[REGULACIÓN] Aprobación *acelerada* de medicamentos

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PMFarma

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Buscar...

INICIO EMPLEO

Noticias

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Enviar a un amigo | Imp

05 Ene. 2018

EMA aumenta sus aprobaciones de nuevos fármacos innovadores en 2017

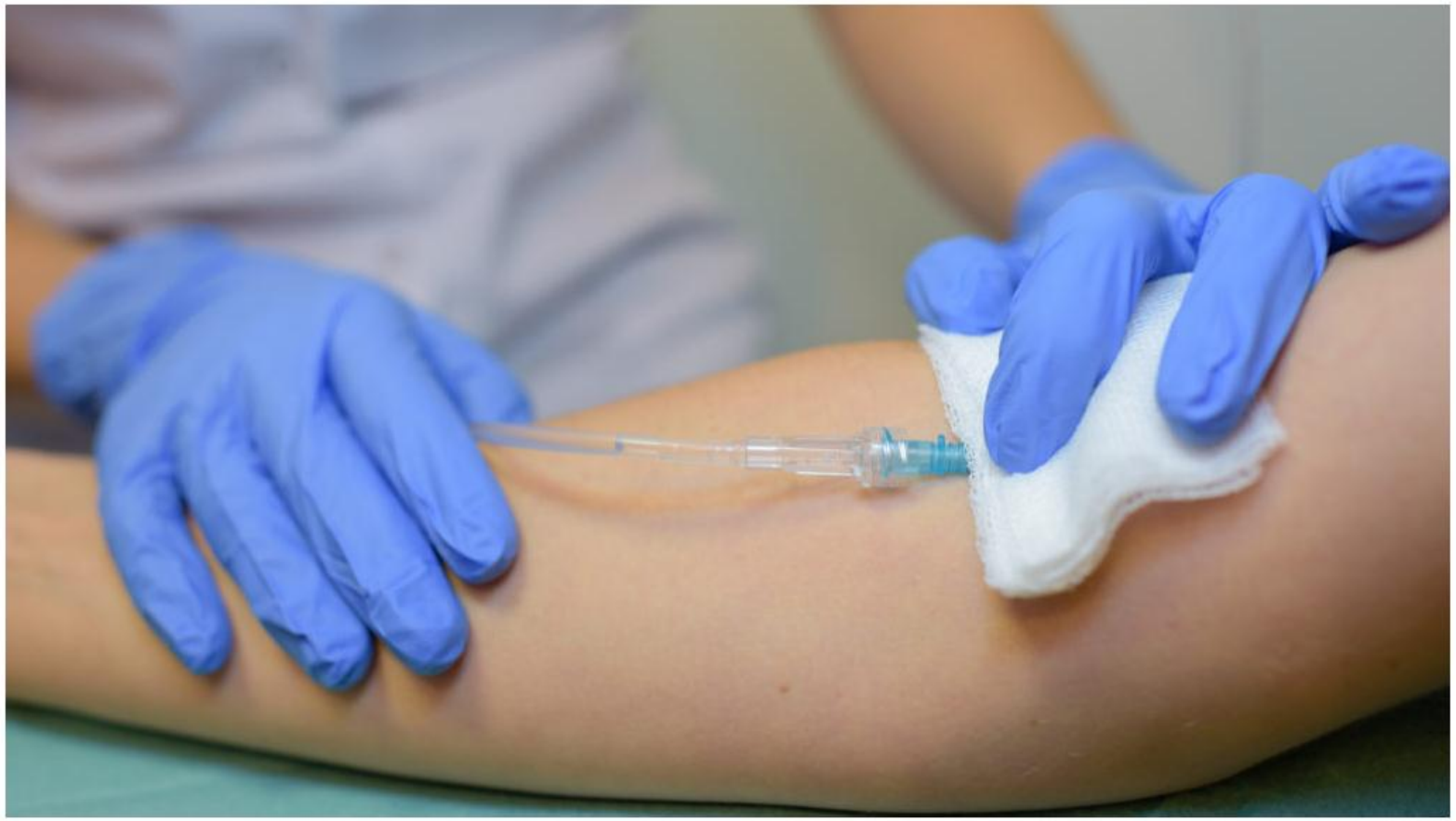
Y la FDA logra su cifra récord en 21 años.

HEALTH

STAT+

New cancer drugs quickly prescribed to patients, but more real-world data needed on effectiveness

By ELIZABETH COONEY @cooney_liz / MAY 10, 2018



EL GLOBAL

jornada de gestión y evaluación

El vértigo a la aceleración del registro puede ser perjudicial para su salud

Almirall ha impulsado un interesante evento en el que se ha abordado el uso de los Big Data y cómo la experiencia en la vida real puede facilitar la toma de decisiones en los sistemas sanitarios.

Pero…

¿qué es antes, la obtención de datos en "vida real" o la decisión de registro?

Marco conceptual…

Existe un grave problema de acceso de los pacientes a la innovación

La causa principal es el complejo y prolongado proceso de registro

Solución: aprobar fármacos exigiendo menos datos en ensayos clínicos y completarlos luego o con "RWD"

¿seguro?

1er ejemplo

CERITINIB

Pacientes con CPNM ALK+ pretratados con crizotinib

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 February 2015
EMA/140022/2015
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Zykadia

ceritinib

On 26 February 2015 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a conditional marketing authorisation for the medicinal product Zykadia, 150 mg, hard capsule, intended for the treatment of adult patients with anaplastic lymphoma kinase (ALK) positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib. The applicant for this medicinal product is Novartis Europharm Ltd. They may request a re-examination of any CHMP opinion, provided they notify the European Medicines Agency in writing of their intention within 15 days of receipt of the opinion.

- Tabular overview of clinical studies

Study (Status) /cut-off date		Primary endpoint	No. of patients	Ceritinib dose
Registration studies for efficacy and safety				
Study X2101 (ongoing; enrolment complete) 14-Apr-2014	Phase 1, multi-center, dose-escalation study in patients with ALK-positive tumors; prior ALK inhibitor therapy was allowed	Escalation phase: MTD Efficacy endpoint: ORR by Investigator per RECIST 1.0	Escalation phase: 59 Expansion phase: 245 Total at 750 mg: 255 [a]	Escalation phase: 50 to 750 mg Expansion phase: 750 mg
Study A2201 (ongoing; enrolment complete) 13-Aug-2014	Phase 2, multi-center, single-arm study in adult patients with ALK-activated NSCLC previously treated with chemotherapy and crizotinib	ORR by Investigator per RECIST 1.1	140	750 mg
Study A2203 (ongoing; enrolment complete) 26-Feb-2014	Phase 2, multi-center, single-arm study in crizotinib-naive adult patients with ALK-activated NSCLC	ORR by Investigator per RECIST 1.1	124	750 mg

Alternativas: docetaxel, pemetrexed

Table 26: Progression-free survival in patients with ALK-positive NSCLC by Investigator assessment (Study X2101, Study A2201, Study A2203)

	NSCLC patients with prior ALK inhibitor		ALK inhibitor naïve NSCLC patients	
	Study X2101 ceritinib 750 mg N=163	Study A2201 ceritinib 750 mg N=140	Study X2101 ceritinib 750 mg N=83	Study A2203 ceritinib 750 mg N=124
Number of patients with PFS event, n (%)	113 (69.3%)	82 (58.6)	33 (39.8)	40 (32.3)
Number of patients censored, n (%)	50 (30.7)	58 (41.4)	50 (60.2)	84 (67.7)
Reasons for censoring				
Ongoing without event	29 (17.8)	51 (36.4)	42 (50.6)	77 (62.1)
Lost to follow-up	1 (0.6)	1 (0.7)	0	0
Withdrew consent	5 (3.1)	2 (1.4)	1 (1.2)	2 (1.6)
Initiation of new anticancer therapy	7 (4.3)	2 (1.4)	3 (3.6)	1 (0.8)
Event documented after ≥ 2 missing tumor assessments [a]	5 (3.1)	1 (0.7)	2 (2.4)	0
Adequate assessment no longer available	3 (1.8)	1 (0.7)	2 (2.4)	4 (3.2)
Median PFS (months) (95% CI)	6.9 (5.6, 8.7)	5.7 (5.3, 7.4)	18.4 (11.1, NE)	11.1 (9.3, NE)
12-month PFS rate	27.2 (19.8, 35.1)	24.5 (14.4, 35.9)	62.3 (50.0, 72.4)	40.3 (19.7, 60.2)

NE = not estimable.
[a] No adequate evaluations for a specific period (more than 4 cycles + 2-week window) prior to data cut-off or without baseline assessment.
Study X2101: Responses assessed by Investigator using RECIST 1.0.
Study A2201, A2203: Responses assessed by Investigator using RECIST 1.1.
Source: [D120 Appendix 1-X2101-Table 14.2-1.5h],[D120 Appendix 1-X2101-Table 14.2-1.6f], [Study A2201-Table 14.2-1.6a], [Study A2201-Table 14.2-1.7], [Study A2203-Table 14.2-1.6a], [Study A2203-Table 14.2-1.7]

