III Post-ASCO Pulmón GIDO
Valencia
21 de Junio 2016

2016 ASCO ANNUAL MEETING
COLLECTIVE WISDOM

#ASCO16

Qué va a cambiar ASCO 2016 en la clínica?

Bartomeu Massutí

ALACANT HOSPITAL GENERAL DEPARTAMENT DE SALUT

Fundación FISABIO Instituto de Investigación Sanitaria y Biomédica de Alicante ISABIAL

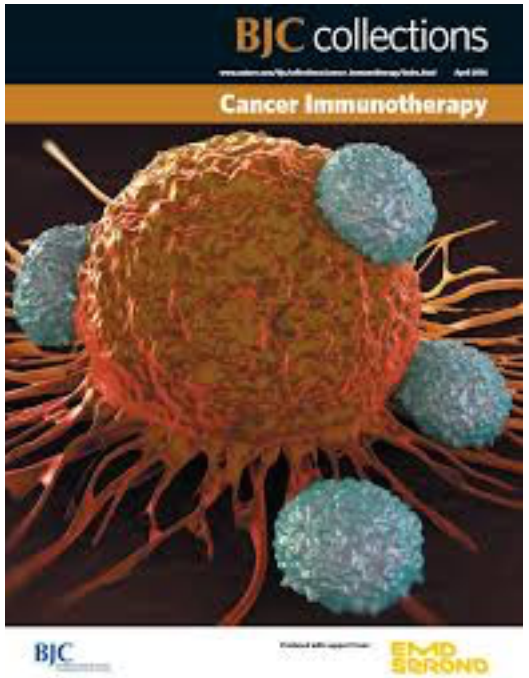
UNIVERSITAS Miguel Hernández

GIDO grup de investigació i divulgació en oncologia

GECP Grupo Español de Cáncer de Pulmón Spanish Lung Cancer Group www.gecp.org


Science
20 December 2013 | $10
Breakthrough of the Year
Cancer Immunotherapy
T cells on the attack
AAAS


nature
THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE
Antitumour immunity enhanced by inhibiting PD-L1/PD-1 and identifying mutant neo-antigens
PAGES 486, 558, 563, 568, 572 & 577
IMMUNE-CHECKPOINT BLOCKADE IN CANCER
PEER REVIEW
ACCEPT YOUR OWN PAPER
How some scientists are duping the system
PAGE 486
MICROSCOPY
THE CASE FOR AIMING HIGHER
Atomic resolution is there for the taking
PAGE 487
ENERGY
'NIGHT-TIME' COOLING BY DAY
New materials enable radiative cooling in sunlight
PAGE 540
NATURE.COM/NATURE
27 November 2014 £10
Vol. 515, No. 7528


BJC collections
Cancer Immunotherapy
BJC
EMD SERONO


FEDERAL RESERVE NOTE
THE UNITED STATES OF AMERICA
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L 34782272 B
WASHINGTON, D.C.
ONE DOLLAR

APRIL 4, 2016

TIME

What if your immune system could be taught to kill cancer?

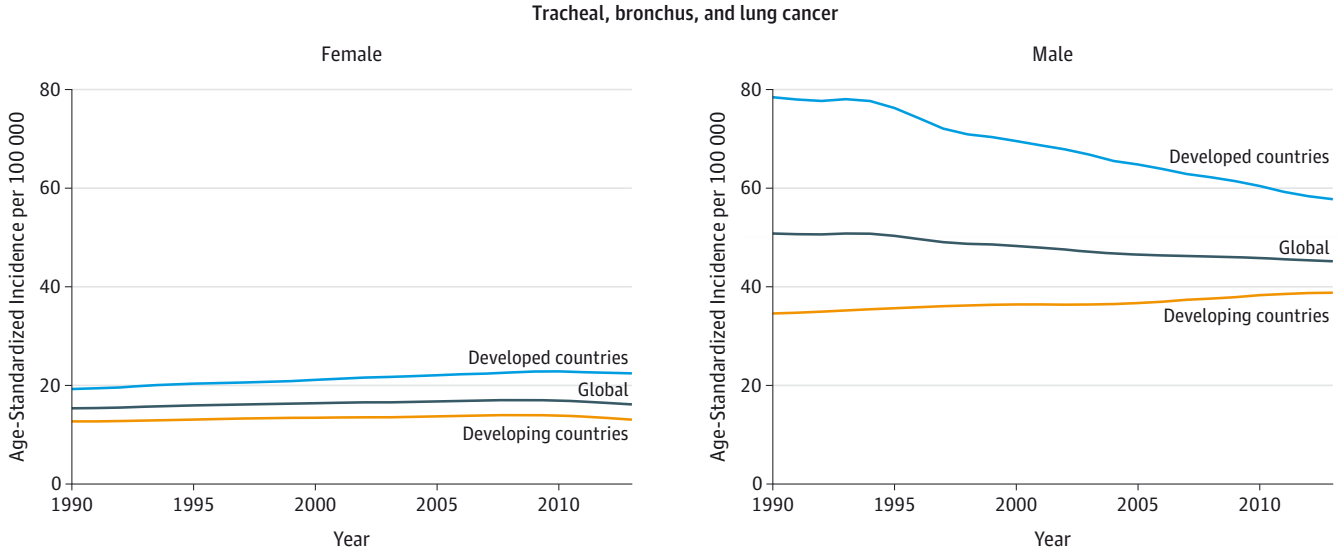
Inside the brutally selective, hugely expensive, lifesaving trials of immunotherapy.

By Alice Park

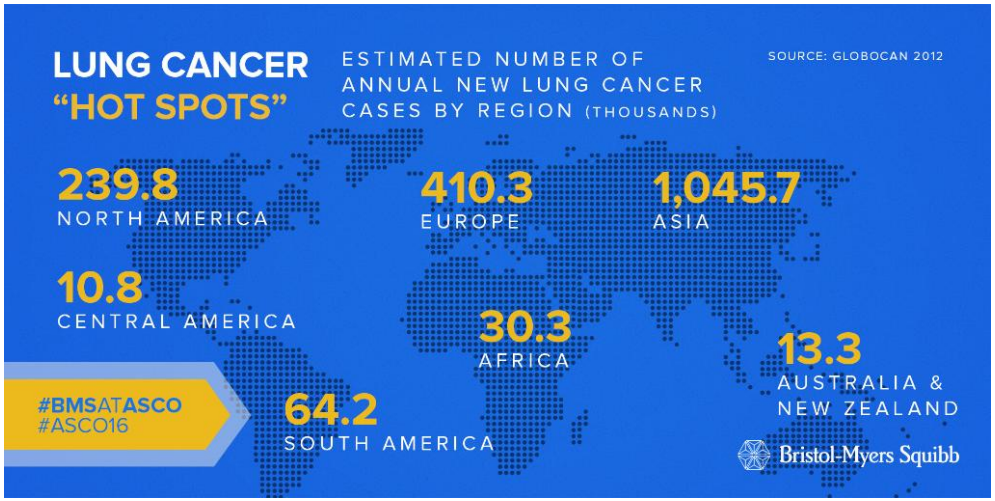
time.com

Tendencias en incidencia Cáncer Broncopulmonar 1990-2013

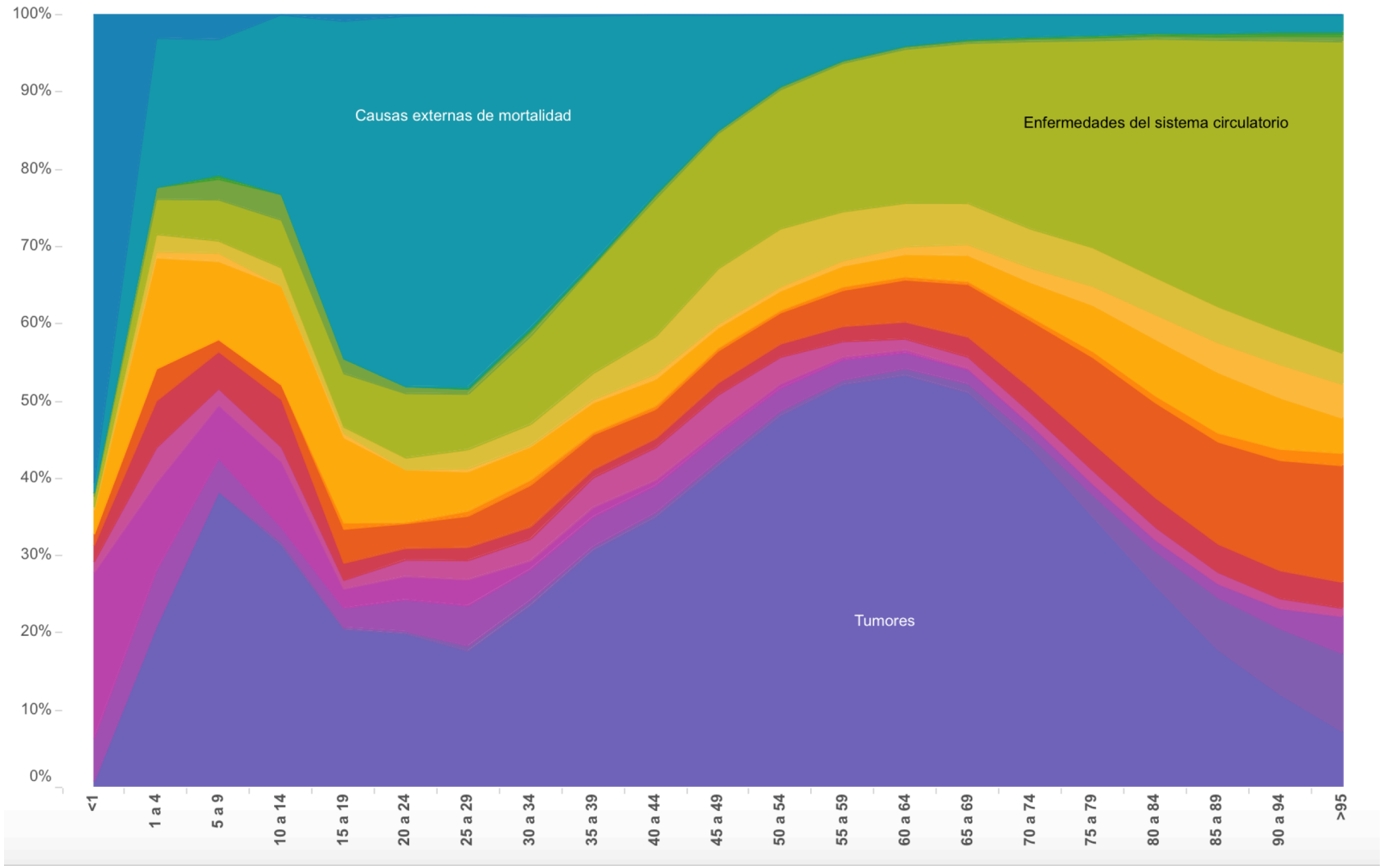
JAMA Oncol. doi:10.1001/jamaoncol.2015.0735 Published online May 28, 2015.



