Efecto lázaro

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Acceso a tratamientos oncológicos para personas con cáncer

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Disclosures

- Dr Enriqueta Felip has the following relationships to disclose:
  - Advisory role or speaker's bureau: Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Eli Lilly, F. Hoffman-La Roche, GlaxoSmithKline, Ipsen, Janssen, Medscape, Merck KGaA, MSD, Novartis, Peptomyc, PeerVoice, Pfizer, Regeneron, Sanofi, Seattle Genetics, Takeda and Turning Point Therapeutics
  - Independent board member: Grifols
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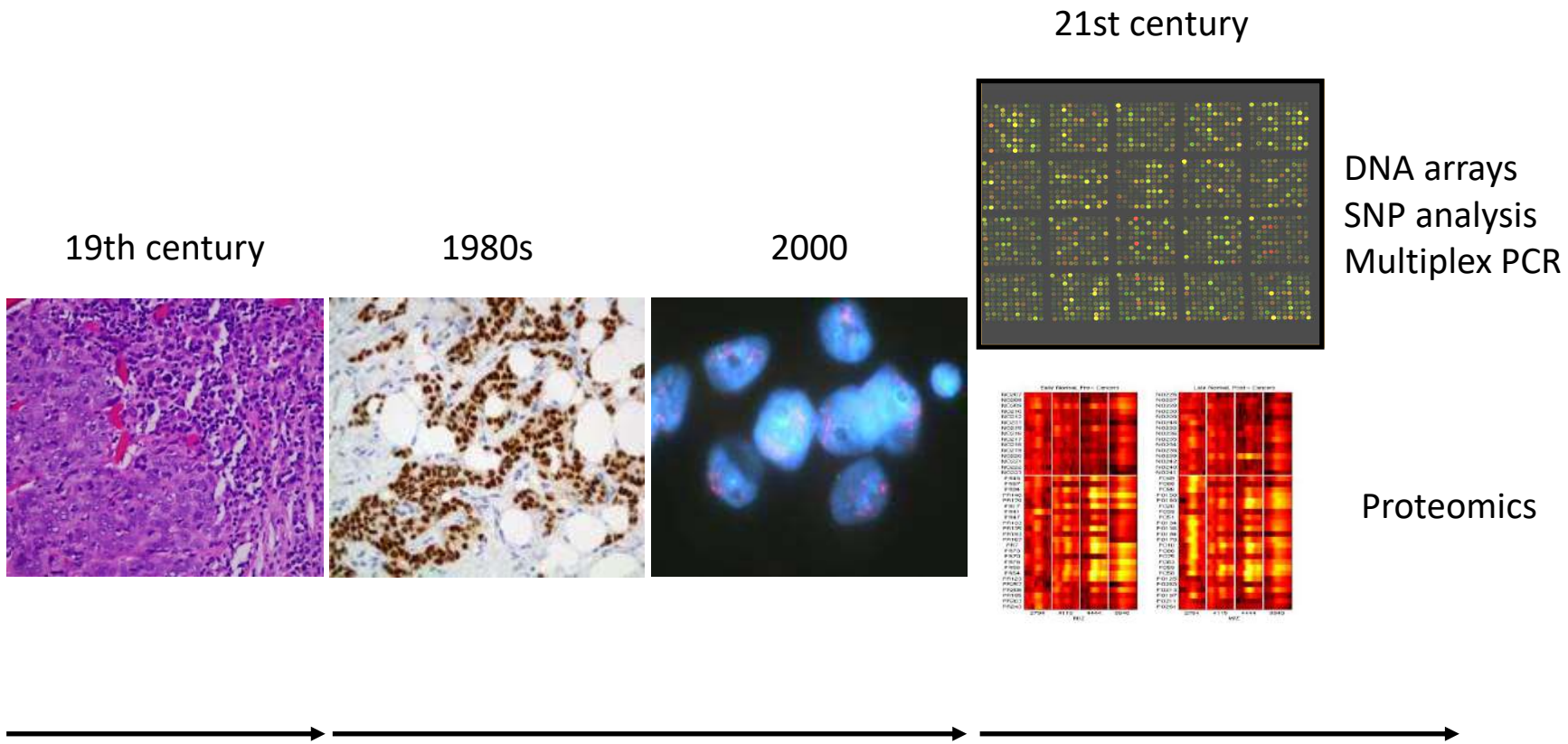
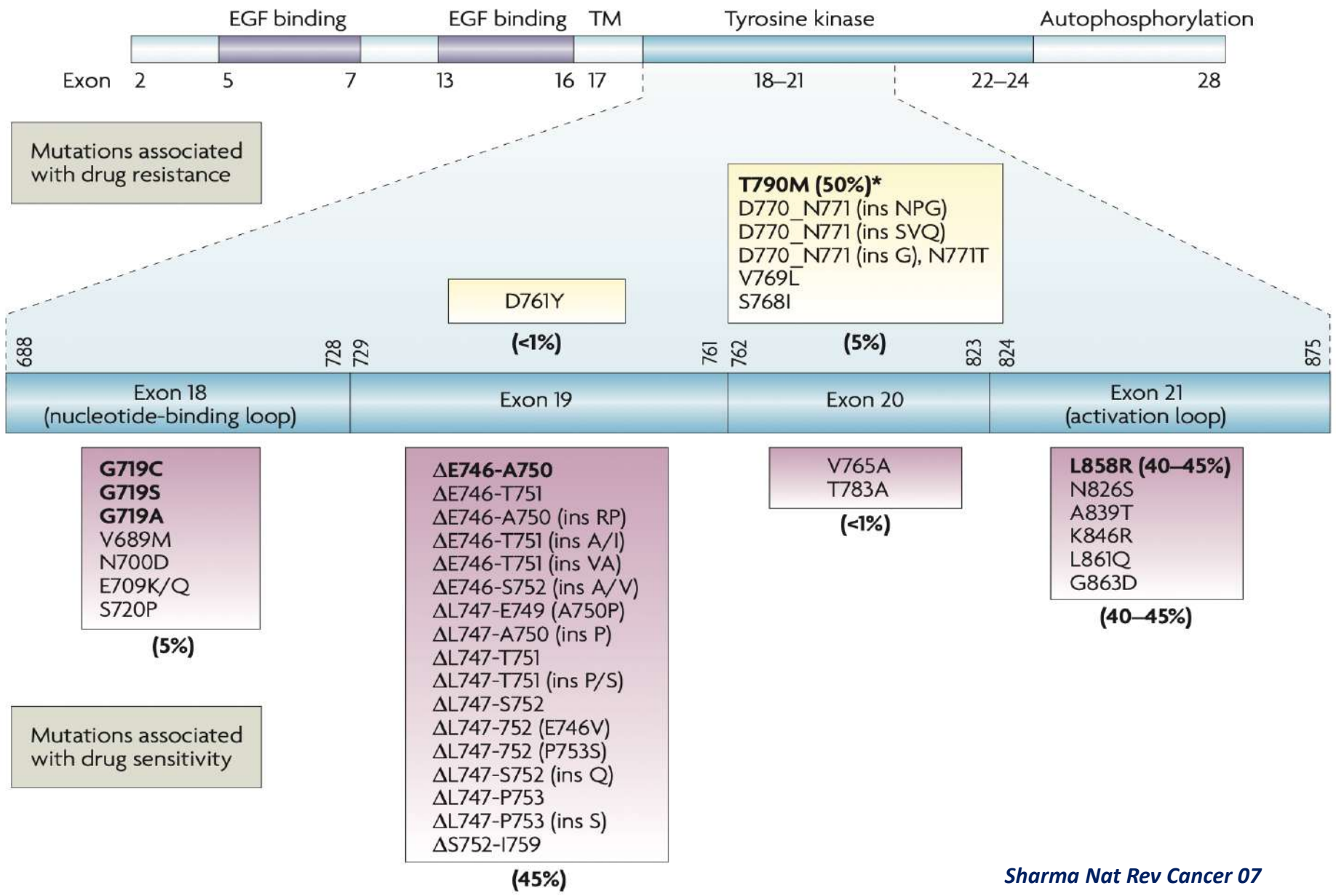
Cáncer: un reto para el siglo XXI …

- El cáncer es un término general que engloba a más de 200 enfermedades
- Cada año, 2,6 millones de personas en la UE son diagnosticadas de cáncer
- Se espera que este número aumente rápidamente a causa del envejecimiento de la población, los estilos de vida y las condiciones ambientales desfavorables
- Sin una acción contundente, el número de casos de cáncer aumentará un 25% en 2035

Evolución del diagnóstico de cáncer



2004: EGFR mutations in lung cancer



Sharma Nat Rev Cancer 07

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JOURNAL OF CLINICAL ONCOLOGY

E D I T O R I A L

The "Lazarus Response" in Treatment-Naïve, Poor Performance Status Patients With Non–Small-Cell Lung Cancer and Epidermal Growth Factor Receptor Mutation

Corey J. Langer, *Thoracic Oncology, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA*

LAZARUS REVISITED

In the treatment of patients with advanced NSCLC, we are on the threshold of customized or individualized medicine. Molecular markers will ultimately identify patients more or less likely to benefit from specific therapies, and should become as important as, if not more important than, disease stage and PS in selecting treatment. Our current empiric therapeutic mentality, one hopes, will ultimately fall by the wayside.

In the new testament of the Bible, Jesus raised Lazarus of Bethany from the dead. In modern medical parlance, the Lazarus phenomenon refers to an event in which a person spontaneously returns to life after resuscitation has been given up. Therapeutic realists have no delusion that miracles of this sort will become routine in oncologic practice. But the judicious application of molecular markers, as practiced by Inoue and colleagues, should go far in combating the gospel of therapeutic nihilism rampant in the management of poor PS patients with advanced NSCLC.

First-Line Gefitinib for Patients With Advanced Non–Small-Cell Lung Cancer Harboring Epidermal Growth Factor Receptor Mutations Without Indication for Chemotherapy

Akira Inoue, Kunihiko Kobayashi, Kazuhiro Usui, Makoto Maemondo, Shoji Okinaga, Iwao Mikami, Masahiro Ando, Koichi Yamazaki, Yasuo Saijo, Akihiko Gemma, Hitoshi Miyazawa, Tomoaki Tanaka, Kenji Ikebuchi, Toshihiro Nukiwa, Satoshi Morita, and Koichi Hagiwara

A B S T R A C T

Purpose
This multicenter phase II study was undertaken to investigate the efficacy and feasibility of gefitinib for patients with advanced non–small-cell lung cancer (NSCLC) harboring epidermal growth factor receptor (*EGFR*) mutations without indication for chemotherapy as a result of poor performance status (PS).

Patients and Methods
Chemotherapy-naïve patients with poor PS (patients 20 to 74 years of age with Eastern Cooperative Oncology Group PS 3 to 4, 75 to 79 years of age with PS 2 to 4, and ≥ 80 years of age with PS 1 to 4) who had *EGFR* mutations examined by the peptide nucleic acid-locked nucleic acid polymerase chain reaction clamp method were enrolled and received gefitinib (250 mg/d) alone.

Results
Between February 2006 and May 2007, 30 patients with NSCLC and poor PS, including 22 patients with PS 3 to 4, were enrolled. The overall response rate was 66% (90% CI, 51% to 80%), and the disease control rate was 90%. PS improvement rate was 79% ($P < .00005$); in particular, 68% of the 22 patients improved from ≥ PS 3 at baseline to ≤ PS 1. The median progression-free survival, median survival time, and 1-year survival rate were 6.5 months, 17.8 months, and 63%, respectively. No treatment-related deaths were observed.

Conclusion
This is the first report indicating that *EGFR* mutation-positive patients with extremely poor PS benefit from first-line gefitinib. Because there previously has been no standard treatment for these patients with short life expectancy other than best supportive care, examination of *EGFR* mutations as a biomarker is recommended in this patient population.

J Clin Oncol 27:1394-1400. © 2009 by American Society of Clinical Oncology

Performance status	
1	3†
2	4†
3	17
4	5

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

Eastern Cooperative Oncology Group, Robert Comis M.D., Group Chair.

The New York Times Magazine

THE HEALTH ISSUE

Learning From the Lazarus Effect

Most clinical trials for cancer drugs are failures. But for a handful of patients, a drug proves to be nearly a cure. What can science learn from these "exceptional responders"?

By Gareth Cook
May 12, 2016

For years, Grace Silva had experienced odd episodes with her throat — bouts of swelling and radiating pain that seemed to resolve with antibiotics — but her doctors couldn't explain what was wrong. Finally, after a flare-up in the summer of 2010, Grace was referred to a specialist, an ear doctor who felt something amiss on the left side of her throat: a lump. The Silva family agreed that it was time to get Grace, then 54, to a thyroid specialist. Grace's daughter Melanie tracked down the name of one at Brigham and Women's Hospital, a 90-minute drive from Grace's brown clapboard split-level near New Bedford, Mass. In September 2010, the specialist delivered the diagnosis: anaplastic thyroid cancer. It was bad, he warned her, and she would need surgery. Grace's other daughter, Karrie, was marrying in a few weeks. "Can't it wait?" Grace asked. It could not. "And whatever you do," the specialist said, "please don't look it up on the Internet."

Of course nobody dreamed of saying these things to Grace at the time. A surgeon removed her tumor, and she was able to attend her daughter's wedding. She then withstood a long stretch of radiation, every weekday for more than a month — vomiting into a bag as her husband, Joe, did his best behind the wheel of their brown Chrysler. Her doctors knew they had to hit the cancer with everything they had. By the end of her treatment in December 2010, Grace, a once-vivacious Portuguese woman with dark eyes and raven hair, had lost more than 30 pounds and could barely eat or talk.

In March 2011, Joe drove Grace back to Dana-Farber. She had started to recover some of her strength, and the day had come to learn the results of her first follow-up scan. The news wasn't good. Less than three months since her last radiation treatment, the cancer had already spread to her lungs. The largest mass, on her right lung, was more than an inch in diameter. This is the way with anaplastic thyroid cancer.

Lorch sat with Grace and Joe in a cream-colored exam room, a red biohazard box nestled under one counter, and explained that all the standard treatments had been exhausted. He told them about an experimental trial for aggressive thyroid cancers that hadn't responded to standard treatments, and Grace agreed to enroll. The drug, everolimus, was used in transplant surgery to prevent rejection, and it had been approved for some use in cancer. Lorch had seen indications that the drug could work in the thyroid, but he didn't have high hopes for the anaplastic cases — its long track record had been too dismal. "Partly we were motivated," Lorch told me, "by the fact that we didn't have anything else."

Two months later, in May, Joe drove Grace to Dana-Farber for her follow-up scan. Lying motionless as the CT scanner began its inquiries, she thought of Isaiah and prayed. If the everolimus had failed to slow the cancer's advance, it would be time to begin the work of getting her affairs in order. But the scan results, plain to even an untrained eye, were shocking: The largest mass had shrunk to half its previous size. Everywhere there were signs of retreat. Lorch said he had never seen such a rout. All six of the other anaplastic thyroid patients on the trial eventually died, but Grace's tumors shrank until they barely registered.

The New York Times Magazine

THE HEALTH ISSUE

Learning From the Lazarus Effect

Most clinical trials for cancer drugs are failures. But for a handful of patients, a drug proves to be nearly a cure. What can science learn from these "exceptional responders"?

