GETTHI

Grupo Español de Oncología Transversal
y Tumores Huérfanos e Infrecuentes

VII SIMPOSIO GETTHI

Sesión 1: Del síndrome Hereditario a la diana terapéutica

4 de noviembre de 2021 - *Formato virtual*

Integración de las plataformas de caracterización genética en la práctica habitual oncológica

Rosa María Rodríguez Alonso. HU Reina Sofía. Córdoba

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Sesión 1: Del síndrome Hereditario a la diana terapéutica

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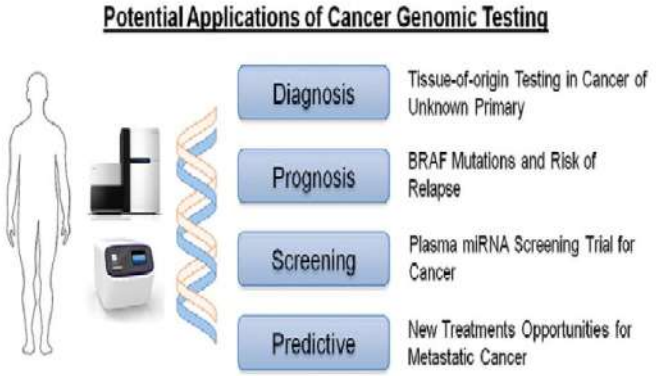
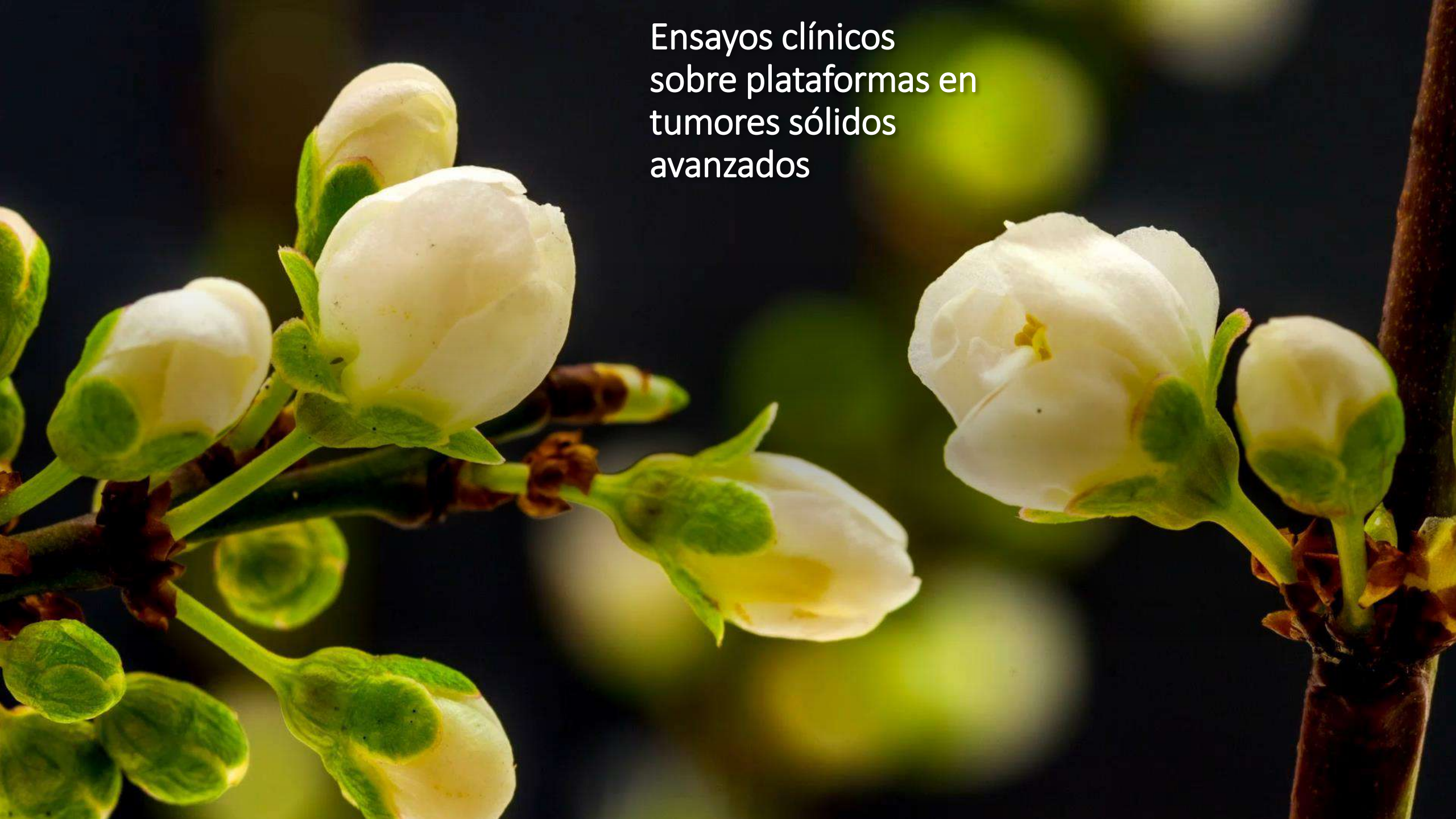
Medicina basada en la evidencia

Cambio de paradigma

¿A quién y cuándo?



Ensayos clínicos sobre plataformas en tumores sólidos avanzados



Integración de las plataformas de caracterización genética en la práctica habitual oncológica

MEDICINA BASADA EN LA EVIDENCIA:

Lo que han demostrado las plataformas de caracterización genética

(en tumores sólidos refractarios)

Ensayos clínicos fases iniciales

Unicéntricos

Distintas plataformas/paneles

Distintas terapias

Bajos porcentajes de "match"
unión perfecta droga dirigida-paciente tras estudio genético

Es difícil encontrar el "match"