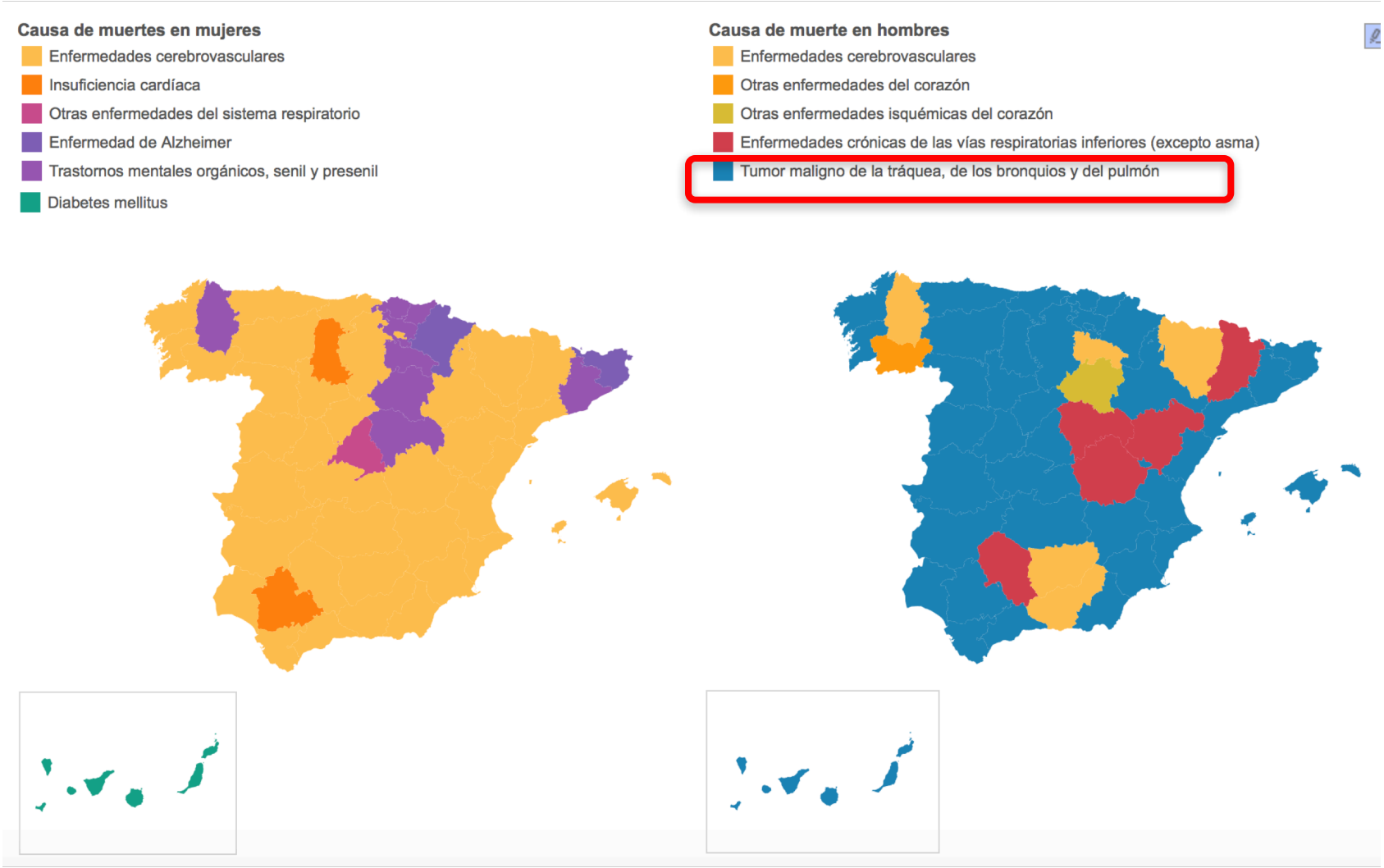
En 1990 y en 2013 el cáncer broncopulmonar continua siendo la primera causa de YLLs con un incremento absoluto del 39.2% pero con una reducción del 17.9% en las tasas ajustadas por edad



Causas de muerte España 2014

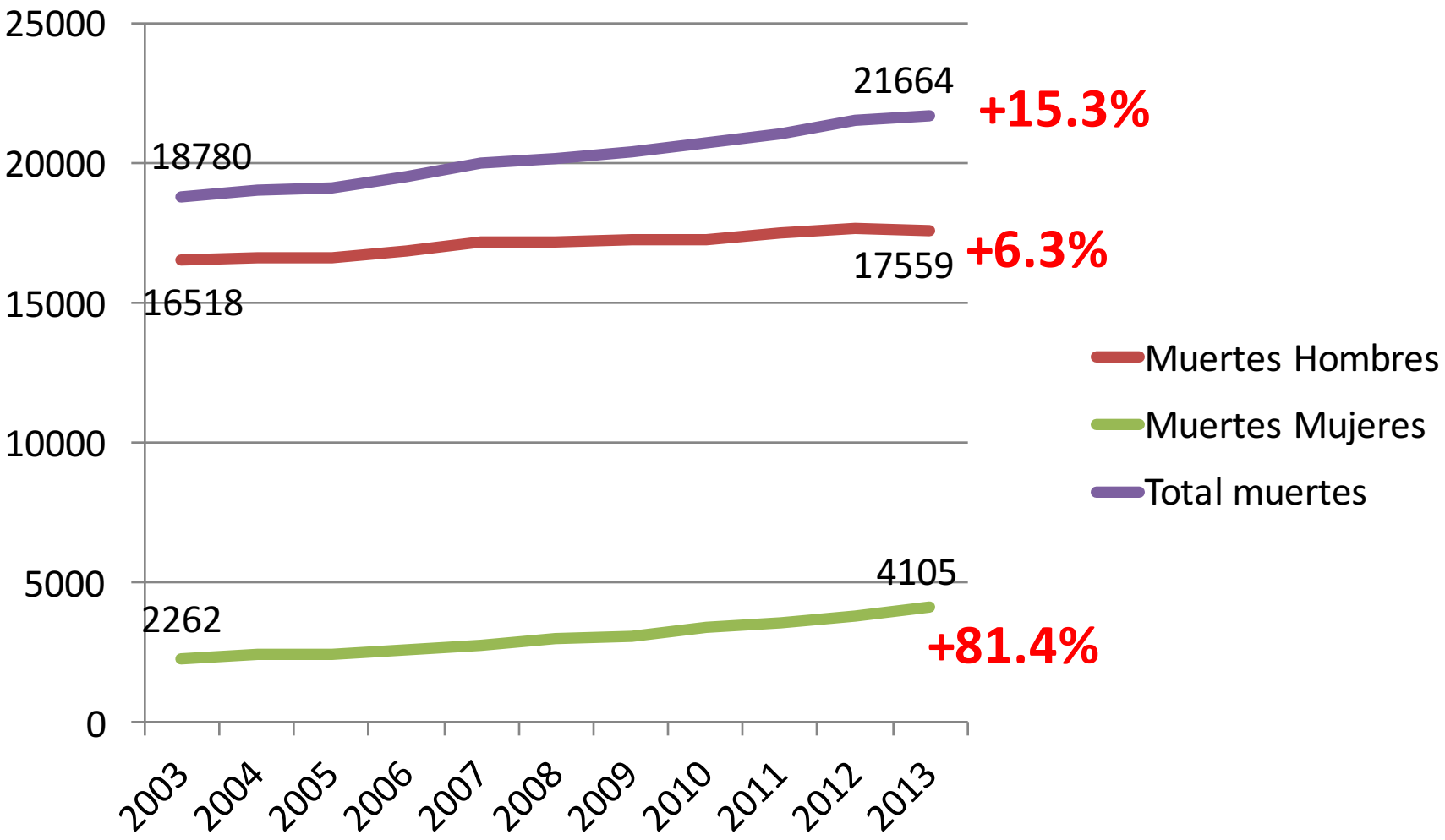


Primera causa de muerte: provincia y sexo

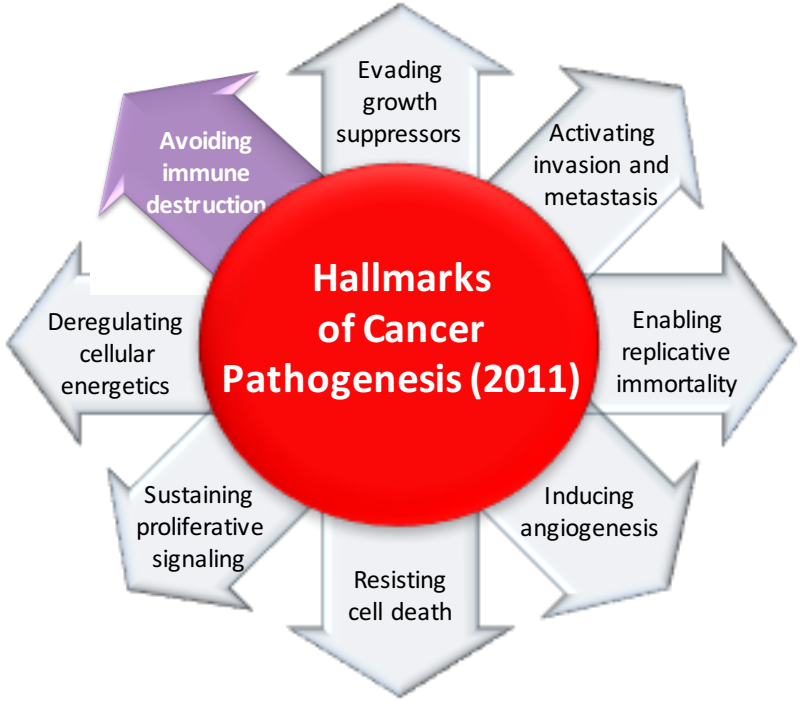


Epidemiología del cáncer de pulmón en España

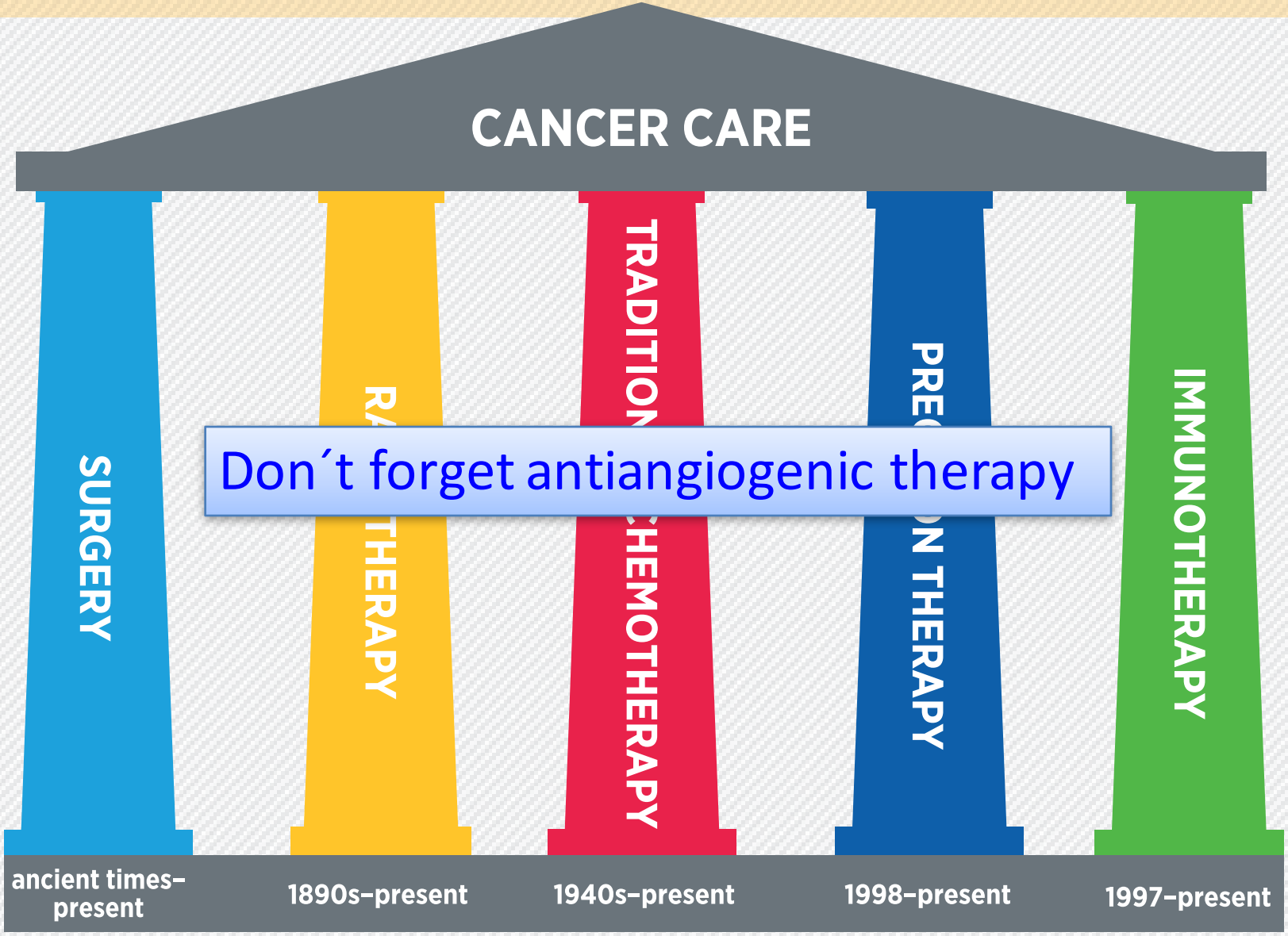
Evolución de la mortalidad por cáncer de pulmón (2003-2013). Fuente: INE



