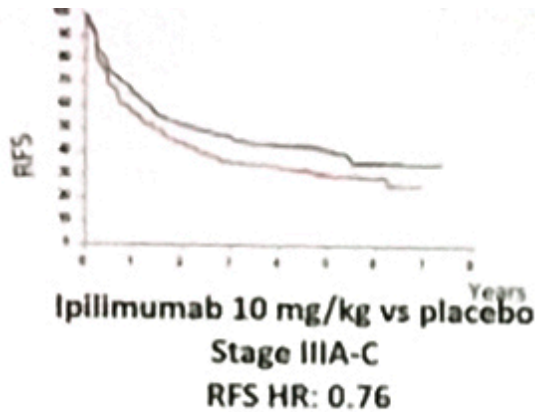
# Adjuvant therapy in High-risk melanoma





# Adjuvant therapy in High-risk melanoma

- Four positive Adjuvant trials



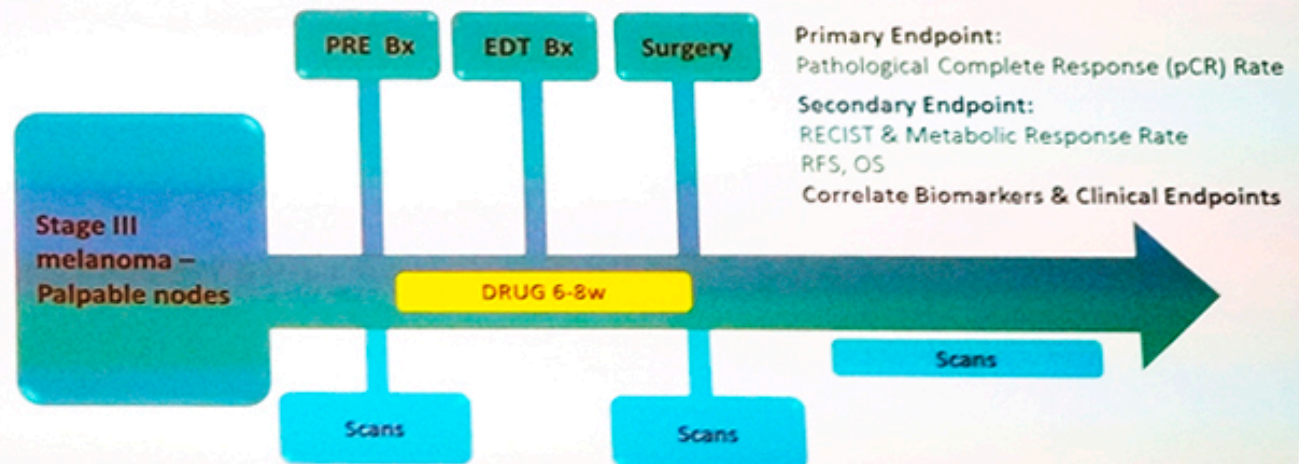


## Neoadjuvant treatment in melanoma

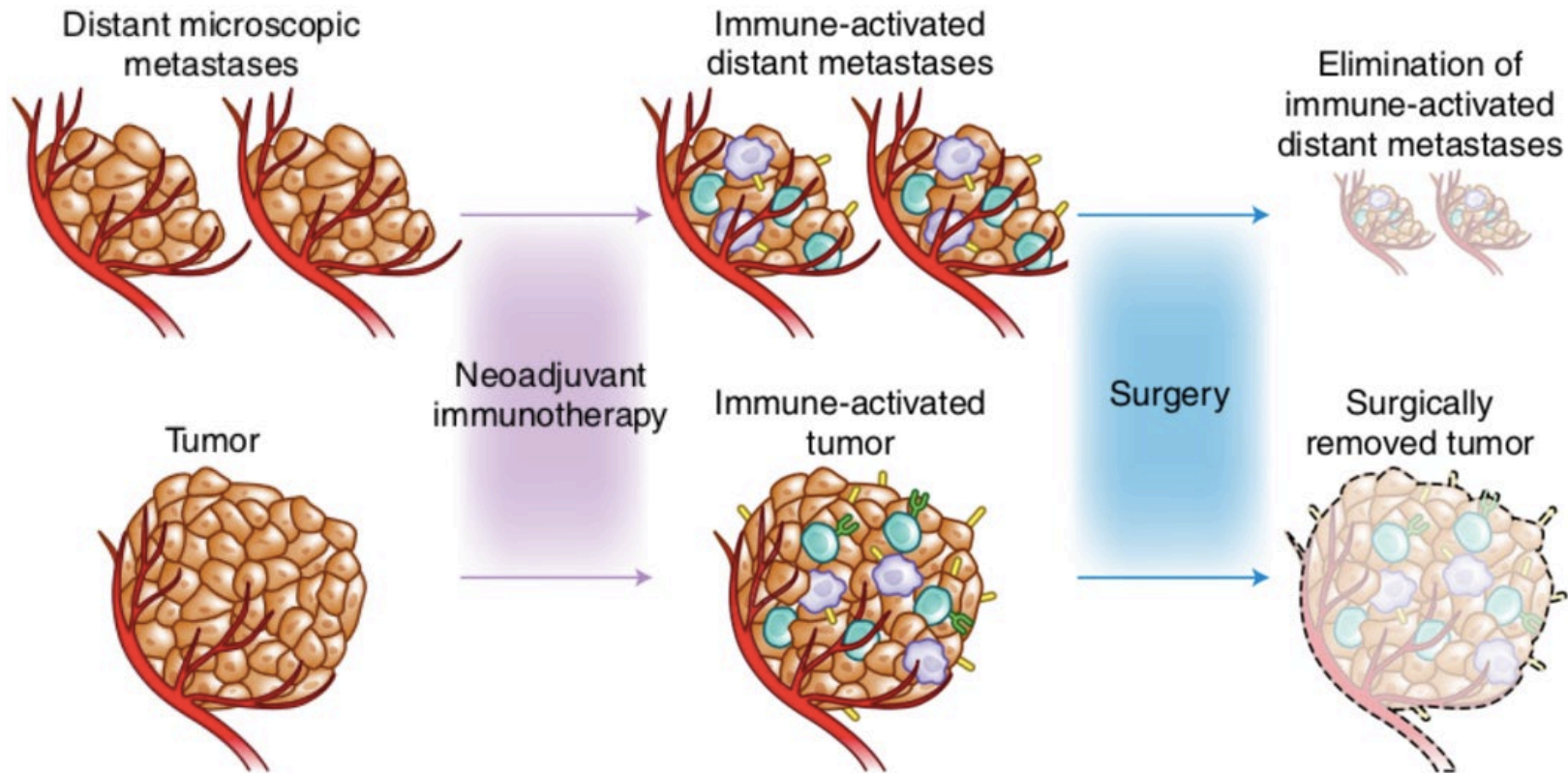
### Neoadjuvant model is well suited for melanoma