TABLE 1. Precision Oncology Efforts Across the Globe

Study	Setting	Assay(s)	Number of Patients	Number of Assays	Number of Patients Matched	Match Rate, %[a]
North America						
MSK-IMPACT	Single-center	DNA: 341- to 410-gene NGS panel (all exons and selected introns)	10,336	10,945	527[b]	11[b]
MD Anderson Personalized Cancer Therapy Program	Single-center	DNA: 10-gene NGS panel (hotspot)	1,144	1,144	211	18
MD Anderson Personalized Cancer Therapy Program	Single-center	DNA: 11- to 50-gene NGS panel (hotspot)	2,000	2,000	83	4
MD Anderson Personalized Cancer Therapy Program	Single-center	DNA: 236 genes	339	339	122	36
PREDICT	Single-center	DNA: 182- to 236-gene NGS panel (Foundation Medicine)	347	347	87	25
IMPACT/COMPACT	Single-center	DNA: 23- to 50-gene NGS panel (hotspot); Protein: PTEN IHC	1,640	1,640	89	5
NCI-MATCH	Multicenter	DNA: 143-gene NGS panel (hotspot); Protein: PTEN, MLH1, MSH2, and Rb IHC	5,540	5,540	686	12
Europe						
MOSCATO	Single-center	DNA: 40- to 75-gene NGS panel (hotspot), CGH WES in limited number of cases; RNA: RNAseq; Protein: MET and phospho-MET IHC	843	843	199	24
Asia						
IMPACT-SG	Single-center	DNA: NGS panel (variable number of genes, hotspot); Protein: ALK, cMET, cMYC, FGFR2 HER2, HGF, MMR, NTRK, PTEN, ROS1, and PD-L1 IHC	1,015	1,064	53	5
IMAC	Single-center	DNA: 50-gene NGS panel (hotspot)	365	365	23	6
NEXT 1	Single-center	DNA: 83- to 381-gene NGS panel (hotspot); Protein: PTEN, MET, and HER2 IHC	588	588	60	10
TOP-GEAR	Single-center	DNA: 114-gene NGS panel (all exons and selected introns)	187	187	25	13
Kyoto University Hospital Study	Single-center	DNA: 215-gene NGS panel (all exons and selected introns)	73	73	9	12

Clinton Y et al. JCO Precision Oncol 2021; 854-858

EC fase II (2015, francés): SHIVA TRIAL *Negativo*

Screening **741 pacientes refractarios**

Incluidos (40% con esa vía alterada): N 293

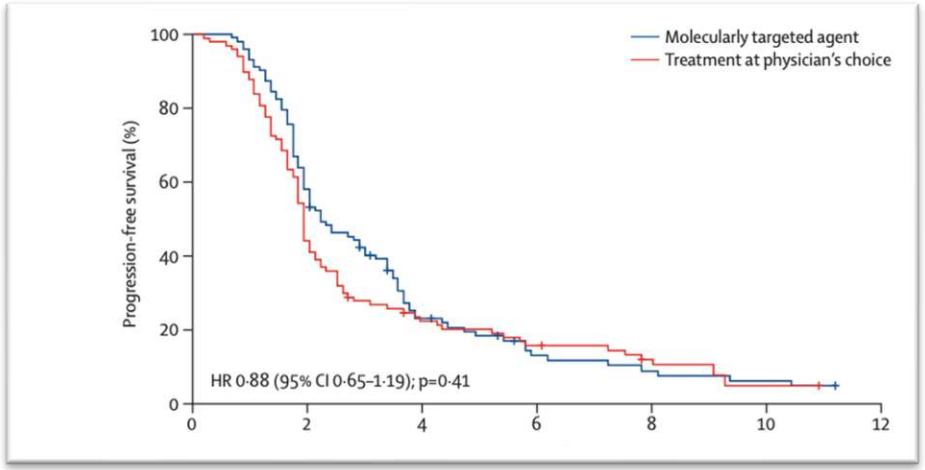
(95 cruzamiento a experimental) **0RR 0-4%**

GRUPO CONTROL: elección investigador

ILP 2 meses, toxicidad > G3 35%

GRUPO EXPERIMENTAL: terapia diana

ILP 2,3 meses, toxicidad > G3 43%



Objetivo primario: Fuera de indicación, la terapia dirigida no aumentaba PFS

Molecular pathway altered		
Hormone receptor pathway	40 (40%)	42 (44%)
PI3K/AKT/mTOR pathway	46 (46%)	43 (45%)
RAF/MEK pathway	13 (13%)	11 (11%)

Tumour type		
Breast adenocarcinoma	22 (22%)	18 (19%)
Ovarian cancer	12 (12%)	17 (18%)
Lung cancer	9 (9%)	10 (10%)
Colorectal cancer	9 (9%)	9 (9%)
Cervical cancer	12 (12%)	7 (7%)
Head and neck squamous cell carcinoma	6 (6%)	5 (5%)
Sarcoma	4 (4%)	4 (4%)
Urothelial carcinoma	2 (2%)	4 (4%)
Pancreatic adenocarcinoma	3 (2%)	2 (2%)
Adenocarcinoma of unknown primary	2 (2%)	3 (3%)
Oesophagogastric cancer	3 (3%)	2 (2%)
Adenoid cystic carcinoma	1 (1%)	3 (3%)
Non-adenoid cystic carcinoma salivary gland tumour	2 (2%)	2 (2%)
Hepatocelular carcinoma	1 (1%)	2 (2%)
Anal squamous cell carcinoma	1 (1%)	2 (2%)
Neuroendocrine tumour	2 (2%)	1 (1%)
Biliary tract carcinoma	1 (1%)	1 (1%)
Nasopharyngeal carcinoma	1 (1%)	1 (1%)
Cutaneous melanoma	1 (1%)	1 (1%)
Mesothelioma	0	1 (1%)
Peritoneal tumour	0	1 (1%)
Ependymoma	1 (1%)	0
Prostate adenocarcinoma	1 (1%)	0
Uveal melanoma	1 (1%)	0
Germline tumour	1 (1%)	0
Kidney cancer	1 (1%)	0

Terapias diana

Erlotinib

Lapatinib
trastuzumab

Sorafenib

Imatinib

Dasatinib

Vemurafenib

Everolimus

Abiraterona

Letrozol

Tamoxifeno

Tourneau et al. Lancet Oncol 2015;16:1324-34

EC no randomizado, prospectivo (2017, francés): MOSCATO 01 TRIAL

Positivo

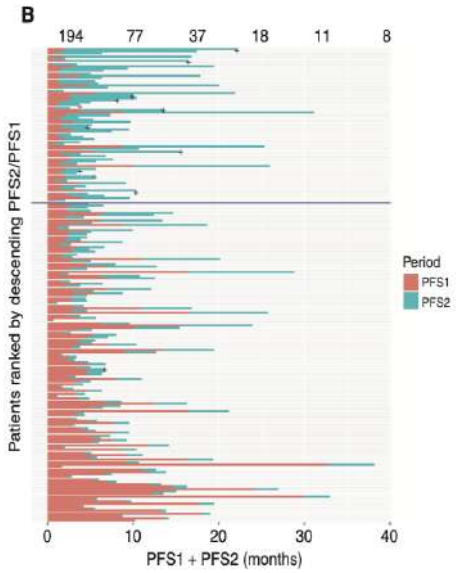
Objetivo primario: 33%(63) pacientes con PFS2/PFS1 <1.3