Table 27: Overall survival in patients with ALK-positive NSCLC (Study X2101, Study A2201, Study A2203)

	NSCLC patients with prior ALK inhibitor		ALK inhibitor naïve NSCLC patients	
	Study X2101 ceritinib 750 mg N=163	Study A2201 ceritinib 750 mg N=140	Study X2101 ceritinib 750 mg N=83	Study A2203 ceritinib 750 mg N=124
Number of deaths, n (%)	**63 (38.7)**	**39 (27.9)**	**16 (19.3)**	**13 (10.5)**
Number of patients censored, n (%)	**100 (61.3)**	**101 (72.1)**	**67 (80.7)**	**111 (89.5)**
Reasons for censoring				
Alive	73 (44.8)	100 (71.4)	58 (69.9)	110 (88.7)
Lost to follow-up	27 (16.6) [a]	1 (0.7)	9 (10.8)[b]	1 (0.8)
Median (month) (95%CI)	**16.7 (14.8, NE)**	**14.0 (10.3, 14.0)**	**NE (19.61, NE)**	**NE**
12-month OS rate (95% CI)	67.2 (58.9, 74.1)	54.9 (38.5, 68.6)	83.0 (72.4, 89.8)	81.5 (64.8, 90.8)

NE = not estimable.
[a] 2 patients classified by the investigator as lost to follow-up, and 24 patients for whom no survival information was available within 14 weeks prior to the cut-off date
[b] 1 patient classified by the investigator as lost to follow-up, and 8 patients for whom no survival information was available within 14 weeks prior to the cut-off date
Source: [D120 Appendix 1-X2101-Table 14.2-2.1d], [D120 Appendix 1-X2101-Table 14.2-1.6f], [Study A2201-Table 14.2-2.1], [Study A2203-Table 14.2-2.1], [Study A2201-Table 14.2-1.7], [Study A2203-Table 14.2-1.7]

Faltan "algunas" cosas…

- No se ha comparado con el estándar
- No conocemos el beneficio en SLP
- No sabemos en qué medida se traduce a SG
- No conocemos la seguridad comparativa
- No tenemos curva de supervivencia (sólo medianas)
- El resultado no es ciego
- No hay comité independiente para medir progresión
- No hay análisis de subgrupos…

- No podemos hacer comparaciones indirectas ajustadas
- No podemos hacer análisis coste/efectividad
- No podemos valorar beneficio en distintos tipos de pacientes

- ¿Cuándo tendremos estos datos?
- ¿Estudios observacionales en pacientes refractarios a quimioterapia y crizotinib? ¿Cuánto tardaremos en conseguirlos? ¿Serán fiables? Hay nuevos tratamientos: alectinib, inmunoterapia…
- ¿precio?

Additional efficacy data needed in the context of a conditional MA

The updated information from the phase I and the phase II studies supporting the ALKi pretreated indication confirm the efficacy results initially observed, and provide reassurance on the robustness of these results. Although a positive benefit-risk profile can be concluded, the data have limitations inherent to the non-comparative nature of the studies supporting the recommendation for a conditional MA.

In order to confirm the positive benefit-risk profile, the applicant will submit the final results of the phase II study A2201 expected by Q2 2016. In addition, 177 patients out of the target 236 patients (75% completed) have been randomized in the ongoing phase III comparative study (A2303). Enrolment is expected to be completed by end of August 2015 and the approval of ceritinib in the EU is not expected to impact completion of recruitment in this study. The final study report of study A2303 will allow a more comprehensive data package to be submitted in Q3 2018.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 May 2017
EMA/CHMP/313473/2017
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (post authorisation)

Zykadia

ceritinib

On 18 May 2017, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending a change to the terms of the marketing authorisation for the medicinal product Zykadia. The marketing authorisation holder for this medicinal product is Novartis Europharm Ltd.

The CHMP adopted a new indication as follows:

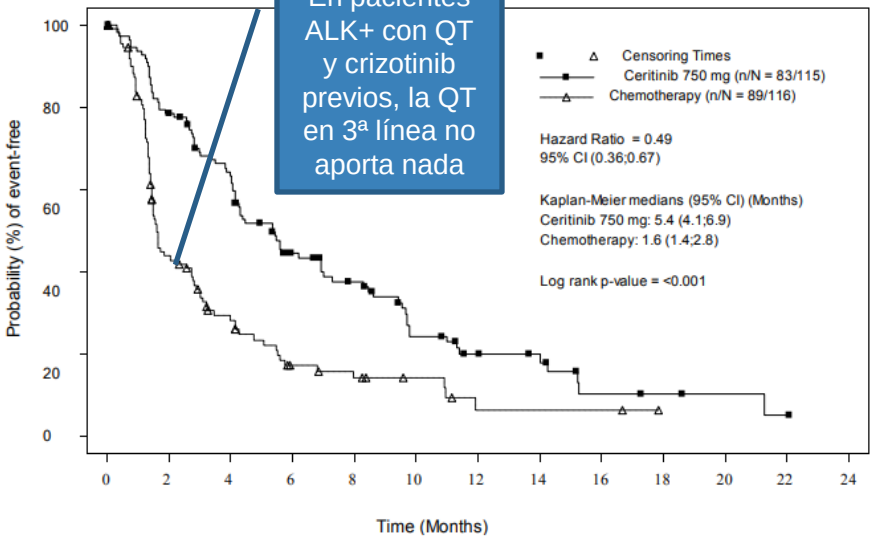
> "Zykadia as monotherapy is indicated for the first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC)."

For information, the full indications for Zykadia will be as follows[2]:

> "**Zykadia as monotherapy is indicated for the first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC).**
>
> Zykadia as monotherapy is indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib."

In addition, since all specific obligations of the conditional marketing authorisation have been fulfilled, the marketing authorisation for Zykadia will be switched from conditional to full approval.

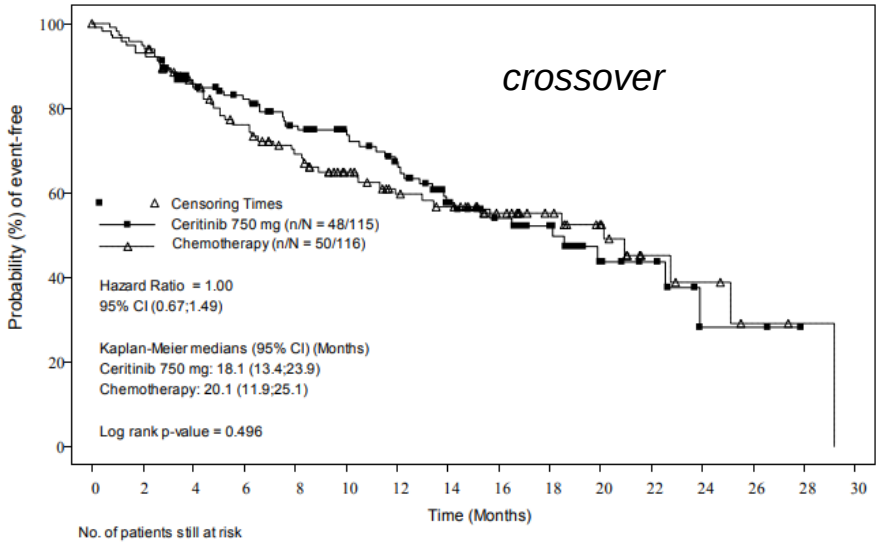
Figure 3 **ASCEND-5 (Study A2303) – Kaplan-Meier plot of progression-free survival as assessed by BIRC**



No. of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24
Ceritinib 750 mg	115	87	68	40	31	18	12	9	4	3	2	1	0
Chemotherapy	116	45	26	12	9	6	2	2	2	0	0	0	0

Figure 4 **ASCEND-5 (Study A2303) – Kaplan-Meier plot of overall survival by treatment arm**



No. of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30
Ceritinib 750 mg	115	107	92	83	71	61	52	37	28	23	13	8	2	2	0	0
Chemotherapy	116	109	91	78	66	53	43	39	29	22	17	7	5	2	1	0

Datos importantes para la negociación de precios y posicionamiento

3,25 años más tarde…

agencia española de **medicamentos y productos sanitarios**

29/05/2018 12:53:59 / *Fuente original*

La última CIPM aprobó seis nuevos principios activos y combinaciones

La última reunión de la Comisión Interministerial de Precios de los Medicamentos (CIPM), celebrada el pasado 26 de abril aprobó la incorporación a la cartera farmacéutica del Sistema Nacional de Salud (SNS) de seis nuevos principios activos y combinaciones.

En concreto, la CIPM propuso aceptar la financiación pública y precio de tres presentaciones de cladribina, comercializado por Merck como Mavenclad para la esclerosis múltiple, así como una presentación de lesinurad, comercializado por Grünenthal como Zurampic para la hiperuricemia.

