



¿A qué paciente tratamos y cuál es el nivel de evidencia?

Prof. Susana Puig
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Conflicts of interest

Speaker: Almirall, BMS, ISDIN, La Roche Posay, Leo, MSD, Novartis, Pfizer, Roche, Regeneron, Sanofi,

Advisory board: Almirall, BMS, ISDIN, La Roche Posay, Leo Pharma, Novartis, Pfizer, Regeneron, Roche, Sanofi, Sun Pharma

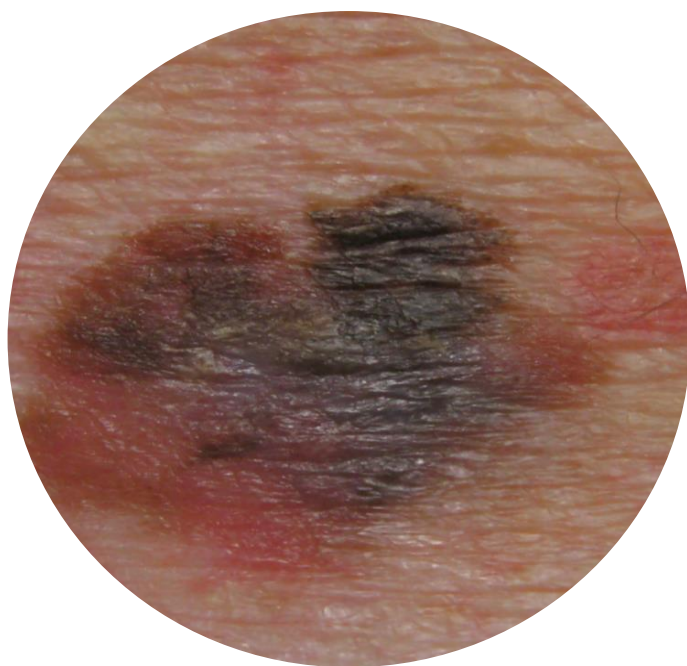
Research and trials: Abbvie, Almirall, Amgen, BMS, Biofrontera, Canfield, Cantabria, Fotofinder, GSK, ISDIN, La Roche Posay, Leo Pharma, MSD, MEDA, Novartis, Polychem, Roche

Husband: Almirall, Amgen, BMS, Biofrontera, Canfield, Cantabria, Fotofinder, GSK, ISDIN, La Roche Posay, Leo, Mavig, Nevisence, Novartis, Polychem, Roche

OTHER: Abbie (educational activities), Lilly (educational activities)

Start ups: Athena Tech & Dermavision Solutions

Diagnóstico de Melanoma



Diagnóstico de Melanoma

¿Estoy curad@?

¿Puede reproducirse?

¿Puede ser mortal?

¿Qué riesgo tengo?

¿Qué puedo hacer para evitarlo?

¿Tiene riesgos?



¿A qué paciente tratamos?



Differences in cutaneous melanoma survival between the 7th and 8th edition of the American Joint Committee on Cancer (AJCC). A multicentric population-based study

Alicia Barreiro-Capurro ^{a,1}, Juan J. Andrés-Lencina ^{f,1}, Sebastian Podlipnik ^{a,1}, Cristina Carrera ^{a,b}, Celia Requena ^c, Esperanza Manrique-Silva ^c, Pietro Quaglino ^d, Luca Tonella ^d, Ane Jaka ^e, Nina Richarz ^e, José L. Rodríguez-Peralto ^f, Pablo Ortiz ^f, Aram Boada ^e, Simone Ribero ^d, Eduardo Nagore ^c, Josep Malvehy ^{a,b}, Susana Puig ^{a,b,*}



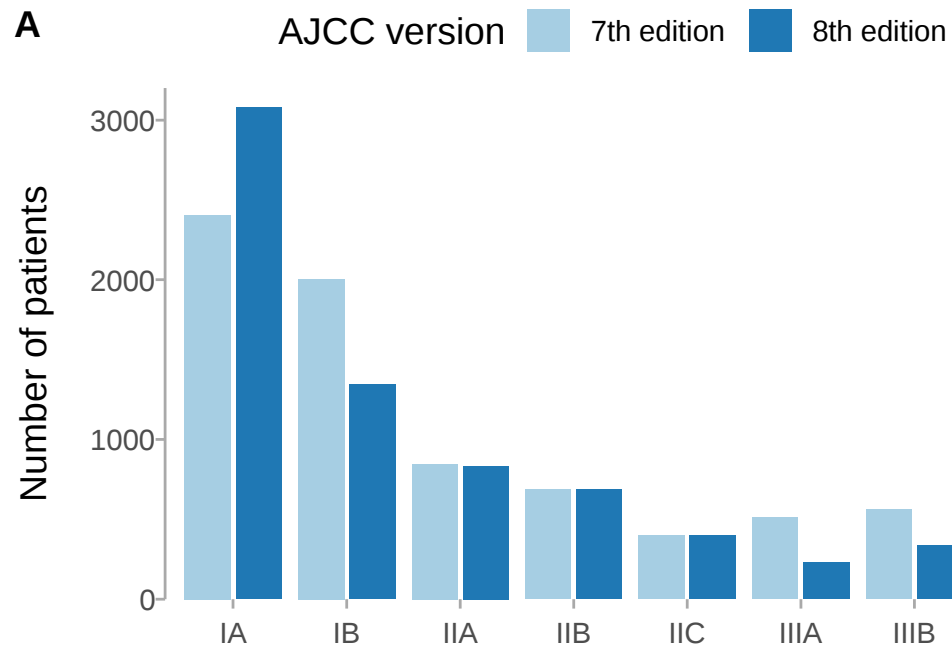
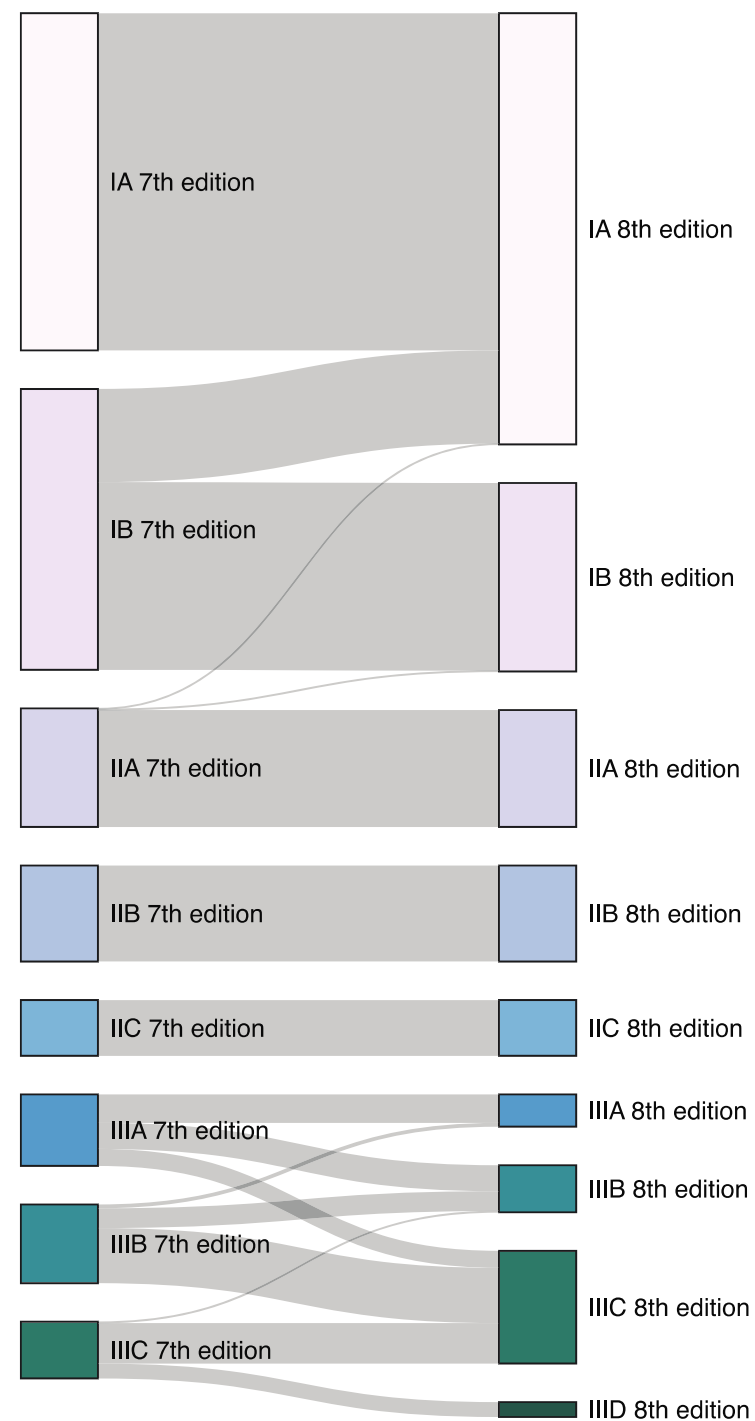
European Journal of Cancer 145 (2021) 29–37

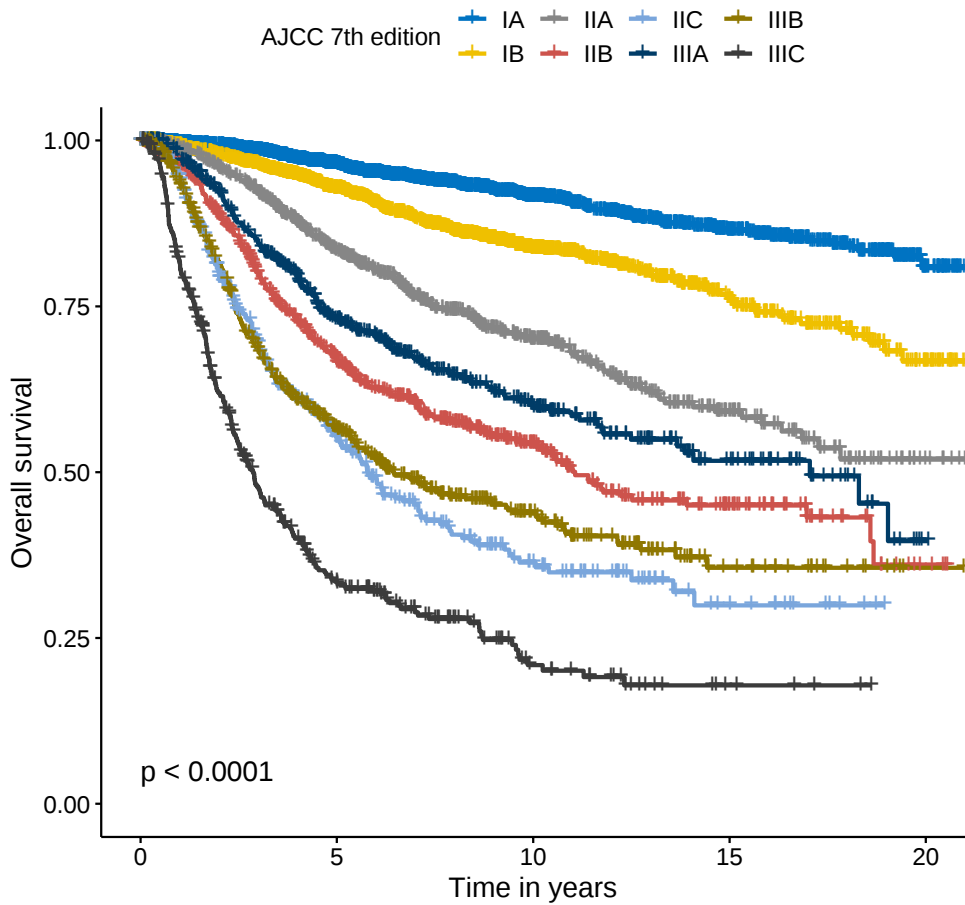
1998-2018

Table 1
Basal characteristics of the cohort.