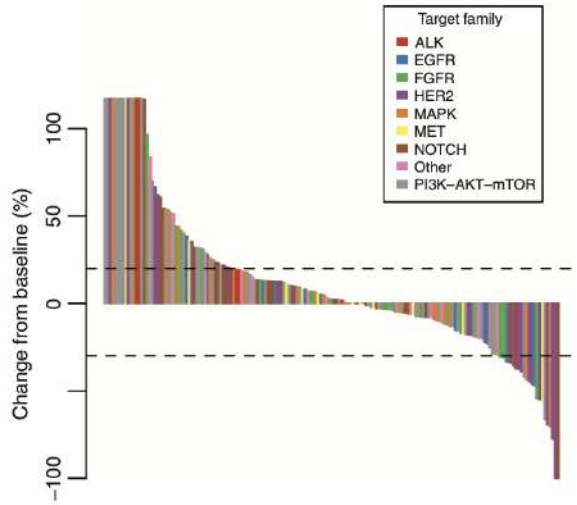
Monocéntrico, comparación intrapaciente

Tumores sólidos refractarios (mediana líneas recibidas: 4)
948 pacientes biopsia (fresca/congelada)
aCGH/RNA-seq/WES

Plataforma molecular: 843 (89%)
Alteración molecular diana: 49%
Match terapia dirigida fases I-II: 19%

Para los autores: ***"la terapia dirigida sugiere mejorar la evolución de un subgrupo (7% del estudio).***
Se necesitan ensayos para valorar la magnitud del beneficio"





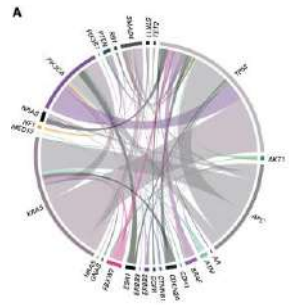
		No. patients with PFS2/PFS1 > 1.3	No. patients (n = 193)	P(PFS2/PFS1 > 1.3)	95% CI	Fisher test for difference in proportions
Tumor type	Melanoma	0	3	0%	0%–71%	
	Breast	13	36	36%	21%–54%	
	Head and neck	8	15	53%	27%–79%	
	Thyroid and other endocrine glands	0	2	0%	0%–84%	
	Ill-defined primary tumor	0	5	0%	0%–52%	
	Digestive	17	45	38%	24%–53%	
	Gynecological, female	4	24	17%	5%–37%	
	Lung	9	32	28%	14%–47%	
	Urological	10	28	42%	19%–65%	
	Mesothelioma and soft tissue	2	3	67%	9%–99%	P = 0.73
Therapy class	ALK	2	6	33%	4%–78%	
	AR	2	5	40%	5%–85%	
	Cell cycle	1	5	20%	1%–72%	
	DNA damage	0	2	0%	0%–84%	
	EGFR	2	12	17%	2%–48%	
	ERBB2	17	26	65%	44%–83%	
	FGFR	7	24	29%	13%–51%	
	IDH	1	2	50%	1%–99%	
	IGF1R	1	1	100%	3%–100%	
	KIT	1	1	100%	3%–100%	
	MAPK	2	12	17%	2%–48%	
	MDM2	0	2	0%	0%–84%	
	MET	3	11	27%	6%–61%	
	NOTCH	6	25	24%	9%–45%	
	PI3K–AKT–mTOR	18	59	31%	19%–44%	P = 0.72

Massard C et al. Cancer Discov 2017; 7 (6): 586-595

EC fase II (2020, USA)
National Cancer Institute:
NCI- Match

Positivo

Objetivo primario:
Aproximadamente 18% de la muestra fue asignada a un grupo de tratamiento activo dentro de fase II



Disease Site	No. of Patients Screened	Patients Screened (%)	No. Assigned to Trial Arm	Patients Screened (%)	No. Enrolled in Trial Arm
Commonest cancers					
Colorectal cancer	848	15.3	116	13.7	85
Breast	685	12.4	122	17.8	85
NSCLC	407	7.3	71	17.4	51
Prostate cancer	139	2.5	32	23.0	25
Total common cancers	2,079	37.5	341	16.4	246

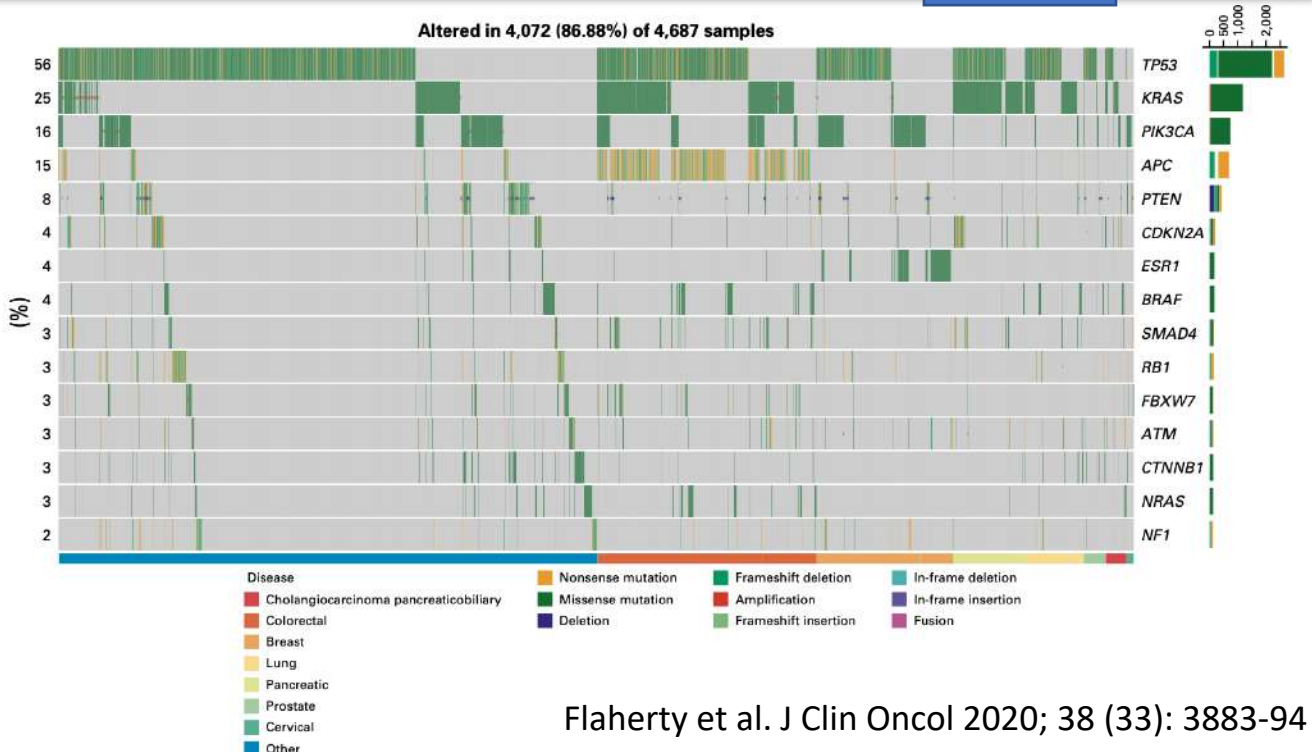
Multicéntrico

Tumores sólidos refractarios (<25% 1ª línea)