The power of this approach was first demonstrated a few years ago, at Memorial Sloan Kettering Cancer Center in Manhattan. In April 2009, Sharon K., who was 68 at the time, had been told by her local doctor that her bladder cancer had morphed into a muscle--invasive form: It had become aggressive and difficult to contain. At Sloan Kettering, she was given chemotherapy, followed by a cystectomy, which involved removing the bladder and fashioning a new one out of a portion of small intestine. "I felt like my insides were going to fall out," said Sharon, who asked that her last name not be used to protect her privacy. Still, a few months later, the cancer returned.

In February 2010, running out of alternatives, Sharon joined a clinical trial at the center, with instructions to take two pills every morning and return for regular checkups. Thousands of trials are open in the United States on any given day, and for people like Sharon, who traveled from Florida to take part, they are an opportunity to take advantage of the latest scientific ideas. But the odds are generally long: Historically, less than 7 percent of cancer drugs tested in humans eventually win F.D.A. approval.

At Sharon's first follow-up scan, the tumors were in recession; within months, they were gone. Her doctors were thrilled. And yet the trial Sharon had joined was a failure. Of the 44 other patients, just one saw his tumor shrink in a meaningful way. Dr. David Solit, a researcher at Sloan Kettering, joined a meeting with his colleagues there to discuss the trial's results, and he remembers the feeling in the room, familiar to anyone in the field. "O.K., we've had no new effective bladder cancer treatments for 30 years, and we did yet another clinical trial that was [based on] a reasonable idea," he recalled. "This is a disappointment. Now let's give up and move on to the next thing."

This idea, more broadly, has been called precision medicine: the hope that doctors will be able to come to a far more exact understanding of each patient's disease, informed by genetics, and treat it accordingly. It is in cancer where this has advanced the furthest, and the exceptional responders provide a glimpse of what precision medicine might mean. When Grace's tumor was sequenced, scientists found a mutation in TSC2, a sister gene to TSC1, the one mutated in Sharon's cancer. Sharon, like Grace, had responded to everolimus, and so the genetic similarity suggested that their cases were not flukes, that their seemingly different cancers shared a deep connection. In this sense, Grace's anaplastic thyroid cancer more closely resembled Sharon's bladder cancer than other thyroid cancers. A more precise oncology would have assigned both to everolimus on purpose, not by chance.

Science. 2012 October 12; 338(6104): 221. doi:10.1126/science.1226344.

Genome Sequencing Identifies a Basis for Everolimus Sensitivity

Gopa Iyer*, **Aphrothiti J. Hanrahan**, **Matthew I. Milowsky**, **Hikmat Al-Ahmadie**, **Sasinya N. Scott**, **Manickam Janakiraman**, **Mono Pirun**, **Chris Sander**, **Nicholas D. Socci**, **Irina Ostrovnaya**, **Agnes Viale**, **Adriana Heguy**, **Luke Peng**, **Timothy A. Chan**, **Bernard Bochner**, **Dean F. Bajorin**, **Michael F. Berger**, **Barry S. Taylor**†, and **David B. Solit**†

Along-standing problem in oncology is the variability of treatment response observed in early stage clinical trials. Drugs that fail to induce disease regression in most patients or prolong median progression-free survival (PFS) are deemed inactive and often abandoned, even when the drug exhibits profound activity in a small number of patients. We hypothesized that sequencing the tumor genomes of such "outlier" patients might identify unique somatic alterations that are the basis of their drug response, information that could in turn inform future clinical development.

We studied the tumor genome of a patient with metastatic bladder cancer who achieved a durable (>2 years) and ongoing complete response to everolimus, a drug targeting the mTORC1 (mammalian target of rapamycin) complex (Fig. 1A). The patient was enrolled in a phase II trial (ClinicalTrials. gov NCT00805 129) that failed to achieve its PFS end point. Whole-genome sequencing of DNA derived from the primary tumor and blood (1) identified 17,136 somatic missense mutations and small insertions and deletions (mutation rate of 6.21 per million bases). Of these, 140 were non-synonymous mutations within protein-coding or noncoding RNA regions of the genome. Structurally, this tumor genome was intact, lacking significant copy number alterations or functional translocations (Fig. 1B). Among confirmed coding mutations were (i) a two-base-pair deletion in the *TSC1* (tuberous sclerosis complex 1) gene, resulting in a frameshift truncation (c.1907_1908del, p.Glu636fs), and (ii) a nonsense mutation in the *NF2* (neurofibromatosis type 2) gene, creating a premature stop codon (c.863C>G, p.Ser288*). These loss-of-function mutations were noteworthy (table S1) because alterations in these genes have been associated with mTORC1 dependence in preclinical models (2). Sequencing of both genes in a second cohort of 96 high-grade bladder cancers identified five additional somatic *TSC1* mutations, whereas no additional *NF2* mutations were detected (fig. S1). Although the NF2 mutation was uncommon in bladder cancers, knockdown of NF2 expression in TSC1-null bladder cancer cells was associated with enhanced sensitivity to mTORC1 inhibition (fig. S1).

Because *TSC1* is mutated in a subset of bladder cancers (3), we explored whether *TSC1* mutation is a biomarker of clinical benefit from everolimus therapy in this disease. We thus analyzed 13 additional bladder cancer patients treated with everolimus in the same trial with

N Engl J Med. 2014 October 9; 371(15): 1426–1433. doi:10.1056/NEJMoa1403352.

Response and Acquired Resistance to Everolimus in Anaplastic Thyroid Cancer

Nikhil Wagle, M.D., **Brian C. Grabiner, Ph.D.**, **Eliezer M. Van Allen, M.D.**, **Ali Amin-Mansour, M.S.**, **Amaro Taylor-Weiner, B.S.**, **Mara Rosenberg, B.S.**, **Nathanael Gray, Ph.D.**, **Justine A. Barletta, M.D.**, **Yanan Guo, Ph.D.**, **Scott J. Swanson, M.D.**, **Daniel T. Ruan, M.D.**, **Glenn J. Hanna, M.D.**, **Robert I. Haddad, M.D.**, **Gad Getz, Ph.D.**, **David J. Kwiatkowski, M.D., Ph.D.**, **Scott L. Carter, Ph.D.**, **David M. Sabatini, M.D., Ph.D.**, **Pasi A. Jänne, M.D., Ph.D.**, **Levi A. Garraway, M.D., Ph.D.**, and **Jochen H. Lorch, M.D.**

Everolimus, an inhibitor of the mammalian target of rapamycin (mTOR), is effective in treating tumors harboring alterations in the mTOR pathway. Mechanisms of resistance to everolimus remain undefined. Resistance developed in a patient with metastatic anaplastic thyroid carcinoma after an extraordinary 18-month response. Whole-exome sequencing of pretreatment and drug-resistant tumors revealed a nonsense mutation in *TSC2*, a negative regulator of mTOR, suggesting a mechanism for exquisite sensitivity to everolimus. The resistant tumor also harbored a mutation in *MTOR* that confers resistance to allosteric mTOR inhibition. The mutation remains sensitive to mTOR kinase inhibitors.

Lazarus response to treatment of patients with lung cancer and oncogenic mutations in the intensive care unit

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Abstract: Novel targeted therapy for patients with non-small-cell lung cancer (NSCLC) and oncogenic mutations along with poor performance status (PS) sometimes evokes a "Lazarus" response. Moreover, for critically ill patients with NSCLC and respiratory failure requiring mechanical ventilation (MV) in the intensive care unit (ICU), only a few case reports have demonstrated positive outcomes with targeted therapy. This perspective review describes in detail the most recently published data in order to highlight the findings and the main pitfalls of targeted therapy for patients with NSCLC in the ICU.

Table 1 Details of included studies of targeted therapies for lung cancer patients in intensive care unit (case reports)

Author, year, reference, journal, study type, case number	Drug (empirical or confirmed), mutation status, previous treatment	Patient characteristics	Ventilator days	PFS
Ahn *et al.* [2013] (21), *J Thorac Oncol*, case report, N=3	Crizotinib (confirmed), ALK, not naive	Respiratory failure in MV	42 days	84 days
	Crizotinib (confirmed), ALK, not naive	Respiratory failure in MV	20 days	8 months
	Crizotinib (confirmed), ALK, not naive	Respiratory failure in MV	17 days	No mention
Geffen *et al.* [2013] (24), *J Thorac Oncol*, case report, N=1	Crizotinib (confirmed), ALK, not naive	Respiratory failure in NIPPV	7 days	>47 weeks
Bosch-Barrera *et al.* [2014] (23), *Lung Cancer*, case report, N=1	Erlotinib (empirical), EGFR exon 19, naive	Respiratory failure in MV	5 days	>6 months
Adam *et al.* [2015] (26), *Lung Cancer*, case report, N=1	Ceritinib (confirmed), ALK, naive	Respiratory failure in MV, vv-ECMO	10 days	>365 days
Tanaka *et al.* [2016] (25), *BMC Res Notes*, case report, N=1	Alectinib (confirmed), ALK, not naive	Oxygen flow rate 10 L/min	No mention	No mention
Jeong *et al.* [2016] (22), *Korean J Crit Care Med,* case report, N=1	Erlotinib (empirical), EGFR exon 19, naive	Respiratory failure in MV	62 days	18 months

Open Access Full Text Article

CASE REPORT

Meningeal "Lazarus Response" to Lorlatinib in a ROS1-Positive NSCLC Patient Progressing to Entrectinib

2021

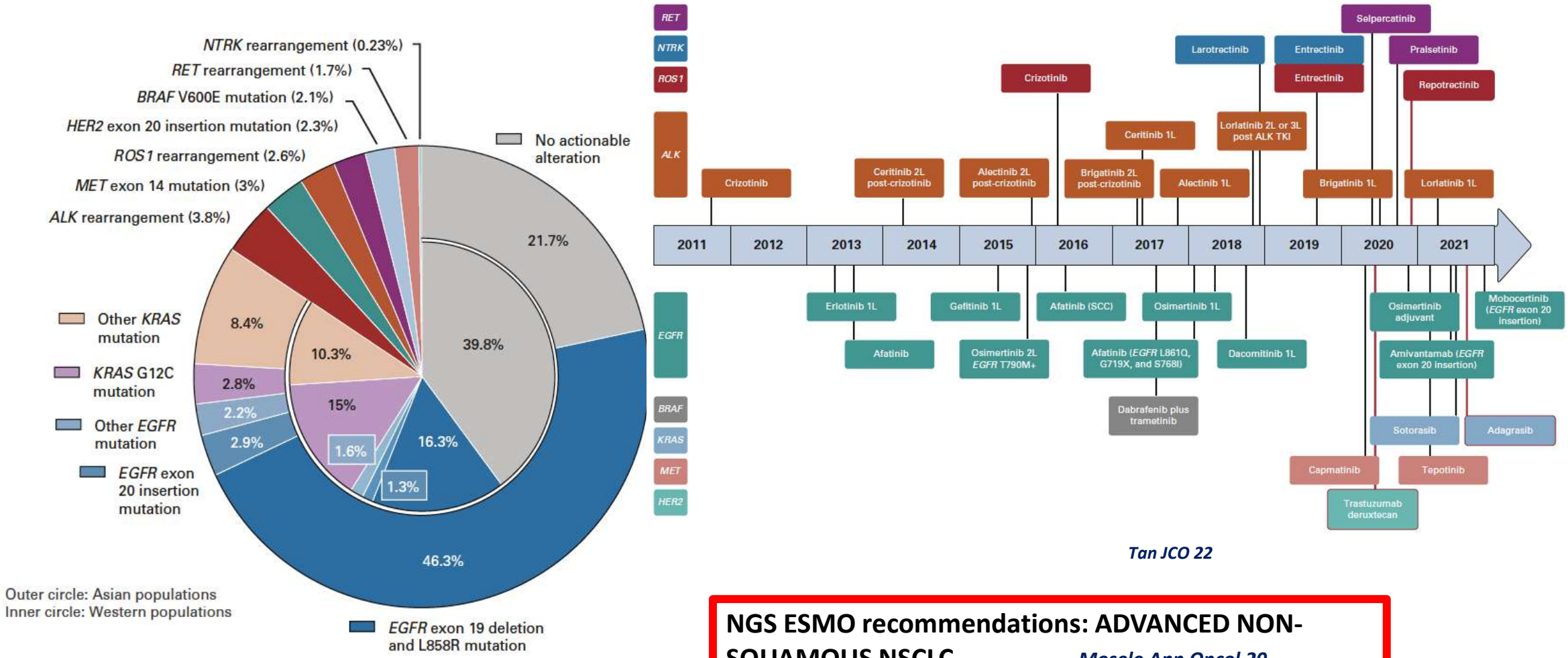
This article was published in the following Dove Press journal:
Cancer Management and Research

Francesco Facchinetti[1,2]
Antonin Levy[3,4]
Samy Ammari[5]
Charles Naltet[6]
Pernelle Lavaud[6]
Mihaela Aldea[6]
Damien Vasseur[7]
David Planchard[6]
Benjamin Besse[2,6]

[1]Predictive Biomarkers and Novel Therapeutic Strategies in Oncology, Inserm U981, Gustave Roussy Cancer Center, Villejuif, France; [2]Université Paris-Saclay, Faculté de Médecine, Le Kremlin-Bicêtre, France; [3]Department of Radiation Oncology, Institut d'Oncologie Thoracique (IOT), Gustave Roussy Cancer Center, Villejuif, France; [4]INSERM U1030, Molecular Radiotherapy, Gustave Roussy, Université Paris-Saclay, Villejuif, France; [5]Department of Radiology, Gustave Roussy Cancer Center, Villejuif, France; [6]Department of Medical Oncology, Institut d'Oncologie

Background: ROS1 tyrosine kinase inhibitors (TKIs) have showed activity and efficacy in *ROS1*-rearranged non-small cell lung cancer (NSCLC). In the clinical practice, besides the utilization of crizotinib, less is known about the best treatment strategies involving additional, new-generation TKIs for the sequential treatment of ROS1-positive NSCLC patients.
Case Presentation: A patient suffering from a *ROS1*-rearranged lung adenocarcinoma, after receiving cisplatin-pemetrexed chemotherapy, was treated with entrectinib, a new-generation ALK/ROS1/NTRK inhibitor. After 16 months, central nervous system (CNS) metastases appeared, without extra-cerebral disease progression. Stereotactic brain radiotherapy was performed and entrectinib was maintained, due to the global systemic disease control. Approximately one month after radiotherapy, thoracic and meningeal progressions were detected, the latter highly symptomatic with neurocognitive disorders, visual hallucinations and worsening of psycho-motor impairment. A lumbar puncture was positive for tumor cells and for an *EZR-ROS1* fusion. The administration of lorlatinib (a third-generation ALK/ROS1 inhibitor) prompted an extremely rapid improvement of clinical conditions, anticipating the positive results observed at radiologic evaluation that confirmed the disease response still ongoing after nine months since treatment start.
Discussion: With the expanding availability of targeted agents with differential activity on resistance mechanism and on CNS disease, choosing wisely the best treatment strategies is pivotal to assure the best clinical outcomes in oncogene-addicted NSCLC patients. Here we have reported lorlatinib reverted an almost fatal meningeal carcinomatosis developing during entrectinib in a ROS1-positive NSCLC patient.