Carácterísticas de la transformacion maligna y potenciales áreas terapéuticas



MORE OPTIONS FOR CANCER CARE



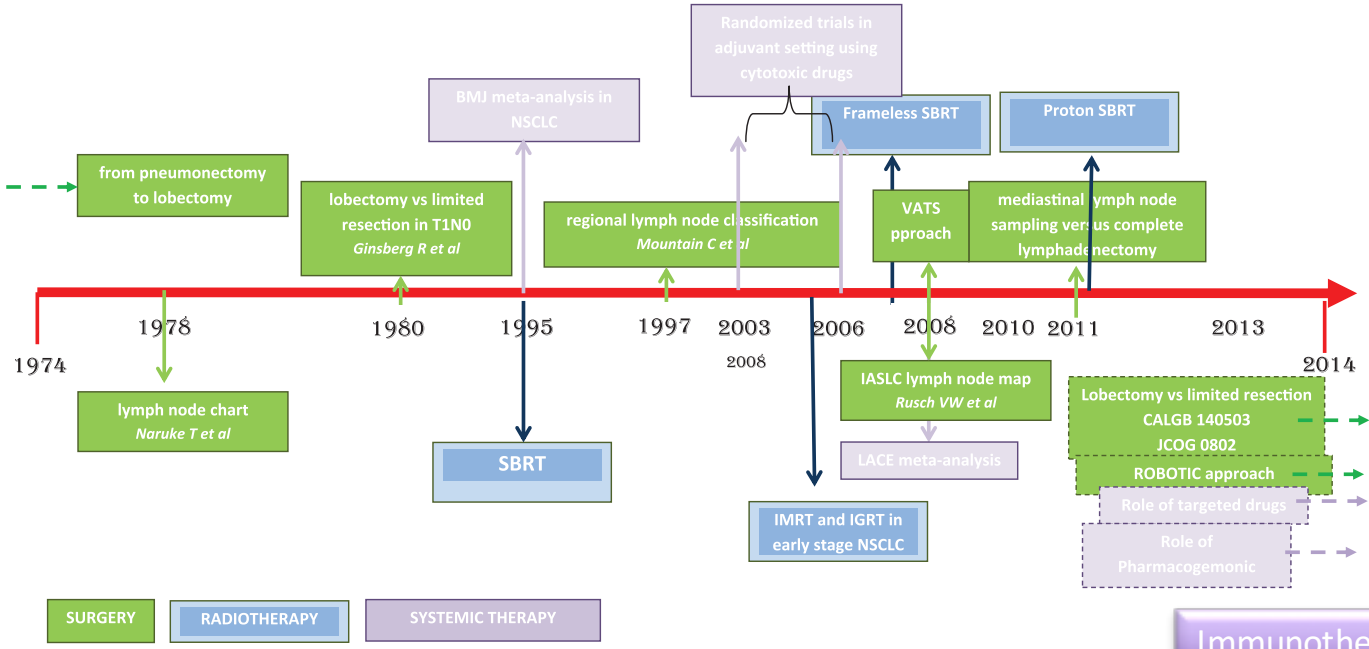
Prevención

Prevención primaria: tabaco vs Prevención secundaria

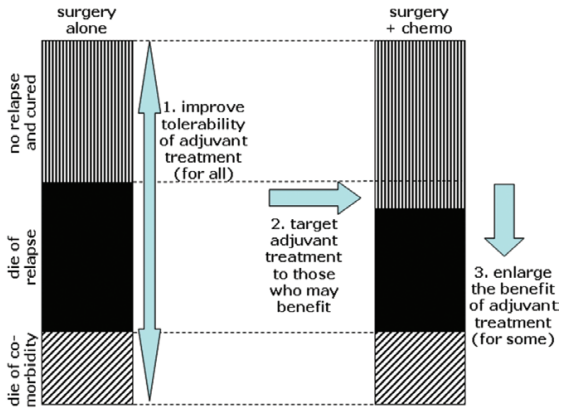
Cribado	Cáncer	Tasa falsos positivos	VPP del Cribado	NNS (episodios cribado para prevenir una muerte)
CT bajas dosis	Pulmon	23%	4%	900
Mamografía	Mama	4%	18%	1200
SOH	Colorrectal	2%	10%	1100

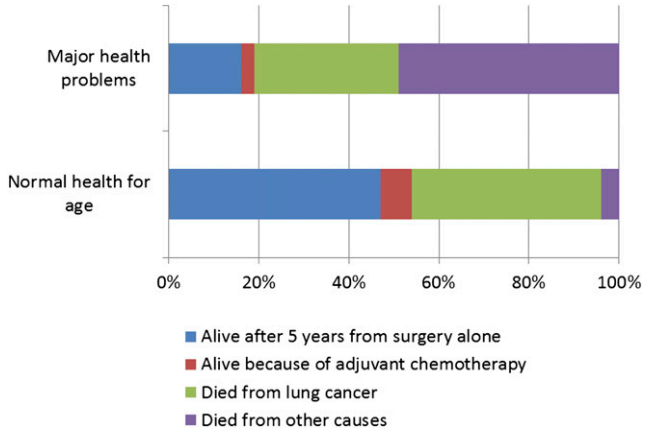
En Europa seguimos esperando a NELSON y al mismo tiempo revisando criterios de caso y procedimientos diagnósticos, evaluación costes
Las medidas antitabáquicas y de deshabituación deben mantenerse

Estadios iniciales



Immunotherapy

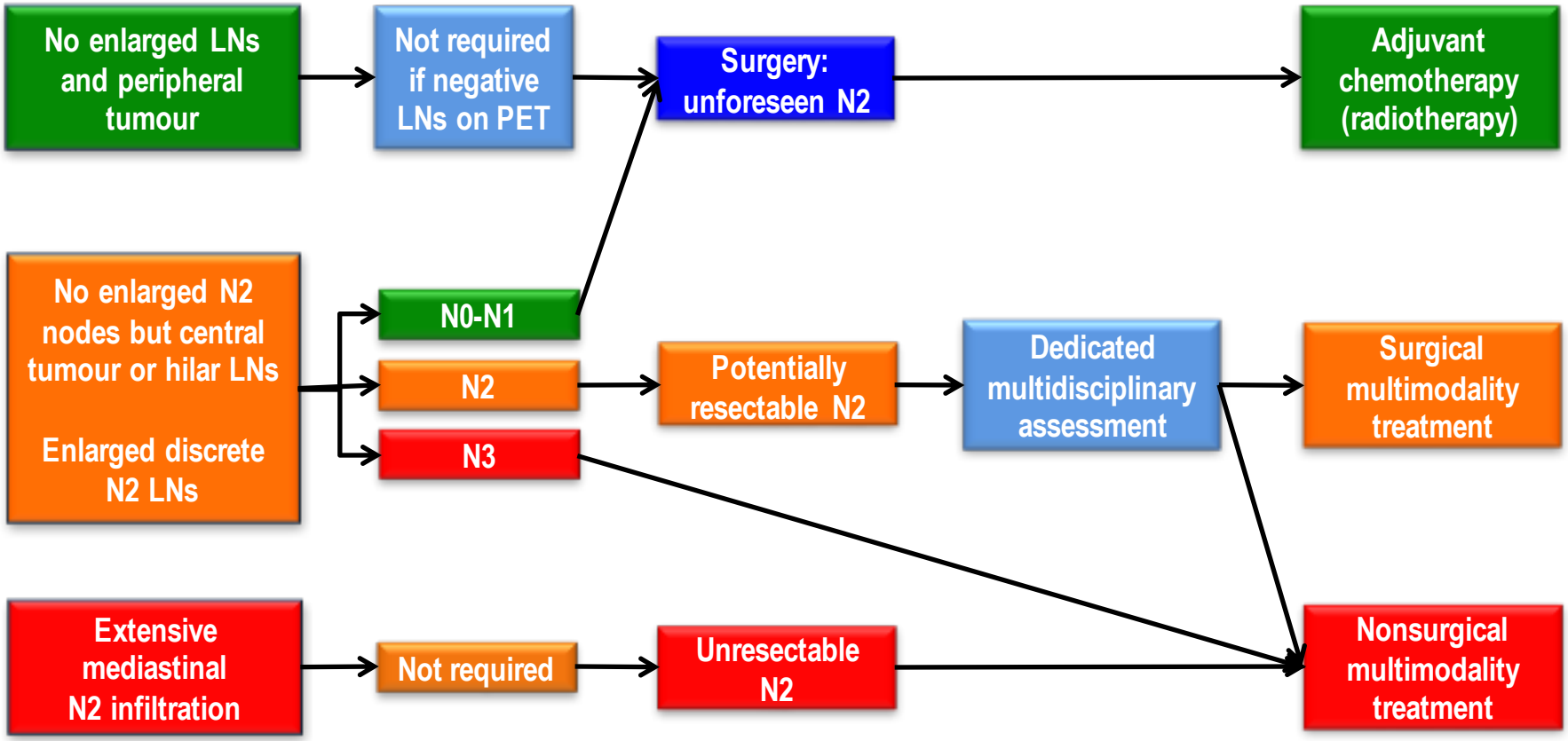




Estadios iniciales ASCO 2016

- QT citotóxica único tratamiento con eficacia demostrada. Tratamientos dirigidos y antiangiogénicos no útiles. Tto con heparina bpm sin impacto
- Expansión e implementación; cumplimiento
- Diferencias biológicas entre la enfermedad inicial y la metastática
- Aprendiendo de los estudios negativos (Silvia Novello)
- Expectativas en la IT (EE CC). Resultados en 2020.