	Overall (N = 7815)
Hospital	
Hospital Clínic de Barcelona	2741 (35.1%)
Instituto Valenciano de Oncología	1687 (21.6%)
University of Turin	1456 (18.6%)
Hospital Germans Trias i Pujol	1131 (14.5%)
Hospital 12 de Octubre	800 (10.2%)
Age	
Median (IQR)	57 (43, 69)
Missing values	37
Gender	
Female	3925 (50.2%)
Male	3890 (49.8%)
Tumor location	
Trunk	2367 (45.2%)
Lower limbs	1206 (23.0%)
Head and neck	654 (12.5%)
Upper limbs	626 (11.9%)
Acral	389 (7.4%)
Missing values	2573
Breslow index	
Median (IQR)	1.3 (0.7, 3.0)
Ulceration	
Absent	5929 (75.9%)
Present	1886 (24.1%)
Histological Subtype	
Superficial spreading melanoma	4945 (63.3%)
Nodular melanoma	1388 (17.8%)
Acral lentiginous melanoma	532 (6.8%)
Lentigo maligna melanoma	373 (4.8%)
Other/unclassified	577 (7.4%)

Abbreviations: IQR, interquartile range.

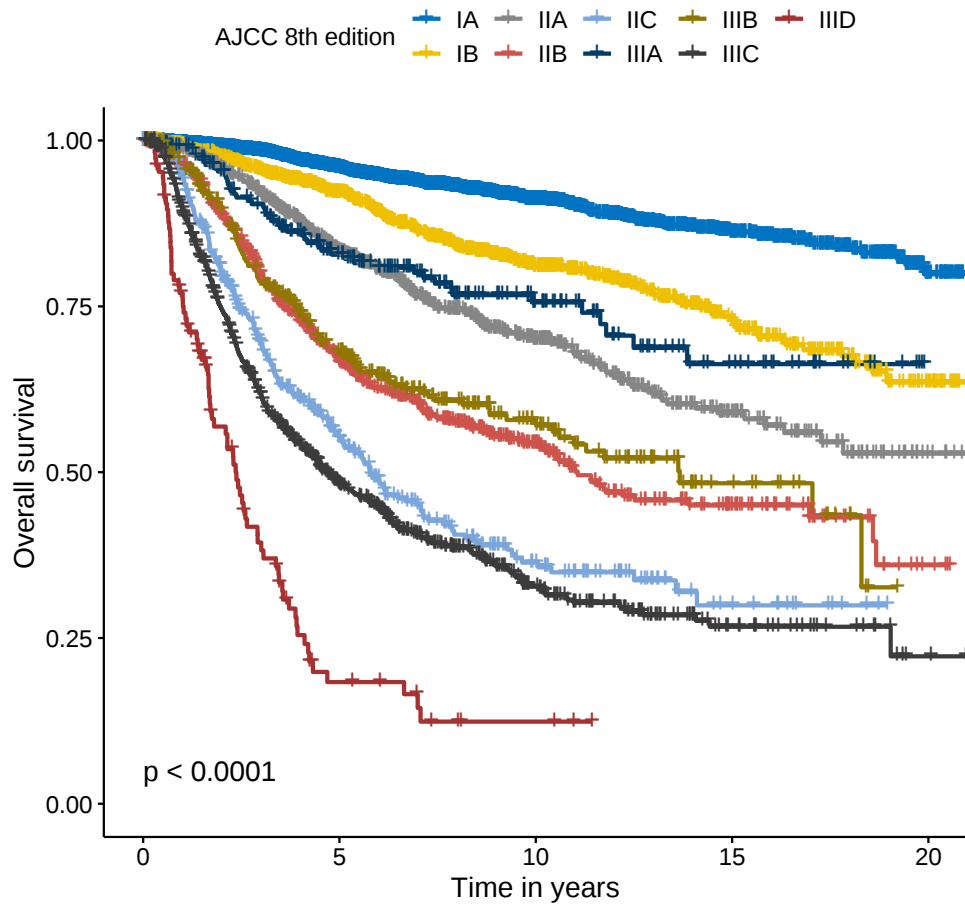
A**B**



AJCC 7th edition

	0	5	10	15	20
IA	2394	1469	769	358	42
IB	1996	1300	573	181	28
IIA	844	523	227	74	7
IIB	683	339	136	46	4
IIC	397	144	53	13	0
IIIA	508	270	118	40	1
IIIB	562	231	94	21	1
IIIC	404	95	25	5	0

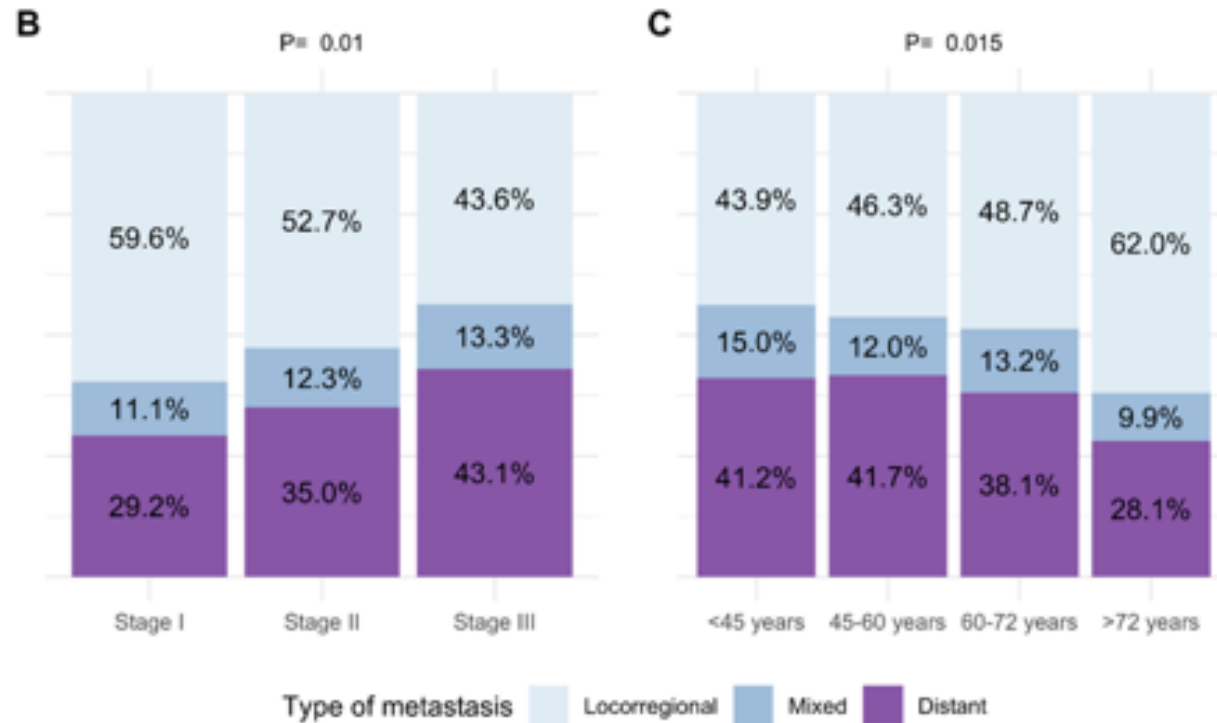
Time in years



AJCC 8th edition

	0	5	10	15	20
IA	3061	1896	932	386	47
IB	1341	881	413	154	23
IIA	832	515	224	73	7
IIB	683	339	136	46	4
IIC	397	144	53	13	0
IIIA	230	134	64	23	0
IIIB	335	167	69	17	0
IIIC	803	283	101	26	2
IIID	106	12	3	0	0

Time in years



Initial stage of cutaneous primary melanoma plays a key role on the pattern and timing of disease recurrence Sümeýre Seda Ertekin,^{1*} Sebastian Podlipnik,^{1,2*} Constanza Riquelme-Mc Loughlin,¹ Alicia Barreiro,^{1,2} Ana Arance,³ Cristina Carrera,^{1,2} Josep Malvehy,^{1,2} Susana Puig.^{1,2} Acta Derm Venereol. 2021 Jul 15;101(7):adv00502.