Además, realizó propuesta favorable de autorización para cuatro medicamentos que se encontraban en fase de alegaciones. Es el caso de Odefsey (tenofovir, alafenamida; emtricitabina; rilpivirina) de Gilead para el VIH/Sida; Trimbow (Formoterol, bromuro de glicopirronio, y beclometasona) para EPOC, de Chiesi; Iluvien (fluocinolona acetónido) de Brill Pharma, para deterioro visual asociado al edema macular diabético crónico; y Zykadia (ceritinib) de Novartis para cáncer de pulmón no microcítico (CPNM) avanzado ALK+.

¿Ha contribuido la aprobación temprana –condicionada– a reducir el tiempo de acceso al mercado?
No. Faltaban datos. No se ha suplido esa carencia con RWD (impensable a corto plazo).
⇒ Era necesario el ECA

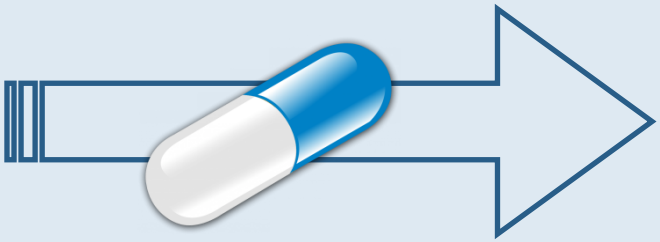
Introducción de un nuevo medicamento en la práctica clínica

EMA

"Fast Track"

aprobación EMA

medicamento en investigación



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EXCEPTIONAL CIRCUMSTANCES

uso del fármaco

uso compasivo

ensayos clínicos

Concepto de "vías adaptadas" (adaptive pathways)

- Se dirige a áreas con ***necesidades médicas no cubiertas***
- Identificar *pequeñas poblaciones con enfermedad grave* en las que **el balance beneficio/riesgo será favorable**
- Identificar áreas en las que la "**real world evidence**" será adecuada para apoyar los datos de ensayos clínicos
- Incorporar a los participantes, como las HTA, en una fase temprana del desarrollo
- Mantener elevados estándares de evaluación **beneficio/riesgo**

thebmj

BMJ 2016;354:i4479 doi: 10.1136/bmj.i4479 (Published 16 August 2016)

NEWS

German body calls for pause in European plan for fast track drug approval

Nigel Hawkes

London

IQWiG (equivalente alemán del NICE): no existe un método con garantías que permita usar RWD para obtener conclusiones fiables

2º ejemplo

IXAZOMIB

Pacientes con mieloma múltiple en recaída

Ninlaro	ixazomib citrate	Multiple Myeloma	21/11/2016	▼	O C	Authorised

Product details

Name	Ninlaro
Agency product number	EMEA/H/C/003844
Active substance	ixazomib citrate
International non-proprietary name (INN) or common name	ixazomib
Therapeutic area	Multiple Myeloma
Anatomical therapeutic chemical (ATC) code	L01XX50
Additional monitoring ▼	This medicine is under additional monitoring. This means that it is being monitored even more intensively than other medicines. For more information, see medicines under additional monitoring.
Treatment of rare diseases O	This medicine has an "orphan designation" which means that it is used to treat life-threatening or chronically debilitating conditions that affect no more than five in 10,000 people in the European Union, or are medicines which, for economic reasons, would be unlikely to be developed without incentives.
Conditional Approval C	Sometimes, the CHMP recommends that a medicine be given 'conditional approval'. This happens when the Committee has based its positive opinion on data which, while not yet comprehensive, indicate that the medicine's benefits outweigh its risks. The company is given obligations to fulfil, such as the performance of further studies. The approval is renewed on a yearly basis until all obligations have been fulfilled, and is then converted from a conditional approval into a normal approval. Conditional approvals can only be granted for medicines that satisfy an 'unmet medical need', meaning the medicine is intended to be used for a disease or condition for which no treatment is readily available, and it is therefore important that patients have early access to the medicine concerned.

En un hospital mediano que atiende a 200.000 habitantes: 100 pacientes

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 June 2016
EMA/358656/2016 rev. 1
EMEA/H/C/003844

Questions and answers

Update of 24 June 2016:

The company that applied for a marketing authorisation for Ninlaro has requested a re-examination of the CHMP's May 2016 opinion. Upon receipt of the grounds of the request, the CHMP will re-examine its opinion and issue a final recommendation.

Refusal of the marketing authorisation for Ninlaro (ixazomib)

On 26 May 2016, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Ninlaro, intended for the treatment of multiple myeloma.

The company that applied for authorisation is Takeda Pharma A/S. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

15 September 2016
EMA/CHMP/603622/2016
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Ninlaro

ixazomib

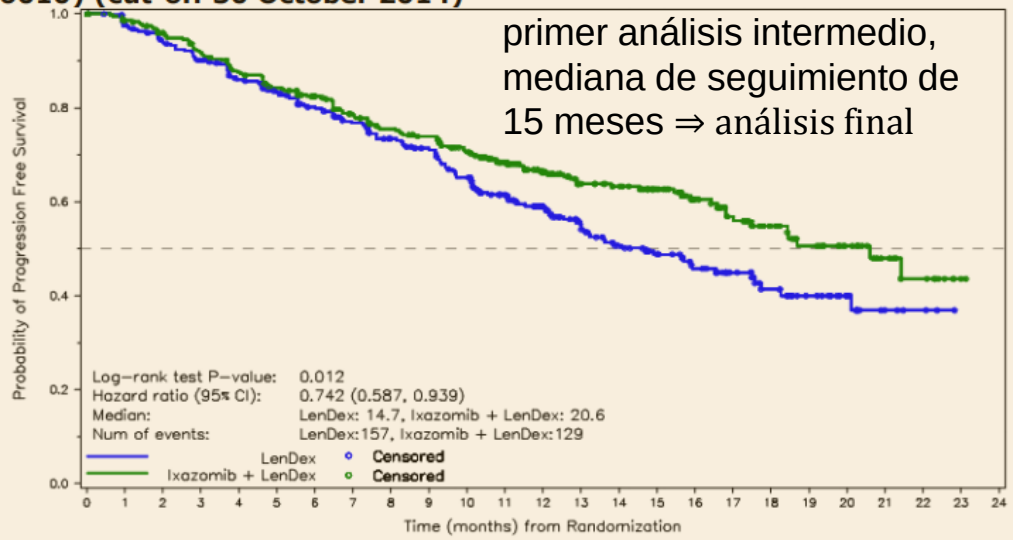
On 15 September 2016, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a conditional[2] marketing authorisation for the medicinal product Ninlaro, intended for the treatment of multiple myeloma. Ninlaro was designated as an orphan medicinal product on 27 September 2011. The applicant for this medicinal product is Takeda Pharma A/S.

Ninlaro will be available as 2.3, 3 and 4 mg hard capsules. The active substance of Ninlaro is ixazomib, a reversible proteasome inhibitor (ATC code: L01XX50).

The benefits with Ninlaro are its ability to delay the progression of multiple myeloma when used in combination with lenalidomide and dexamethasone. The most common side effects are diarrhoea, constipation, thrombocytopenia, peripheral neuropathy, nausea, peripheral oedema, vomiting and back pain.

The full indication is: "Ninlaro in combination with lenalidomide and dexamethasone is indicated for the treatment of adult patients with multiple myeloma who have received at least one prior therapy." It is proposed that treatment must be initiated and monitored under the supervision of a physician experienced in the management of multiple myeloma.

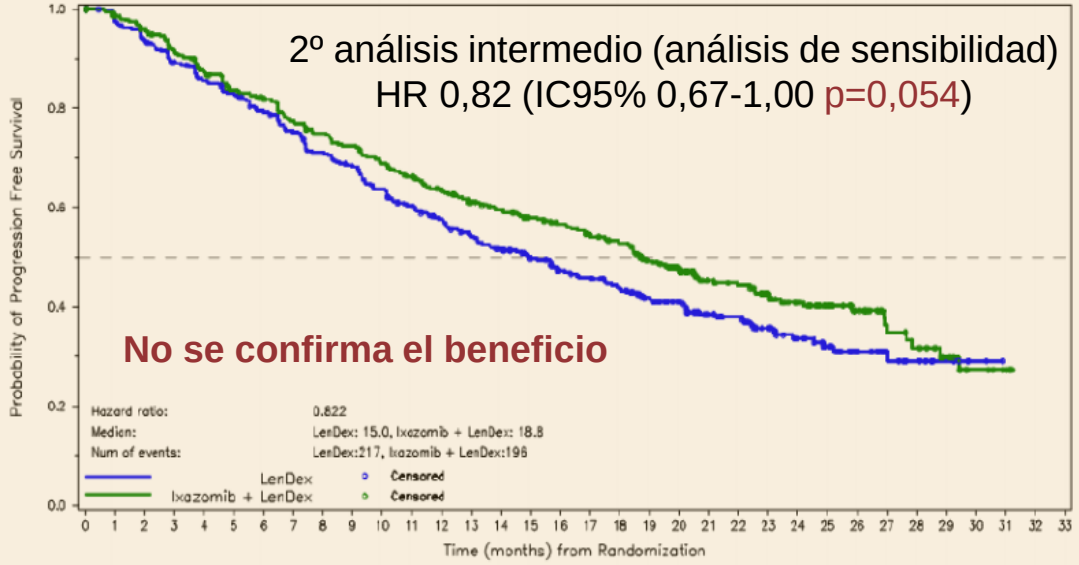
Figure 7. Kaplan-Meier Plot of Progression-Free Survival Based on IRC Assessment (ITT) (Study C16010) (cut-off 30 October 2014)