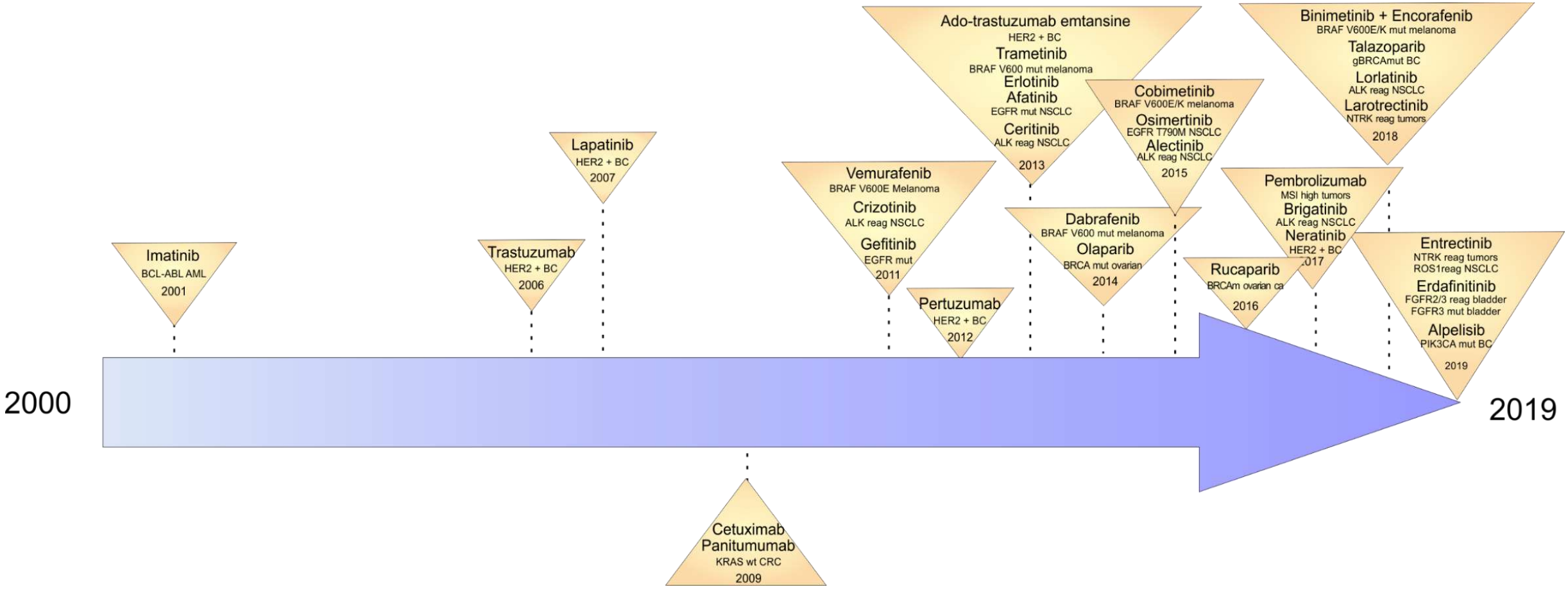
Stage IV non-squamous NSCLC



Tan JCO 22

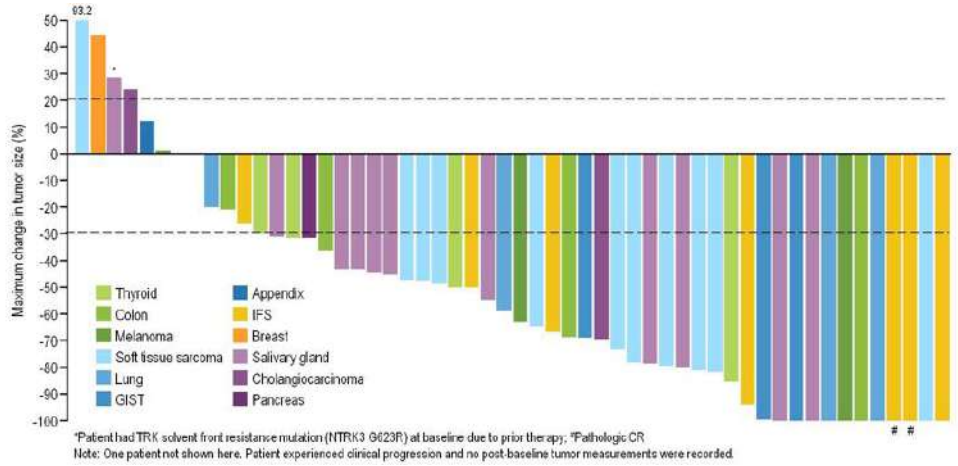
NGS ESMO recommendations: ADVANCED NON-SQUAMOUS NSCLC *Mosele Ann Oncol 20*

Precision medicine clinical trials: evolving field

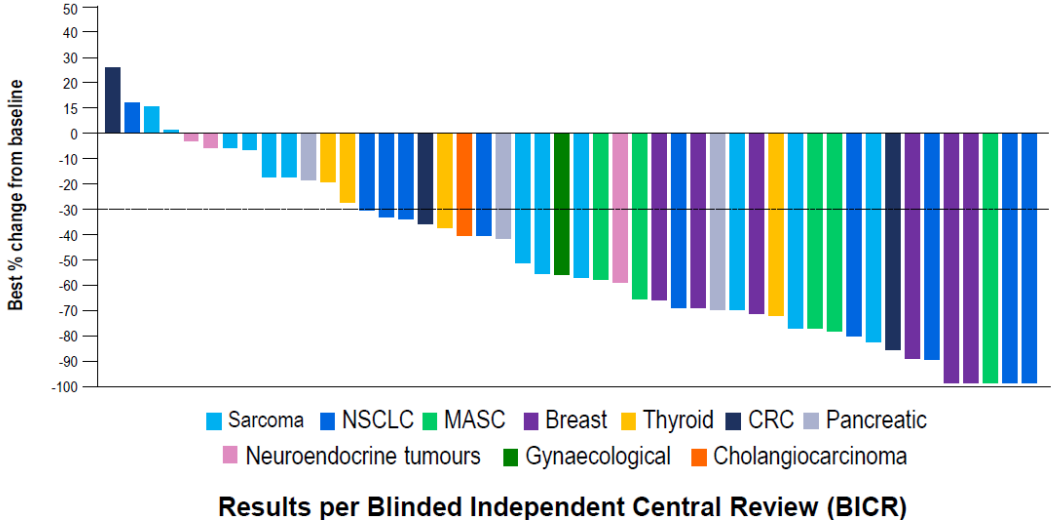


NTRK translocations occur in 0.3% of population, TRK inhibitors are very active

Larotrectinib in NTRK fusion tumors



Entrectinib in NTRK fusion tumors



Hyman D et al. 2017 ASCO Annual Meeting. LBA 2501

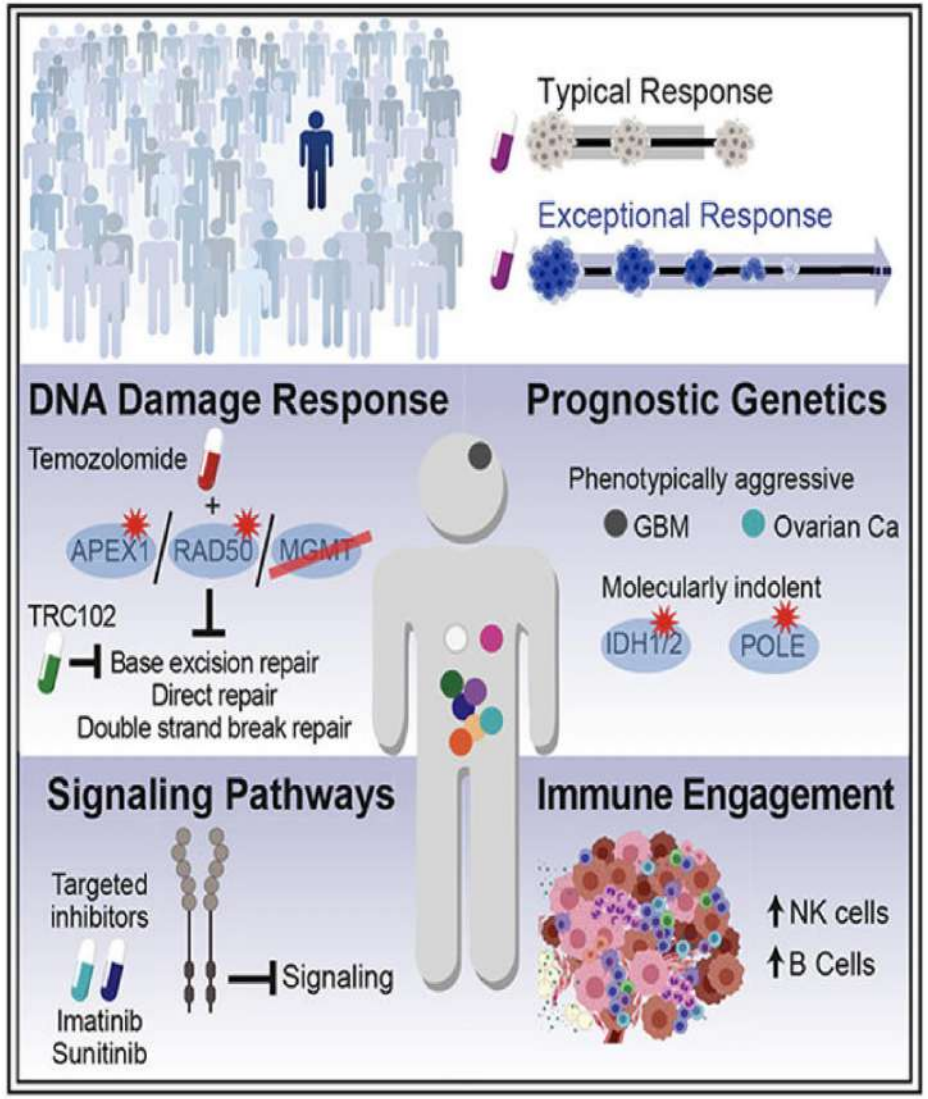
Demetri, ESMO 2018, Abstract 5033

Cancer Cell. 2021 January 11; 39(1): 38–53.e7. doi:10.1016/j.ccell.2020.10.015.

Molecular Features of Cancers Exhibiting Exceptional Responses to Treatment

David A. Wheeler[1,2,17], Naoko Takebe[3,17], Toshinori Hinoue[4], Katherine A. Hoadley[5], Maria F. Cardenas[1,2], Alina M. Hamilton[5], Peter W. Laird[4], Linghua Wang[6], Adrienne Johnson[7], Ninad Dewal[7], Vincent Miller[7], David Piñeyro[8,10], Manuel Castro de Moura[8], Manel Esteller[8,9,10,11], Hui Shen[4], Jean Claude Zenklusen[12], Roy Tarnuzzer[12], Lisa M. McShane[3], James V. Tricoli[3], Paul M. Williams[13], Irina Lubensky[3], Geraldine O'Sullivan-Coyne[3], Elise C. Kohn[3], Richard F. Little[3], Jeffrey White[3], Shakun Malik[3], Lyndsay Harris[3], Carol Weil[3], Alice P. Chen[3], Chris Karlovich[13], Brian Rodgers[3], Lalitha Shankar[3], Paula Jacobs[3], Tracy Nolan[14], Jianhong Hu[1], Donna M. Muzny[1], Harshavardhan Doddapaneni[1], Viktoriya Korchina[1], Julie Gastier-Foster[15], Jay Bowen[15], Kristen Leraas[15], Elijah F. Edmondson[16], James H. Doroshow[3], Barbara A. Conley[3], S. Percy Ivy[3,18], Louis M. Staudt[12,18,19,*]

A small fraction of cancer patients with advanced disease survive significantly longer than patients with clinically comparable tumors. Molecular mechanisms for exceptional responses to therapy have been identified by genomic analysis of tumor biopsies from individual patients. Here, we analyzed tumor biopsies from an unbiased cohort of 111 exceptional responder patients using multiple platforms to profile genetic and epigenetic aberrations as well as the tumor microenvironment. Integrative analysis uncovered plausible mechanisms for the therapeutic response in nearly a quarter of the patients. The mechanisms were assigned to four broad categories—DNA damage response, intracellular signaling, immune engagement, and genetic alterations characteristic of favorable prognosis—with many tumors falling into multiple categories. These analyses revealed synthetic lethal relationships that may be exploited therapeutically and rare genetic lesions that favor therapeutic success, while also providing a wealth of testable hypotheses regarding oncogenic mechanisms that may influence the response to cancer therapy.



In Brief

Profiling multi-platform genomics of 110 cancer patients with an exceptional therapeutic response, Wheeler et al. identify putative molecular mechanisms explaining this survival phenotype in ~23% of cases. Therapeutic success is related to rare molecular features of responding tumors, exploiting synthetic lethality and oncogene addiction.

Table 1.