Estadios localmente avanzados

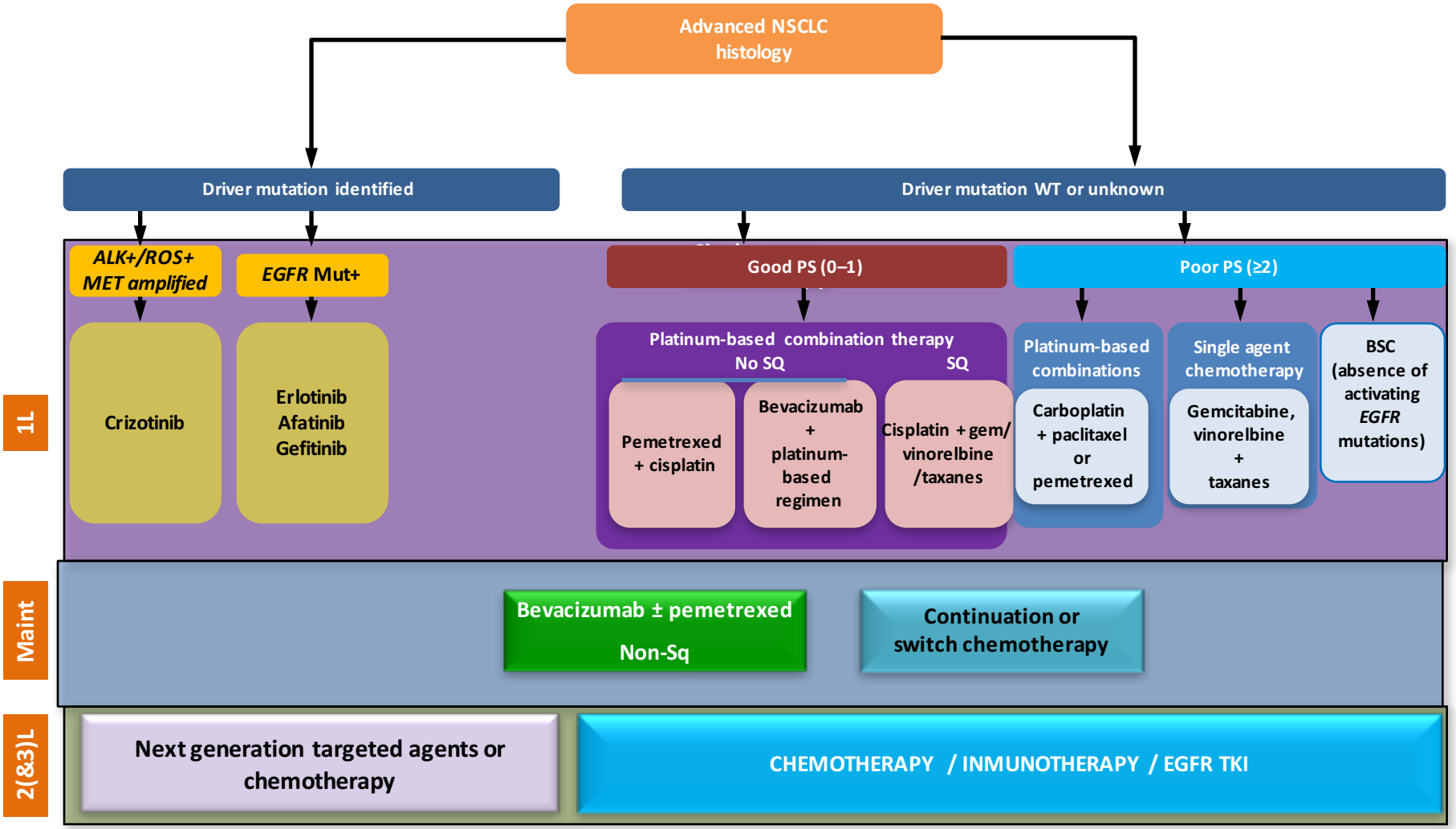


Eberhardt WE, et al. 2nd ESMO Consensus Conference in Lung Cancer: locally advanced stage III non-small-cell lung cancer. Ann Oncol 2015; 26: 1573-88

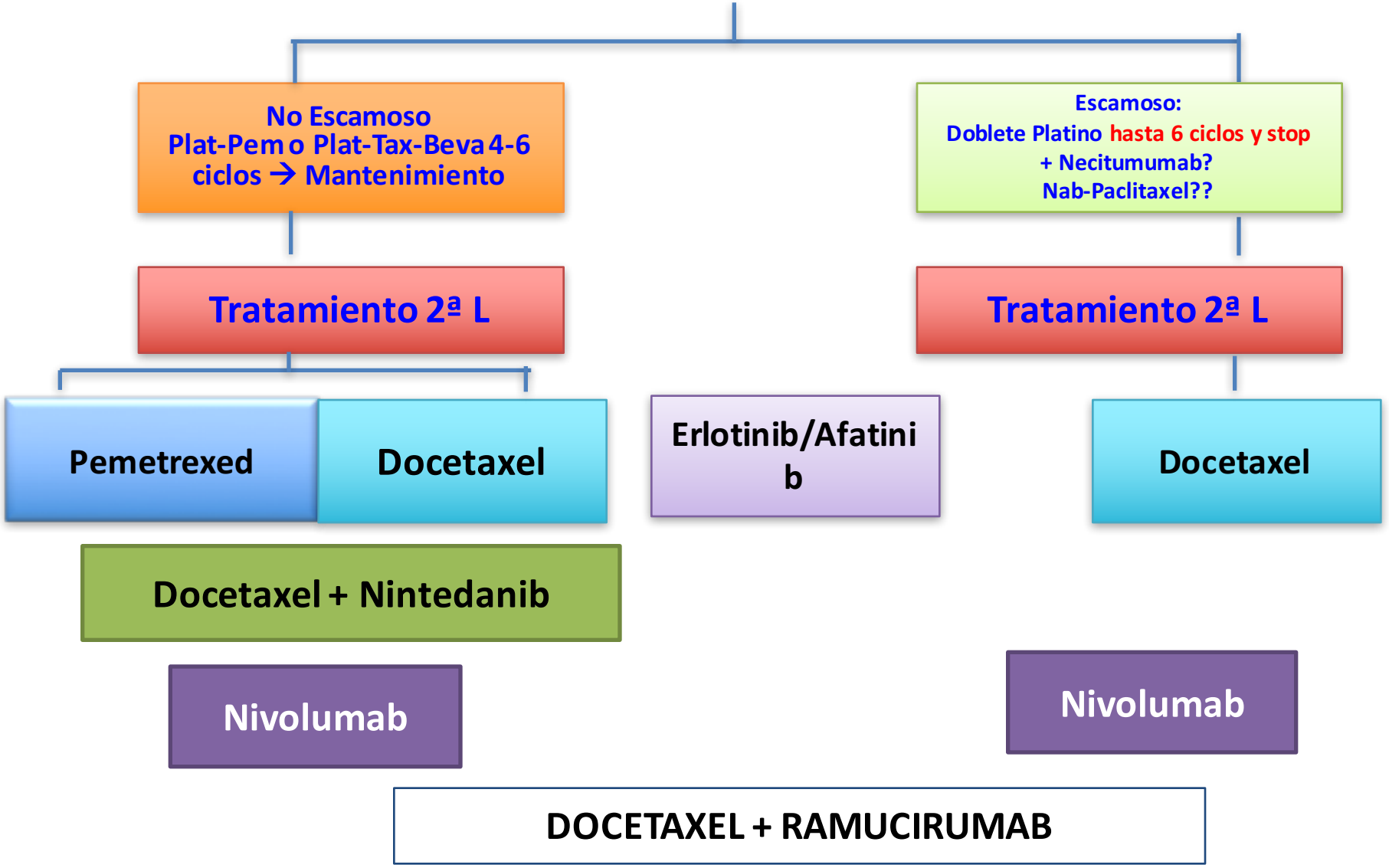
Estadios localmente avanzados: ASCO 2016

- RT con protones?. No a nuestro alcance. Fase III en curso pero comparacion con IMRT NS.
- IMRT para todos (sería deseable). Actualizacion y planificacion tecnología. Controles de calidad?
- QT/RT concomitante como óptimo
- Selección de pacientes. Escalas de valoración geriátrica útiles
- Utilidad del seguimiento y reestadificación periódica
- Dada la heterogeneidad la información sistematizada de ASCO no podrá nunca sustituir la valoración multidisciplinaria de un Comité comprometido

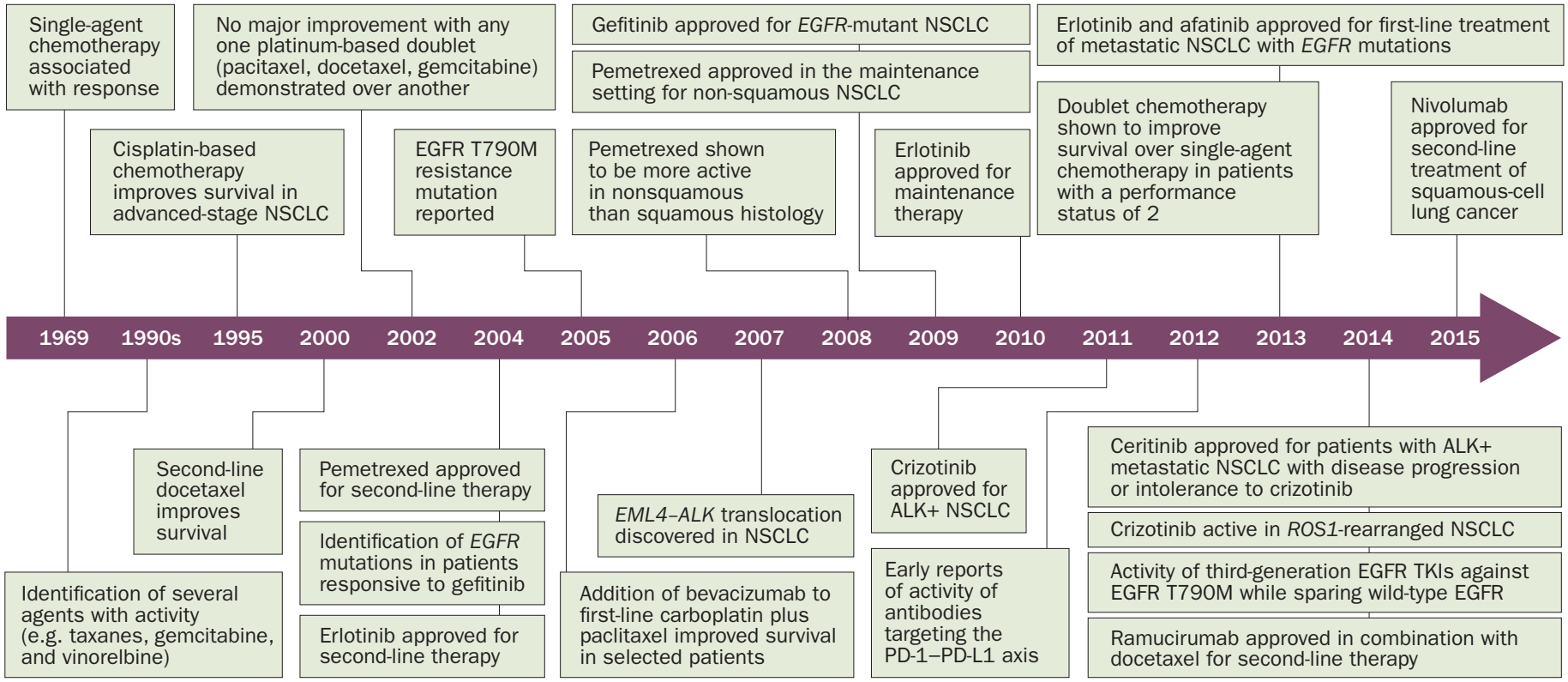
Potential treatment algorithm for advanced NSCLC



Estrategia terapéutica global (CPCNP)
ESTADIO IV



Hitos en el tratamiento sistémico del Cáncer de Pulmón metastático



Estadios avanzados/metastáticos sin mutaciones conductoras tratables: sobrepasando la barrera de 12 meses de supervivencia

- Combinaciones basadas en platino (histología como factor de decisión) en 1ª línea
- Adición de biológicos desde el inicio (Bevacizumab no-escamoso) (Necitumumab o ¿Veliparib? en Escamoso)
- Duración del tratamiento de mantenimiento (tiempo en tratamiento) (pemetrexed/bevacizumab/erlotinib/sunitinib)
- Tratamientos 2ª linea: citotoxicos, erlotinib,afatinib, nindetanib, ramucirumab, selumitinib, ganetespib, **inmunoterapia**)
- PFS vs OS como objetivos primarios. PROs?
- Tratamiento activo de soporte precoz

Estadios avanzados/metastáticos sin mutaciones conductoras tratables: ASCO 2016

- Tratamientos locales en la enfermedad oligometastática (HR 0.36) después de tratamiento QT inducción en pacientes seleccionados
- Paclitaxel semanal + Beva en 2/3 L
- Organizar tratamiento soporte y accesibilidad (via web?) (colaboración con otras especialidades y niveles asistenciales)