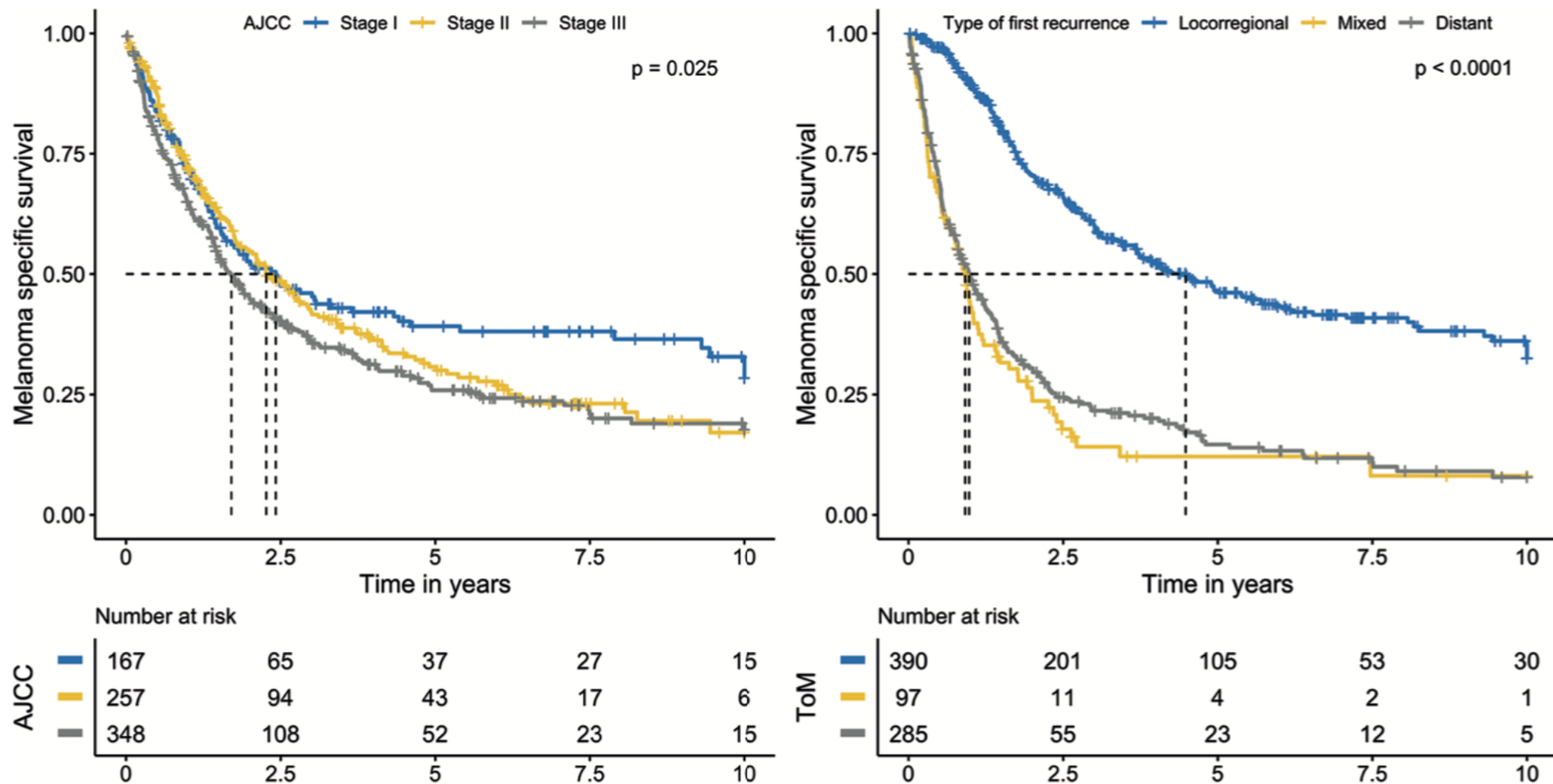
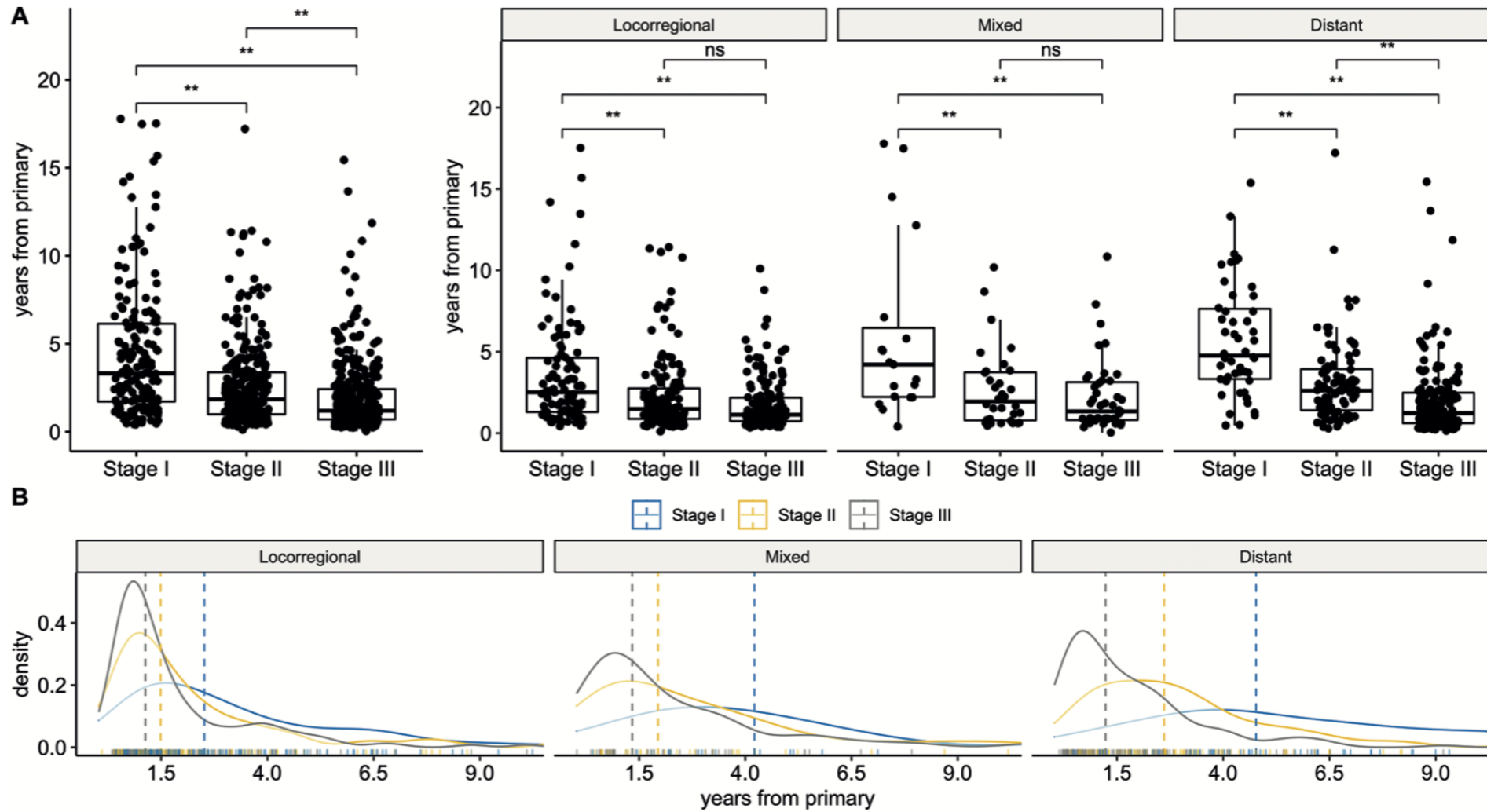


Fig. 3. Kaplan–Meier curves of post-recurrence melanoma specific survival according to the initial stage at diagnosis and metastatic pattern. Below the x-axis is displayed the number of patients at risk at each 2.5-year interval. AJCC: American Joint Committee on Cancer.

Initial stage of cutaneous primary melanoma plays a key role on the pattern and timing of disease recurrence Sümeyle Seda Ertekin,^{1*} Sebastian Podlipnik,^{1,2*} Constanza Riquelme-Mc Loughlin,¹ Alicia Barreiro,^{1,2} Ana Arance,³ Cristina Carrera,^{1,2} Josep Malvehy,^{1,2} Susana Puig.^{1,2} Acta Derm Venereol. 2021 Jul 15;101(7):adv00502.

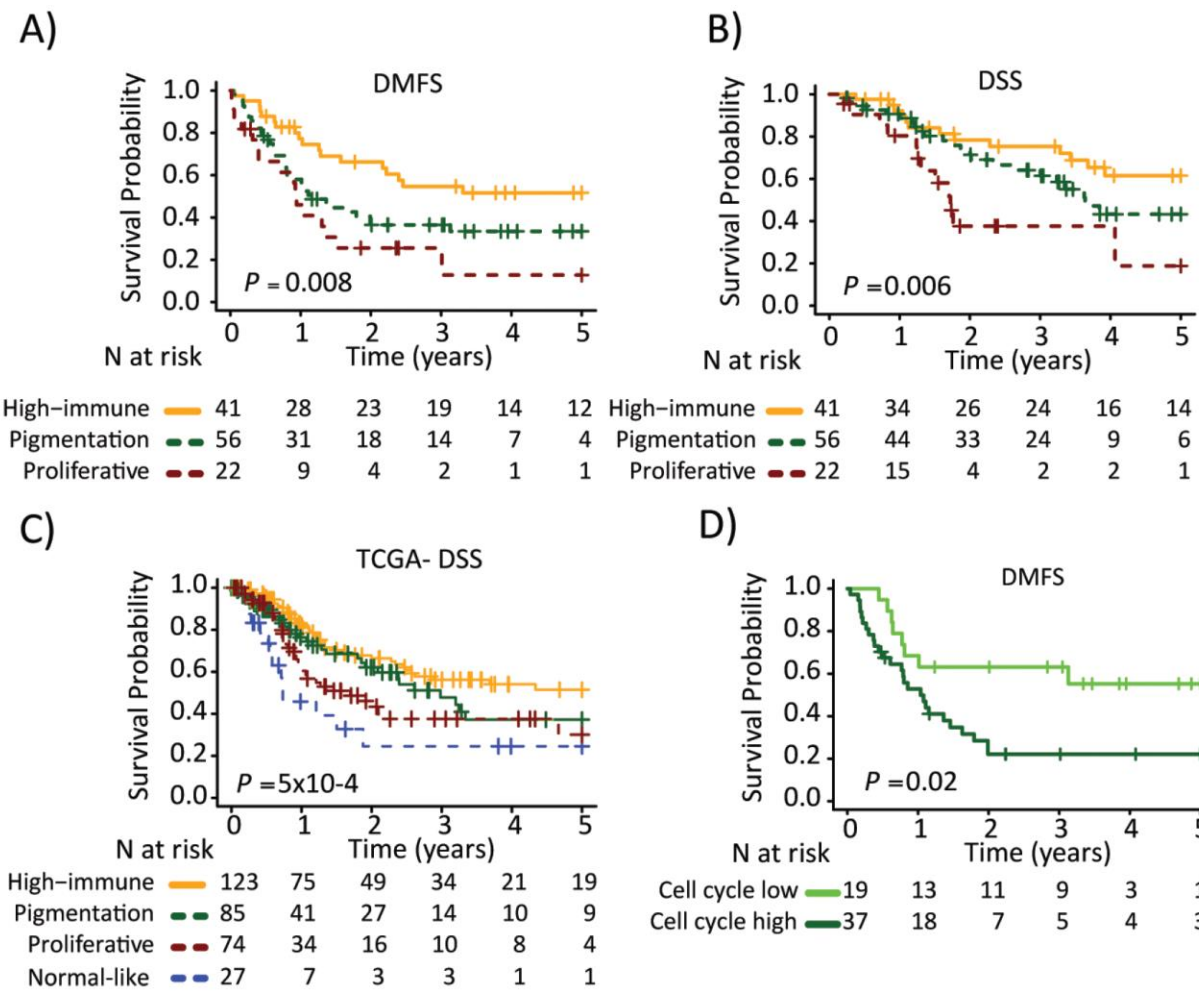


N=784

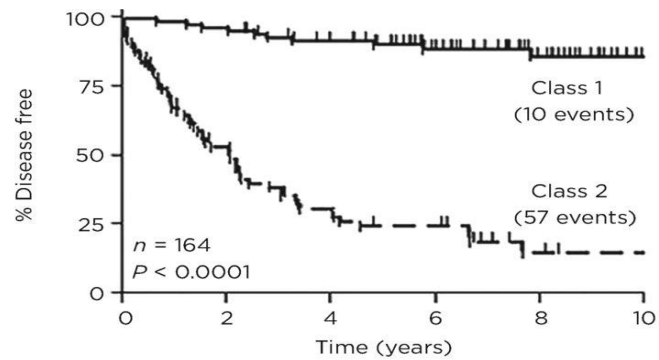
Initial stage of cutaneous primary melanoma plays a key role on the pattern and timing of disease recurrence Sümeyre Seda Ertekin,^{1*} Sebastian Podlipnik,^{1,2*} Constanza Riquelme-Mc Loughlin,¹ Alicia Barreiro,^{1,2} Ana Arance,³ Cristina Carrera,^{1,2} Josep Malvehy,^{1,2} Susana Puig.^{1,2} *Acta Derm Venereol.* 2021 Jul 15;101(7):adv00502.