Number of Patients at Risk

LenDex	362	340	325	308	288	274	254	237	218	208	188	157	130	101	85	71	58	46	31	22	15	5	3	0	0
Ixazomib + LenDex	360	345	332	315	298	283	270	248	233	224	206	182	145	119	111	95	72	58	44	34	26	14	9	1	0

Figure 8. Kaplan-Meier Plot of Progression-Free Survival (IRC Assessments)—EMA Censoring Rule, ITT Population (data cut-off 12 July 2015)



Number of Patients at Risk

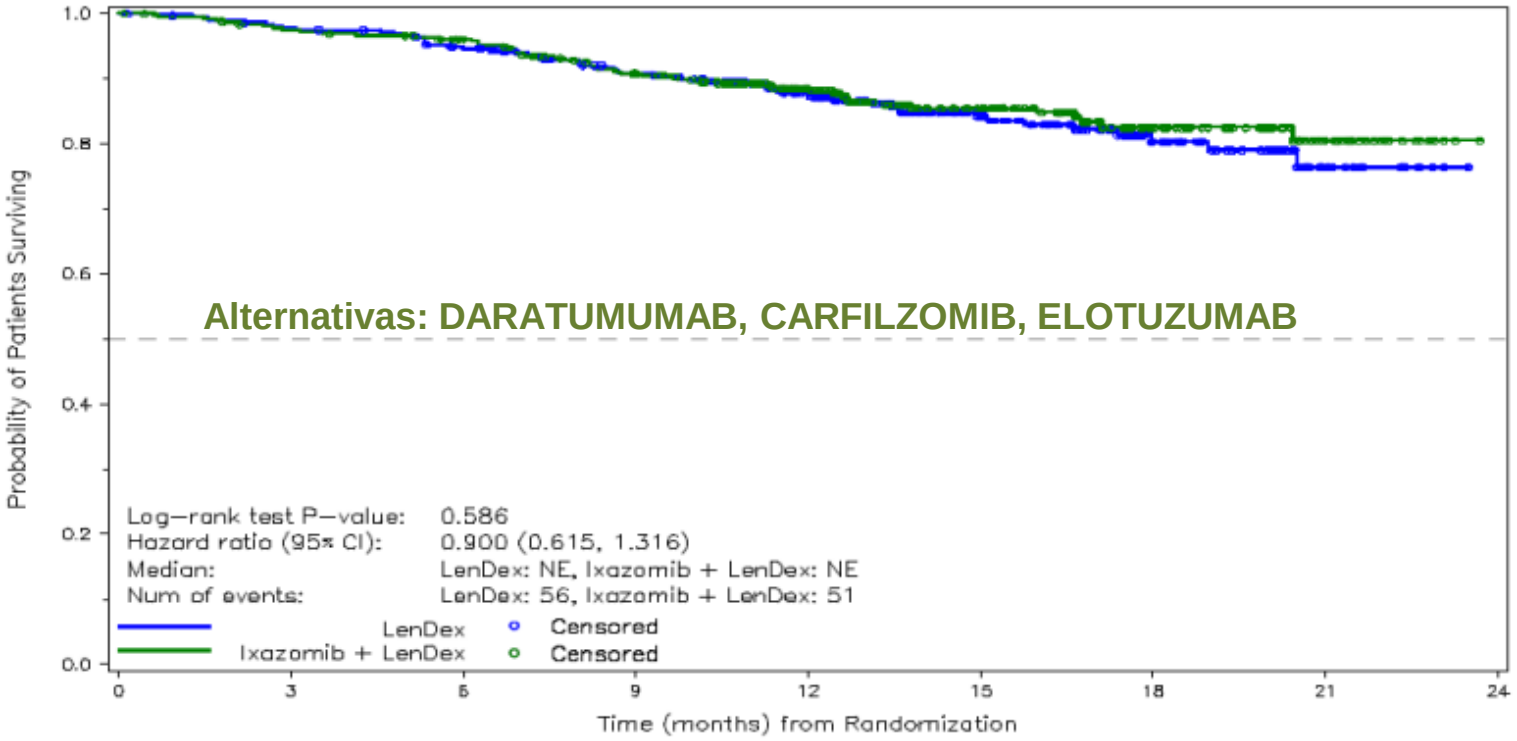
LenDex	362	347	333	314	300	289	275	260	245	235	218	205	194	180	170	157	144	139	128	112	99	80	69	56	44
Ixazomib + LenDex	360	346	336	318	303	287	281	263	254	246	233	223	210	198	190	181	174	166	158	140	119	93	84	74	62

LenDex	36	23	16	12	6	2	0	0	0																
Ixazomib + LenDex	50	37	24	20	14	7	4	0	0																

Secondary endpoint: Overall survival

As of 30 October 2014, the 18-month survival rate was 83% in the ixazomib regimen and 80% in the placebo (**Figure 10**).

Figure 10. Kaplan-Meier Plot of Overall Survival—ITT Population (Study C16010) (cut-off 30 October 2014)



Number of Patients at Risk

LenDex	362	351	333	303	230	145	79	18	0
Ixazomib + LenDex	360	347	333	304	230	152	81	28	0

R/0003	Renewal of the marketing authorisation.	20/07/2017	18/09/2017	SmPC, Annex II, Labelling and PL	The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for NINLARO, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.

No se aporta confirmación de beneficio significativo en SLP

Figure 4. An overview of conditional marketing authorisations granted by the year of authorisation and current status

"Real World" Data on the Efficacy and Safety of Ixazomib in Combination with Lenalidomide and Dexamethasone in Relapsed/Refractory Multiple Myeloma: A Combined Study from the Greek, Czech and UK Databases

Evangelos Terpos, Nadjoua Maouche, Jiri Minarik, Eirini Katodritou, Matthew W Jenner, Hana Plonkova, Maria Gavriatopoulou, Grant Vallance, Tomas Pika, Maria Kotsopoulou, Jaimal Kothari, Tomas Jelinek, Eftathios Kastritis, Robin Aitchison, Meletios A. Dimopoulos, Karthik Ramasamy, and Roman Hajek

Blood 2017 130:3087;

"la mediana de seguimiento de los pacientes fue de 9,1 meses"

"la mediana de SLP para el total de pacientes fue 27,6 meses (95% CI: 11.3-27.6). (en el ECA fue 18.8 meses)

Conclusión

"Nuestros resultados corroboran los datos del ensayo clínico en un escenario de "Mundo Real" y sugieren que ILd es una opción oral atractiva en mieloma múltiple en recaída o refractario"

"los pacientes con exposición previa limitada y ASCT parecen beneficiarse más del régimen Ild".

Sin embargo…

¿Cómo se hace inferencia causal en un estudio descriptivo?

¿Cómo analiza el beneficio por subgrupos?

Carecemos de la curva K-M y los pacientes a riesgo

Estudio de SLP extremadamente inmaduro: mediana de 27 meses estimada con sólo 9 meses de seguimiento ?!

ESTUDIO DESCRIPTIVO: ¿muestra el beneficio REAL?

1,5 años despues…

- Ixazomib no está financiado en España
- Por tanto, la aprobación condicionada, en lugar de esperar a confirmar los datos, no ha facilitado su acceso (y probablemente es mejor así)
- Por desgracia, seguimos sin datos confirmatorios del beneficio en SLP, a pesar de lo cual se sigue renovando la autorización
- Los “RWD” (estudios descriptivos en este caso) no pueden aportar la certidumbre sobre el beneficio que el ECA no aporta.