Cases with Strong Hypothesis for Exceptional Response

Case Number	Cancer Type	Treatment Associated with Exceptional Response	Response	Duration (months)	Exceptional Responder Category				Key Molecular Findings[b]
					DDR	Signaling Pathway	Immune[a]	Prognostic Genetics	
0072	oligoastrocytoma (G3)	irinotecan	CR	57			t	+	• IDH1 p.R132H; 1p, 19q loss (prognostic genetics)
0151	astrocytoma (G3)	bevacizumab, irinotecan	PR	96			n	+	• IDH1 p.R132H, ATRX p.D497fs (prognostic genetics)
0187	glioblastoma multiforme	cediranib, cilengitide (NCT00979862)	CR	111			b	+	• IDH1 p.R132H (prognostic genetics)
0305	astrocytoma (G3/4)	cabozantinib (NCT01068782)	CR	60			b	+	• IDH1 p.R132L, ARTX p.I2050N (prognostic genetics)
0394	glioblastoma multiforme	RT, TMZ	CR	117	+			+	• IDH1 p.R132H, ATRX p.M1839K (prognostic genetics) • MGMT, DDB2 promoter me (DDR)
0486	astrocytoma, grade 3	RT, TMZ, irinotecan (NCT00099125)	CR	145	+			+	• IDH1 p.R132C, ATRX p.E991fs (prognostic genetics) • MGMT, DDB2, POLE4 promoter me (DDR)
0366	glioblastoma multiforme	gliadel wafer, RT, TMZ	CR	135	+				• inactivating translocation APEX1 (DDR) • MGMT, EXO5 promoter methylation (DDR) • low MGMT and APEX1 expression (DDR)
0256	astrocytoma anaplastic	bevacizumab, irinotecan	CR	103	+		n/a	+	• MSI: MLH1 p.R100*; POLE p.V411L (DDR, prognostic genetics, immune)
0075	breast ductal adenocarcinoma, ER− PR− Her2+	trastuzumab, carboplatin, docetaxel	CR	76	+		t		• BRCA2 p.W563*, BRIP1 p.S601*, TOP1 p.F329fs; BRCA1[c] del (DDR)
0197	breast ductal adenocarcinoma, ER− PR− Her2+	trastuzumab, capecitabine	CR	72	+	+			• germline POLQ p.S1632* (DDR) • high ERBB2 expression (signaling pathway)
0512	breast ductal adenocarcinoma, ER+ PR− Her2+	anastrazole, trastuzumab	PR	30		+	tnb		• high CYP19A; Low ERBB2 expresssion (signaling pathway) • ERBB2 amplification (signaling pathway)
0513	breast ductal adenocarcinoma, ER+ PR+ Her2+	trastuzumab, pertuzumab (NCT01615068)	CR	37		+	t		• high ERRB2, ERBB3 expression (signaling pathway) • ERBB2 amplification (signaling pathway)
0399	cholangiocarcinoma	gemcitabine, cisplatin	CR	18	+		b		• TP53 p.R248Q, BRCA2 p.A1648fs[c] (DDR)
0493	cholangiocarcinoma	gemcitabine, cisplatin	CR	12	+				• TP53 p.C135F, extensive chromosome instability, mTOR p.T2380A (DDR)
0349	colon adenocarcinoma	irinotecan	CR	56	+		nb		• ATM p.R337C (DDR) • high TOP1 expression (DDR)

Case Number	Cancer Type	Treatment Associated with Exceptional Response	Response	Duration (months)	Exceptional Responder Category				Key Molecular Findings[b]
					DDR	Signaling Pathway	Immune[a]	Prognostic Genetics	
0474	colon adenocarcinoma	TMZ, TRC102 (NCT01851369)	PR	45	+				• MGMT promoter me, low MGMT expression germline RAD50 p.N1238N (DDR)
0483	rectal adenocarcinoma	bevacizumab, capecitabine, oxaliplatin	CR	53	+		b		• BRCA1 exons 7–8 del,[c] POLN splice site mutation (DDR)
0454	endometrial carcinoma	temsirolimus, carboplatin, taxol (NCT00977574)	CR	70	+	+	t b	+	• MSI: MLH1 promoter me (DDR, immune) • PIK3CA p.Y1021C, PTEN fs (signaling pathway) • BRCA2 p.T3033fs, SLX4 p.G142fs, WRN p.G327fs (DDR)
0096	gastrointestinal stromal	sunitinib	CR	9		+			• KIT exon 11 del: YEVQ (signaling pathway) • KDR, FLT1, FLT3 expression (signaling pathway)
0214	gastrointestinal stromal	imatinib	CR	70		+	tnb		• KIT exon 11 del: EVQWKVVE (signaling pathway) • high KIT; deficient SDHB expression (signaling pathway)
0392	GE junction adenocarcinoma	EOX	CRs	32	+	+			• TP53 p.G245S, germline EXO1 p.D249N (DDR)
0190	lung, non-small cell	afatinib	CR	6		+	t		• EGFR del exon 19 (signaling pathway)
0428	Lung, squamous cell	carboplatin, taxol	CR	25	+		tn		• PALB2 p.W898*, DDB1 p.Q466fs, (2) TP53 p.R158H, fs
0009	ovarian carcinoma, clear cell and serous features	bevacizumab	PR	41		+	tbn	+	• POLE p.V411L (prognostic genetics) • high VEGFA expression (signaling pathway)
0396	pancreatic adenocarcinoma	FOLFOX	CR	10	+				• TP53 splice site, germline BRCA1 p.K339fs (DDR)
0401	urothelial carcinoma	nivolumamb (NCT023387996)	CR	16			t		• high PD1, PDL1; highest IFNG expression (immune)[d]

Abbreviations and treatments: afatinib, tyrosine kinase inhibitor targeting EGFR; cilengitide, binds α-integrins inhibiting angiogenesis; cediranib, inhibitor of VEGF receptor; CR, complete response; PR, partial response; DDR, DNA damage repair, which includes the following pathways: homology-dependent recombination; nucleotide excision repair; base excision repair; nonhomologous end joining; EOX, epirubicine, oxaloplatin, capecitabin; FOLFOX, folinic acid, 5FU, oxaliplatin; gliadel wafer, infused with carmustine (bis-chloroethylnitrosourea [BCNU]), an alkylating agent; imatinib, tyrosine kinase inhibitor targeting PDGFR, ABL, KIT, DDR1, ABL2, NQO2 (N-ribosyldihydronicotinamide:quinone reductase; and oxidoreductase); me, DNA methylation; TMZ, temozolomide; TRC102, methoxyamine, inhibitor of BER through binding to apurinic/apyrimidinic sites. Causes TOP2-dependent irreversible strand breaks and apoptosis; RT, radio therapy.

[a] Immune categories. Three cell types were of interest (see text) with single letter designations: t, T cell; n, NK cell $CD56^{dim}$; b, B cell. Each letter indicates when an ER tumor was in the upper quartile for infiltration by the given immune cell (see the STAR Methods), n/a, not available.

[b] All reported genetic alterations are clonal.

[c] See also Figure S3A and S3B.

2020 Annual Report

New Targeted Therapies Transform Lives

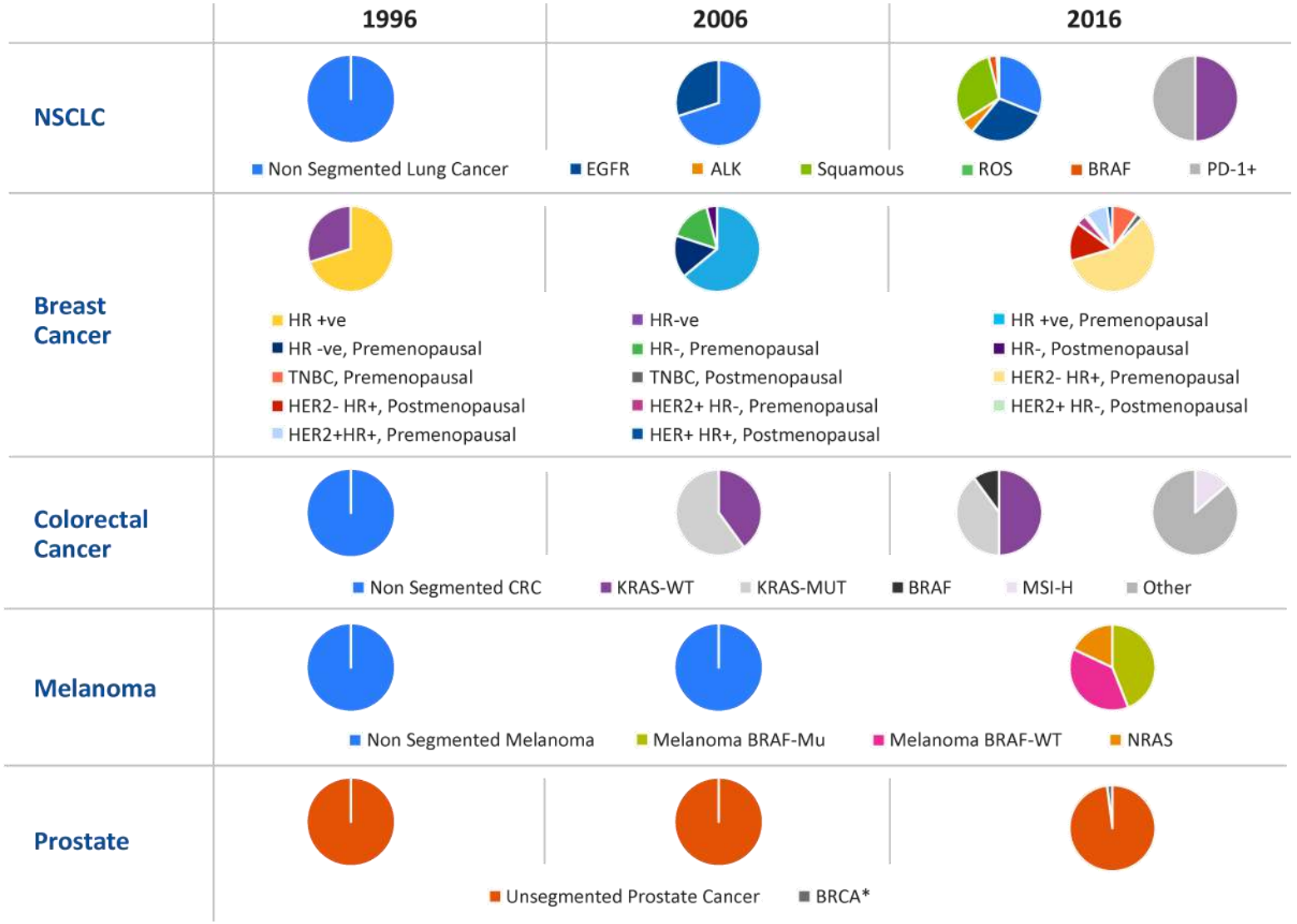
Chief of the Early Drug Development Service Alexander Drilon says targeted therapies can help some patients achieve a "Lazarus effect" — dramatic improvement when they've run out of other options.

"We've seen sick patients who were practically knocking on death's door," says Alexander Drilon, Chief of Memorial Sloan Kettering's Early Drug Development (EDD) Service. "Targeted therapy then achieved a Lazarus effect — their cancer-related symptoms dramatically improved, and they went back to living their lives the way they did prior to their cancer diagnosis."

In just the past three years, the US Food and Drug Administration has approved three drugs developed by the EDD and Dr. Drilon's team, working with pharmaceutical companies. In May 2020, selpercatinib (Retevmo™) was approved to treat lung and thyroid cancers driven by *RET* fusions or mutations. In August 2019, entrectinib (Rozlytrek™) was approved for lung cancer driven by *ROS1* fusions and all cancers driven by *NTRK* fusions. In November 2018, larotrectinib (Vitrakvi®) was approved for adult and pediatric tumors driven by *NTRK* fusions. All of these drugs are targeted therapies, which block the cancer-causing genes and directly attack tumors while mostly sparing healthy cells.

Doctors in the EDD Service specialize in developing new therapies for cancers, including those with specific gene changes. "Immunotherapy can work extremely well for some cancers," Dr. Drilon says, adding that his patients often ask if these drugs are an option. "But for cancers caused by a mutation or fusion, targeted therapy can work much better." Unlike therapies that activate the immune system to fight the cancer, targeted therapy drugs like selpercatinib, entrectinib, and larotrectinib turn off the signals that tell cancer cells to grow and divide.

Biomarker-based segmentation



IQVIA, Global Oncology Trends 2017

Lazarus syndrome in nonsmall cell lung cancer patients with poor performance status and major leukocytosis following nivolumab treatment

Nivolumab appears efficacious in highly PD-L1-expressing NSCLC with poor PS, resulting in Lazarus syndrome http://ow.ly/X92e30coTsB

Cite this article as: Pluvy J, Brosseau S, Naltet C, *et al*. Lazarus syndrome in nonsmall cell lung cancer patients with poor performance status and major leukocytosis following nivolumab treatment. *Eur Respir J* 2017; 50: 1700310 [https://doi.org/10.1183/13993003.00310-2017].

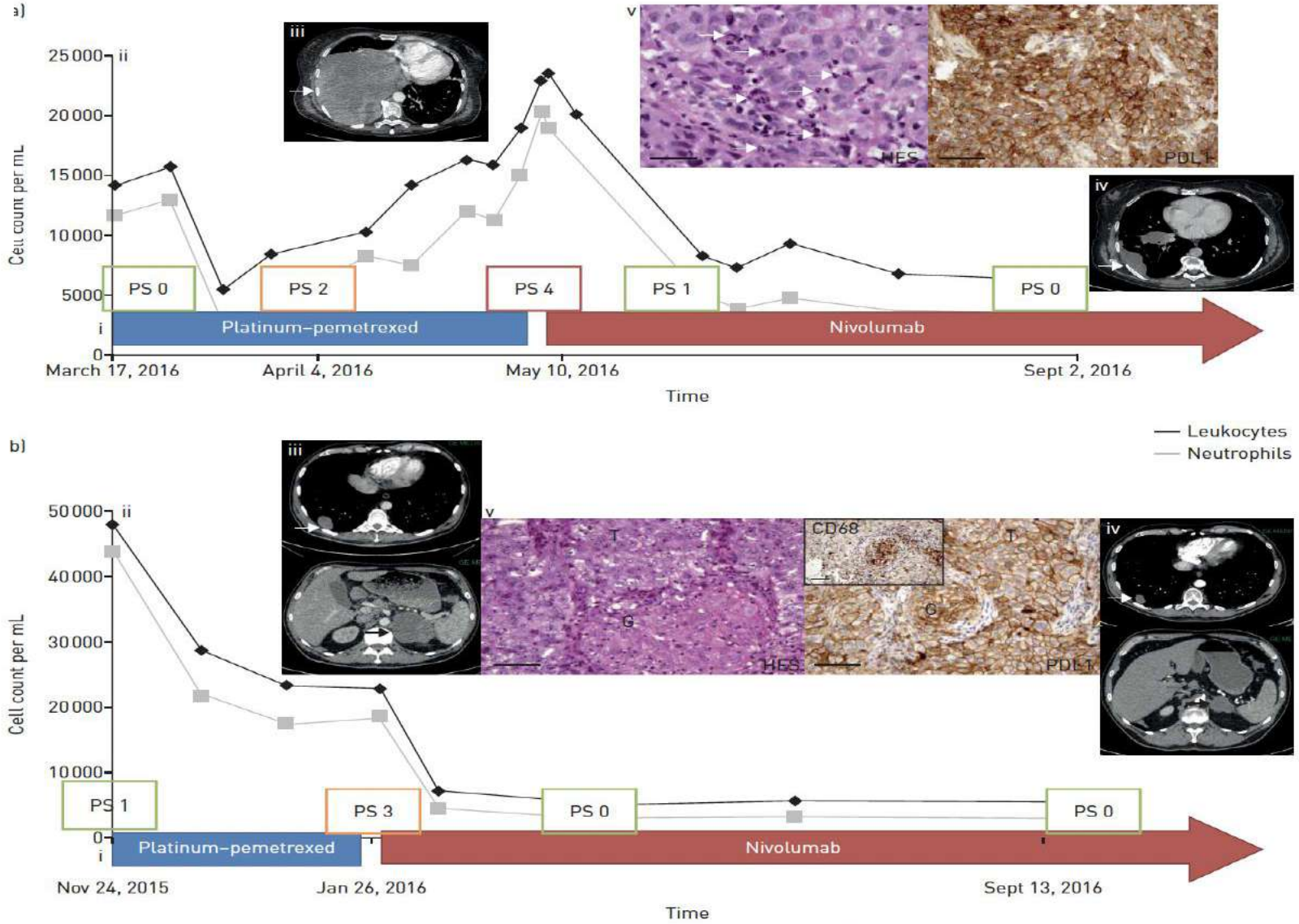
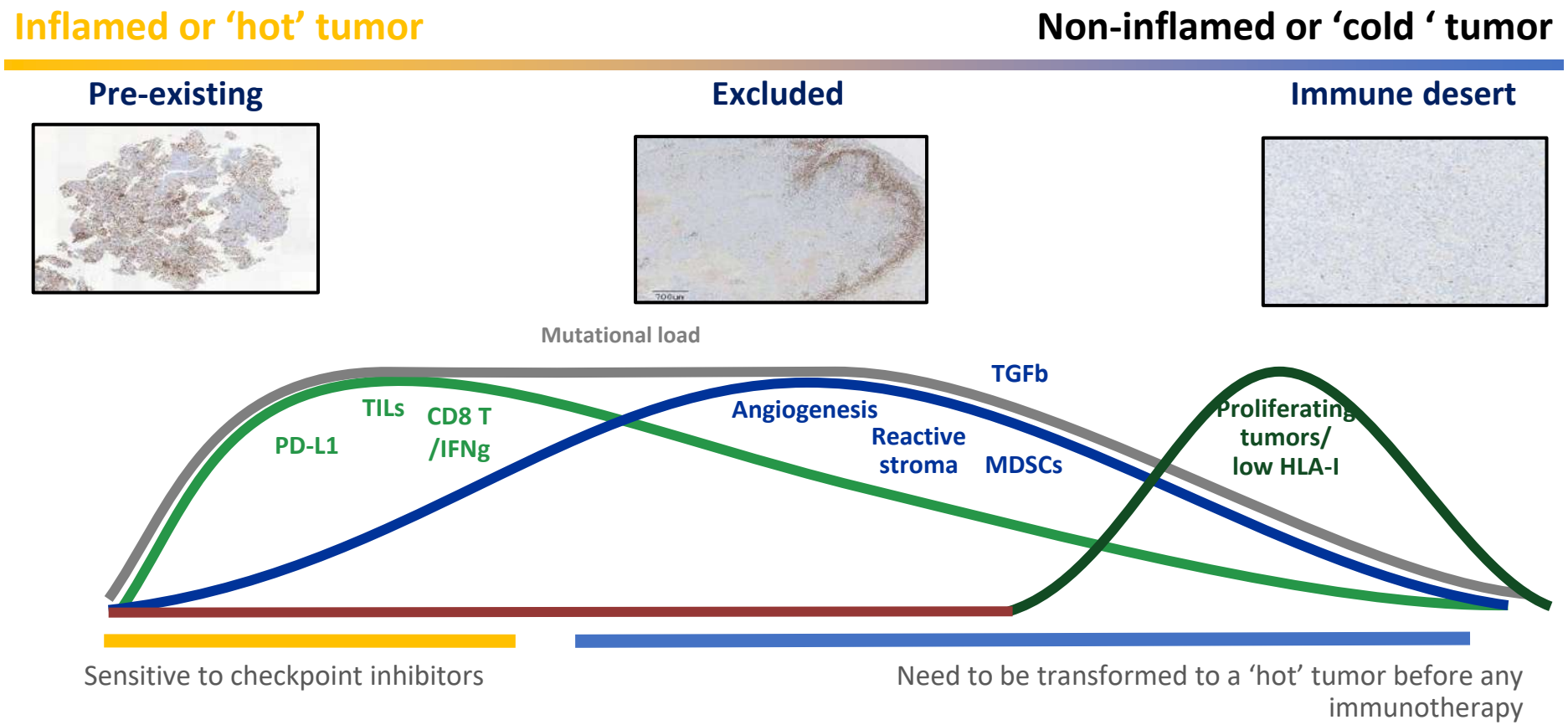