Molecular stratification of metastatic melanoma using gene expression profiling : Prediction of survival outcome and benefit from molecular targeted therapy

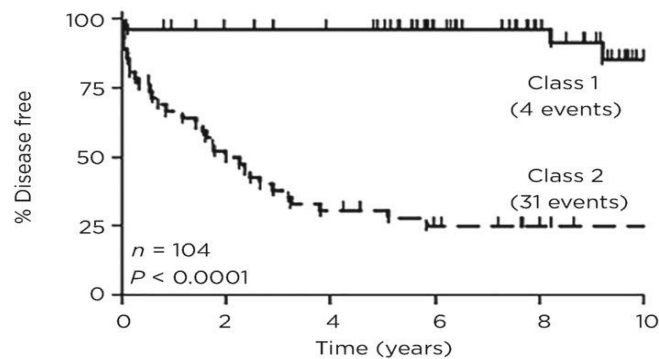
Helena Cirenajwis¹, Henrik Ekedahl², Martin Lauss¹, Katja Harbst¹, Ana Carneiro^{1,3}, Jens Enoksson⁴, Frida Rosengren¹, Linda Werner-Hartman¹, Therese Törngren¹, Anders Kvist¹, Erik Fredlund⁵, Pär-Ola Bendahl¹, Karin Jirstrom⁴, Lotta Lundgren^{1,3}, Jillian Howlin¹, Åke Borg¹, Sofia K. Gruvberger-Saal¹, Lao H. Saal¹, Kari Nielsen⁶, Markus Ringnér¹, Hensin Tsao^{7,8}, Håkan Olsson^{1,3}, Christian Ingvar², Johan Staaf¹, Göran Jönsson¹



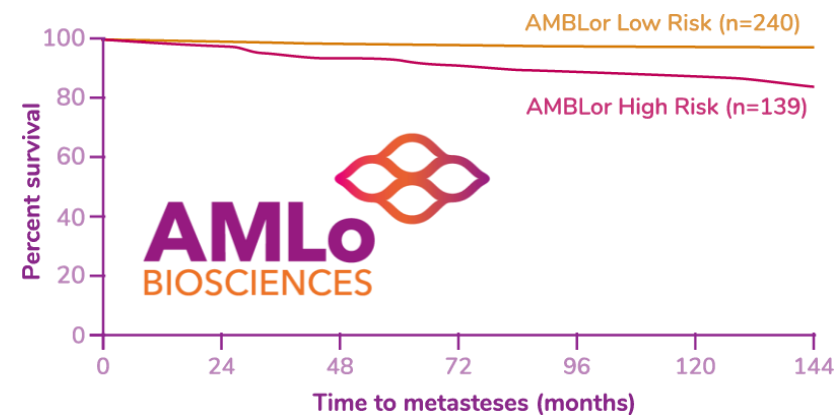
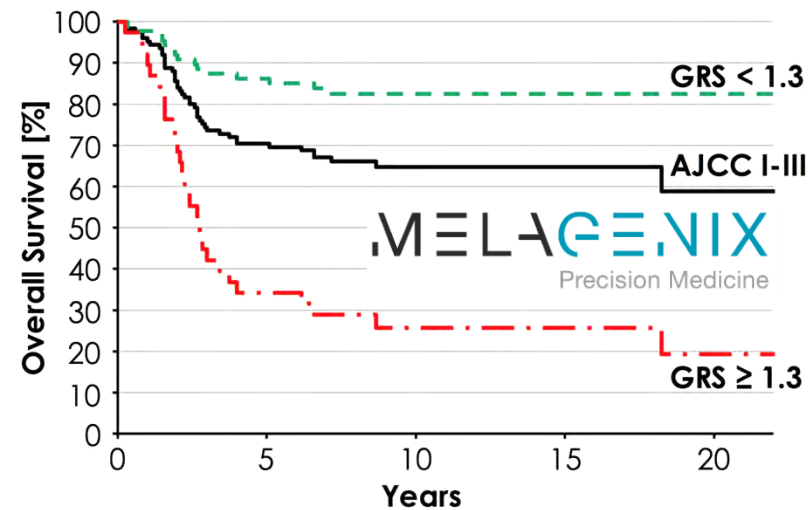
MELANOMA



Year	0	2	4	6	8	10
At risk (class 1)	88	85	74	51	31	11
At risk (class 2)	76	38	21	16	5	2



Year	0	2	4	6	8	10
At risk (class 1)	61	56	53	38	23	5
At risk (class 2)	43	22	14	9	4	2



Early outcome of a 31-gene expression profile test in 86 AJCC stage IB-II melanoma patients. A prospective multicentre cohort study

S. Podlipnik,^{1,*} C. Carrera,¹ A. Boada,² N.A. Richarz,² J.L. López-Estebarez,³ F. Pinedo-Moraleda,³ M. Elosua-González,³ M.M. Martín-González,⁴ R. Carrillo-Gijón,⁴ P. Redondo,⁵ E. Moreno,⁵ J. Malveyh,¹ S. Puig¹

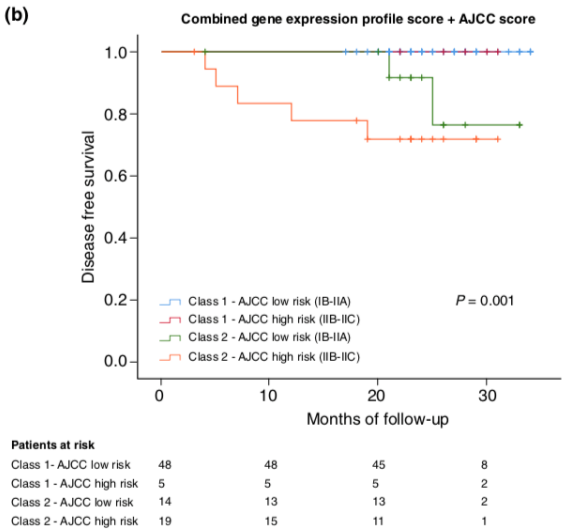
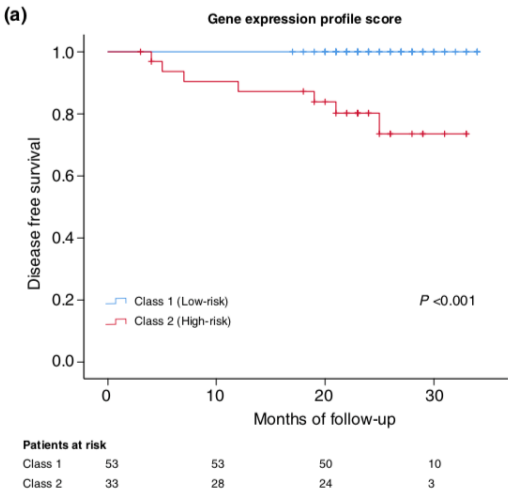
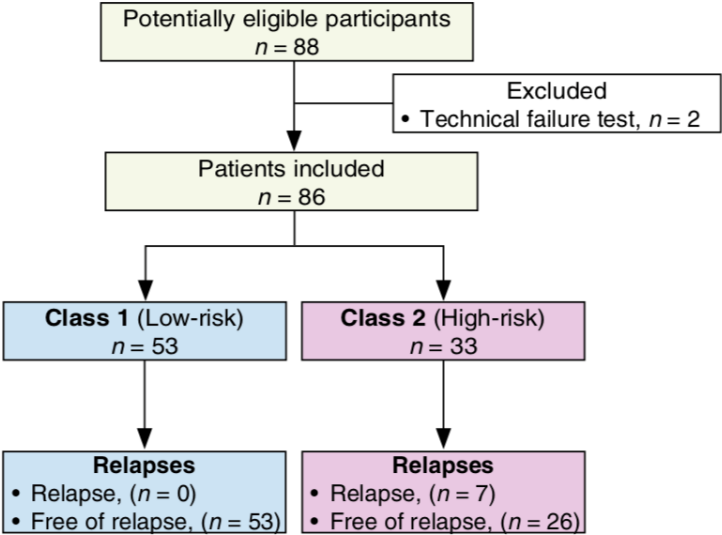


Table 2 Univariable and multivariate Cox regression analysis of prognostic factors in 86 melanoma patients for relapse free survival

Factor (high-risk variable)	Univariate		Multivariate	
	HR (95% CI)	p	HR (95% CI)	p
GEP (Class 2)	28.37 (3.46–3682.91)	<0.01	18.82 (1.81–2,549.76)	0.01
AJCC risk group (IIB-IIC)	6.33 (1.52–35.28)	0.01	1.52 (0.36–8.77)	0.58
Age of onset (>50)	7.26 (0.88–942.67)	0.07	3.7 (0.43–486.05)	0.29

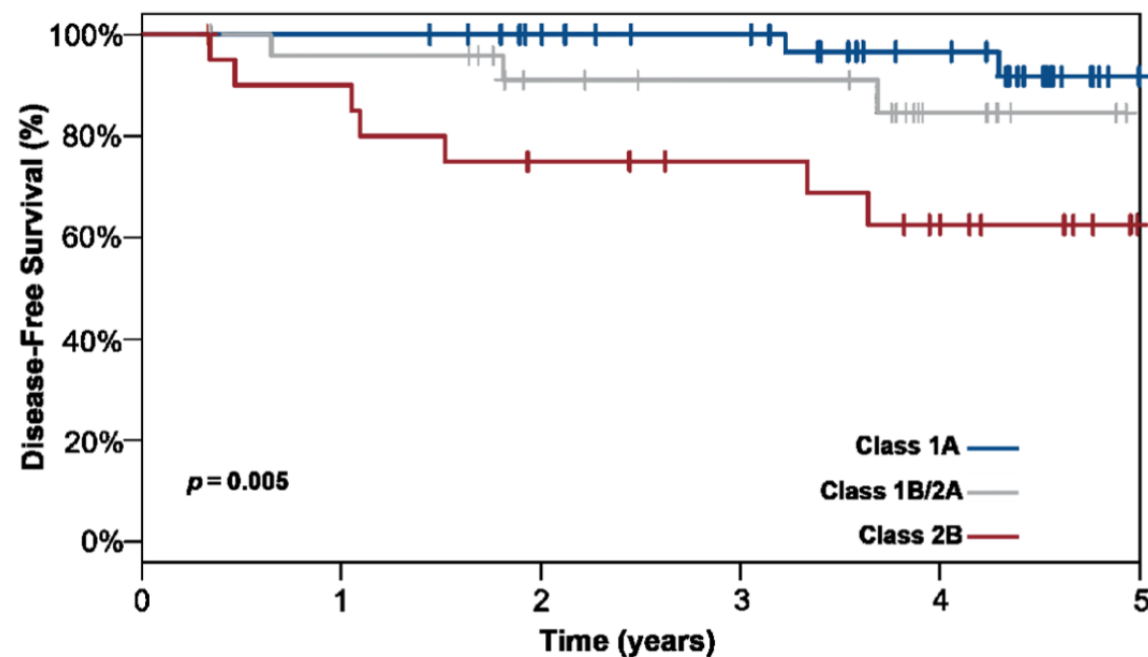
AJCC, American Joint Committee on Cancer; CI, Confidence interval; GEP, gene expression profile.