Introducción de un nuevo medicamento en la práctica clínica

EMA

"Fast Track"

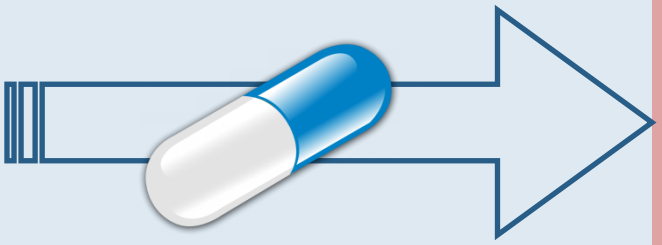
aprobación EMA

financiación SSP

CIMP

IPT

medicamento en investigación



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uso compasivo

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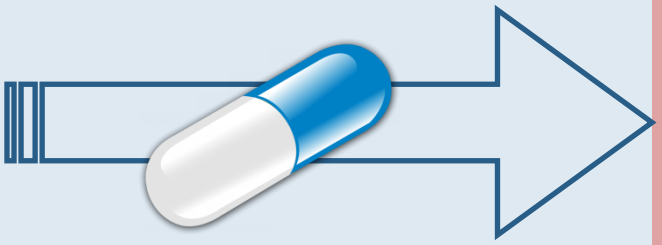

CIMP

IPT

Comisiones
-locales
-regionales

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estudios observacionales "RWD"

-----información-----

-------promoción-------

uso del fármaco

uso compasivo

ensayos clínicos

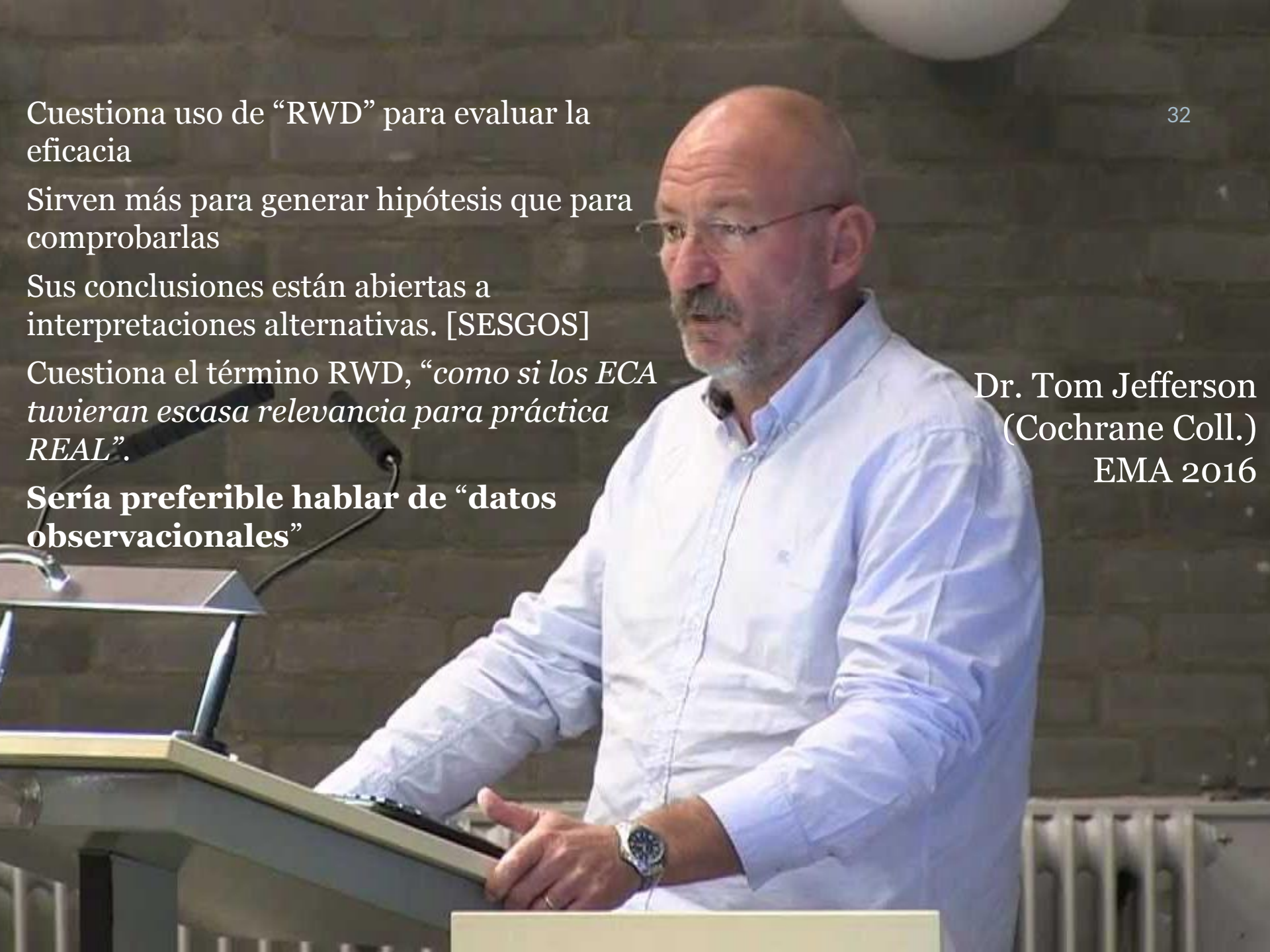
Cuestiona uso de “RWD” para evaluar la eficacia

Sirven más para generar hipótesis que para comprobarlas

Sus conclusiones están abiertas a interpretaciones alternativas. [SESGOS]

Cuestiona el término RWD, “*como si los ECA tuvieran escasa relevancia para práctica REAL*”.

Sería preferible hablar de “datos observacionales”



Dr. Tom Jefferson
(Cochrane Coll.)
EMA 2016

“Real World” Data

Reciente EUFEMISMO para renombrar a los **estudios no experimentales**, con altísima probabilidad de sesgos

La innovación y la 'mente abierta' facilitarán que la FH siga latiendo más allá del 2020

■ Big Data y Real World Evidence son dos claves para el progreso y para planificar e investigar aspectos desconocidos

Sanofi organizó el III Foro de Modernización de los Servicios de Farmacia Hospitalaria.

Temas relacionados:

Big Data - Farmacia Hospitalaria - Farmacoeconomía - Innovación - Inversión en I+D - Investigacion - Pacientes - Horizonte 2020 - Gasto farmacéutico de hospital - RWE - Resultados en salud - Seguridad del Paciente - sanofi - eficiencia - Hospital Clínico San Carlos - Servicio de Farmacia - Hospital Clínico San Carlos - SEFH - SEFH - Sociedad Española de Farmacia Hospitalaria - España - Madrid - Sanofi - Real World Evidence - Sociedad Española - SEFH - Instituto - Farmacia Hospitalaria (SEFH - Farmacia Hospitalaria - big data - Real World Evidence (RWE - Servicios - Nuevas Tecnologías - RWE - gamificacion - III Foro - Farmacia del Hospital Clínico San Carlos - farmacoeconomia - 3D - farmacoepidemiología - Acceso al Mercado - brainstorming - Incliva - Administraciones - Miguel Ángel Calleja - ENRIQUE CAMPILLO - E. CAMPILLO - José Manuel Martínez - Dionisio López - Mª Jesús Alsar - Josep Redon i Mas - José Luis Marco - Investigación - España-- - Madrid - Comunidad Valenciana

+6

ENRIQUE CAMPILLO Madrid | 12 may 2018 - 08:00 h | ElGlobal.net

Los ESTUDIOS OBSERVACIONALES, BIEN HECHOS (cohortes con buen análisis multivariante / índice de propensión) son **muy útiles** para CONFIRMAR y COMPLETAR los ensayos clínicos aleatorizados ⇨ **papel del FH en entorno clínico multidisciplinar**

NO PARA SUSTITUIR LOS ENSAYOS CLÍNICOS ⇨ **papel del FH en evaluación e información** (existe interés comercial en ello para reducir más los requisitos del registro)

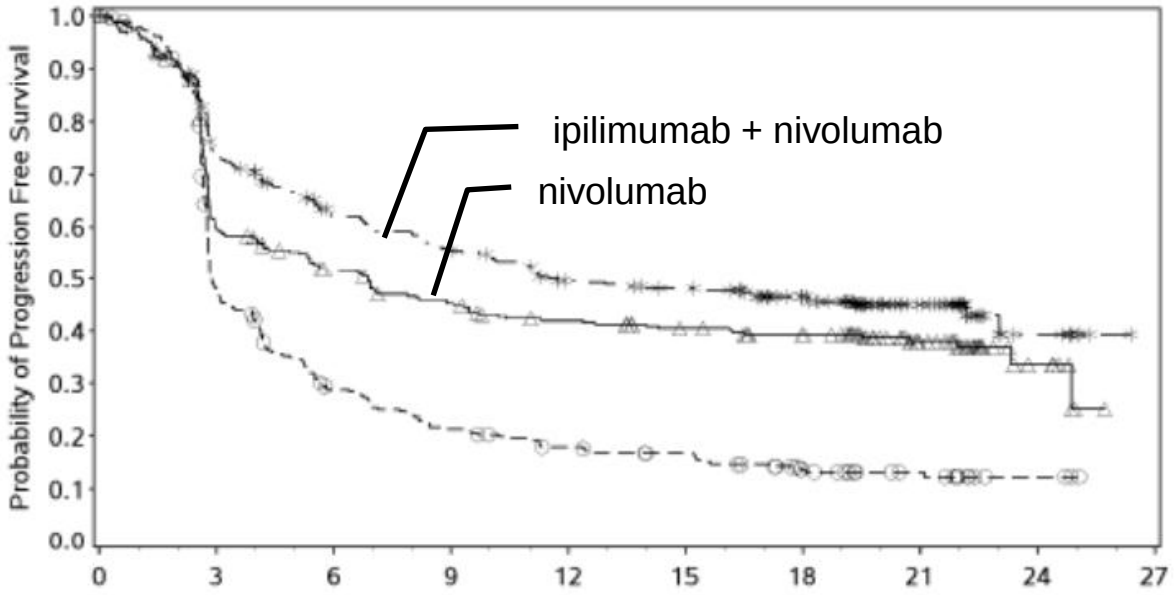
3er ejemplo

El “régimen”

ipilimumab + nivolumab
en melanoma

(nueva indicación)