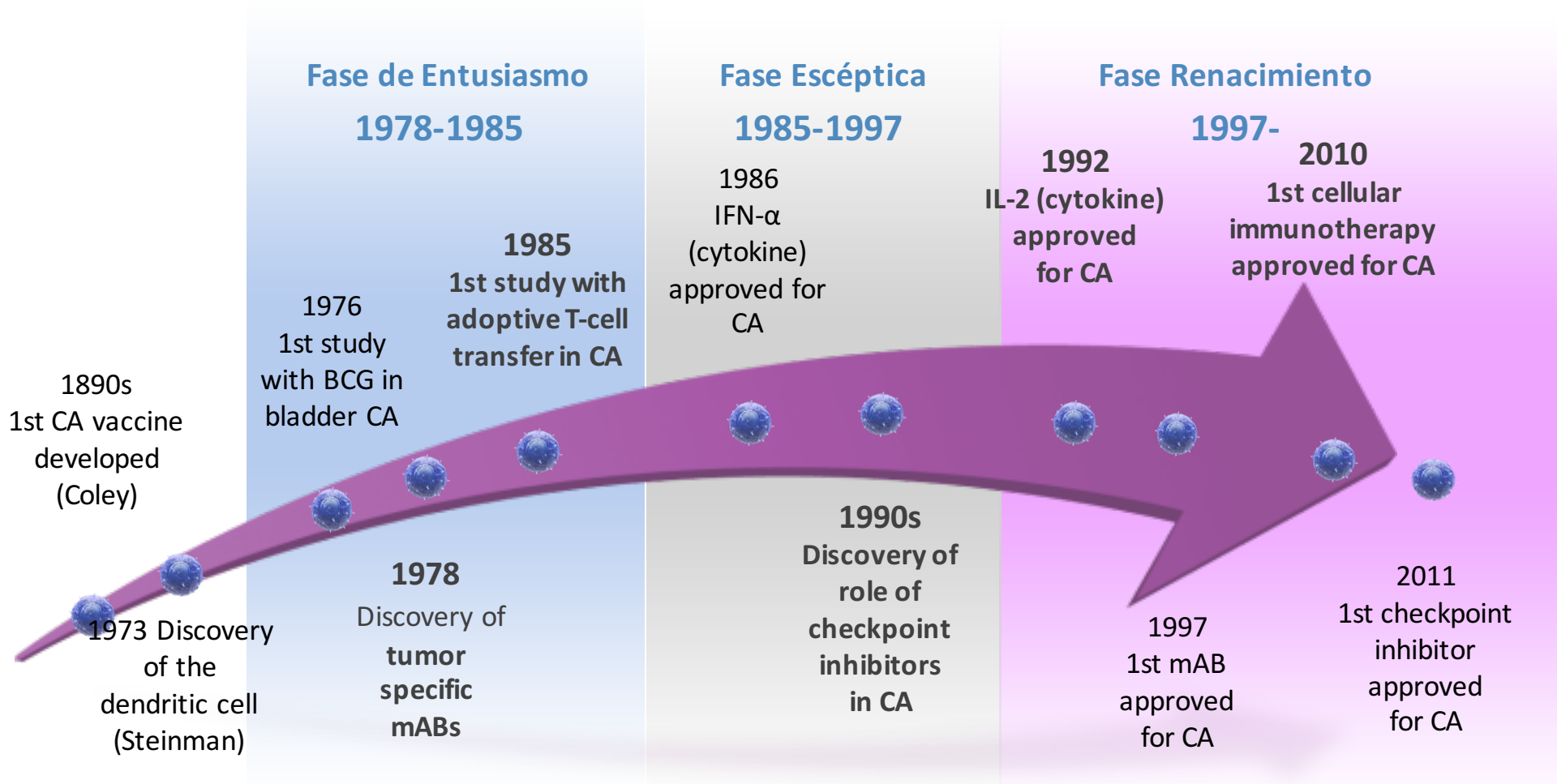
Tratamientos dirigidos a dianas genetico-moleculares

- Dianas tratables: EGFR, ALK, ROS1, BRAF, HER2
- Identificación, procesamiento muestra
- Mecanismos de resistencia
- Líneas sucesivas de tratamientos

Tratamientos dirigidos a dianas genetico-moleculares: ASCO 2016

- Heterogeneidad y biopsia líquida
- NGS / CGS
- EGFR:
  - Rociletinib suspendido desarrollo
  - Olmutinib
  - Osimertinib: eficacia en T790M + y en SNC
  - EC en 1ª línea (pero secuencia?)
- ALK:
  - Alectinib en 1ª linea
  - Brigatinib en 2ª línea
- Resultados en dianas adicionales: RET (Vandetanib) MET (Crizotinib) BRAF (Trametinib+Dabrafenib)

Renacimiento de la Inmunoterapia



Adapted with permission from Lesterhuis WJ, et al[2] and Kirkwood JM, et al. *J Clin Oncol*. 2008;26(20):3445-3455.

BCG, Bacille Calmette-Guerin; mABs, monoclonal antibodies; CA, cancer; IFN-α, interferon alpha; IL-2, interleukin-2

1. Kirkwood JM, Ferrone S, et al. *CA Cancer J Clin*. 2012;62(5):309-335.
2. Lesterhuis WJ, Punt CJ, et al. *Nat Rev Drug Discov*. 2011;10(8):591-600.
3. Krummel MF, Allison JP. *J Exp Med*. 1995;182(2):459-465.
4. Lotze M. In: *Cancer: Principles & Practice of Oncology*. 9th ed. 2011.
5. Leget GA, Czuczman MS. *Curr Opin Oncol*. 1998;10(6):548-551.

Escape from immune control is a hallmark of cancer

Elimination

Cancer immunosurveillance

- **Effective antigen processing/presentation**
- **Effective activation and function of effector cells**
  - e.g. T cell activation without co-inhibitory signals

Equilibrium

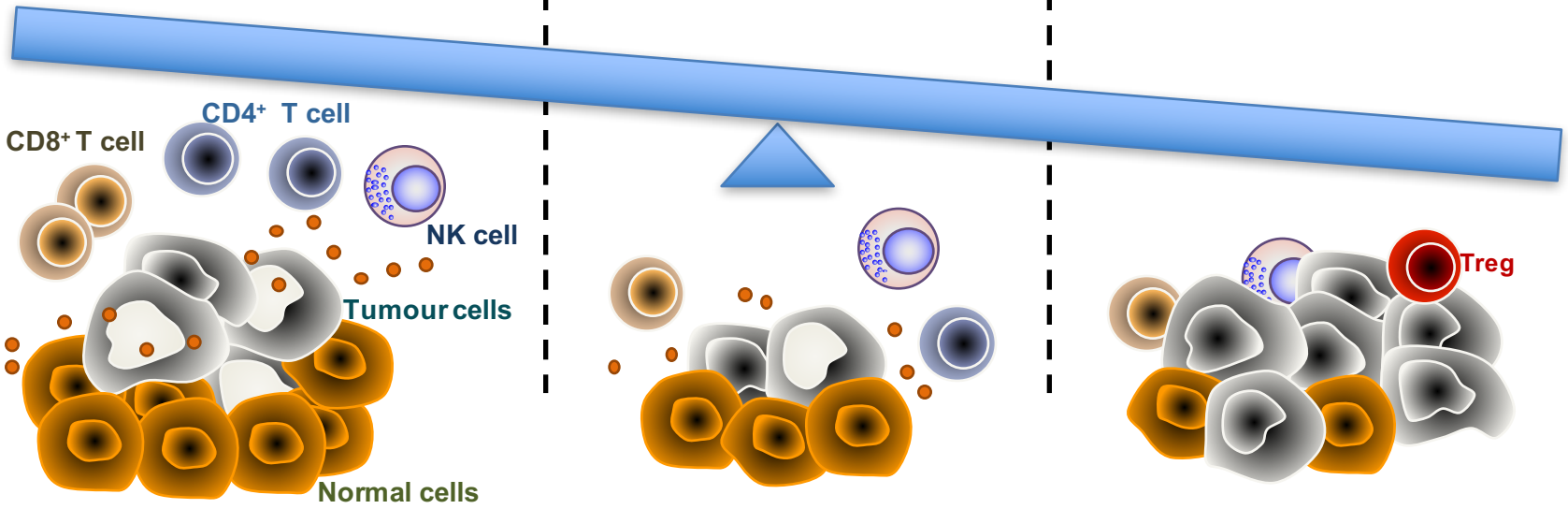
Cancer dormancy

- **Genetic instability**
- **Tumour heterogeneity**
- **Immune selection**

Escape

Cancer progression

- **Tumours avoid elimination through the outgrowth of tumour cells that can suppress, disrupt or 'escape' the immune system**
- **Reduced immunogenicity**

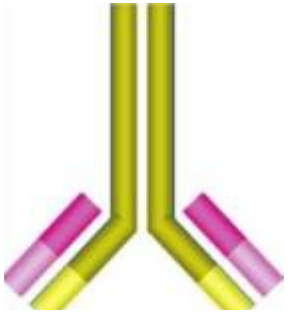


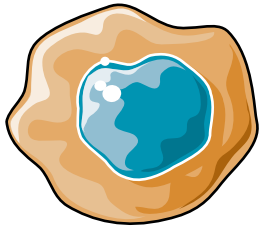
NK = natural killer; Treg = regulatory T cells.

Vesely M and Schreiber R. *Ann N Y Acad Sci.* 2013;1284:1–5.

Paradigm shift with immuno-stimulatory Ab

Historical Paradigm: Targeting Tumor Cells

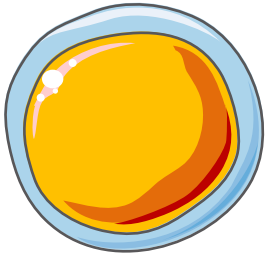


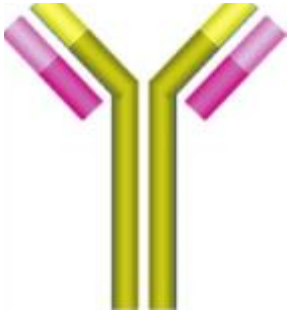


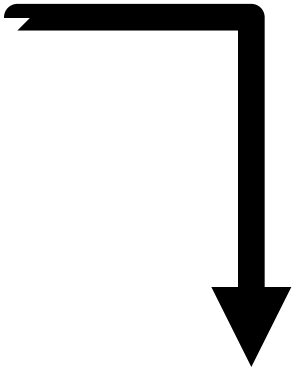
Tumor Cell

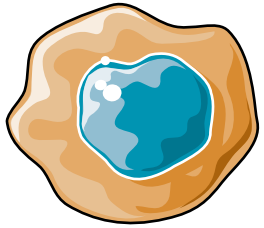
New Paradigm: Targeting Immune Cells

Lymphocyte

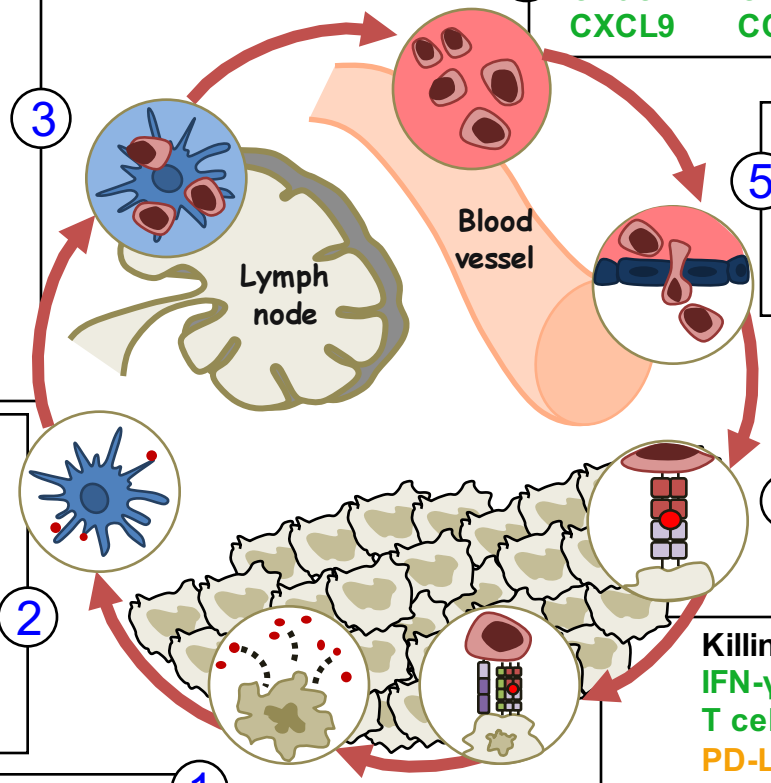








Stimulatory and Inhibitory Molecules During Immune Tumor Surveillance



Priming and activation
CD28/B7.1
CD137/CD137L
OX40/OX40L
CD27/CD70
HVEM
GITR
IL-2
IL-12
CTLA-4/B7.1
PD-L1/PD-1
PD-L1/B7.1
prostaglandins