5954 pacientes analizados con NGS/IHQ: **143** alteraciones

Plataforma molecular realizada con éxito: **5524(93%)**
Alteración molecular diana: 37.6%
Mutaciones de resistencia: 11.9%

Para los autores: **"es factible hacer screening para dianas moleculares moderadamente frecuentes"**



Flaherty et al. J Clin Oncol 2020; 38 (33): 3883-94

Ensayos en desarrollo con terapias dirigidas por paneles multigenes

TAPUR (ASCO) n3123

ALK, ROS1, MET	Crizotinib
CDKN2A, CDK4, CDK6	Palbociclib
CSF1R, PDGFR, VEGFR	Sunitinib
mTOR, TSC	Temsirolimus
ERBB2	Trastuzumab+pertuzumab
BRAFV600E/D/K/R	Vemurafenib+cobimetinib
NRAS, KRAS, NRAF	Cetuximab
BCR-ABL, SRC, KIT, PDGFRB, EPHA2, FYN, LCK, YES1	Dasatinib
RET, VEGFR1/2/3, KIT, PDGFRB, RAF-1, BRAF	Regorafenib
BRCA1, BRCA2, ATM	Olaparib
POLE, POLD1, high mutational load	Pembrolizumab
MSI-high, high mutational load and others	Nivolumab+ipilimumab

DRUP (Netherlands) n400

KRAS, BRAF, NRAS wild type	Panitimumab
BRCA1, BRCA2, ATM	Olaparib
BRAF	Dabrafenib
Molecular profile that can potentially be targeted by nilotinib	Nilotinib
Molecular profile that can potentially be targeted by trametinib	Trametinib
Molecular profile that can potentially be targeted by erlotinib	Erlotinib
HER-2 overexpression, amplification or mutated	Trastuzumab+pertuzumab
BRAF mutated tumors	Vemurafenib+cobimetinib
Molecular profile that can potentially be targeted by vismodegib	Vismodegib
Molecular profile that can potentially be targeted by regorafenib	Regorafenib
Molecular profile that can potentially be targeted by nivolumab	Nivolumab

Malone et al. Genome Med 2020; 12 (8): 1-19

Ensayos en desarrollo con terapias dirigidas por paneles multigenes

The Drug Rediscovery Protocol (DRUP Trial) (DRUP)

Netherlands Cancer Institute

ClinicalTrials.gov Identifier: NCT02925234

Recruitment Status : Recruiting
First Posted : October 5, 2016
Last Update Posted : March 11, 2021

TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (TAPUR)

ClinicalTrials.gov Identifier: NCT02693535

Recruitment Status : Recruiting
First Posted : February 26, 2016
Last Update Posted : August 25, 2021

American Society of Clinical Oncology

Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR)

Canadian Cancer Trials Group

ClinicalTrials.gov Identifier: NCT03297606

Recruitment Status : Recruiting
First Posted : September 29, 2017
Last Update Posted : March 9, 2021

Esperando resultados…

Integración de las plataformas de caracterización genética en la práctica habitual oncológica

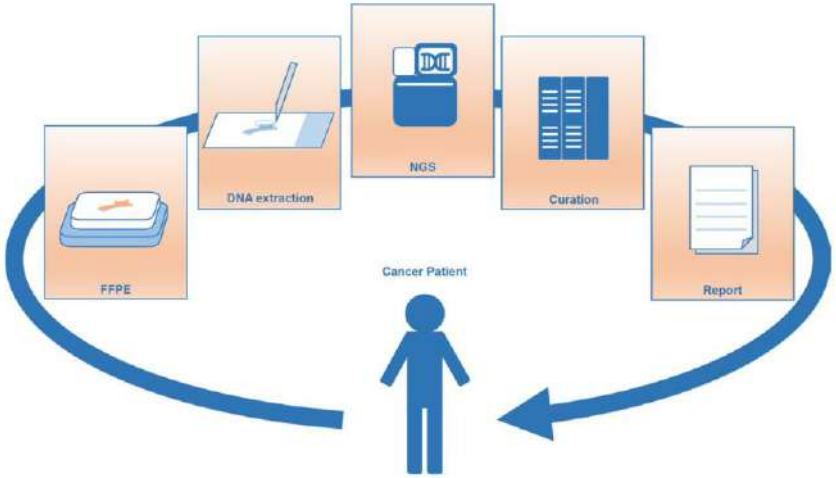
CAMBIO DE PARADIGMA:

Novedades tecnológicas

Biopsia líquida

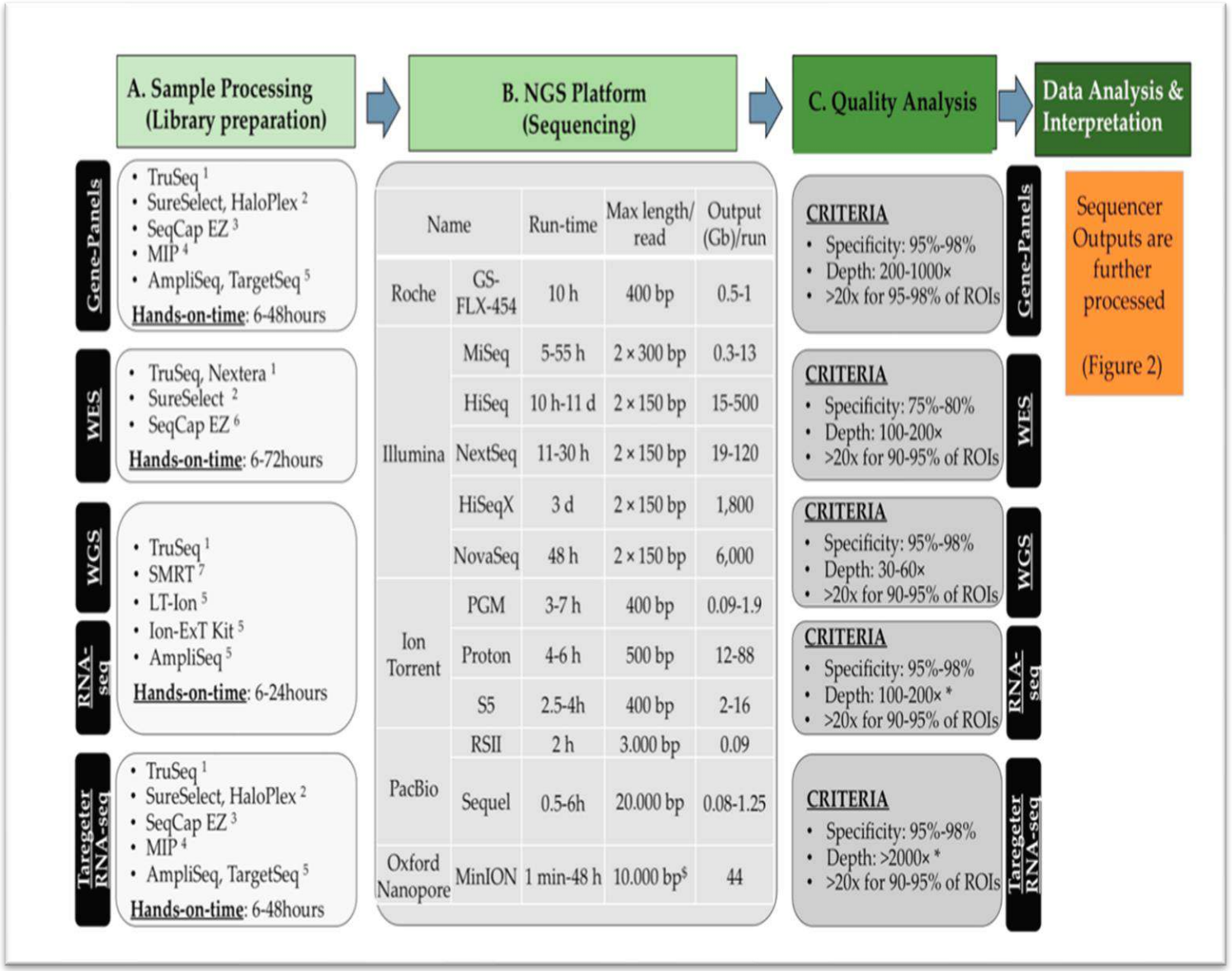
Aprobación de fármacos

Estudio de biomarcadores



O cómo evolucionar para enfrentarse a la nueva realidad en tumores sólidos

La revolución técnica: plataformas moleculares en cáncer



Kamps et al. Int J Mol Sci 2017; 18:308-365

NGS: secuenciación simultánea de millones de fragmentos de DNA, amplificados previamente por PCR: SECUENCIACIÓN PARALELA MASIVA

Sequencing method	Number of articles	Total number of patients	Weighted average of the proportion of successfully sequenced (%)	Weighted average of the proportion of successfully sequenced patients with at least 1 mutation detected (%)	Weighted average of the proportion of successfully sequenced patients with actionable targets identified (%)
1 Targeted gene panel	47	20 577	90.04 (range: 53.53-100.00)	83.22 (range: 30.56-100.00)	54.56 (range: 15.87-100.00)
2 Whole exome sequencing (WES) and/or RNA sequencing	5	559	89.27 (range: 79.37-100.00)	82.20 (range: 82.69-100.00)	39.02 (range: 37.62-75.00)
3 Other method (eg single gene deep sequencing)	4	687	88.79 (range: 80.80-100.00)	63.12 (range: 50.00-71.88)	58.75 (range: 50.00-71.88)

"Es coste-efectiva: aproximadamente 37% detección dianas terapéuticas"

Tan et al. Clin Gen 2018; 93:533-544

Estandarización, abaratamiento técnico

Liquid biopsy in oncology: a consensus statement of the Spanish Society of Pathology and the Spanish Society of Medical Oncology

Technology	Advantages	Disadvantages
rtPCR or qPCR	Quick	Low sensitivity
	Simple	Low specificity
	Economical	Detects already known mutations
ddPCR	High sensitivity	Limited to multiplexing variant detection in a single reaction
	High specificity	Detects already known mutations
	Quick	
	Simple	
	Relatively economical	
BEAMing	Quick	Lacks validation?
	Slightly invasive	
	Simple	
	Relatively economical	
NGS	High precision	Complicated preparation of specimens
	High reproducibility	Limited to certain DNA regions
	Detects new mutations	Requires a complex bioinformatic analysis
	Price progressively becoming lower	

BEAMing beads, emulsification, amplification and magnetics, *ddPCR* droplet-digital polymerase chain reaction, *NGS* next generation sequencing, *qPCR* quantitative PCR, *rtPCR* real time PCR