Figure 9: Kaplan-Meier Plot of Progression Free Survival per Investigator (all randomised subjects) - Study CA209067 (Nov 2015 DBL)



Number of Subjects at Risk

Nivolumab	316	177	148	127	114	104	94	46	8	0
Nivolumab + Ipilimumab	314	219	174	156	133	126	103	48	8	0
Ipilimumab	315	137	78	58	46	40	25	15	3	0

Nivolumab (events: 183/316), median and 95% CI: 6.87 (4.34, 9.46)
Nivolumab + Ipilimumab (events: 161/314), median and 95% CI: 11.50 (8.90, 22.18)
Ipilimumab (events: 245/315), median and 95% CI: 2.89 (2.79, 3.42)

Nivolumab vs Ipilimumab - hazard ratio and 99.5% CI: 0.55 (0.42, 0.73); p-value: <0.0001
Nivolumab + Ipilimumab vs Ipilimumab - hazard ratio and 99.5% CI: 0.42 (0.32, 0.56); p-value: <0.0001
Nivolumab + Ipilimumab vs Nivolumab - hazard ratio and 95% CI: 0.76 (0.62, 0.95)

Symbols represent censored observations.

<10% pacientes se benefician
↑ efectos adversos por la adición de ipilimumab

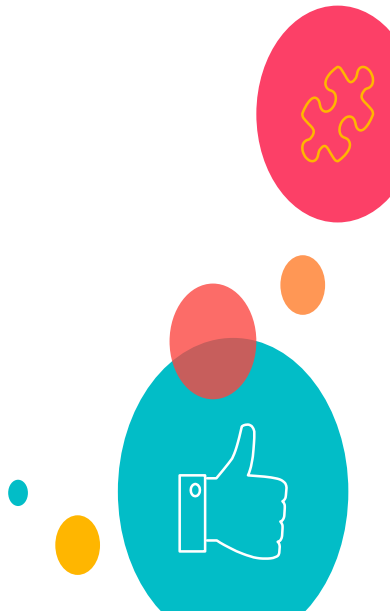
¿efecto sobre supervivencia?

Conduct of the study

The most relevant amendment was the amendment number 6. The study was originally designed with a single primary endpoint of overall survival. The study was modified to have the co-primary endpoints of PFS

and OS. This amendment only changes the statistical analysis plan and did not change the conduct of the study. The rationale to add PFS as co-primary endpoint was the increased number of anti-melanoma therapies, which can be used after progression, impacting on OS. This amendment was introduced after 945 patients were treated. The Amendment number 7 allowed to collect radiographic images in order to carry out a retrospective re-assessment of responses by an independent review of radiologic data. Amendment 8 allowed patients who discontinued study drug to be followed for a collection of outcomes and survival follow up data.

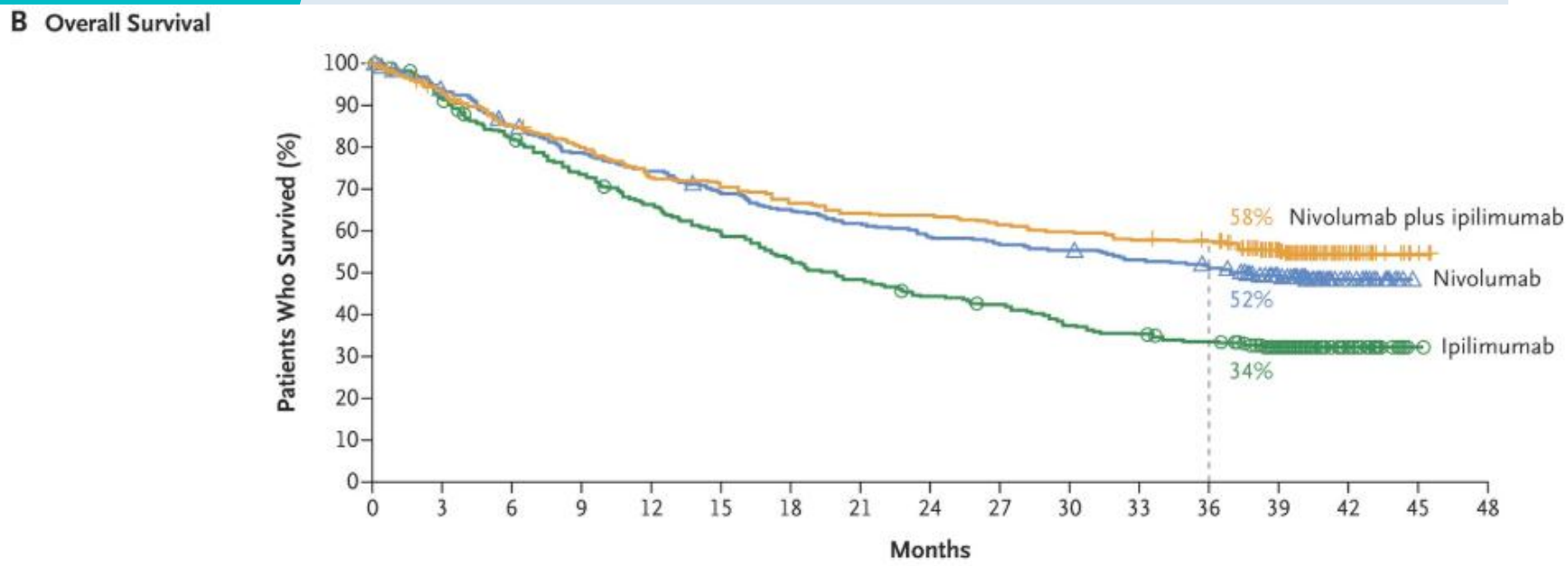
"In terms of OS, the data is not yet mature. More mature data are required and expected by the end 2016 (annex II condition)".



1,5 años más tarde…

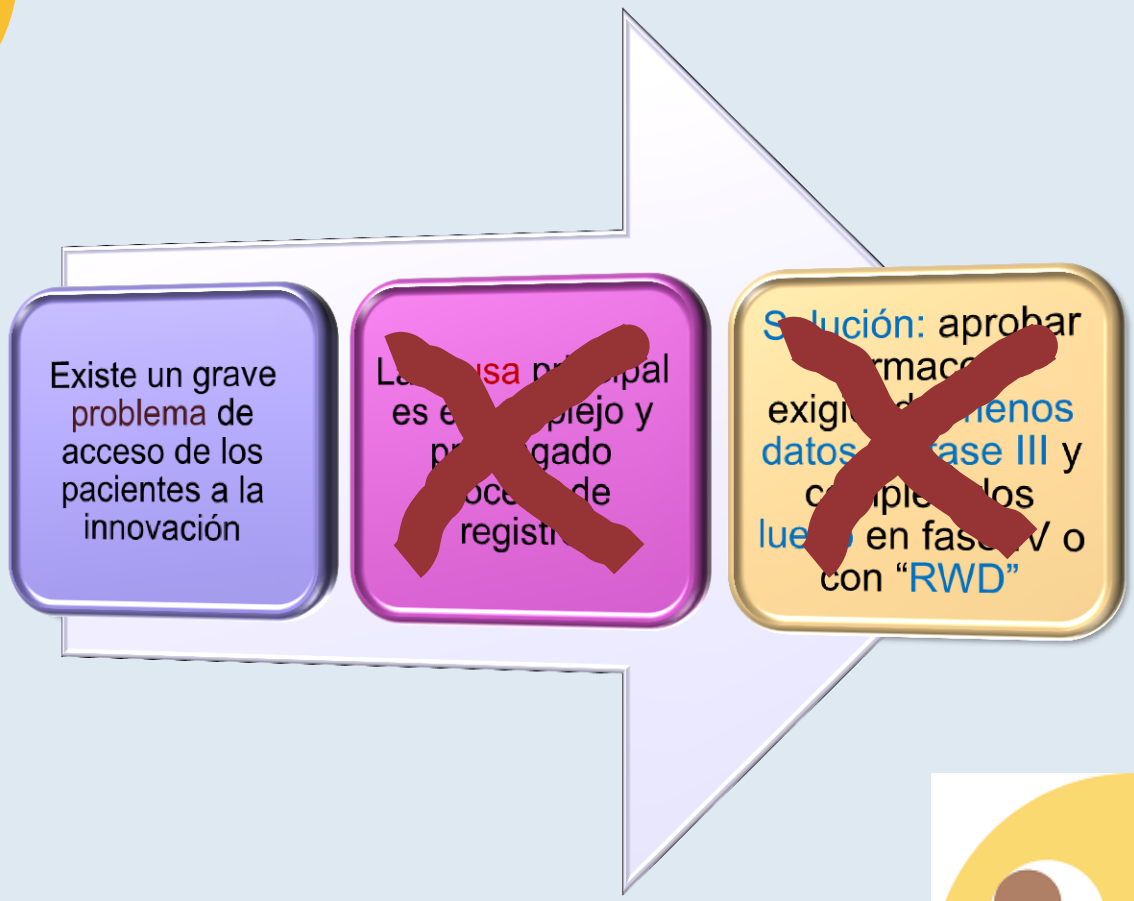
- NEJM

In a descriptive analysis, the hazard ratio for death with nivolumab plus ipilimumab versus nivolumab was **0.85 (95% CI, 0.68 to 1.07).**