FIGURE 1 a) "Lazarus"-type response in a 47-year-old woman with metastatic nonsmall cell lung cancer (NSCLC): biological, pathological, clinical and radiologic findings timeline. i) Timeline of performance status (PS) evolution and therapies. ii) Leukocyte and neutrophil counts over time. iii) Computed tomography (CT) scan before starting nivolumab showing extensive mass in the right lung. iv) Latest findings of CT scan, with important partial response. v) Haematoxylin and eosin stain (HES) (left panels; scale bar=50 μm) and tumour programmed death ligand 1 (PD-L1) immunostaining (right panels; scale bar=50 μm), with rabbit mAb E1L3N monoclonal antibody from Cell Signaling Technology at 1/400 dilution using Leica BOND-MAX autostainer. Arrowheads indicate neutrophils infiltrating tumour cells. b) Rapid response for a man PS 3 with metastatic lung adenocarcinoma: biological, pathological, clinical and radiologic findings timeline. i) Timeline of PS evolution and therapies. ii) Leukocyte and neutrophil count over time. iii) CT scan before initiation of nivolumab, showing inferior right lobe mass, left adrenal gland metastasis. iv) Latest CT scan, showing persistent partial response. v) Positive HES (left panels; scale bar=100 μm), and tumour PD-L1 immunostaining (right panels; scale bar=100 μm) with rabbit mAb E1L3N monoclonal antibody from Cell Signaling Technology at 1/400 dilution using Leica BOND-MAX platform. Inset in upper right panel displays CD68 immunostaining (scale bar=50 μm) (clone KP1 from Dako at 1/100 dilution), showing the granulomatous tumour stroma. T: tumour cells; G: granuloma.

Immune phenotypes and cancer

The tumor biology of each patient generates a different immune response. Phenotypes must be defined in individual patients



Hegde et al, Clin Cancer Res 2016

Case Report: A Case Study Documenting the Activity of Atezolizumab in a PD-L1-Negative Triple-Negative Breast Cancer

Fara Brasó-Maristany[1,2†], Miriam Sansó[3,4†], Nuria Chic[1,2], Débora Martínez[1,2], Blanca González-Farré[1,5], Esther Sanfeliu[1,5], Lucio Ghiglione[2], Esther Carcelero[6], Javier Garcia-Corbacho[1,2], Marcelo Sánchez[7], Dolors Soy[6], Pedro Jares[8], Vicente Peg[9], Cristina Saura[9,10,11], Montserrat Muñoz[1,2], Aleix Prat[1,2,3,10,11,12‡] and Ana Vivancos[3*‡]*

[1] Translational Genomics and Targeted Therapies in Solid Tumors, August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain, [2] Department of Medical Oncology, Hospital Clínic of Barcelona, Barcelona, Spain, [3] Cancer Genomics Group, Vall d'Hebron Institute of Oncology, Barcelona, Spain, [4] Department of Oncology and Hematology, Health Research Institute of the Balearic Islands (IdISBa), Palma de Mallorca, Spain, [5] Department of Pathology, Hospital Clínic de Barcelona, Barcelona, Spain, [6] Department of Pharmacy, Hospital Clínic of Barcelona, Barcelona, Spain, [7] Department of Radiology, Hospital Clínic of Barcelona, Barcelona, Spain, [8] Molecular Biology Core, Hospital Clinic of Barcelona, Barcelona, Spain, [9] Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology (VHIO), Medical Oncology Service, Barcelona, Spain, [10] SOLTI Cooperative Group, Barcelona, Spain, [11] Department of Oncology, Institut Oncològic Baselga (IOB) Institute of Oncology, Quironsalud Group, Barcelona, Spain, [12] Department of Medicine, University of Barcelona, Barcelona, Spain

Front Oncol 2021

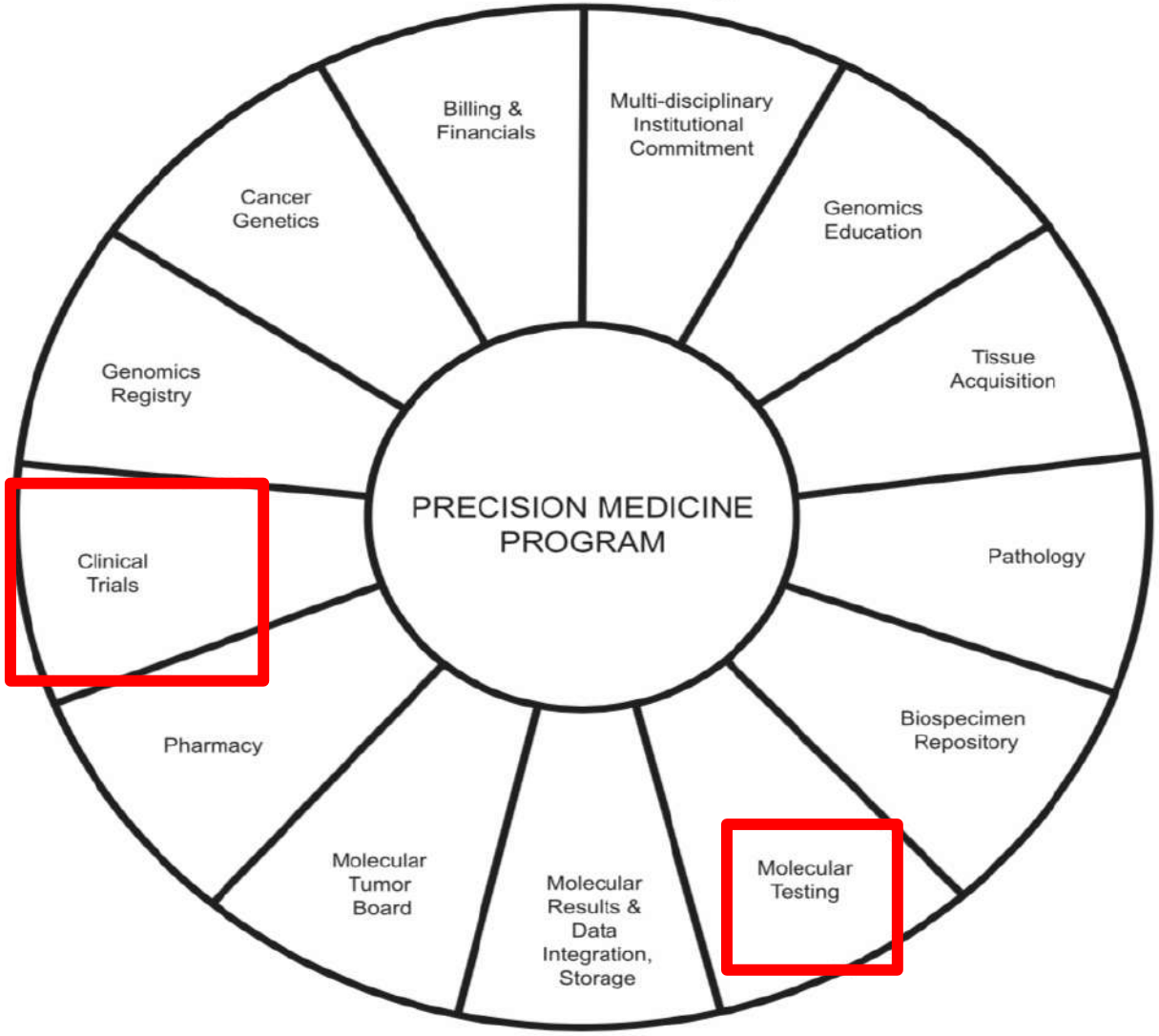
The immune checkpoint inhibitor atezolizumab is approved for PD-L1-positive triple-negative breast cancer (TNBC). However, no activity of atezolizumab in PD-L1-negative TNBC has been reported to date. Here, we present the case study of a woman with TNBC with low tumor infiltrating lymphocytes and PD-L1-negative disease, which achieved a significant response to atezolizumab monotherapy and durable response after the combination of atezolizumab and nab-paclitaxel. The comprehensive genomic analysis that we performed in her tumor and plasma samples revealed high tumor mutational burden (TMB), presence of the APOBEC genetic signatures, high expression of the tumor inflammation signature, and a HER2-enriched subtype by the PAM50 assay. Some of these biomarkers have been shown to independently predict response to immunotherapy in other tumors and may explain the durable response in our patient. Our work warrants further translational studies to identify biomarkers of response to immune checkpoint inhibitors in TNBC beyond PD-L1 expression and to better select patients that will benefit from immunotherapy.

Retos de atención clínica en oncología

- Diagnóstico precoz, programas de diagnóstico rápido
- Adaptar el tratamiento a las necesidades del paciente: pediatría, pacientes ancianos...
- Implementación de programas de medicina de precisión
- Acceso a fármacos
- Ensayos clínicos
- Atención integral a largos supervivientes
- Datos de vida real
- Establecer una red de infraestructuras integrales contra el cáncer *dentro y entre todos los estados miembros de la UE para aumentar la calidad de la investigación y la atención y para garantizar que "cada ciudadano o paciente de la UE tenga acceso y pueda beneficiarse de una investigación y atención del cáncer de alta calidad”*

Precision oncology

FIGURE 1. Attributes of a Successful Precision Medicine Program



Jennifer L. Ersek

NGS ESMO recommendations

Tumor type	NGS recommendation	Level I Alterations	Level II Alterations	Level III Alterations
NON-SQUAMOUS NSCLC	**YES (Daily practice)**	***EGFR , ALK, MET, BRAF ^{V600E}, ROS1, RET, NTRK***	*EGFR* (exon 20 insertions), *MET* (focal amplifications), *KRAS^{G12C}, ERBB2*	*BRCA1/2, PIK3CA, NRG1*
METASTATIC COLORECTAL CANCER	**YES (With cost considerations)**	*BRAF ^{V600E}* MSI-H, *NTRK* fusions	*ERBB2 amplifications*	*PIK3CA, ATM, MET, AKT1^{E17K} RET, ALK*
ADVANCED CHOLANGIO CARCINOMA	**YES (Daily practice)**	*IDH1, FGFR2, MSI-H, NTRK*	*BRAF ^{V600E}*	*ERBB2, PIK3CA, BRCA 1/2, MET*
CANCER OF UNKNOWN PRIMARY (CUP)	**YES**	No evidence		
OVARIAN CANCER	**YES (Daily practice)**			
ADVANCED PROSTATE CANCER	**YES (Daily practice)**	*BRCA1/2, ATM MSI-H*	*PTEN, PALB2*	*PIK3CA, AKT1^{E17K}*