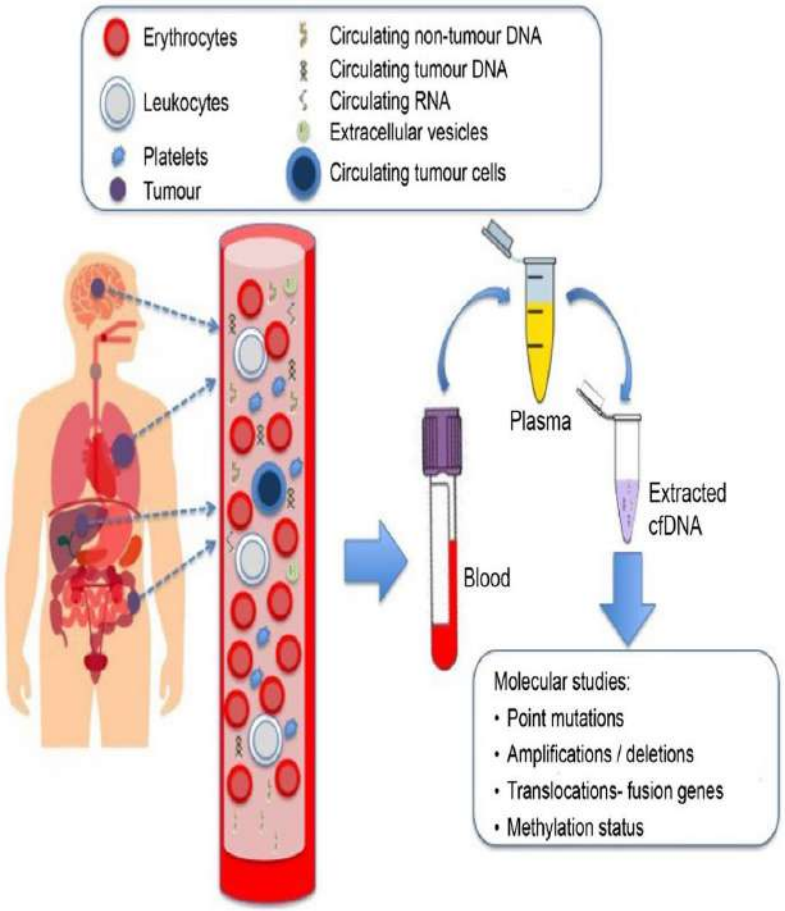


Table 2 Validity and clinical utility of liquid biopsy in clinical practice

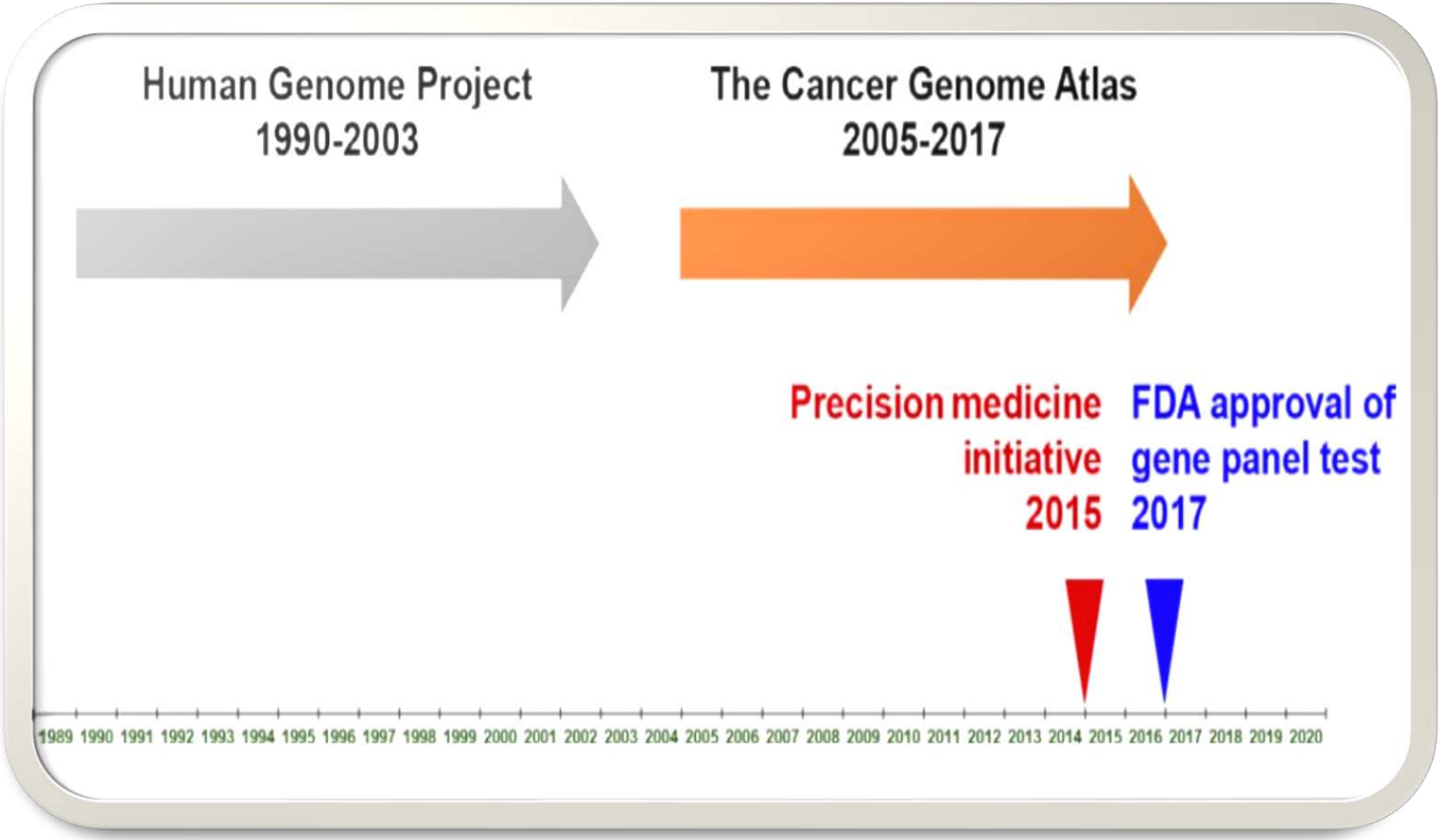
	Approval status
Screening	Not approved
Minimal residual disease	Not approved
Advanced disease	Approved for NSCLC and CRC
Disease monitoring	Not approved
Resistance mechanisms	Approved for *T790M* in NSCLC
Immunotherapy	Not approved

CRC colorectal cancer, *NSCLC* non-small cell lung cancer

¿Aumentar la accesibilidad a la medicina personalizada?
¿Estudiar mecanismos de resistencia?
Biopsia líquida vs NGS en parafina…80-90% concordancia

Remon J et al. Clin Transl Oncol 2020 22:823-834

Cambio de paradigma…



Nagahashi et al. Cancer Sci 2019; 110(6):6-15

Table 4 Active tissue-agnostic clinical trials

Target	Therapeutic Agent(s)	Selected Clinical Trials[a]
ALK	Entrectinib	NCT02568267
		NCT02650401
		NCT03375437
	Repotrectinib	NCT03093116
		NCT04094610
BRAF	PLX8394	NCT02428712
DNA Repair Deficieny	Atezolizumab/Rucaparib	NCT04276376
FGFR	Debio1347	NCT01948297
		NCT03834220
MSI-H/dMMR	HLX10	NCT03941574
	INCB099280	NCT04242199
	INCB099318	NCT04272034
	QL1604	NCT04326829
	Tislelizumab	NCT03736889
RET	Pralsetinib	NCT03037385
	Selpercatinib	NCT04280081
		NCT04320888
	TPX-0046	NCT04161391
ROS1	Entrectinib	NCT02568267
		NCT02650401
		NCT03375437
	Repotrectinib	NCT03093116
		NCT04094610
TRK	DS-6051b	NCT02279433
		NCT02675491
	Entrectinib	NCT02568267
		NCT02650401
		NCT03375437
	Larotrectinib	NCT02465060
		NCT02576431
		NCT02637687
		NCT03213704
		NCT03834961
	Repotrectinib	NCT03093116
		NCT04094610
	Selitrectinib	NCT03215511
		NCT04275960

Selignson N et al. Clin Pharm Ther 2020; 109(2):334-342

Aprobación de fármacos: agencias reguladoras

Medidas clásicas *(EMA):*
Objetivos basados en RECIST 1.1 y Supervivencia

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Endpoint	Start	Event	Censored Events	Pros	Cons
PFS (Progression-Free Survival)	Randomization	Disease progression; Death	Last date of radiological assessment	Earlier read out Effect on survival not diluted by subsequent therapies	Death might not be related to disease but to comorbidities
TTP (Time to Progression)	Randomization	Disease progression	Death	Earlier read out Effect on survival not diluted by subsequent therapies	Does not take into account death related to treatments
TTF (Time to Treatment Failure)	Randomization	Disease progression; Adverse events; Patient choice; Death	-	Earlier read out Effect on survival not diluted by subsequent therapies Best indicator of the treatment's specific tolerance	Does not completely reflect the duration of treatment efficacy, since patients might still be responding to treatment although they had an adverse event or decided to stop treatment Death might not be related to disease but to comorbidities
FFS (Failure-Free Survival)	The first day of treatment	Disease progression	Adverse event Death	Earlier read out Effect on survival not diluted by subsequent therapies Best indicator of the treatment's specific efficacy	Death and adverse events related to treatments are not taken into account
DOR (Duration of Response)	Date of response	Disease progression	Death	Measures duration of response that might be of importance for some treatments such as immunohterapies	Only applies to the responding patient population
OS (Overall Survival)	Randomization	Death	Last date patient seen alive	Direct measure of clinical benefit, Easily measured, Gold standard endpoint	affected by post-progression and cross over therapies; require prolonged Follow up; includes non-cancer related deaths