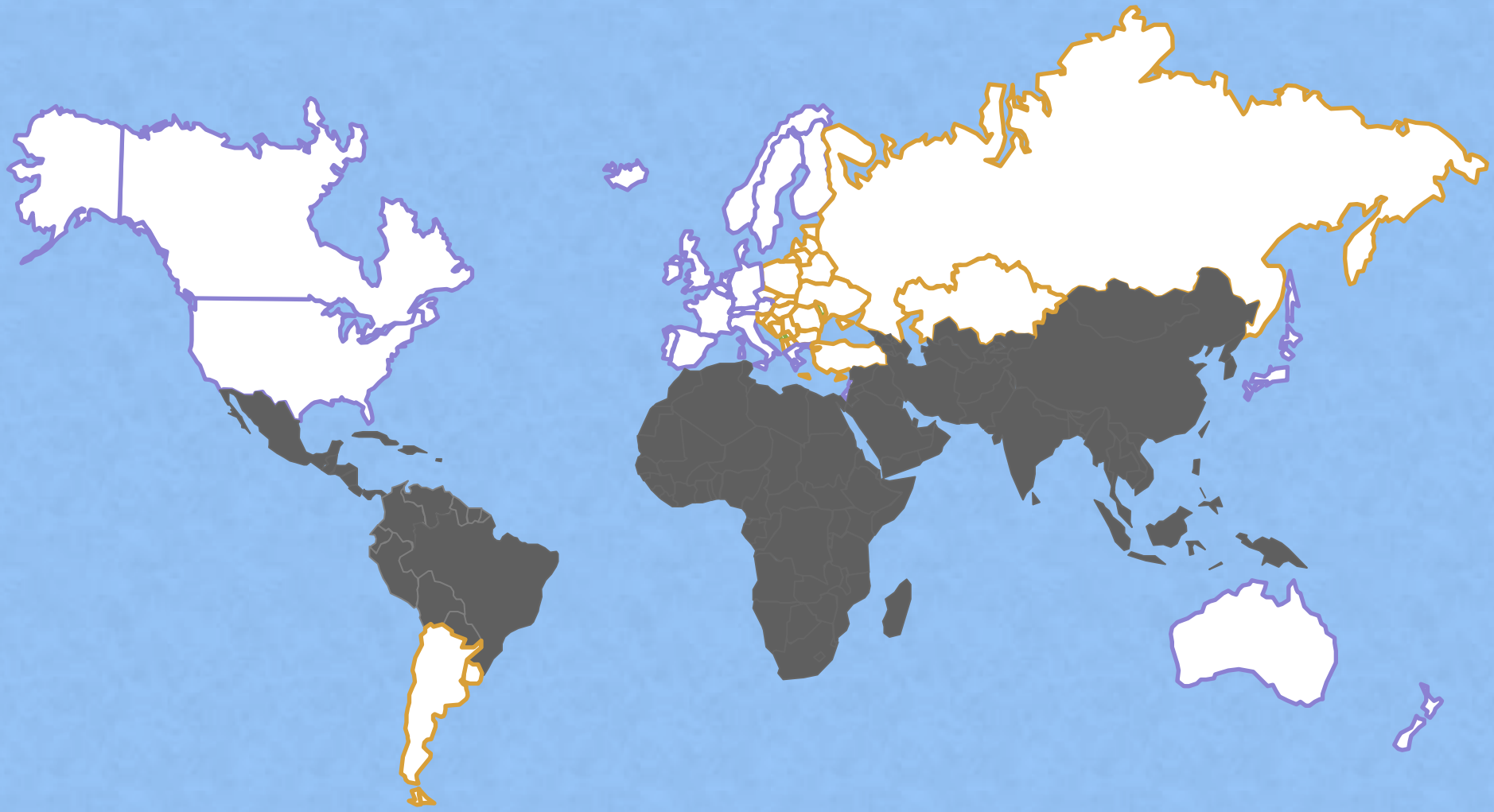


No. at Risk																	
Nivolumab plus ipilimumab	314	292	265	247	226	221	209	200	198	192	186	180	177	131	27	3	0
Nivolumab	316	292	265	244	230	213	201	191	181	175	171	163	156	120	28	0	0
Ipilimumab	315	285	253	227	203	181	163	148	135	128	117	107	100	68	20	2	0