- Prototype tumour for IO drug development
- Accessible tissue
- Rapid results

Abstract #9503  
2019 ASCO  
Annual Meeting

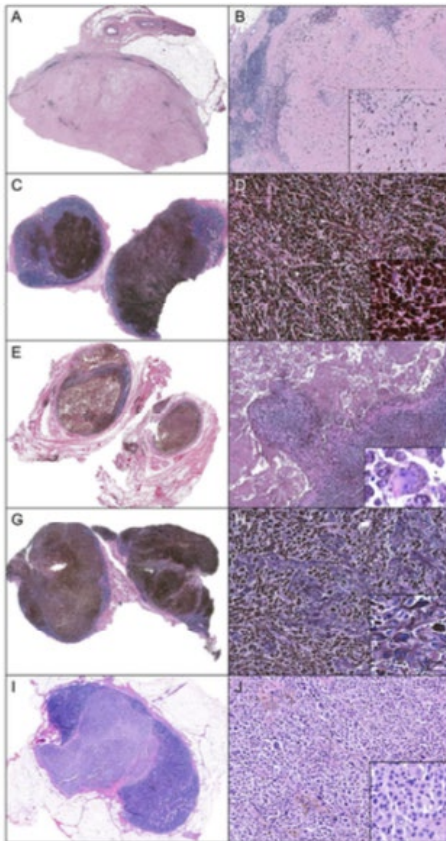


# Neoadjuvant treatment in melanoma



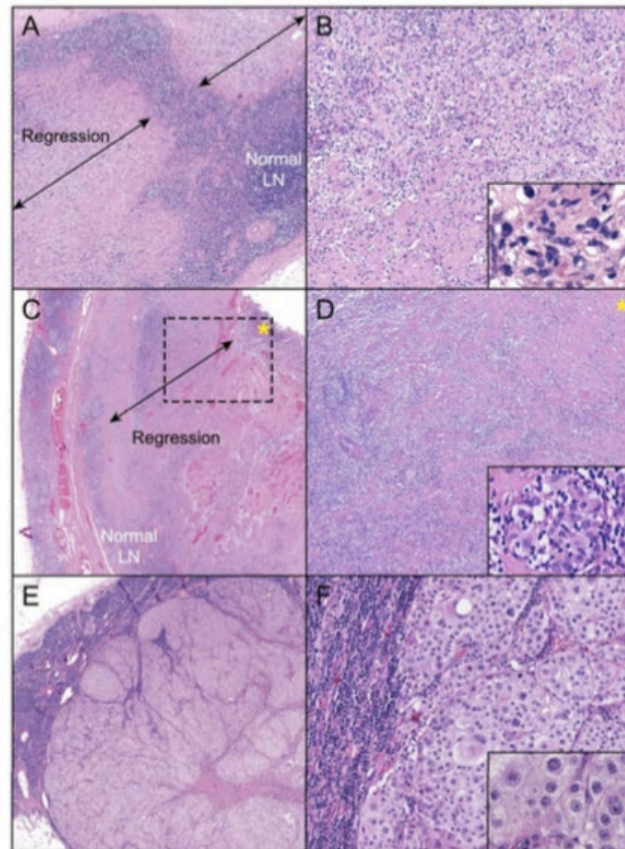
# Pathological response

## Targeted therapy



- hyalinized fibrosis
- melanosis (melanophages)

## Checkpoint inhibitor



- immune-mediated
- tumor regression immune infiltrate
- features of wound healing/repair



## Neoadjuvant treatment in melanoma

### Modern melanoma NST trials

Trial	Regimen	N	pCR (%)	med RFS (mo)	med FU (mo)
Amaria Lancet Oncol 2018	Dab/Tram	21	58	19.7	18.6
Long Lancet Oncol 2019*	Dab/Tram	35	49	23.0	27.0
Blank Nat Med 2018	Ipi+nivo	10	33	NR	32
Amaria Nat Med 2018	Nivo	12	25	NR	20
	Ipi+nivo	11	45	NR	
Huang Nat Med 2019	Pembro	30	19	NR	18
Rozeman Lancet Oncol 2019*	Ipi+nivo	86	57 <sup>^</sup>	NR	8.3

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## Dermatologic surgery & pearls

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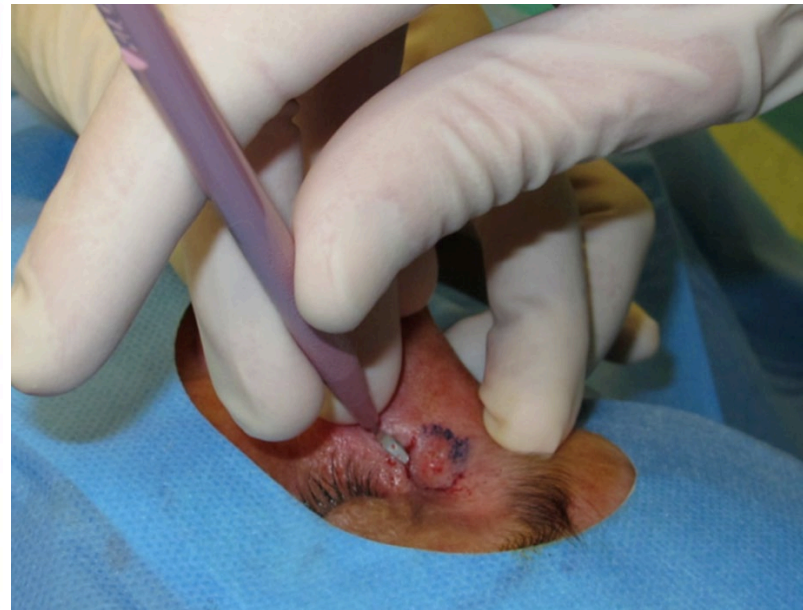
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# Evaluation of the quality of the surgical piece in Mohs micrographic surgery for periocular basal cell carcinomas using a conventional scalp Vs Slit Knife

- Periocular BCC
- Quality evaluation of the surgical piece by pathologists (0-10 scale)
- Quality of the surgical piece obtained with slit knife is slightly higher to the conventional scalp when performing MMS for periocular BBC.



## Factors Associated with wound dehiscence following cutaneous excisions performed by over 400 dermatology providers

- Electronic medical record database
- n = 6.362 procedures
- Factors: Age, sex, smoking status, suture method (interrupted, mattress, running), anatomic location (extremities, head/trunk), wound length
- Skin wound dehiscence (SWD) incidence rate: 0,53%

### Correlation with SWD

Age  
Anatomic location  
Wound length

### No correlation with SWD

Sex  
Smoking status  
Suture method

## Basal cell carcinoma and electrochemotherapy: the InspECT experience (2008-2018)

- Intratumoral or intravenous injection of Bleomycin followed by the delivery of electric pulses
- Retrospective study
- 503 BCC in 277 patients
- Curative intent: OR 97%
- Paliative intent: OR 73%
- Multivariate analysis
  - Tamaño < 3 cm
  - Head & neck location
  - No previous treatments
  - Deep tumor margins covered during ECT
- Median follow-up time was 14 months (range 2-21 months)
- Recurrence at 12 months: 10%