Article

Using a 31-Gene Expression Profile Test to Stratify Patients with Stage I–II Cutaneous Melanoma According to Recurrence Risk: Update to a Prospective, Multicenter Study

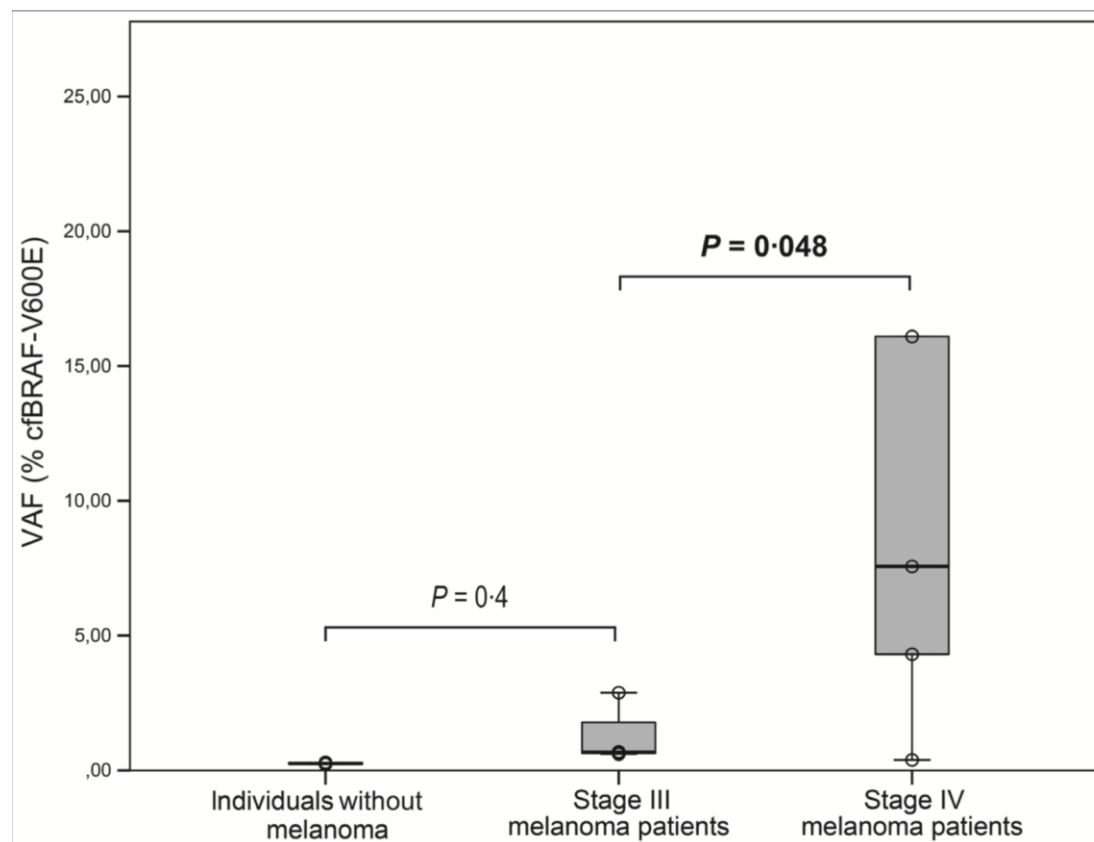
Sebastian Podlipnik ¹ , Aram Boada ² , Jose L. López-Estebarez ³ , Manuel M. Martín-González ⁴, Pedro Redondo ⁵ , Brian Martin ⁶, Ann P. Quick ⁶ , Christine N. Bailey ⁶, Sarah J. Kurley ⁶, Robert W. Cook ^{6,*} and Susana Puig ^{1,7,8}



Population	3-yr DFS (95%CI)	Recurrences		
		All (% population)	Loco-Regional (% of events)	Distant (% of events)
Class 1A (n = 40)	100% (100-100%)	2/40 (5.0%)	2/2 (100%)	0/2 (0%)
Class 1B/2A (n = 25)	91.04% (79.9-100%)	3/25 (12.0%)	2/3 (66.7%)	1/3 (33.3%)
Class 2B (n = 21)	75.0% (58.2-96.6%)	7/21 (33.3%)	4/7 (57.1%)	3/7 (42.9%)

Detection of cell-free circulating *BRAF*^{V600E} by droplet digital polymerase chain reaction in patients with and without melanoma under dermatological surveillance

N. Calbet-Llopart ¹ M. Potrony ^{1,2} G. Tell-Martí ^{1,2} C. Carrera ^{1,2} A. Barreiro ¹ P. Aguilera ^{1,2}
S. Podlipnik ¹ S. Puig ^{1,2} J. Malvehy ^{1,2} and J.A. Puig-Butillé ^{2,3}

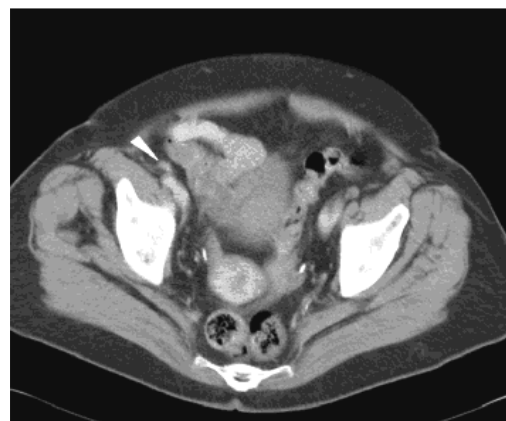
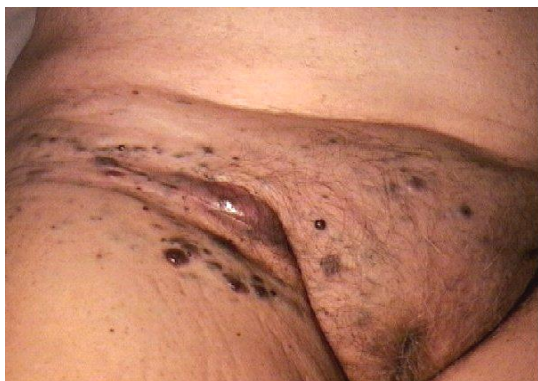


¿Qué nivel de evidencia?



TREATMENT OF PATIENTS WITH PROGRESSIVE UNRESECTABLE METASTATIC MELANOMA WITH A HETEROLOGOUS POLYVALENT MELANOMA WHOLE CELL VACCINE

Ramon VILELLA^{1,*}, Daniel BENITEZ¹, Jordi MILÀ¹, Antoni VILALTA², Ramon RULL³, Francisco CUELLAR², Carles CONILL⁴, Sergi VIDAL-SICART⁵, Josep COSTA⁶, Eva YACHI², Josep PALOU², Josep MALVEHY², Susana PUIG², Rosa MARTI², Begoña MELLADO⁷ and Teresa CASTEL²



- Mujer 45 años
- Melanoma Breslow > 2.5 mm y m1 cutánea
- BSGC –
- Melanoma Vacunas (4 años)
- 5 libre de enfermedad 2004.....
- Shock



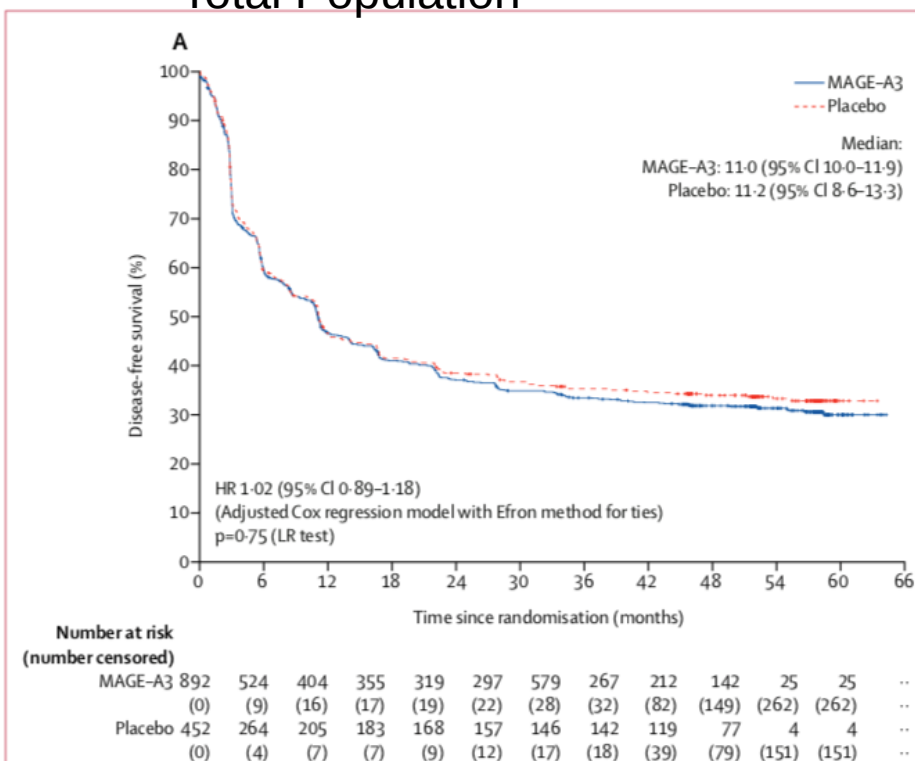


MAGE-A3 immunotherapeutic as adjuvant therapy for patients with resected, MAGE-A3-positive, stage III melanoma (DERMA): a double-blind, randomised, placebo-controlled, phase 3 trial

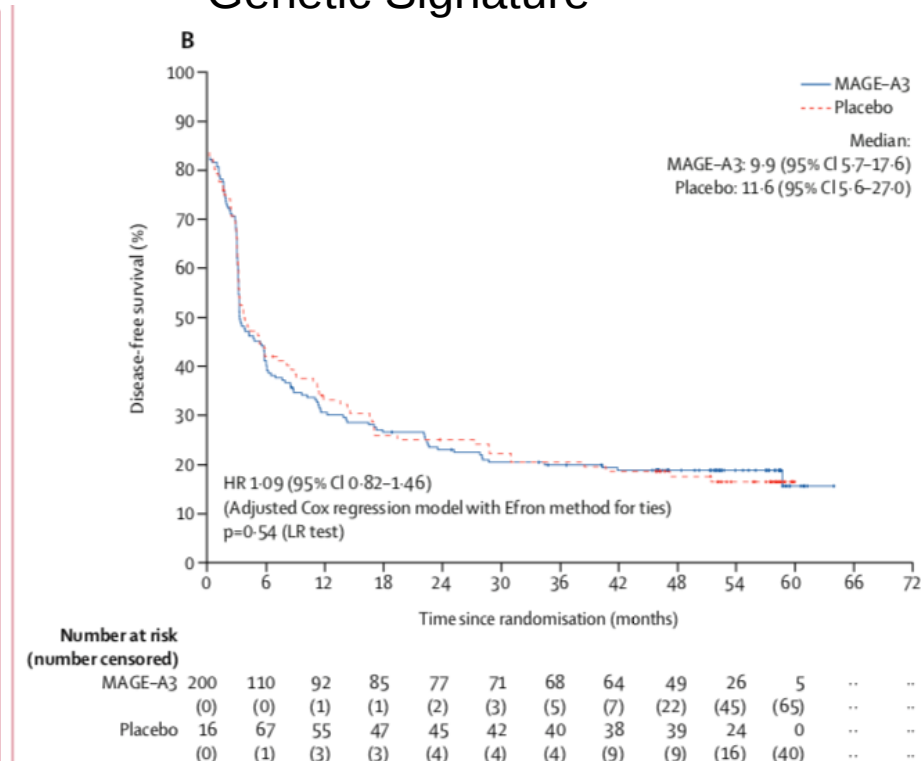
Lancet Oncol 2018; 19: 916–29

Brigitte Dreno, John F Thompson, Bernard Mark Smithers, Mario Santinami, Thomas Jouary, Ralf Gutzmer, Evgeny Levchenko, Piotr Rutkowski, Jean-Jacques Grob, Sergii Korovin, Kamil Drucis, Florent Grange, Laurent Machet, Peter Hersey, Ivana Krajsova, Alessandro Testori, Robert Conry, Bernard Guillot, Wim H J Kruit, Lev Demidov, John A Thompson, Igor Bondarenko, Jaroslaw Jaroszek, Susana Puig, Gabriela Cinat, Axel Hauschild, Jelle J Goeman, Hans C van Houwelingen, Fernando Ulloa-Montoya, Andrea Callegaro, Benjamin Dizier, Bart Spiessens, Muriel Debois, Vincent G Brichard, Jamila Louahed, Patrick Therasse, Channa Debruyne, John M Kirkwood