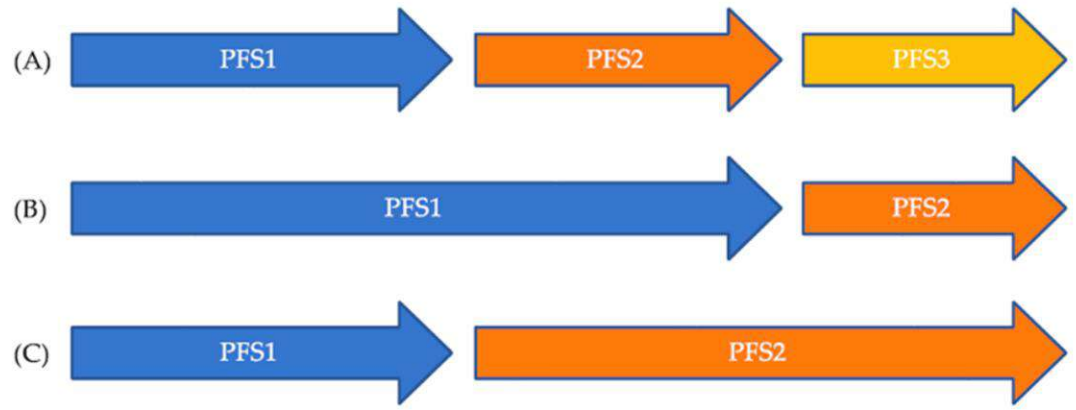


Figure 1. Illustration of the PES ration. (**A**) Expected natural history of cancer in the recurrent and/or metastatic setting with decreasing efficacy of treatments over time; (**B**) PES ratio < 1 suggesting a decreased efficacy of the second drug over the first; (**C**) PES ratio > 1 suggesting a benefit from the new treatment over the first.

Du Rusquet P et al. Cancers 2021; 13: 2758-2768

The FDA Oncology Center of Excellence and precision medicine

- Desde enero 2017: **Oncology Center of Excellence (OCE)**

Nuevos objetivos:

SG y además: ORR y PFS….

“Unmet medical need”

- Fast-track designation…amenazante para la vida: cáncer…comentar desde fase I…
- Breakthroug therapy designation…órgano de consulta
- Accelerated approval: Debut mayo 2017: Pembrolizumab MSI-H or dMMR
- Priority review: de 12 a 8 meses…

Goldberg Ket al. Exp Biol Med 2018; 243: 308-312

Medidas actualizadas *(FDA):* Objetivos basados en tasa de respuesta

U.S. FOOD & DRUG ADMINISTRATION

Table 2. Selected clinical trials using each patient as his/her own control to assess efficacy.

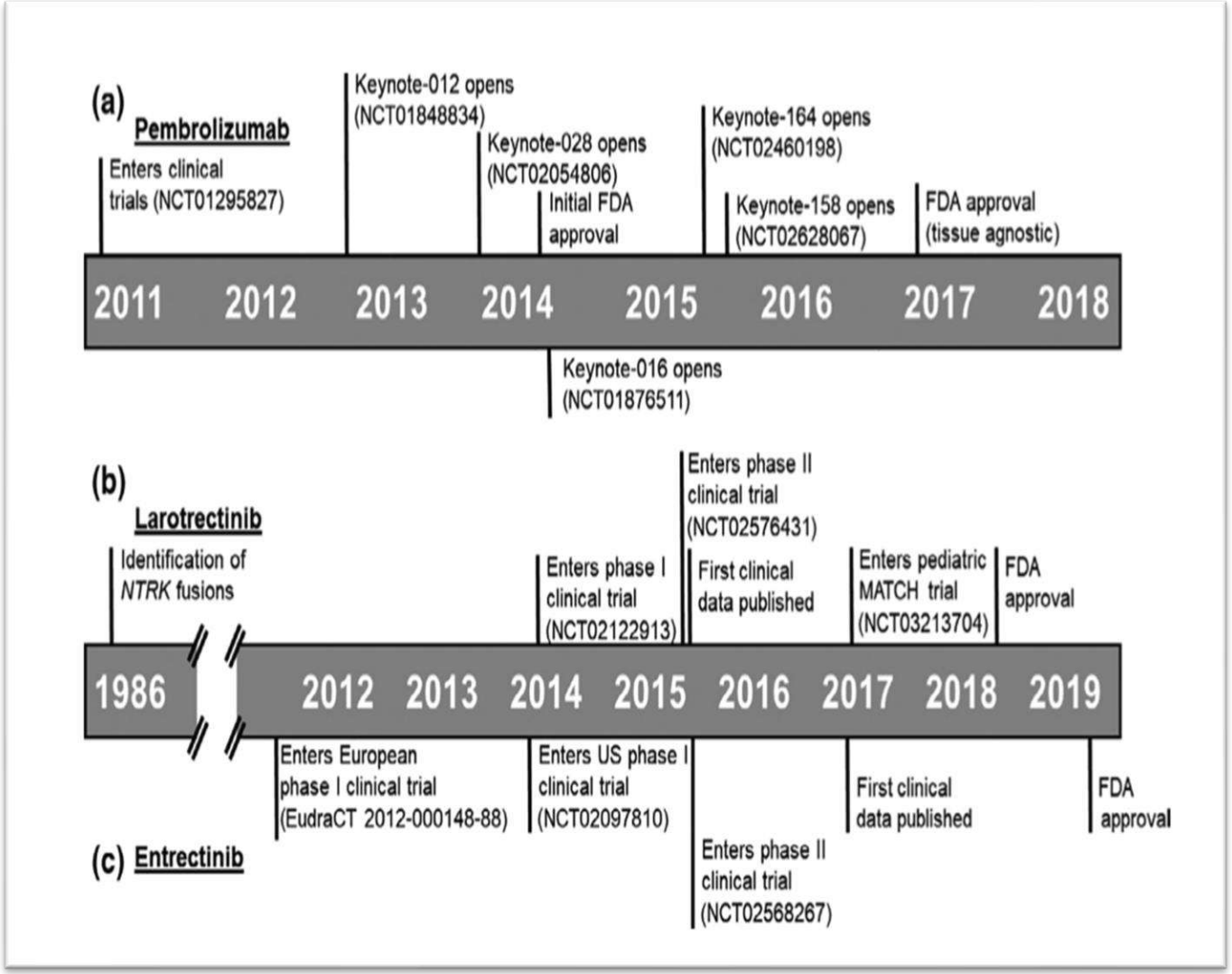
Study	Von Hoff's Study [49]	SHIVA01 [51,56]	MOSCATO-01 [53]	I-PREDICT [54]	WINTHER [55]
Threshold used for PFS ratio	1.3	1.3	1.3	1.3	1.5
No. of patients included	106	741	1035	149	303
No. of patients treated with matched therapy (%)	66 (62%)	170 (23%)	199 (19%)	73 (49%)	107 (35%)
No. of evaluable patients for the PFS ratio (%)	66 (62%)	95 (13%)	193 (19%)	53 (36%)	107 (35%)
Proportion of patient with a PFS ratio >1.3	27%	37% [1] 61% [2]	33%	45%	25%
Median PFS1 (months)	-	2.0 [1] 2.3 [2]	-	-	-
Median PFS2 (months)	-	2.1 [1] 2.8 [2]	2.3	3.7	2.0

[1] Patients crossing from physician's choice to matched therapy; [2] Patients crossing over from matched therapy to physician's choice.