Cancer antigen presentati
TNF-α
IL-1
IFN- α
CD40L/CD40
CDN
ATP
HMGB1
TLR
IL-10
IL-4
IL-13

Release or cancer cell antigens
Immunogenic cell death
Tolerogenic cell death

Trafficking of T cells to tumors
CX3CL1
CXCL9
CXCL10
CCL5

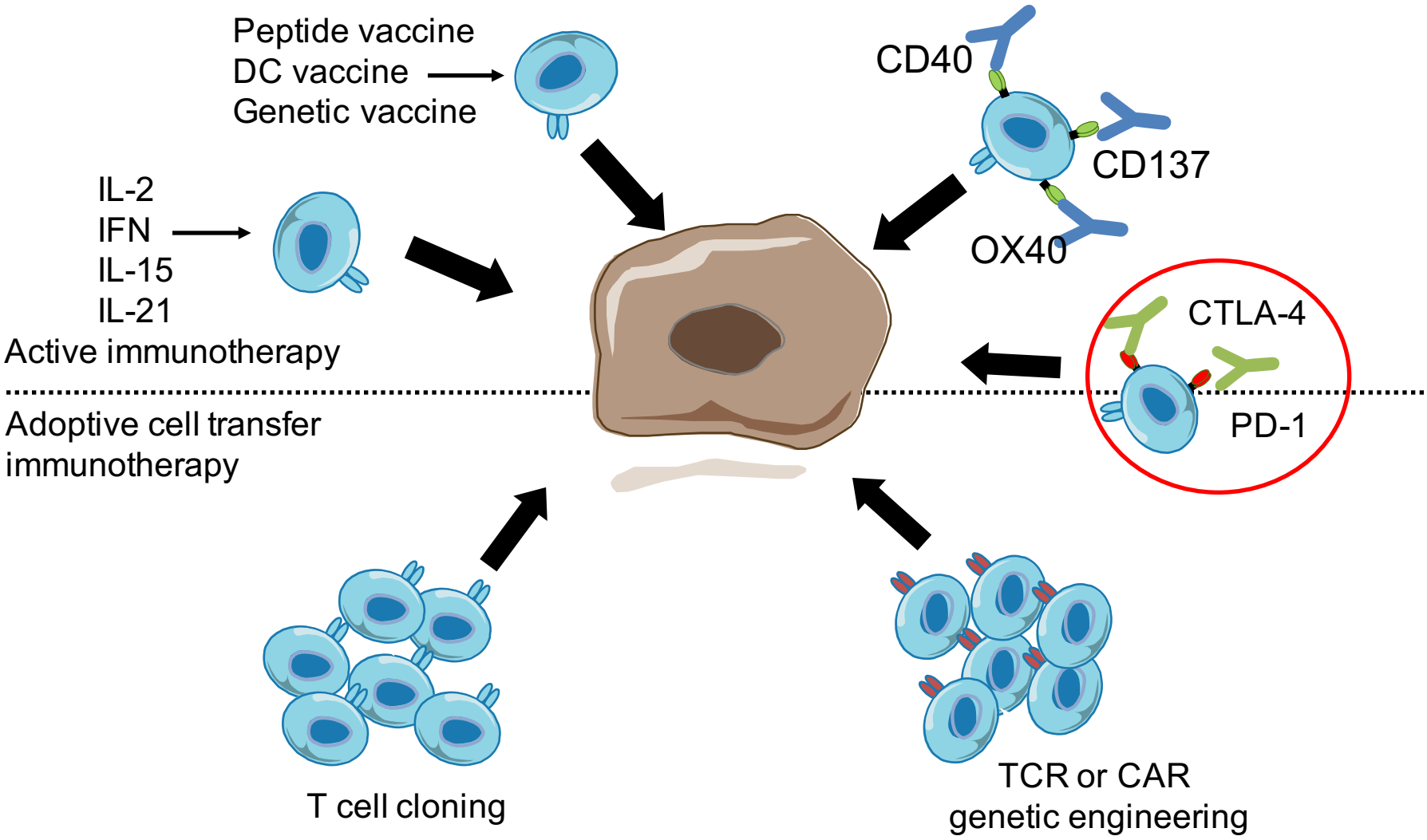
Infiltration of T cells into tumors
LFA1/ICAM1
Selectins
VEGF
Endothelin B receptor

Recognition of cancer cells by T cells
T-cell receptor
Reduced pMHC on cancer cells

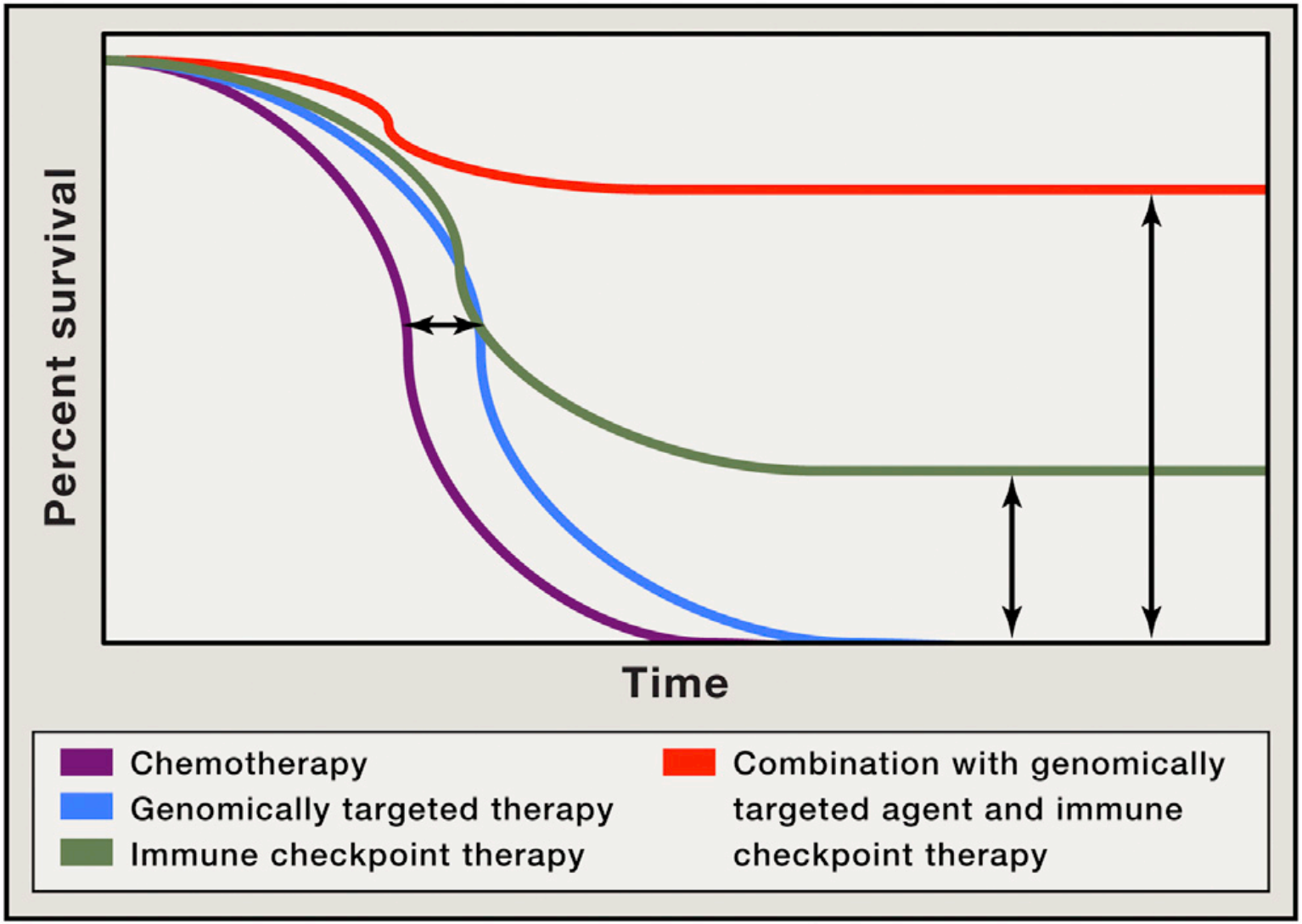
Killing of cancer cells
IFN-γ
T cell granule content
PD-L1/PD-1
PD-L1/B7.1
IDO
TGF-β
BTLA
VISTA
LAG-3
Arginase
MICA/MICB
TIM-3/phospholipids

Chen DS, et al. Immunity. 2013;39:1-10.