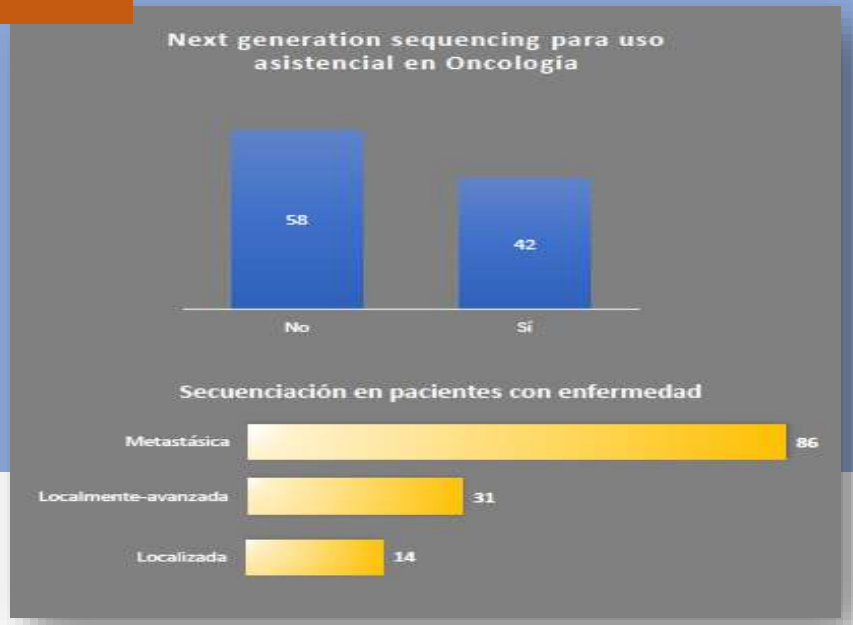
Mosele Ann Oncol 20

Encuesta SEAP-SEOM de medicina de precisión

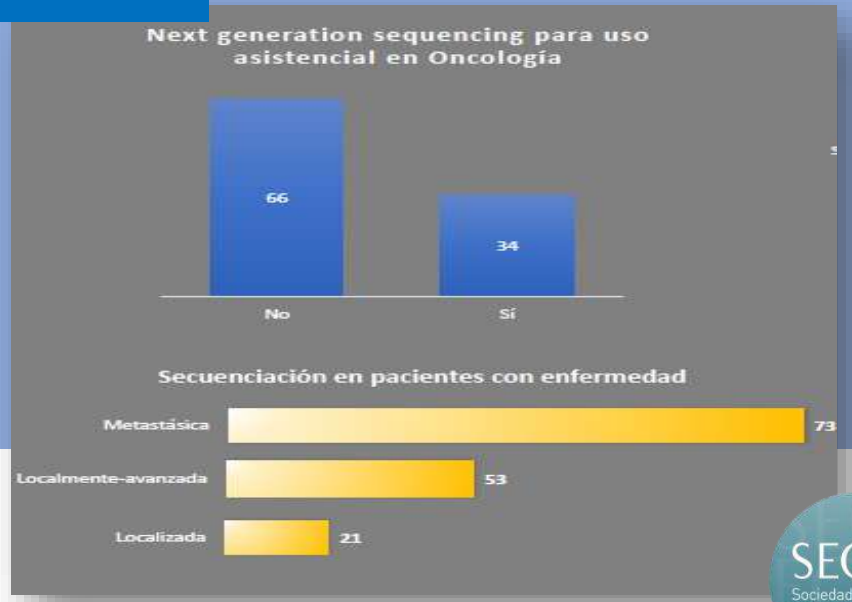
Encuesta a los Servicios de Oncología Médica y Anatomía Patológica (Diciembre 21)

- 40% de los encuestados tiene acceso a la NGS asistencial
- 49% tiene acceso a la biopsia líquida

ONCÓLOGOS



PATÓLOGOS



SEOM
Sociedad Española de Oncología Médica

Druggable targets meet oncogenic drivers: opportunities and limitations of target-based classification of tumors and the role of Molecular Tumor Boards

R. Danesi[1], S. Fogli[1†], S. Indraccolo[2], M. Del Re[1], A. P. Dei Tos[3], L. Leoncini[4], L. Antonuzzo[5], L. Bonanno[6], V. Guarneri[6,7], A. Pierini[8], G. Amunni[9*] & P. Conte[6,7]

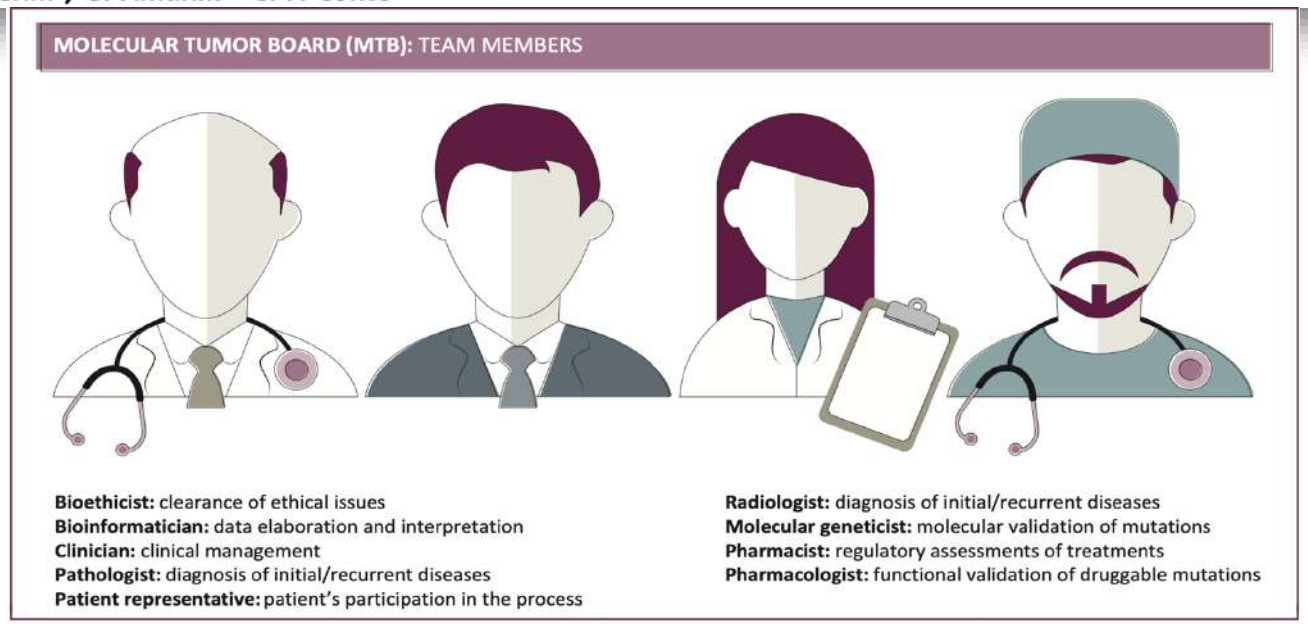


Figure 2. **Composition and function of the Molecular Tumor Board (MTB).**

CONCLUSIONS

An increasing number of new targeted drugs demonstrated clinical benefits in multiple cancer types. The availability of new technologies (e.g. next generation sequencing) and approaches (e.g. liquid biopsy) allow clinicians to better select patients based on their genetic make-up. Therefore, in the era of precision medicine, integration of different professional skills is mandatory and the establishment of MTB may represent the most important asset to support clinicians in translating new scientific knowledge into daily clinical practice. Target-based classification is increasingly used to integrate the histology-based classification of tumors, which remains the backbone of cancer diagnosis and management.

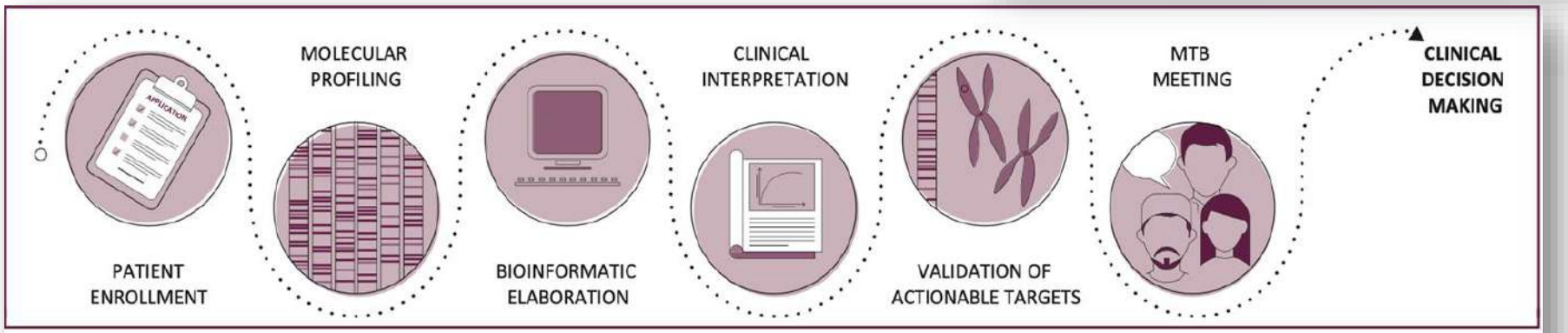
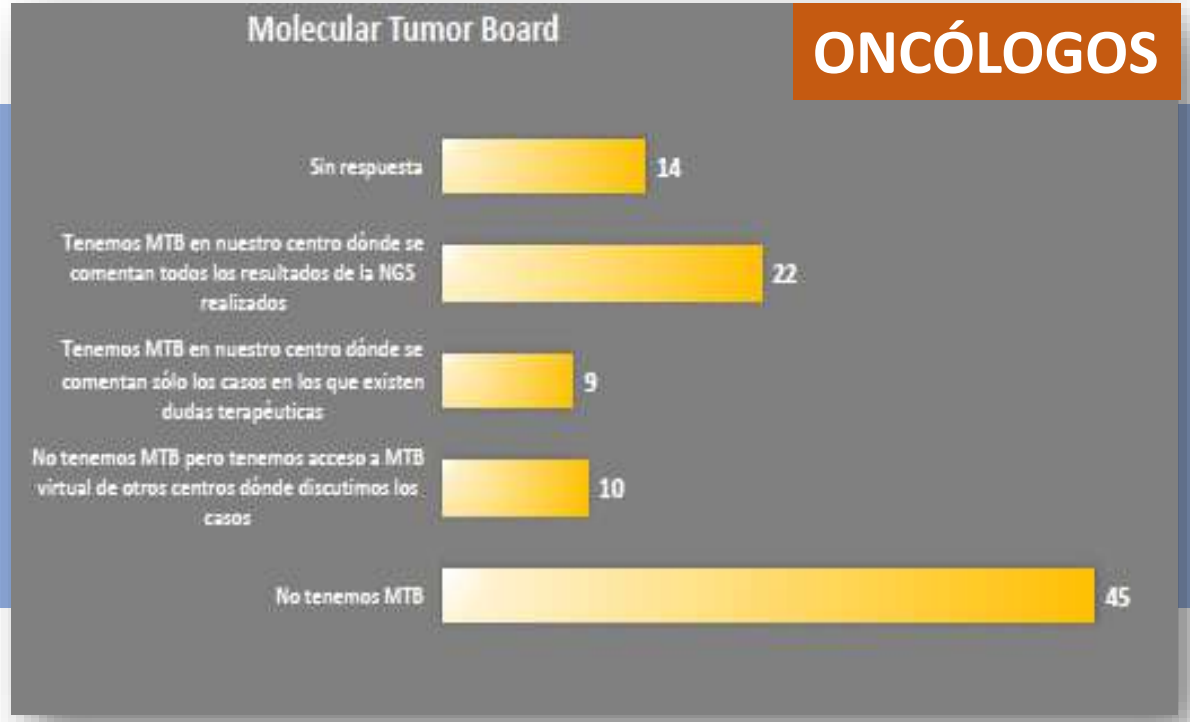
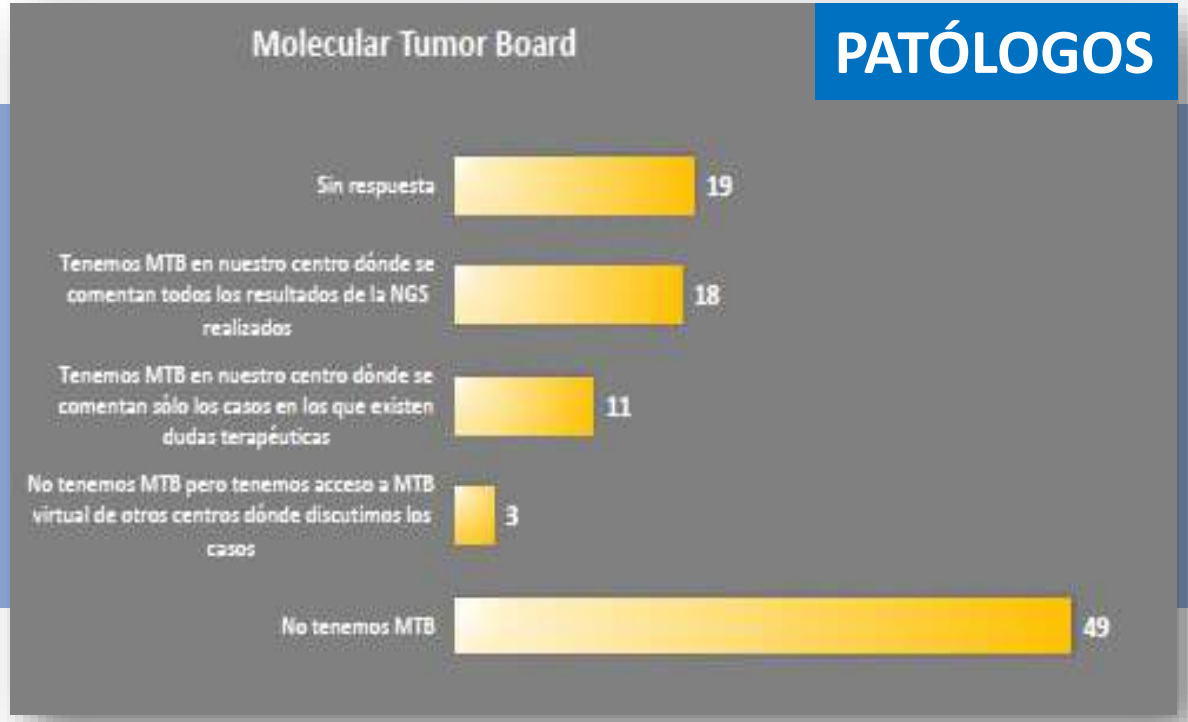


Figure 3. **Work flow—from patient enrollment to pharmacological treatment selection.**

Resultados: molecular Tumor Board

- El **30% de los centros españoles** dispone de **MTB** dónde se discuten los **casos de NGS**





Centres de referència (n=11): Designats basat en criteris d'experiència prèvia amb panells, recerca competitiva en aquest àmbit, disponibilitat de professionals amb expertesa i de la tecnologia:

- Equips multidisciplinars: hematòlegs clínics, patòlegs, oncòlegs mèdics, biòlegs moleculars, bioinformàtics, entre altres.
- **Comitè de Tumors:** per avaluar casos de resultats dubtosos.
- **Panels diferenciats (4)** segons: tumors sòlids, hematològics, infantils i línia germinal (mama-ovari i resta).
- **Circuits establerts** per realitzar estudis genètics pels centres externes indicats a la Instrucció.