Total Population



Genetic Signature

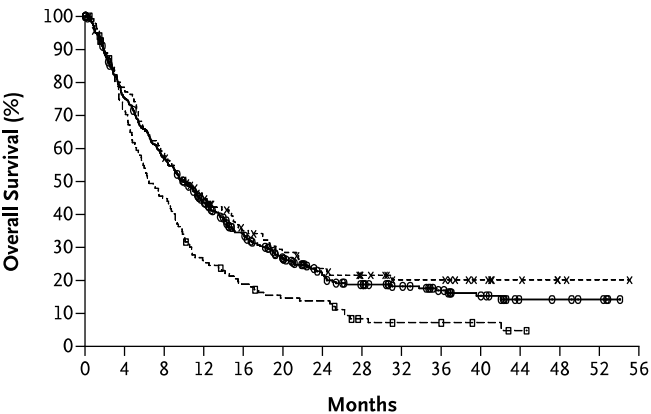


ORIGINAL ARTICLE

Improved Survival with Ipilimumab in Patients with Metastatic Melanoma

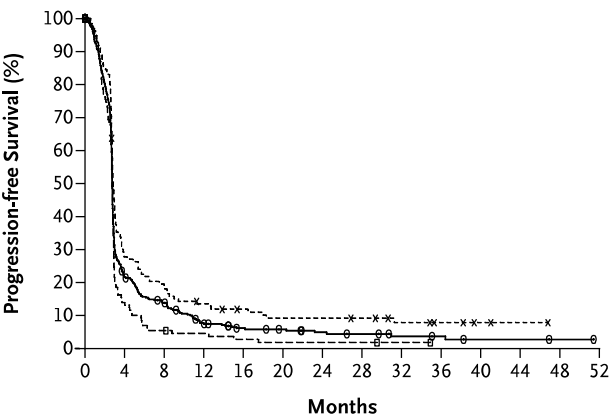
F. Stephen Hodi, M.D., Steven J. O'Day, M.D., David F. McDermott, M.D., Robert W. Weber, M.D., Jeffrey A. Sosman, M.D., John B. Haanen, M.D., Rene Gonzalez, M.D., Caroline Robert, M.D., Ph.D., Dirk Schadendorf, M.D., Jessica C. Hassel, M.D., Wallace Akerley, M.D., Alfons J.M. van den Eertwegh, M.D., Ph.D., Jose Lutzky, M.D., Paul Lorigan, M.D., Julia M. Vaubel, M.D., Gerald P. Linette, M.D., Ph.D., David Hogg, M.D., Christian H. Ottensmeier, M.D., Ph.D., Celeste Lebbé, M.D., Christian Peschel, M.D., Ian Quirt, M.D., Joseph I. Clark, M.D., Jedd D. Wolchok, M.D., Ph.D., Jeffrey S. Weber, M.D., Ph.D., Jason Tian, Ph.D., Michael J. Yellin, M.D., Geoffrey M. Nichol, M.D., Axel Hoos, M.D., Ph.D., and Walter J. Urba, M.D., Ph.D.

A Overall Survival



No. at Risk												
Ipi plus gp100	403	297	223	163	115	81	54	42	33	24	17	7
Ipi	137	106	79	56	38	30	24	18	13	13	8	5
gp100	136	93	58	32	23	17	16	7	5	5	3	1

B Progression-free Survival



No. at Risk												
Ipi plus gp100	403	85	52	27	17	14	10	8	5	4	2	2
Ipi	137	37	26	17	13	10	10	9	6	4	2	1
gp100	136	18	7	5	3	2	2	2	1	0	0	0

SHORT COMMUNICATION



1

Induced Vitiligo due to Talimogene Laherparepvec Injection for Metastatic Melanoma Associated with Long-term Complete Response

Pablo IGLESIAS^{1#}, Simone RIBERO^{1,2#}, Alicia BARREIRO¹, Sebastian PODLIPNIK¹, Cristina CARRERA¹, Josep MALVEHY^{1,3} and Susana PUIG^{1,3}

¹Dermatology Department, Hospital Clinic Barcelona, University of Barcelona, Villarroel 170, ES-08036 Barcelona, Spain, ²Medical Sciences Department, Section of Dermatology, University of Turin, Turin, Italy and ³Centro de Investigación Biomédica en Red en Enfermedades Raras (CIBERER), Barcelona, Spain. E-mail: susipuig@gmail.com #Both authors contributed equally to this paper.

Accepted Oct 3, 2018; Epub ahead of print Oct 3, 2018

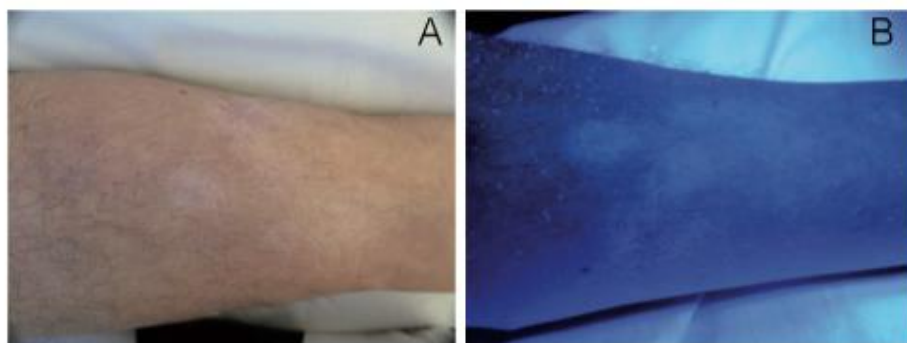


Fig. 1. Case 1. (A) Well-defined hypochromic lesions with non-pigmented hairs on the pretibial area. Those lesions appeared at the sites of the previous melanoma metastases. (B) At 20 months from the complete response the vitiligo plaques were still visible and stable in size, as seen under Wood's lamp.



Fig. 2. Case 2. (A) Induced vitiligo after 2 months from the achievement of a complete response of melanoma metastases with T-VEC treatment. (B) Induced vitiligo on the dorsum of the hand. (C) Distribution of the induced vitiligo on the neck/chest and on the typical localization around the mouth, as seen under Wood's lamp.

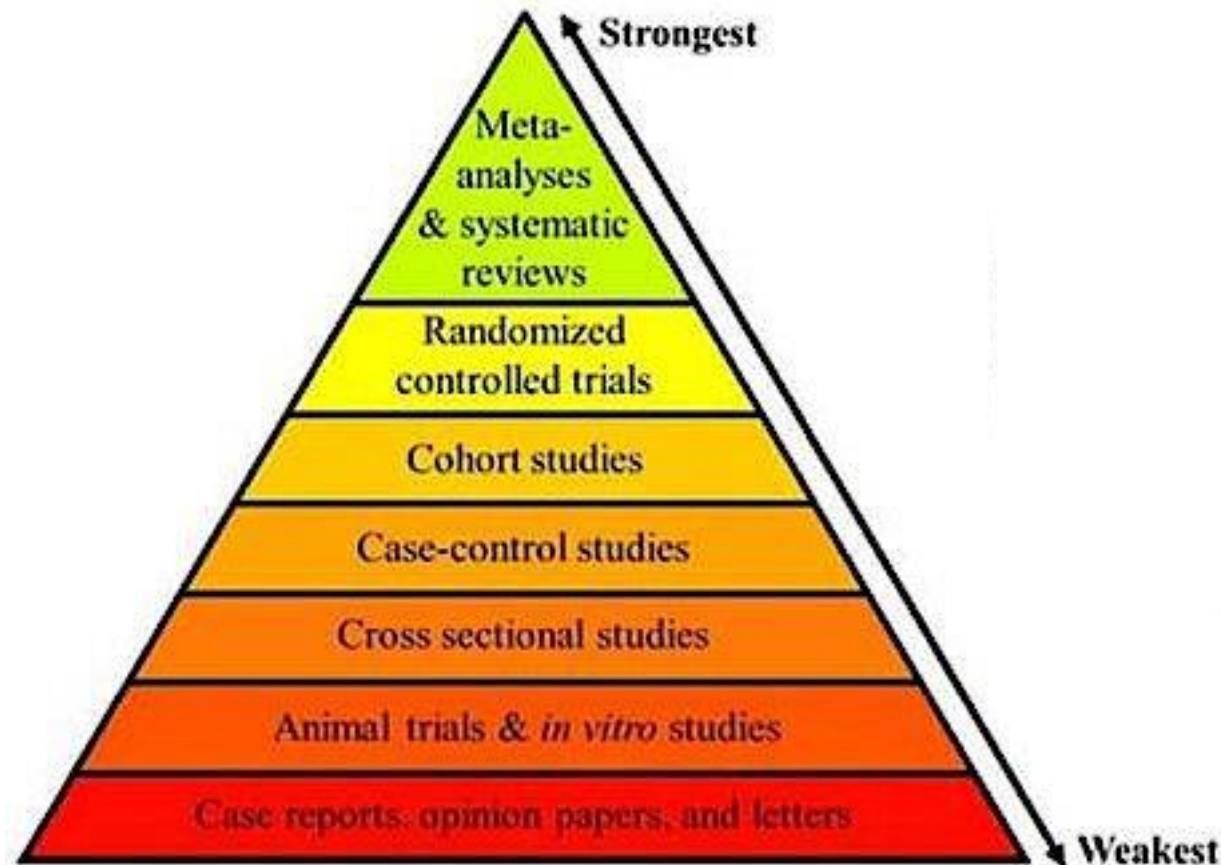




Nivel de evidencia científica

1. Metanálisis de ensayos clínicos controlados aleatorizados.
2. Ensayos clínicos controlados aleatorizados.
3. Ensayos clínicos controlados no aleatorizados.
4. Series de casos y otros diseños de estudios observacionales.