General Approaches for Cancer Immunotherapy

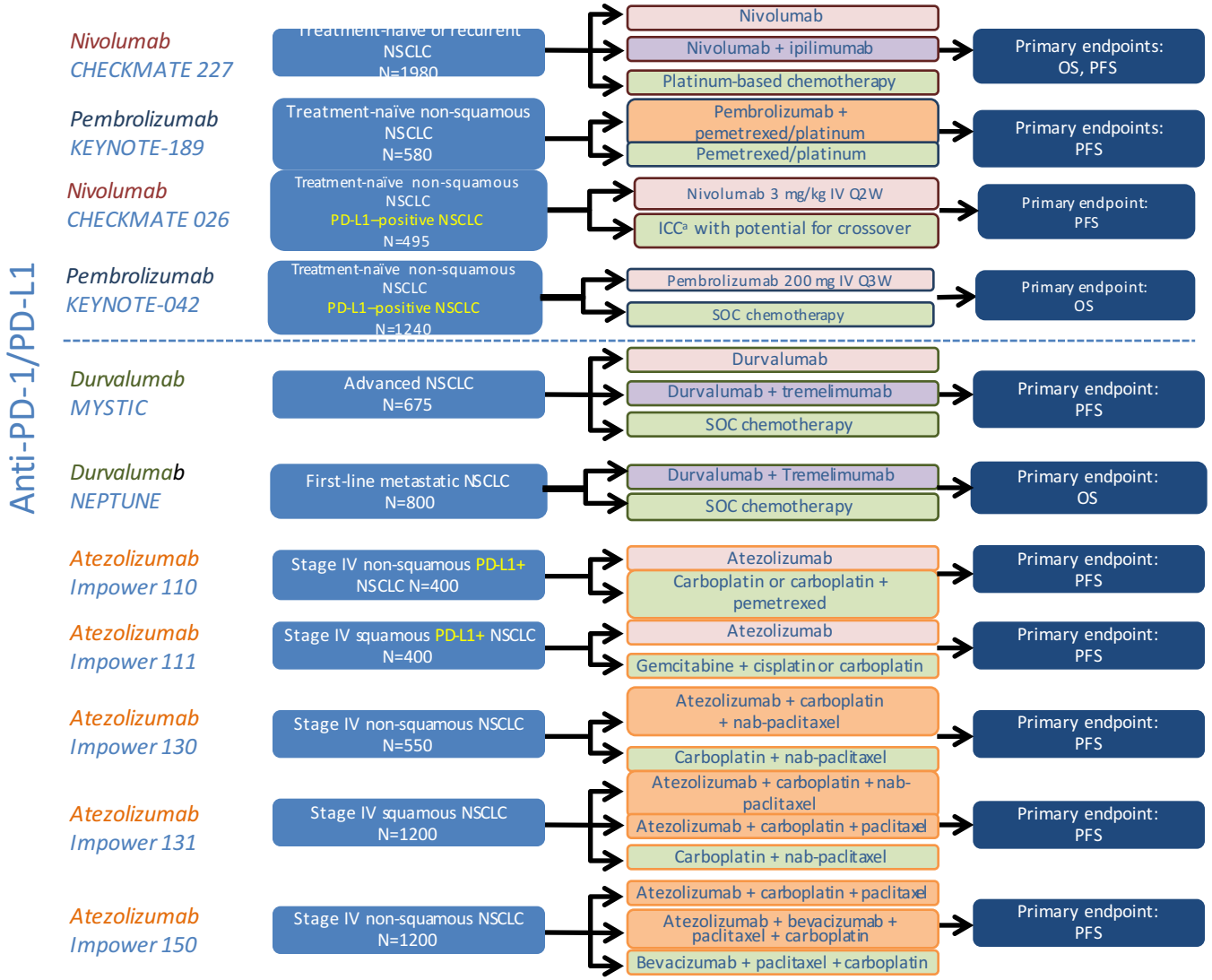


Theoretical survival with different treatment approaches

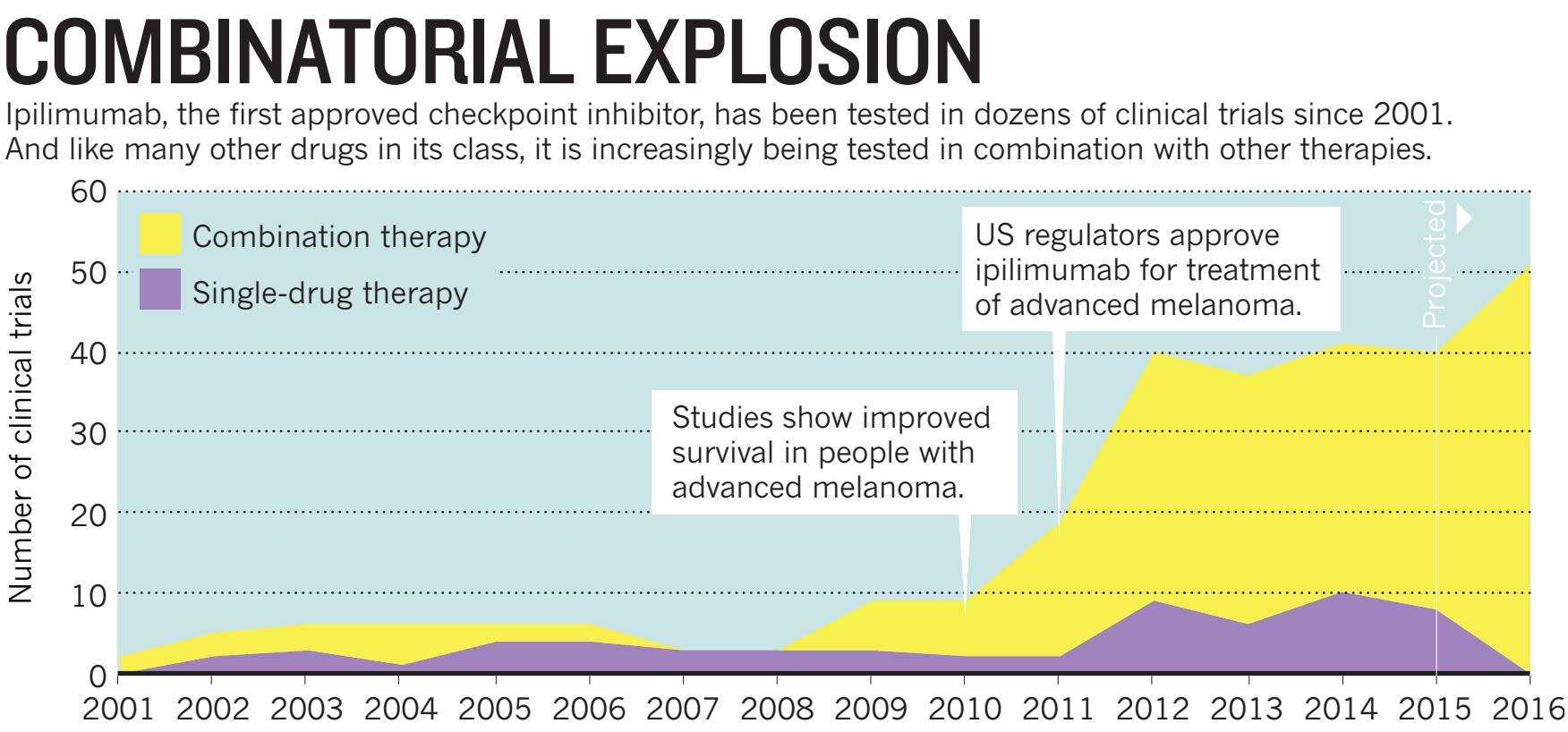


Cell 161, April 9, 2015

Phase 3 anti-PD1/-PD-L1 combination trials in 1st-line advanced NSCLC (>10,000 patients)



Inmunoterapia combinación



Inmunoterapia: ASCO 2016

- Nuevos fármacos anti-PD-1 y anti-PD-L1
- Combinaciones Anti-CTL-4 y Anti-PD1/L1
- Marcadores predictivos:
  - Expresión PD-L1
  - Carga mutacional (TMB)
  - TIL
  - Immunoscore
- Combinaciones con otros tratamientos: IT/RT/QT?
- Criterios de valoración específicos
- Tratamiento post-progresión?

Carcinoma microcítico

- Limitaciones de los tratamientos actuales
- Expectativas de tratamientos 2ª línea no confirmadas
- Expansión del beneficio y de la indicación del tratamiento con RT
- Tratamientos biológicos dirigidos no eficaces
- Tratamientos inmunoterapia específica en investigación

Carcinoma microcítico ASCO 2016

- RT: continua siendo relevante en estadios iniciales
- BD no superior to OD. Dosis biologicas equivalentes?
- 66 Gy en BD mejor cumplimiento
- Combinación Ipilimumab + Nivolumab
- ADC frente a DLL3 (Rovalpituzumab Tesirina). DLL3 expresion > 50% factor predictivo (en curso de validación)

Mesotelioma

- Incidencia todavía creciente
- Controversias en la extensión de la cirugía (experiencia)
- Tratamiento QT con Platino+Inh TS
- Posibilidad mejoria con antiangiogénicos
- 2/3 L únicamente investigación

Mesotelioma ASCO 2016

- Expectativas en IT no confirmadas:
  - Avelumab?
  - Tremelimumab no eficacia en 2/3 L

Baja carga mutacional MPM?

Componentes del valor en Oncología

Superv
Mediana
Median
Sup 5-a
SLE SLP

EAs
EAGs
Discont.
CDV

Resp
Benef.
Clinico
Durac. R
Biomarc

Impacto
Pres.
Umbral
C/E
Analisis
ICER

The Oncologist®

Economics of Oncology Practice

The Financial Toxicity of Cancer Treatment: A Pilot Study Assessing Out-of-Pocket Expenses and the Insured Cancer Patient's Experience

S. Yousuf Zafar,[a] Jeffrey M. Peppercorn,[a] Deborah Schrag,[b] Donald H. Taylor,[c] Amy M. Goetzinger,[d] Xiaoyin Zhong,[a] Amy P. Abernethy[a]

VOLUME 33 · NUMBER 10 · APRIL 1 2015

JOURNAL OF CLINICAL ONCOLOGY E D I T O R I A L

Can Money Really Be No Object When Cancer Care Is the Subject?

Leonard B. Saltz, *Memorial Sloan Kettering Cancer Center, New York, NY*

VOLUME 34 · NUMBER 7 · MARCH 1, 2016

JOURNAL OF CLINICAL ONCOLOGY COMMENTS AND CONTROVERSIES

The Value of Considering Cost, and the Cost of Not Considering Value

Leonard B. Saltz, *Memorial Sloan Kettering Cancer Center, New York, NY*

High Cancer Drug Prices in the United States: Reasons and Proposed Solutions

By Hagop Kantarjian, MD, David Steensma, MD, Judit Rius Sanjuan, Adam Elshaug, MPH, PhD, and Donald Light, PhD

thebmj

BMJ 2015;351:h5376 doi: 10.1136/bmj.h5376 (Published 7 October 2015) Page 1 of 1

NEWS

Rising drug prices drive US manufacturers' revenues, analysis finds

Michael McCarthy

Discussion | Cancer drug prices are rising faster than the prices in other sectors of health care, drawing concern from patients, physicians, and policy researchers.[5,6] We found little difference in the median wholesale price of 21 novel drugs and 30 next-in-class drugs approved over a 5-year period (next-in-class drugs, $119 765; novel drugs, $116 100; P = .42). Our results suggest that the price of cancer drugs is independent of novelty. Additionally, we found little difference in price among drugs approved based on time-to-event end points and drugs approved on the basis of RR. Our results suggest that current pricing models are not rational but simply reflect what the market will bear.

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Measuring the Value of Prescription Drugs

Peter J. Neumann, Sc.D., and Joshua T. Cohen, Ph.D.

New Math on Drug Cost-Effectiveness

Peter B. Bach, M.D., M.A.P.P.

Journal of Economic Perspectives—Volume 29, Number 1—Winter 2015—Pages 139–162

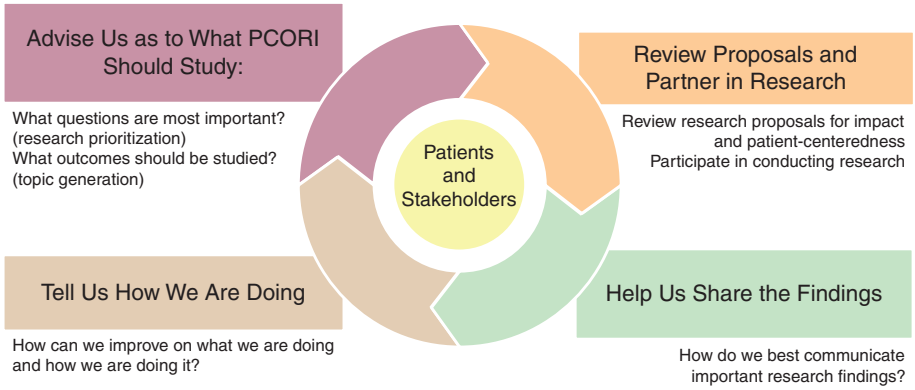
Pricing in the Market for Anticancer Drugs†