NGS

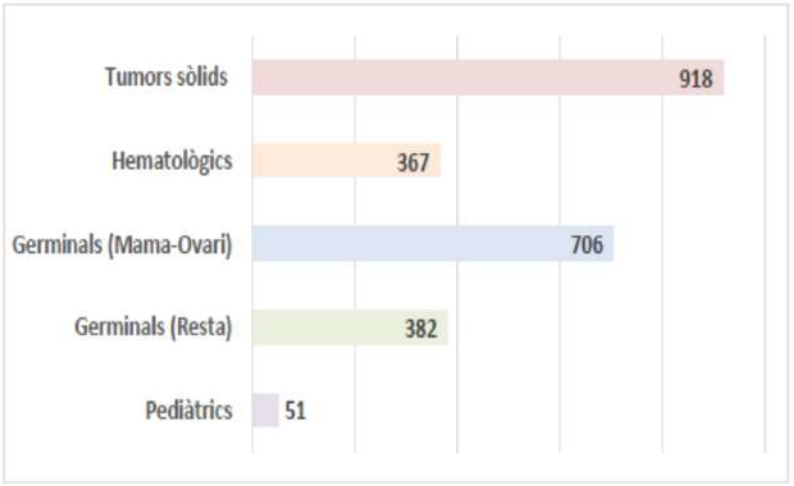
Panel sòlid	Panel Hematològic	Panel Hereditari	Panel Pediàtric
• H. Vall d'Hebron • H. Clínic • H. Bellvitge • ICO • H. Sant Pau • H. Mar	• H. Vall d'Hebron • H. Clínic • HGTiP • H. Sant Pau • H. Mar	• H. Vall d'hebron • H. Clínic • H. Sant joan de Reus • ICO • H. Parc Taulí • CS Terrassa • H. Sant Pau • H. Mar	• H. Sant Joan de Déu • H. Vall d'Hebron

MTB inter-hospital 2021-22

S/Seguiment de l'activitat

Resum activitat 2022

- Primer trimestre: **2.424 mostres totals**



- Estimació creixement anual del Programa (2021-2022):

Any 2021: 3.206 casos registrats (5,5 mesos) -> 6.995 anuals estimats

Any 2022: 2.424 casos registrats (3 mesos) -> 9.696 anuals estimats

Increment anual 39%

⇩

Millora del Programa (circuits)
Nous tractaments / marcadors
Recaigudes

Generalitat de Catalunya

/Salut

OBSERVATORIO Medicina de Precisión

- Mapa con respuestas por CCAA a la encuesta de SEOM sobre Medicina de Precisión

Miembros de la Comisión

- Dra. Enriqueta Felip Font *(Coordinadora)*
- Dra. Pilar Garrido López *(Coordinadora)*
- Dr. Javier de Castro Carpeño
- Dr. Ramon Colomer i Bosch
- Dra. Carmen Esteban Esteban
- Dr. Juan de la Haba Rodríguez
- Dr. Antonio González Martín
- Dr. Rafael López López
- Dr. Aleix Prat Aparicio
- Dr. David Vicente Baz

OBSERVATORIO Medicina de Precisión SEOM Sociedad Española de Oncología Médica

Medicina de Precisión

Respuestas por CCAA a la encuesta de SEOM

SEOM ha elaborado un informe interno que esboza la situación de la estrategia de Medicina Precisión en Oncología en las Comunidades Autónomas con el fin de poder contribuir a establecer las bases para mejorar la implementación de la medicina personalizada en nuestro país, de manera homogénea y equitativa y ponernos a disposición de las Consejerías de Salud y del Ministerio de Sanidad.
Este informe SEOM se ha realizado mediante encuesta a facultativos especialistas de Oncología Médica, miembros de SEOM, en representación del colectivo de su Comunidad Autónoma.

Nota sobre la navegación por los mapas: *Si accede desde su ordenador, puede hacer zoom sobre el mapa haciendo doble click en cualquier parte del mismo.*

¿Existe una Estrategia de Medicina de Precisión en Oncología en tu Comunidad?

¿Nos puedes resumir los puntos más importantes?

¿Cuál es el órgano de gobernanza y quiénes lo constituyen?

¿Se han definido centros de referencia?

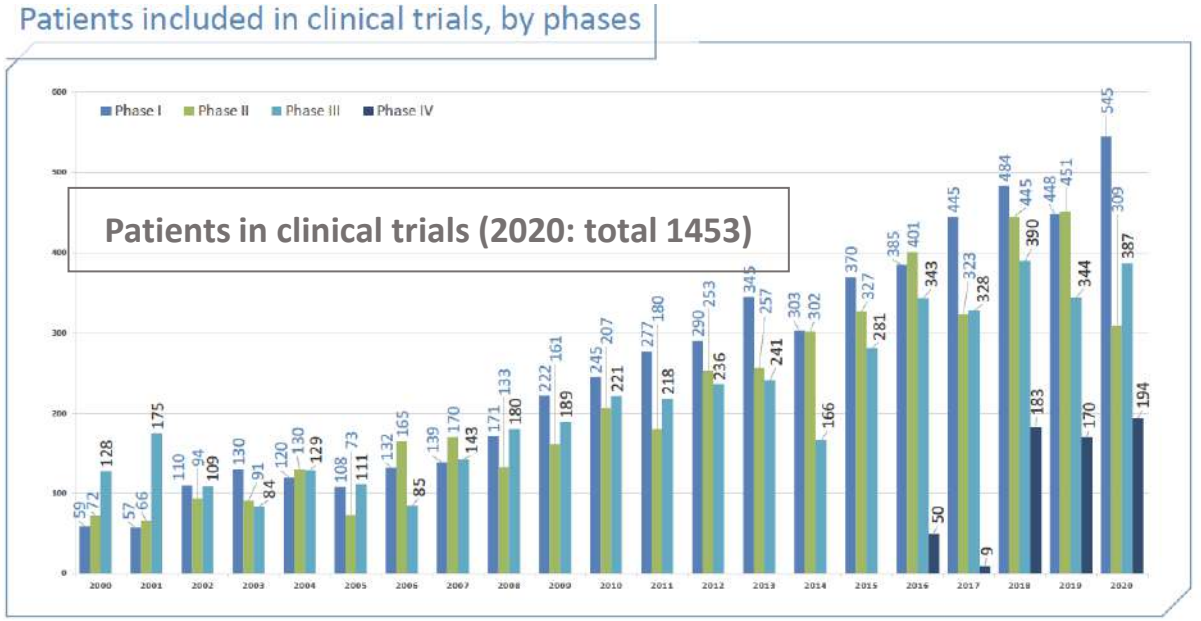
¿Qué nivel de implantación tiene?

¿Qué tecnología integra (NGS, inmunohistoquímica etc.)?

¿Quién sufraga esa tecnología?

Clinical trials, VHIO

Number of active clinical trials (2020: total 791)



Since 2012, UITM has participated in clinical trials leading to **30**
FDA-approved drugs for the treatment of specific cancer types

VHIO has been pioneer in the development of a molecular prescreening program. The Program, under continuous development, has been through several phases including a personalized Onco-panel of 70 genes, and nowadays with a 400+ gene panel equivalent to gold standards in the field like FoundationOne or MSKCC- IMPAKT.
Around 1500 patients benefit from the program yearly

Actualidad de la OEC VHIO

EECC:

- Herramienta fundamental para avanzar
- Oportunidad terapéutica para los pacientes

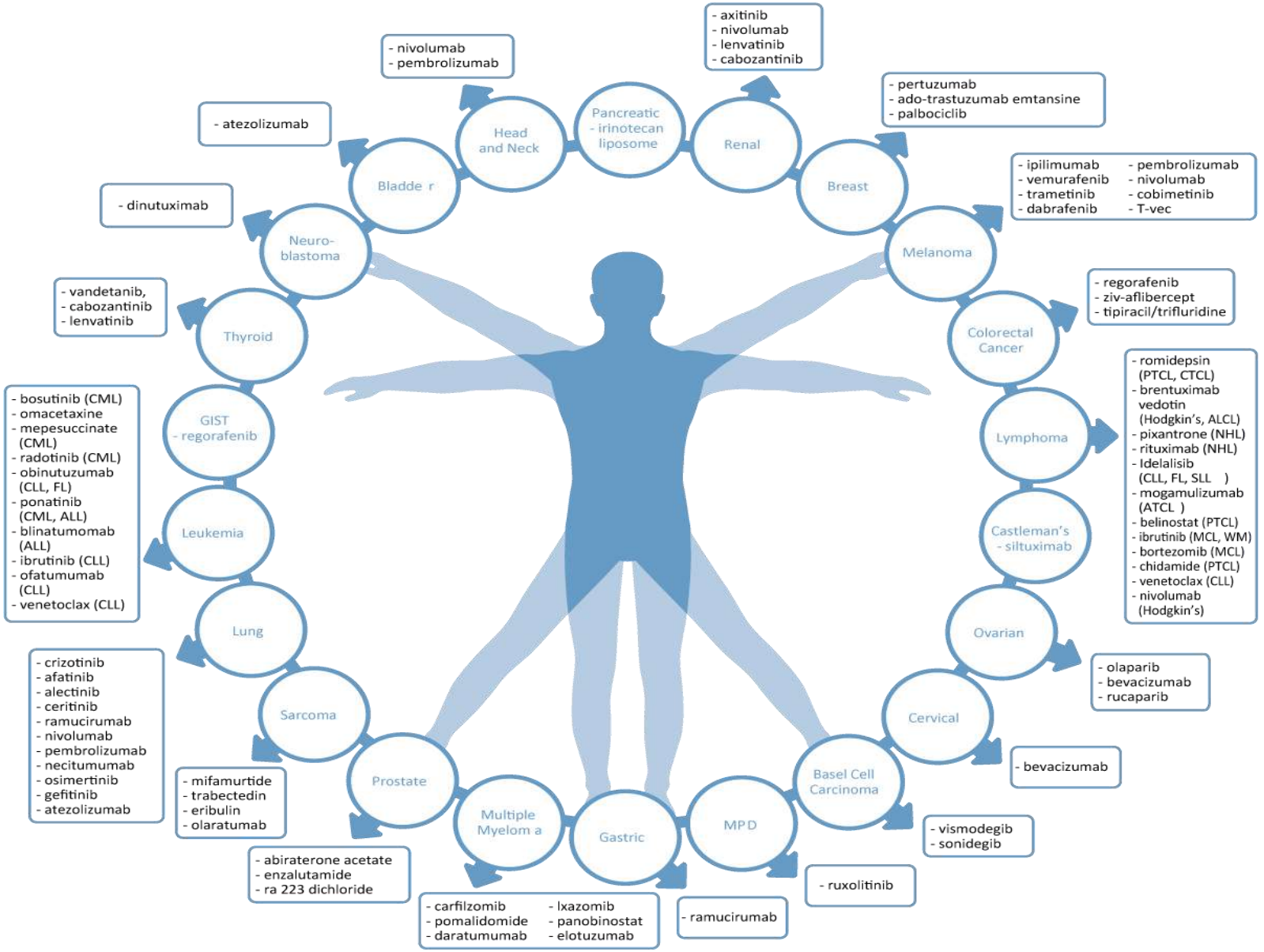
- > 350 ensayos
- > 1200 pacientes incluidos /año
- > 1400 pacientes en seguimiento

- **Trabajan > 120 profesionales**:
  - Equipo médico
  - Coordinadores de estudio
  - Gestores de datos
  - Enfermeras
  - Farmacia
  - Personal administrativo
  - Unidad de Calidad y Procesos

Aspectos que deben abordarse para estar preparados para seguir creciendo de forma eficiente

- **Organización:** diferentes profesionales y liderazgos, intereses distintos, sueldos diferentes
- **Dispersión geográfica de espacios y optimización:** actividad en diferentes espacios, dificultad de seguir creciendo en el hospital
- **Comunicación:** asegurar la comunicación interna y externa
- **Gestión de necesidades/expectativas individuales de los profesionales**
  - Carrera profesional
  - Formación continuada
  - Alta rotación de profesionales que son captados por su gran experiencia
  - Captación de talento
- **Calidad:** mantener el crecimiento con incorporación de nuevo personal y con los máximos estándares de calidad
- **Innovación**: incorporación de nuevas metodologías (digitalización, inteligencia artificial)
- **Sostenibilidad económica:** estructura administrativa y de gestión sólida

New active substance (NAS) approvals in oncology by indication, 2013-2017



The cancer treatment landscape has continued to evolve since 2013, and now includes new medicines targeting 23 different cancer types.

From 2013 to 2017, there were 61 unique NAS molecules with 76 indication approvals, with many being approved for more than one indication.

Source: QuintilesIMS, ARK R&D Intelligence, Feb 2017; QuintilesIMS Institute, Mar 2017

SEOM, SEFH y SEHH presentan propuestas de mejora del proceso de incorporación de fármacos al Ministerio de Sanidad y a la AEMPS

Escrito en 12 Mayo 2022

La Sociedad Española de Oncología Médica, la Sociedad Española de Farmacia Hospitalaria (SEFH) y la Sociedad Española de Hematología y Hemoterapia (SEHH) han elaborado un **documento con propuestas para mejorar el proceso de incorporación de los fármacos oncohematológicos de valor a la Cartera Básica de Servicios del Sistema Nacional de Salud**. Este documento ha sido enviado conjuntamente por las tres sociedades al Ministerio de Sanidad y a la Agencia Española del Medicamento y Productos Sanitarios (AEMPS), tras mantener conversaciones previas y se está a la espera de mantener reuniones con ambas entidades. SEFH SEHH y SEOM llevan tiempo trabajando en proyectos de interés para los pacientes con cáncer, incluyendo la elaboración de documentos que mejoren el trabajo multidisciplinar, disminuyan la variabilidad asistencial y promuevan la equidad en el tratamiento oncológico, la transparencia en los procesos y la seguridad clínica. Esta alianza ha dado un paso más y supone un gran avance para **establecer una línea de trabajo de las tres sociedades con el Ministerio de Sanidad y la AEMPS en beneficio de los pacientes con cáncer.**

La SEFH anuncia su retirada del documento de propuestas de mejora del proceso de incorporación c enviado al Ministerio de Sanidad y a la AEMPS

Última actualización: Jueves, 19 Mayo 2022 10:14

La Sociedad Española de Farmacia Hospitalaria (SEFH) anuncia que no va a continuar en la defensa o exposición del documento con propuestas para mejorar el proceso d fármacos oncohematológicos de valor a la Cartera Básica de Servicios del Sistema Nacional de Salud, que había elaborado con la Sociedad Española de Hematología y Hem SEOM.