Hierarchy of Scientific Evidence





Mayo 2018

Jonathan Fox. Accountability Research Center, Making All Voices Count

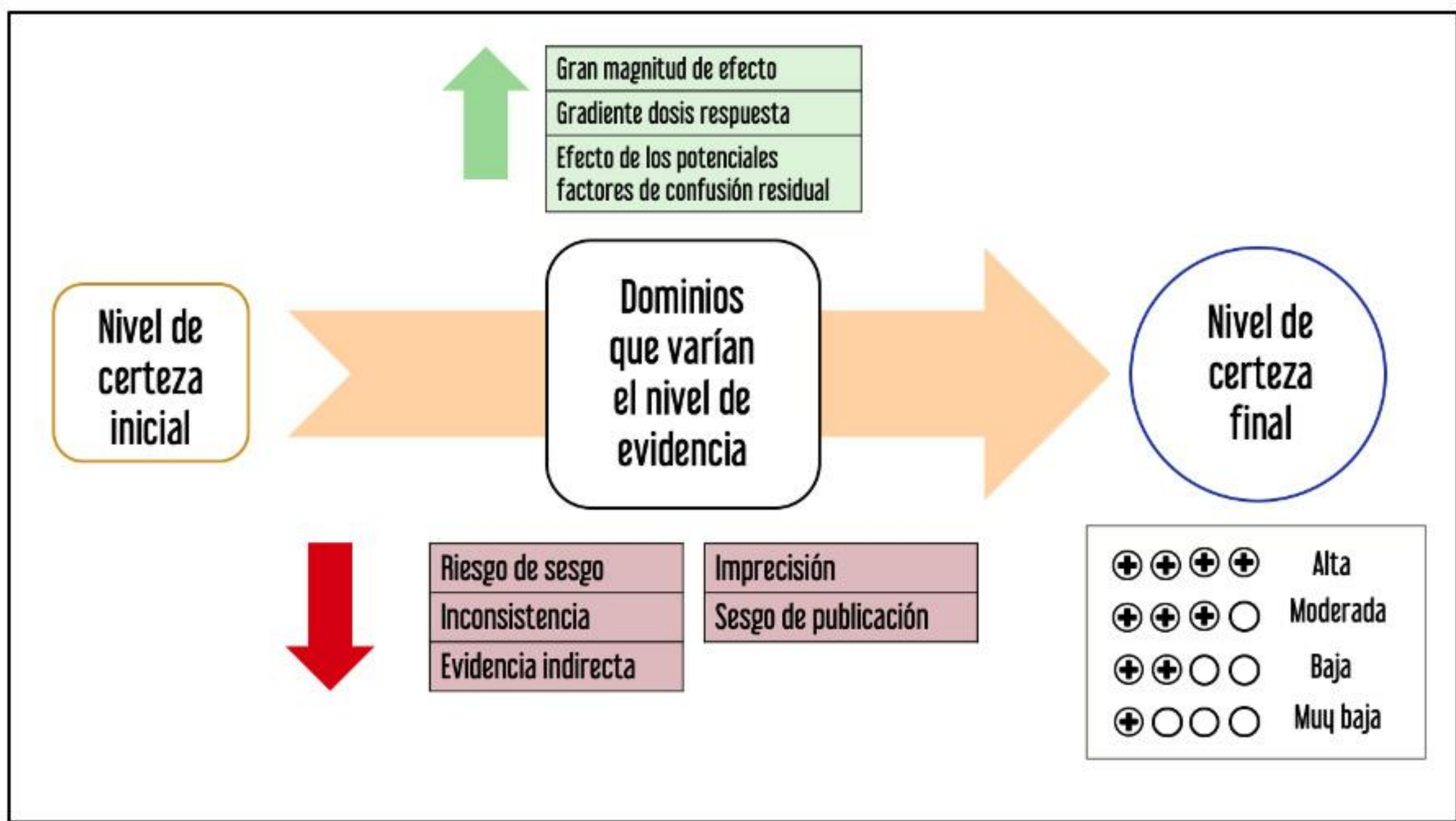
Pirámide tradicional

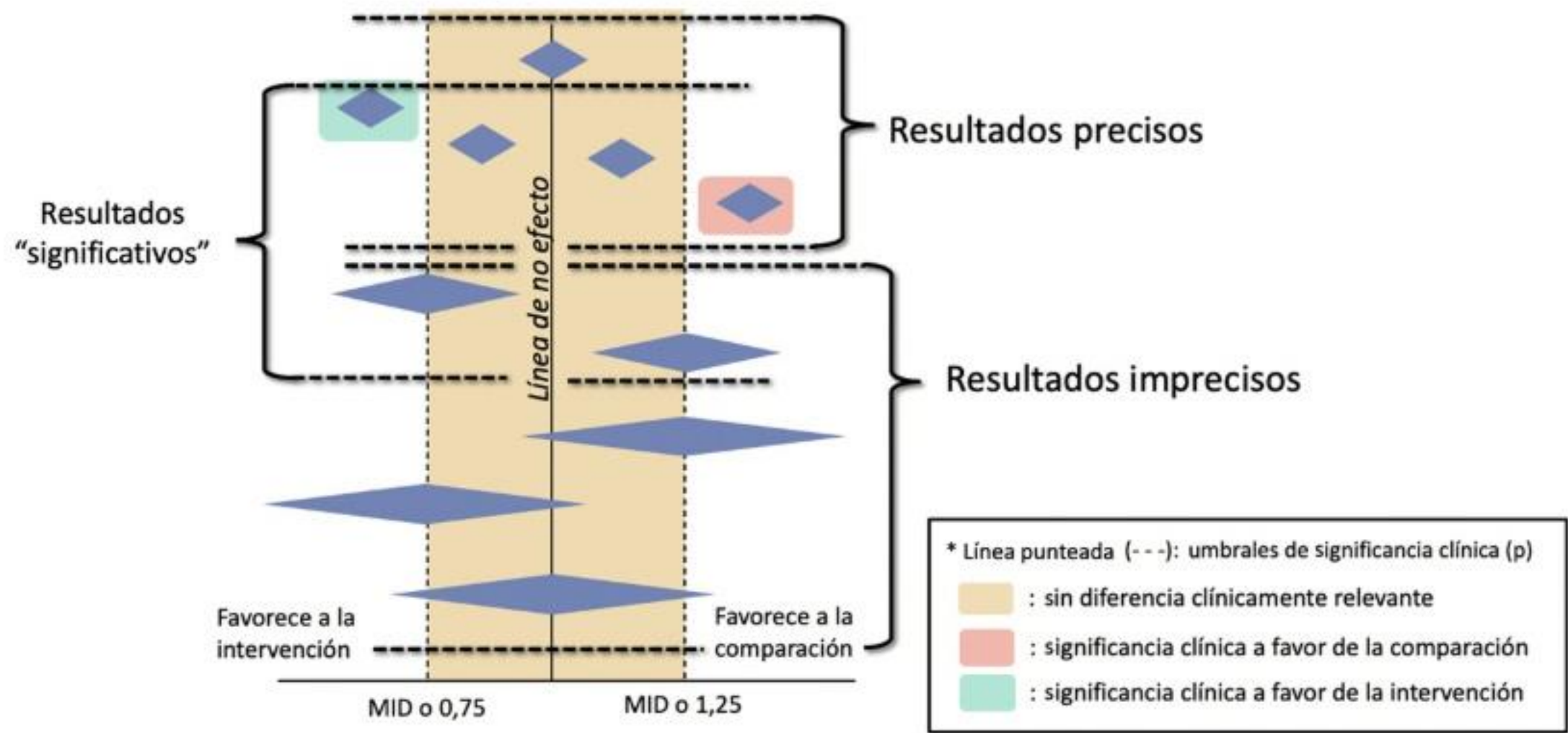


Modelo actual



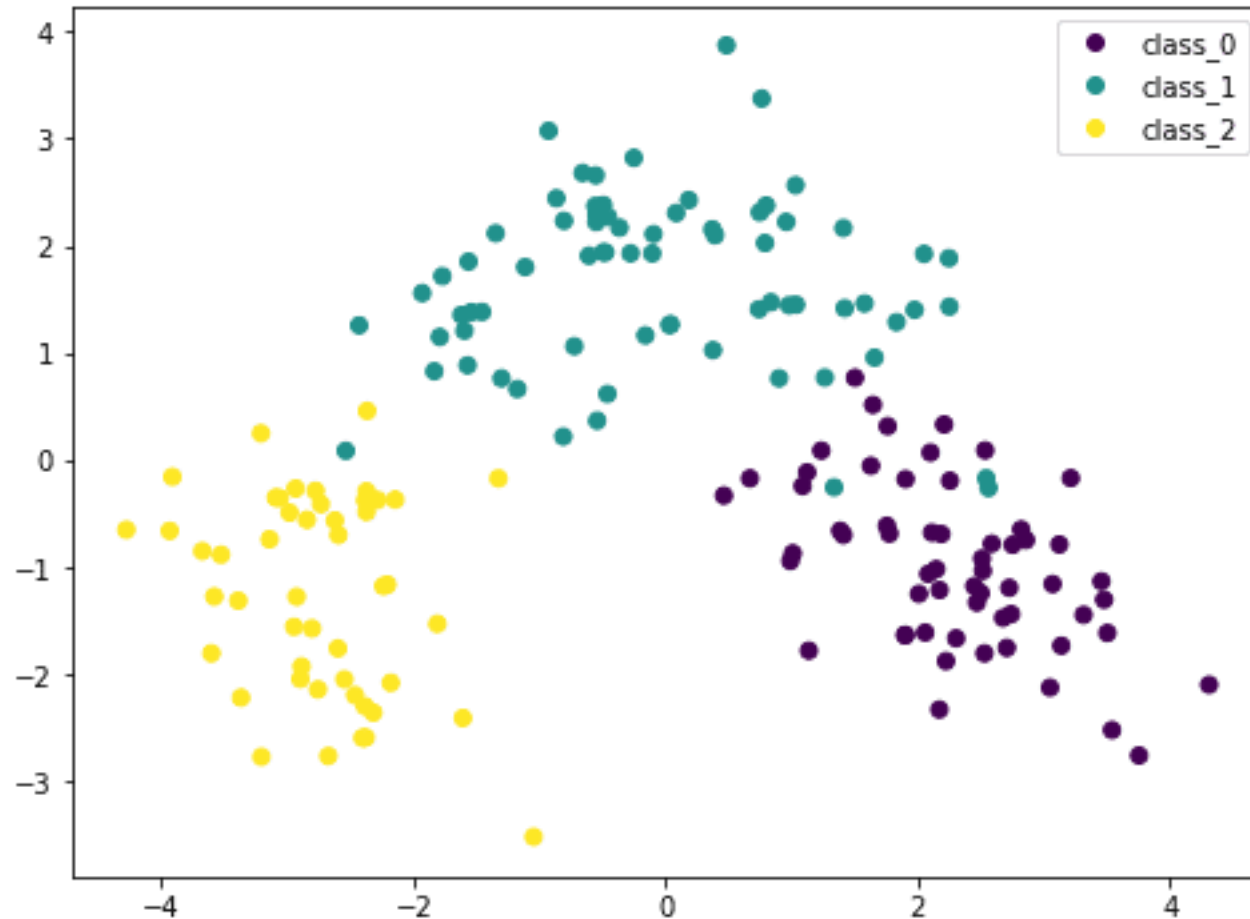
Fuente: adaptada y traducida desde el artículo: *Proposed new evidence-based medicine pyramid*⁵.





MID: diferencia mínima importante.
Fuente: figura confeccionada por los autores.