David H. Howard, Peter B. Bach, Ernst R. Berndt, and Rena M. Conti

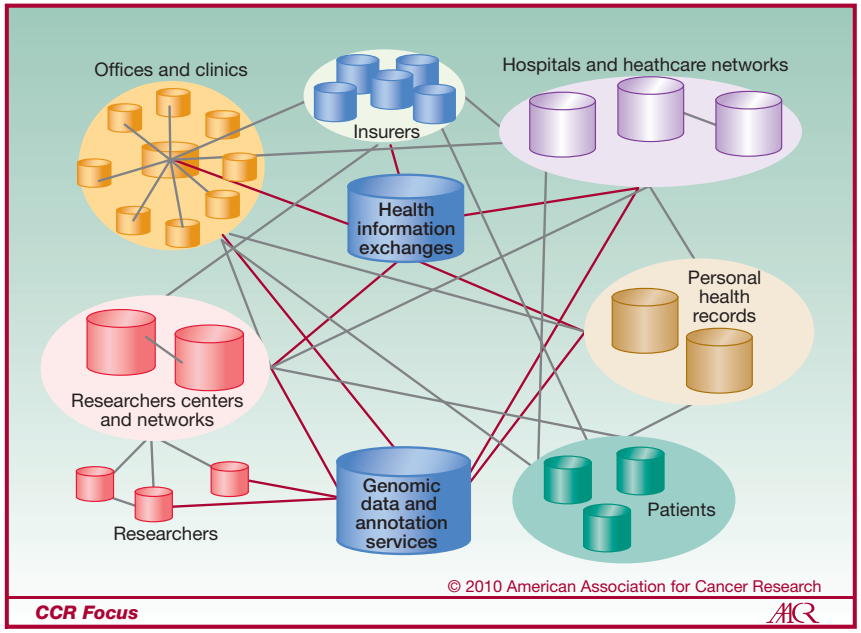
A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS)

N. I. Cherny[1*], R. Sullivan[2], U. Dafni[3], J. M. Kerst[4], A. Sobrero[5], C. Zielinski[6], E. G. E. de Vries[7] & M. J. Piccart[8,9]

Approaching Patient´s Outcomes and cost-effectivenes and cost-utility in research: the future, the needs



Achieving health equity via ACA. IOM NAP 2015



A Call for Value in Cancer Research

JAMA Oncology January 2016 Volume 2, Number 1

A focus on both the empirical study and actual practice of value-driven research will accelerate efforts to lower research costs and increase the body of knowledge derived from scarce research funding

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A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS)

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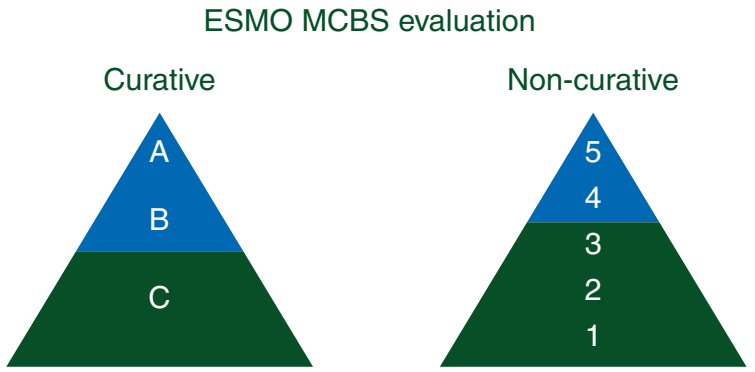
Table 2. Maximal preliminary scores

Treatments with curative intent (form 1)
>5% improvement of survival at ≥3-year follow-up
Improvements in DFS alone HR <0.60 (primary end point) in studies without mature survival data
Treatments with non-curative intent (form 2)
Primary outcome OS (form 2a)
Control ≤12 months
HR ≤0.65 *AND* gain ≥3 months *OR*
Increase *in* 2-year survival alone ≥10%
Control >12 months
HR ≤0.70 *AND* gain ≥5 months *OR*
Increase *in* 3-year survival alone ≥10%
Primary outcome PFS (form 2b)
Control ≤6 months
HR ≤0.65 *AND* gain ≥1.5 months
Control >6 months
HR ≤0.65 *AND* gain ≥3 months



Curative-Evaluation form 1: for new approaches to adjuvant therapy or new potentially curative therapies

Non-curative-Evaluation forms 2a, b or c: for therapies that are not likely to be curative

ASCO Value Framework Updated

Step 1: Determine the regimen's CLINICAL BENEFIT		
1.A. Is hazard ratio (HR) for death reported?	**YES.** Assign an HR Score for death by subtracting the HR from 1, and then multiplying the result by 100. Write this number in the box labeled "HR Score (death)." **Proceed to 1.F.**	**HR Score (death)**
	No. Proceed to 1B.	
1.B. If HR for death is not reported, is median overall survival (OS) reported?	**YES.** Assign an OS Score by calculating the percentage (ie, fractional) difference in median overall survival between the two regimens and multiply the result by 100. Write this number in the box labeled "OS Score." **Proceed to 1.F.**	**OS Score**
	NO. Proceed to 1.C.	
1.C. If OS data are not reported, is hazard ratio (HR) for disease progression reported?	**YES.** Assign an HR Score for disease progression by subtracting the HR from 1, multiplying the result by 100, and then multiplying this number by 0.8. Write this number in the box labeled "HR Score (progression)." **Proceed to 1.F.**	**HR Score (progression)**
	NO. Proceed to 1.D.	
1.D. If HR for disease progression is not reported, is median progression-free survival (PFS) reported?	**YES.** Assign a PFS Score by calculating the percentage (ie, fractional) difference in median progression-free survival between the two regimens and multiply the result by 100. Multiply this number by 0.8. Write this number in the box labeled "PFS Score." **Proceed to 1.F.**	**PFS Score**
	NO. Proceed to 1.E.	
1.E. If median PFS is not reported, is response rate (RR) reported?	**YES.** Assign an RR Score by adding the complete response (CR) and partial response (PR) rates, multiply by 100, then multiply this number by 0.7. Write this number in the box labeled "RR Score." **Proceed to 1.F.**	**RR Score**
1.F. Calculate the Clinical Benefit Score	Insert the score for HR death, HR PFS, median OS, or median PFS. **Note: You should have a score for only 1 of the clinical benefit scales above.** Write the total in the box labeled "Clinical Benefit Score." **Proceed to Step 2.**	**Clinical Benefit Score**

Step 2: Determine the regimen's TOXICITY		
Does the new regimen represent an improvement in toxicity over the standard of care/ comparator?	For each of the regimens being assessed, compare the number and frequency of clinically relevant toxicities, and assign a Toxicity Score) as shown below. Each clinically meaningful toxicity (ie, exclude laboratory results only) is assigned a score between 0.5 and 2.0 based on grade and frequency: For every grade 1 or 2 toxicity with a frequency < 10%, record 0.5 points. For every grade 1 or 2 toxicity with a frequency ≥ 10%, record 1.0 points. For every grade 3 or 4 toxicity with a frequency < 5%, record 1.5 points. For every grade 3 or 4 toxicity with a frequency ≥ 5%, record 2.0 points. Calculate the total number of toxicity points for each regimen. Calculate the percentage difference in total toxicity points between the two regimens, then multiply by 20 to obtain a toxicity score. If the regimen being evaluated is more toxic than the comparator, subtract the toxicity score of the regimen from the clinical benefit score. If the regimen is less toxic than the comparator, add the toxicity score of the regimen to the clinical benefit score. **If there are unresolved symptomatic treatment-related toxicities at 1 year after completion of treatment, subtract 5 additional points from the clinical benefit score.** The maximum points that can be awarded is 20. **Proceed to Step 3.**	**Toxicity Score**

Step 3: Determine Bonus Points		
3.A. TAIL OF THE CURVE. Identify the time point on the survival curve that is 2X the median OS (or PFS) of the comparator regimen. Is there a 50% or greater improvement in proportion of patients alive with the test regimen at this time point (assuming ≥ 20% surviving with standard)?	**YES.** If yes, award 20 points if the improvement is in OS, and 16 points (0.8 x 20) if the improvement is in PFS, and place this number in the box labeled "Tail of the Curve Bonus Points." **Proceed to Step 3.B.**	**Tail of the Curve Bonus Points**
	NO. No bonus points are awarded. **Proceed to Step 3.B.**	
3.B. PALLIATION BONUS. Is an improvement in cancer-related symptoms reported?	**YES.** If a statistically significant improvement in cancer-related symptoms is reported for the regimen being evaluated, award 10 points, and place this number in the box labeled "Palliation Bonus." **Proceed to Step 3.C.**	**Palliation Bonus**
	NO. No bonus points are awarded. **Proceed to Step 3.C.**	
3.C. QoL BONUS. Is an improvement in QoL reported?	**YES.** If a statistically significant improvement in QoL is reported for the regimen being evaluated, award 10 points, and place this number in the box labeled "QoL Bonus." **Proceed to Step 3.D.**	**QoL Bonus**
	NO. No bonus points are awarded. **Proceed to Step 3.D.**	
3.D. TREATMENT-FREE INTERVAL BONUS. Are data related to treatment-free interval reported?	**YES.** If a statistically significant improvement in treatment-free interval is reported for the regimen being evaluated, multiply the percentage improvement by 20 and award points. **Proceed to 3.E.**	**Treatment-Free Interval Bonus**
	NO. No bonus points are awarded. **Proceed to Step 3.E.**	
3.E. Calculate Total Bonus Points	Add the Palliation Bonus Points (Step 3.A), the Treatment-Free Interval Bonus Points (Step 3.B), and the QoL Bonus Points (Step 3.C.). Write this number in the box labeled "Total Bonus Points." The maximum points available for Bonus Points is 60. **Proceed to Step 4.**	**Total Bonus Points**

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Step 4: Determine the regimen's NET HEALTH BENEFIT		
Calculate the Net Health Benefit	Add the Clinical Benefit Score (Step 1), Toxicity Score (Step 2), and Bonus Points (Step 3). This yields a Net Health Benefit Score. Write this number in the box labeled "Net Health Benefit." Proceed to **Step 5.**	**Net Health Benefit**

Step 5: Determine the regimen's COST	
Insert the drug acquisition cost (DAC) and patient co-pay based on how much the treatment regimen costs per month.	**Cost (per month)** **DAC:** _____ **Patient Payment:** _____

Step 6: Summary Assessment: Advanced Disease Framework				
Clinical Benefit	**Toxicity**	**Bonus Points**	**Net Health Benefit**	**Cost (per month)**
				DAC: _____ Patient Payment: _____

DOI: 10.1200/JCO.2016.68.2518

	AUS	CHI	IND	SA	UK	US
Median generic monthly prices (US$)	226	532	159	120	458	654
Median patented monthly prices (US$)	2,741	3,173	1,515	1,708	2,587	8,694
GDPcap (US$)	46,550	13,324	5,808	13,094	39,826	54,370
Generic Median monthly price as % of GDPcap	3	48	33	11	14	14
Patented Median monthly price as % of GDPcap	71	288	313	157	78	192

DHCC in each country in Euros (€) per capita adjusted for purchasing power parity (PPP) in 2014.

< 100 €/ capita	100-200 €/ capita	>200 €/ capita
Bulgaria / 66	Cyprus / 105	Austria / 266
Croatia / 81	Denmark / 163	Belgium / 227
Czech Republic / 91	Finland / 125	France / 212
Estonia / 69	Greece / 127	Germany / 265
Latvia / 62	Hungary / 105	Luxembourg / 323
Lithuania / 79	Ireland / 164	Netherlands / 264
Poland / 81	Italy / 161	Sweden / 223
Portugal / 81	Malta / 134	
Romania / 55	Slovakia / 107	
	Slovenia / 139	
	Spain / 129	
	United Kingdom / 136	

Coste-utilidad: Spain Post-ASCO 2016

Bartomeu Massuti @bmassutis · Jun 18 View translation

El umbral de coste-efectividad español está entre 20.000 y 25.000 euros diariofarma.com/2016/06/16/el-…

Coneste umbral C/E Txs oncologicos no caben

El umbral de coste-efectividad español está entre 20.000 y 25.000 eur…

El umbral de coste-efectividad en España no se había determinado hasta ahora, pero un estudio coordinado por la experta en Economía de la Salu...

diariofarma.com

No basta saber, se debe también aplicar…

No es suficiente querer, se debe también hacer…

W. Goethe


LO SUYO NO ESTÁ CUBIERTO POR LA PÓLIZA, PERO LE PODEMOS TRATAR DE ALGO MÁS ECONÓMICO

Ben agraït
Muchas gracias

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