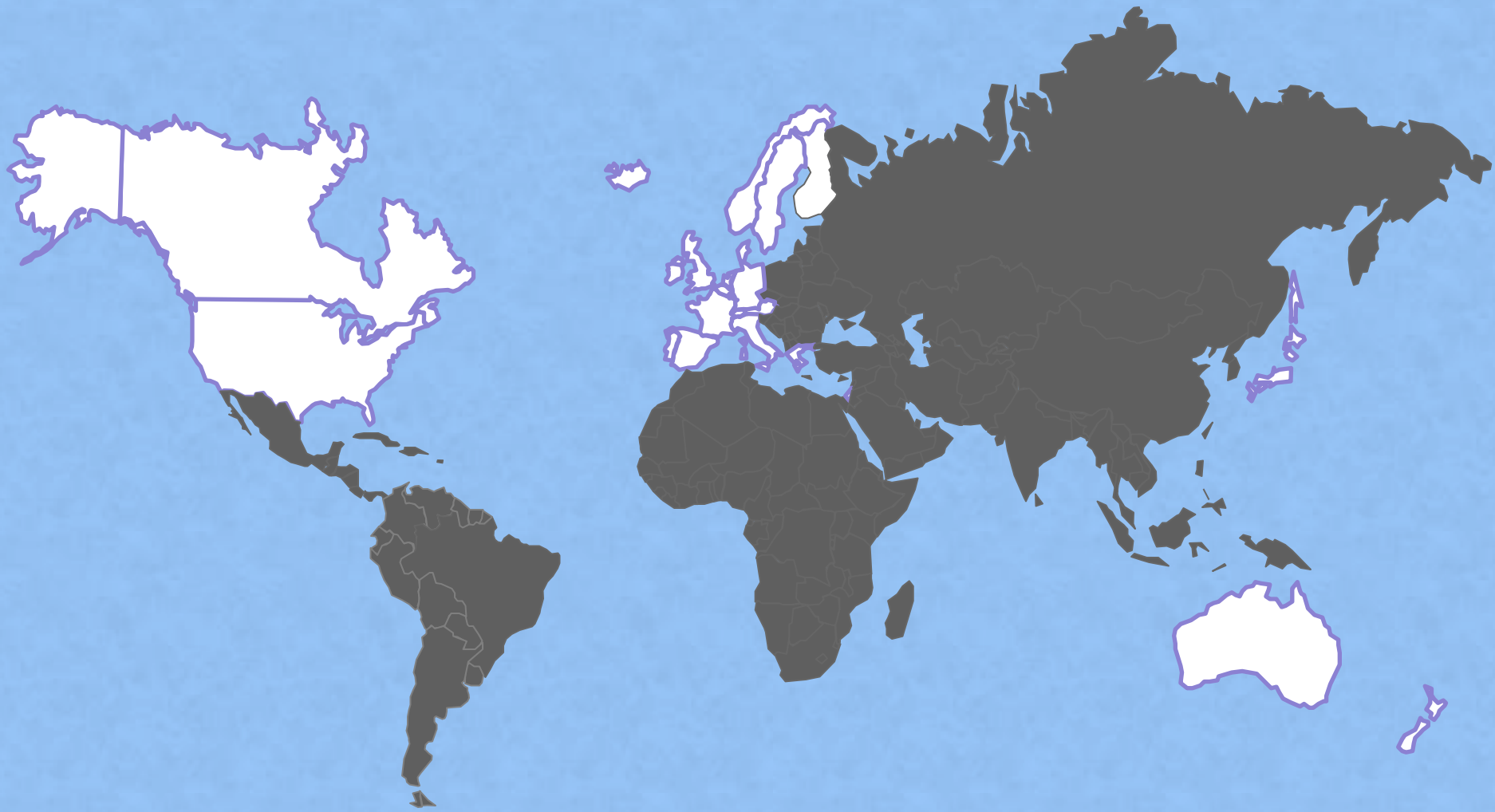
Marco conceptual…



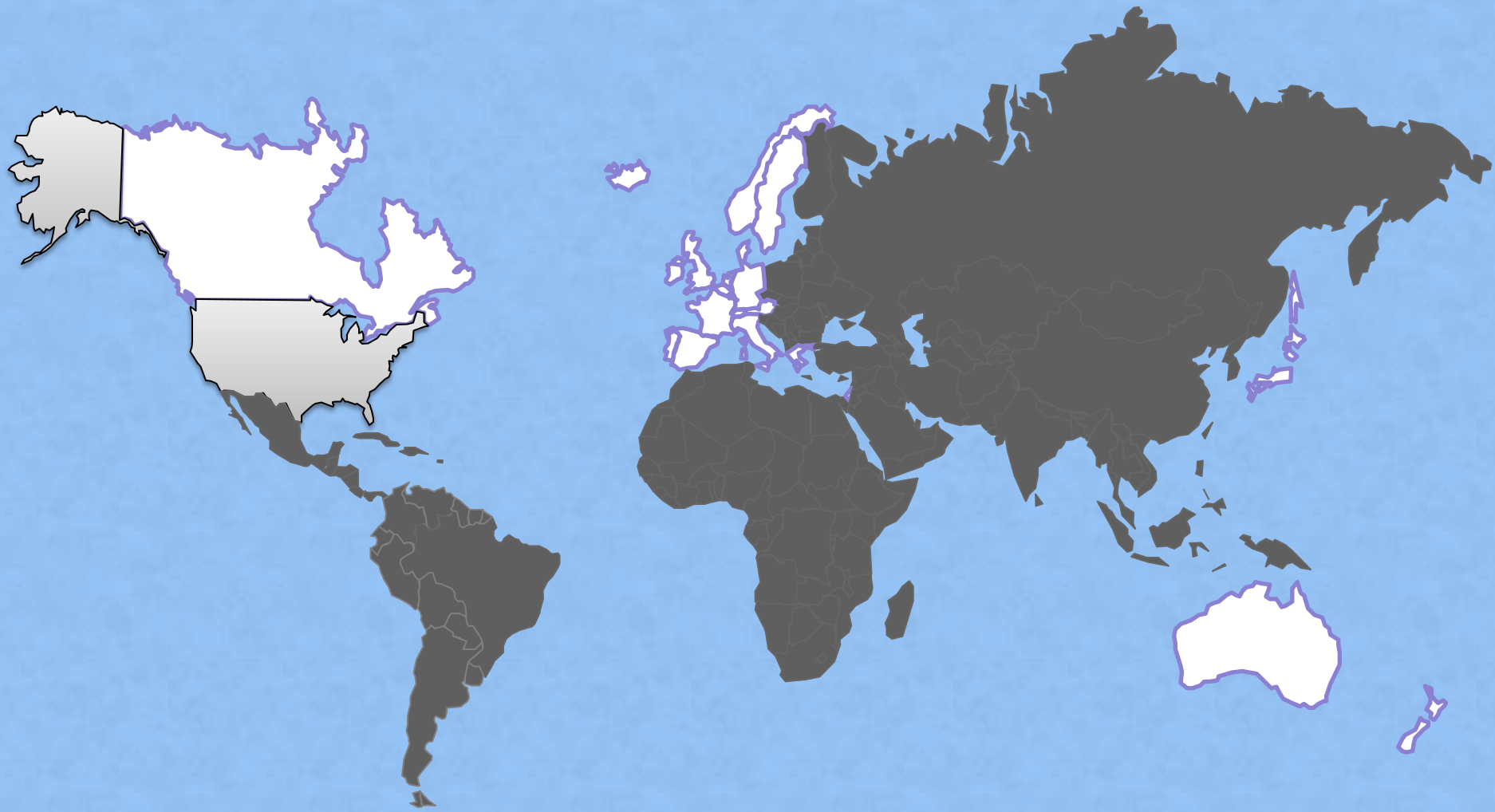
Acceso de los PACIENTES a los nuevos medicamentos (1)



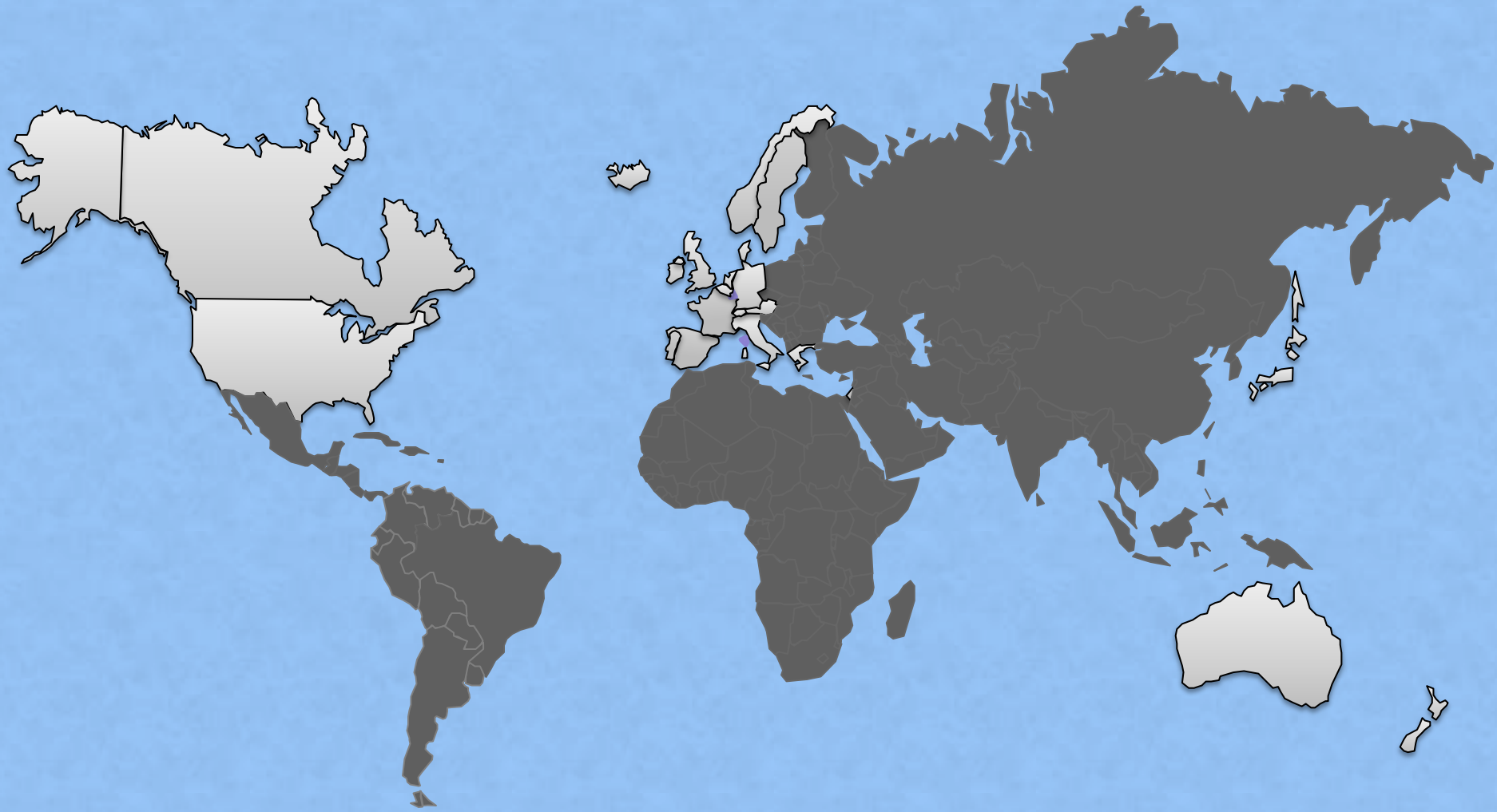
Acceso de los PACIENTES a los nuevos medicamentos (2)



Acceso de los PACIENTES a los nuevos medicamentos (2)



Acceso de los pacientes a los nuevos medicamentos (3)



VIDA SANA

Los oncólogos advierten de la carrera "insostenible" del precio de los medicamentos

Publicado el 11 de Septiembre de 2017 - 14: 24

CRISTINA CASTRO

EP

"Cada vez tenemos más medicamentos contra el cáncer, pero cada vez cuestan más y en algún punto esto se va a volver insostenible", ha advertido el presidente electo de la Sociedad Europea de Oncología Médica (ESMO), Josep Tabernero, durante el encuentro que reúne estos días en Madrid a 24.000 profesionales sanitarios relacionados con el cáncer.

¡Gracias!

¿alguna pregunta?