Maching learning PCA



Case Report

Dermatology

Dermatology
DOI: 10.1159/000433527

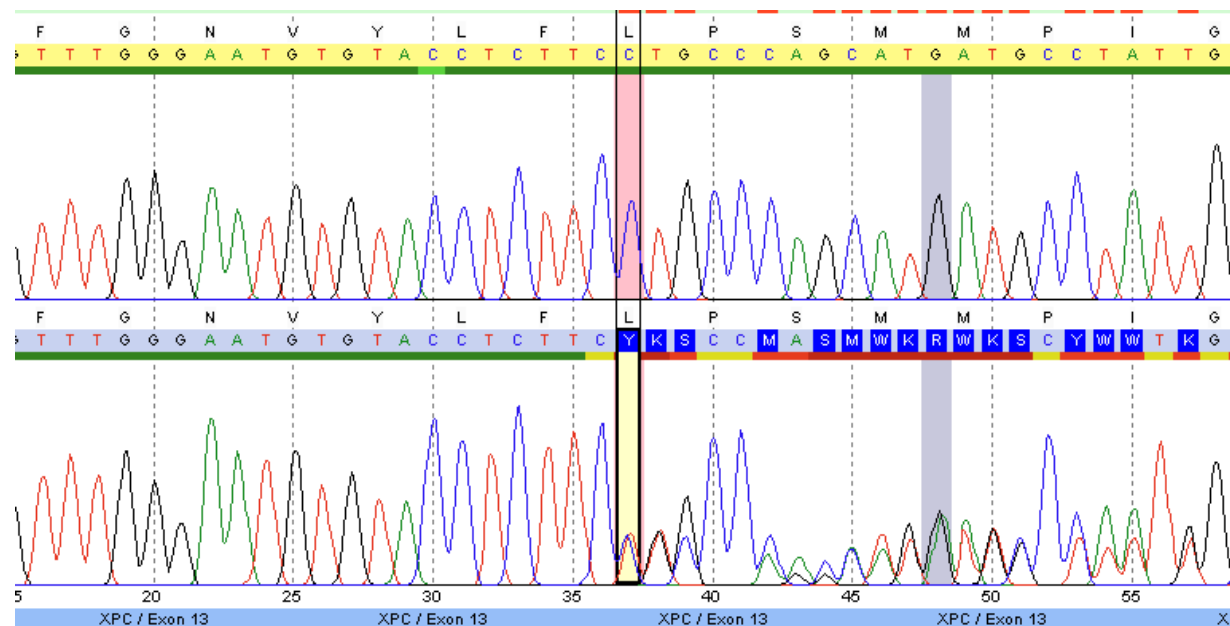
Received: January 21, 2015
Accepted after revision: May 20, 2015
Published online: August 5, 2015

Atypical Clinical Presentation of Xeroderma Pigmentosum in a Patient Harboring a Novel Missense Mutation in the XPC Gene: The Importance of Clinical Suspicion

Marina Meneses^a Marion Chavez-Bourgeois^a Celia Badenas^{b, d} Salvador Villablanca^a
Paula Aguilera^a Antoni Bennàssar^a Llúcia Alos^{c, e} Susana Puig^{a, d, e} Josep Malvehy^{a, d}
Cristina Carrera^{a, d, e}

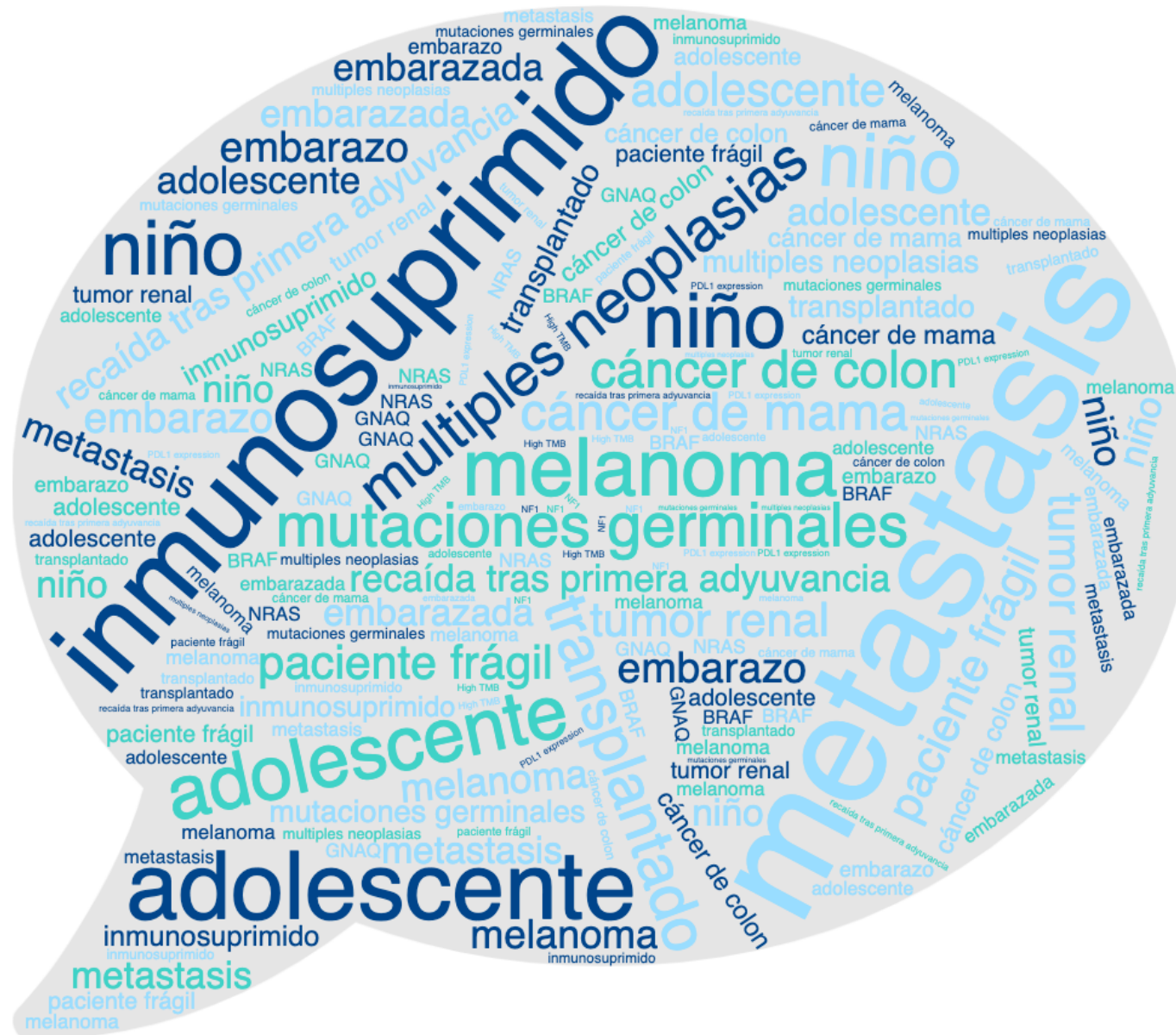
^aMelanoma Unit, Dermatology Department and ^bMelanoma Unit, Biochemistry and Molecular Genetics Service, IDIBAPS, Hospital Clinic of Barcelona, ^cMelanoma Unit, Pathology Department, Hospital Clinic of Barcelona, ^dCIBER de Enfermedades Raras, Instituto de Salud Carlos III, and ^eUniversity of Barcelona, Barcelona, Spain

XPC EXON 13 p.Leu763Cysfs*4 (c.2287delC) already described



WT

Patient



Mission Cancer

Novel health care strategies for MELanoma in Children, Adolescents and YOUNG Adults (MELCAYA)

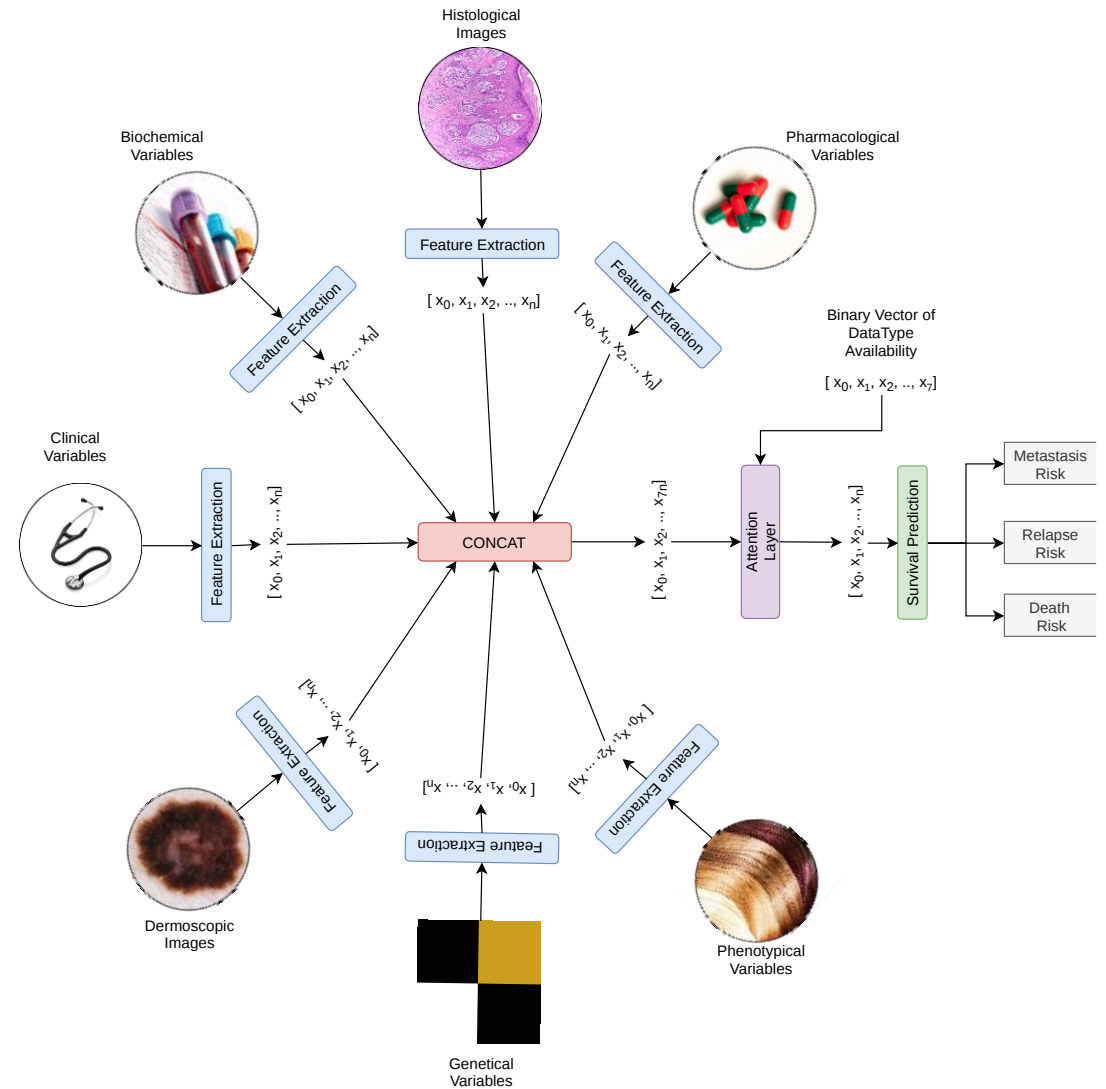
2023-2026

Coordinattor: Susana Puig



This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No 101096667.





iTOBOs: Intelligent Total Body Scanner for Early Detection of Melanoma (EU H2020)

- **New diagnostics** for the early detection of melanoma, exploiting **all the available information** of the patient.
- This **holistic assessment tool** should understand the specific characteristics of every patient in order to enable a **personalised, early detection of melanoma**.