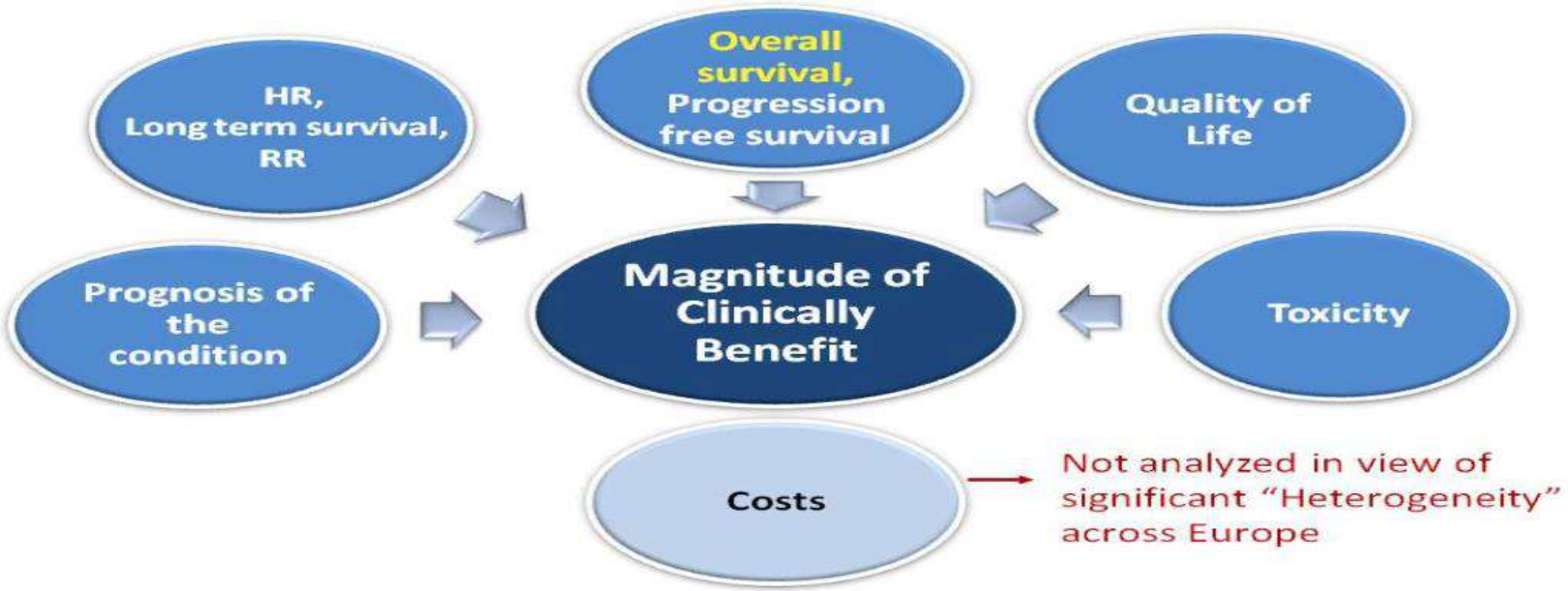
- Garantizar la transparencia y trazabilidad de los procesos de registro de un nuevo medicamento o indicación.
- Indicar la duración de la fase piloto del Plan de Consolidación de los informes de Posicionamiento Terapéutico (IPT), variables de valoración de los resultados y planes posteriores.
- Garantizar la participación de expertos multidisciplinares en la elaboración de los IPTs.
- Asesoría de las sociedades científicas de expertos en elaboración de los IPTs y la evaluación de medicamentos por áreas terapéuticas.
- Publicar las fases en las que se encuentra la elaboración de los IPTs y transparencia en los tiempos de elaboración.
- Valorar la medición del beneficio clínico del medicamento mediante la inclusión de los criterios de la escala ESMO (ESMO-MCBS).
- Revisión periódica de los IPTs.
- Hacer pública la red de evaluadores de REvalMed y su área profesional.
- Hacer públicas las alegaciones que se realizan a los IPTs y las respuestas a las mismas.
- Publicar los criterios que llevan a la financiación de un medicamento o de una indicación, y emitir un informe justificativo cuando se resuelva la no financiación de un medicamento o indicación.
- Cuando se indica que existen alternativas terapéuticas a un medicamento para una indicación debe indicarse cuales son.

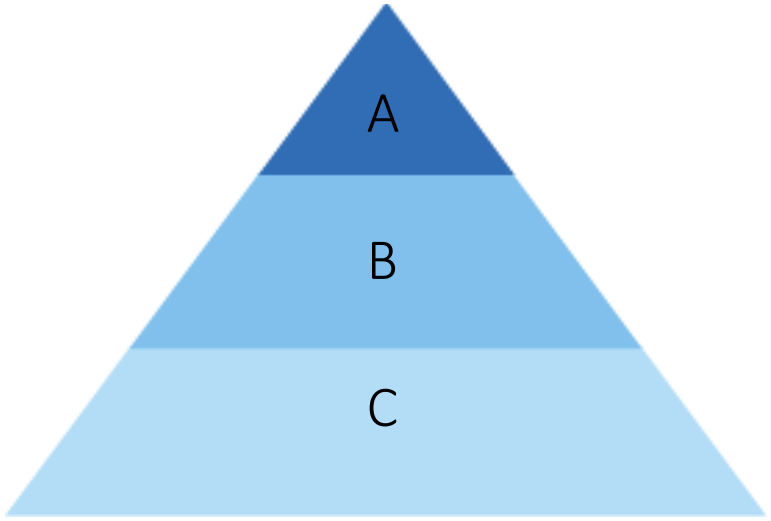
Innovación oncológica: iniciativas para la sostenibilidad

- ESMO magnitude of clinical benefit scale
- Value based payment
- Biosimilars
- Academic research

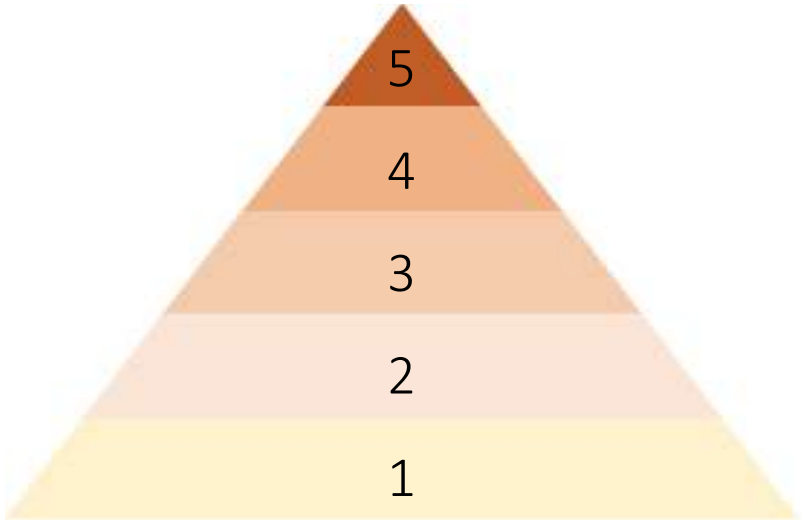
ESMO-MCBS

Factors taken into account for ESMO-MCBS





Curative



Non-curative

Definitions of Real-World Data and Real-World Evidence

Section 505F(b) of the FD&C Act defines RWE as "data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than traditional clinical trials" (21 U.S.C. 355g(b)).[5] In developing its RWE program, FDA believes it is helpful to distinguish between the sources of RWD and the evidence derived from that data. Evaluating RWE in the context of regulatory decision-making depends not only on the evaluation of the methodologies used to generate the evidence but also on the reliability and relevance of the underlying RWD; these constructs may raise different types of considerations. For the purposes of this framework, FDA defines RWD and RWE as follows:

Real-World Data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.

Real-World Evidence (RWE) is the *clinical* evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD.

Supporting FDA's Regulatory Decisions of Effectiveness

In limited instances, FDA has accepted RWE to support drug product approvals, primarily in the setting of oncology and rare diseases. When approval is based on a single-arm interventional trial — often when using a parallel assignment control arm is unethical or not feasible and usually when the effect size is expected to be large, based on preliminary data — the supportive RWE has consisted of data on historical response rates drawn from chart reviews, expanded access, and other practice settings.

"FDA will work with its stakeholders to understand how RWE can best be used to increase the efficiency of clinical research and answer questions that may not have been answered in the trials that led to the drug approval, for example how a drug works in populations that weren't studied prior to approval."

Janet Woodcock, M.D., Director, CDER

Format: Abstract

Full text links

Cancer Discov. 2019 Mar;9(3):310. doi: 10.1158/2159-8290.CD-NB2019-005. Epub 2019 Jan 23.

FDA to Consider Real-World Evidence.

[No authors listed]

Abstract

The **FDA** released a framework outlining how it plans to incorporate **real-world evidence** into the **drug** review process. The agency will consider **real-world evidence** to support the approval of new indications for approved drugs and to support or satisfy post-approval study requirements.

Datos de vida real

- Limitación sistemas informáticos
- Política protección de datos
- De quién son los datos de los pacientes de un hospital concreto?

European Commission

Proposed Mission

CONQUERING CANCER: MISSION POSSIBLE

Report of the Mission Board for Cancer

Independent Expert Report

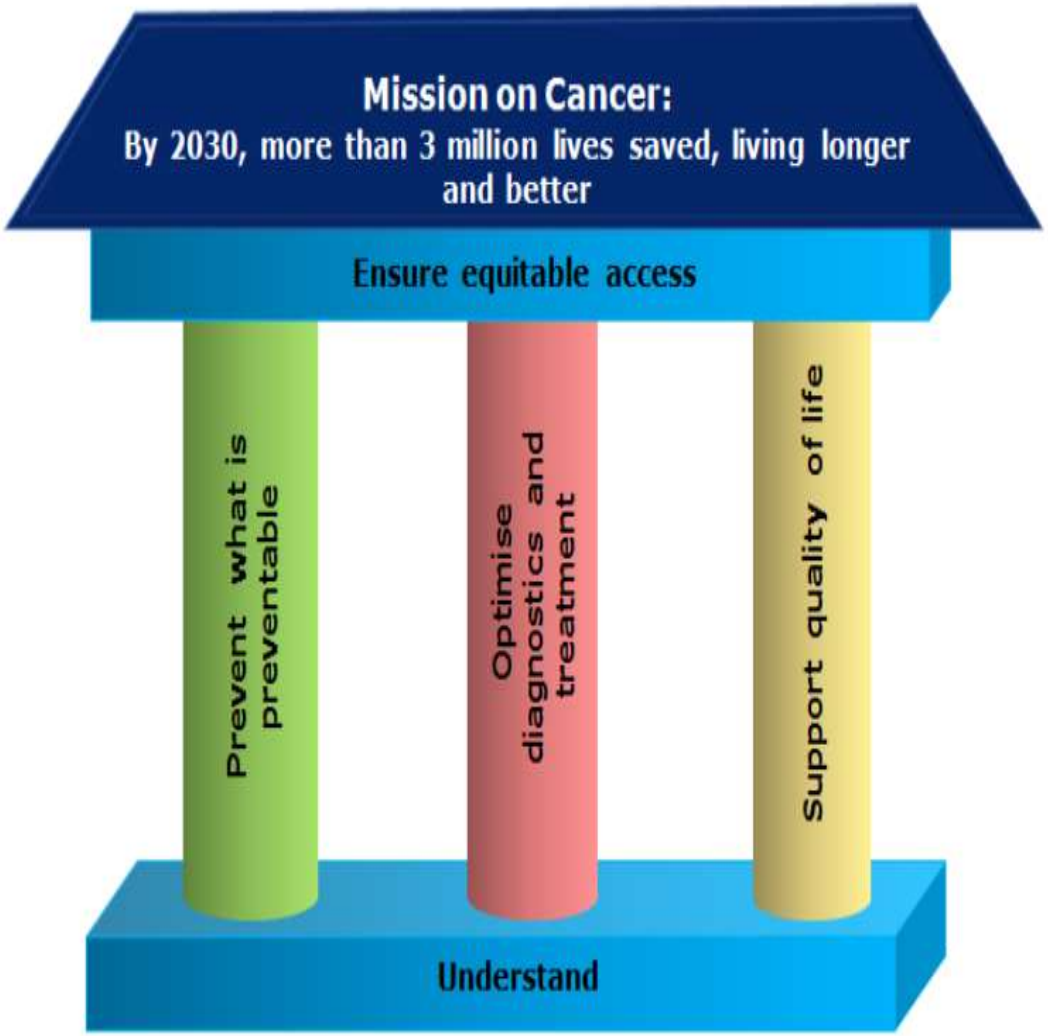
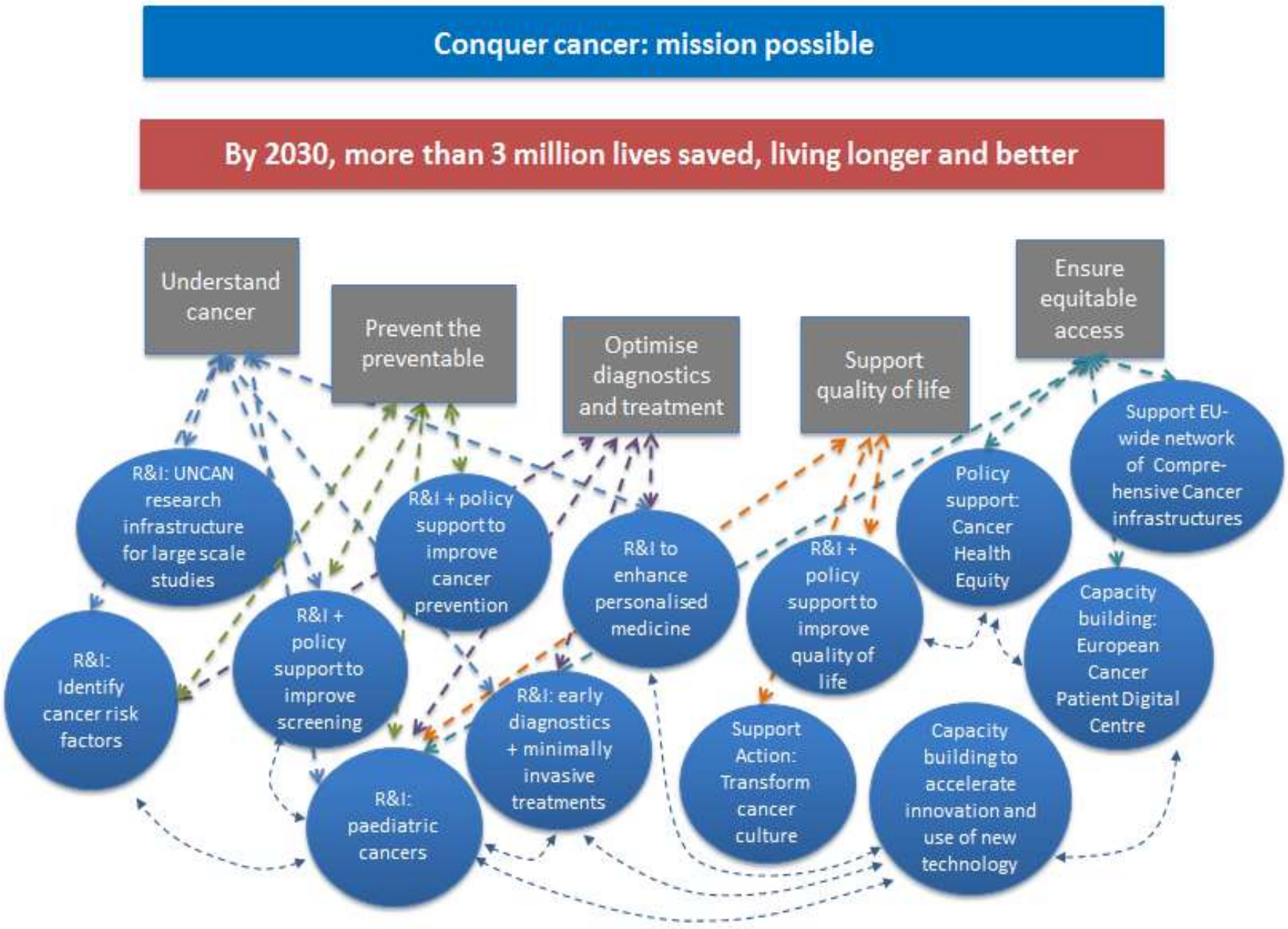


Figure 1. Intervention areas for action

Misión cáncer, 5 áreas de intervención

La misión contra el cáncer abordará todos los cánceres, incluidos los cánceres poco frecuentes en hombres y mujeres, cánceres en niños, adolescentes/adultos jóvenes y ancianos, cánceres en personas socioeconómicamente vulnerables, que viven en ciudades, zonas rurales o remotas, en todos los países miembros



Gràcies!!!

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