En ausencia de comparador estándar…

Du Rusquet P et al. Cancers 2021; 13: 2758-2768

Aprobaciones agnósticas “basket”, “umbrella”, “octopus”….



Selignson N et al. Clin Pharm Ther 2020; 109(2):334-342

MSI/dMMR (KN-016, 164, 012, 028, 158)

Table 1 Clinical response to pembrolizumab in microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) cancers

Cancer type[11]	*n* (%)	Overall response rate (% (95% CI))	Duration of response (range, months)
Total	149 (100%)	39.6% (31.7–47.9)	1.6[a]–22.7[a]
Colorectal	90 (60.4%)	36% (26–46%)	1.6[a]–22.7[a]
Noncolorectal	59 (39.6%)	46% (33–59%)	1.9[a]–22.1[a]
Endometrial	14 (9.4%)	36% (13–65%)	4.2[a]–17.3[a]
Biliary	11 (7.4%)	27% (6–61%)	11.6[a]–19.6[a]
Gastric or GE junction	9 (6.0%)	56% (21–86%)	5.8[a]–22.1[a]
Pancreatic	6 (4.0%)	83% (36–100%)	2.6[a]–9.2[a]
Small intestinal	8 (5.4%)	38% (9–76%)	1.9[a]–9.1[a]
Breast	2 (1.3%)	PR, PR	7.6–15.9
Prostate	2 (1.3%)	PR, SD	9.8[a]

TMB: 10 mutations/Mb

13% pacientes cáncer refractario

Pembrolizumab: ORR 29 vs 6%

Aprobación FDA 2020

Fusión NTRK

Larotrectinib (LOXO-TRK-14001, SCOUT, NAVIGATE)

ORR 75%

PFS 10.4 meses

Entrectinib (STARTRK-1/2, ALKA-372-001):

ORR 57%

PFS 11.2 meses

Biomarcadores predictivos para terapias dirigidas en cáncer aprobados

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

FDA U.S. FOOD & DRUG ADMINISTRATION

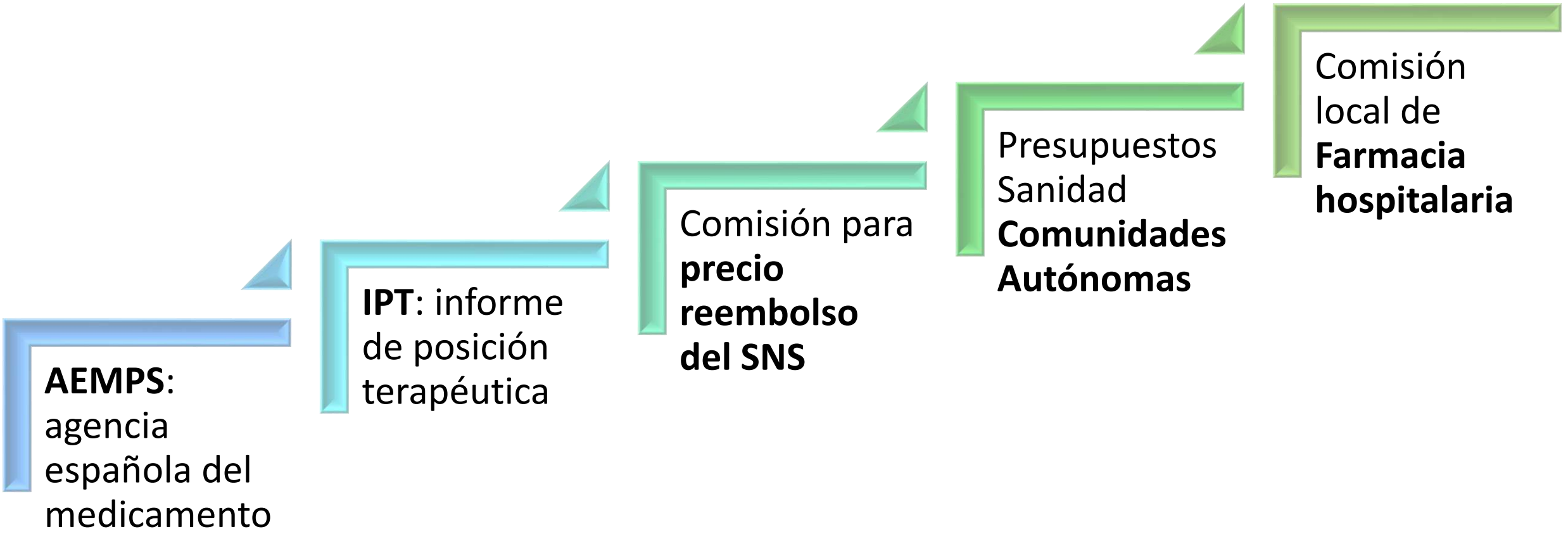
¿actualización mensual?

Table 1 FDA and EMA approved biomarker matching targeted drugs and routine molecular pathology testing [2, 3]

Gene/protein	Anticancer agent	Indications	Biomarker	Routine testing
ALK	Crizotinib, ceritinib, alectinib, lorlatinib, brigatinib	NSCLC	*ALK* translocation	FISH, IHC
Androgen receptor (AR)	Abiraterone, enzalutamide, dalurotamide, apalutamide	Prostate cancer	AR expression	IHC
BCL-2	Venetoclax	Chronic myeloid leukemia	BCL-2 protein expression, *BCL-2* amplification/ translocation	IHC, FISH
BCR/ABL	Imatinib, dasatinib, nilotinib, bosutinib, ponatinib	Chronic myeloid leukemia	*BCR/ABL1* fusion	IHC (FISH, DNA/ RNA sequencing), PCR[1]
BRAF	Dabrafenib+trametinib, vemurafenib+cobimetinib, encorafenib+binimetinib	Melanoma, NSCLC, anaplastic thyroid cancer, hairy cell leukemia	*BRAF* V600E/K mutations	IHC, PCR[1], DNA sequencing
BRCA	Olaparib, talazoparib, rucaparib	Breast cancer, ovarian cancer	Germline/somatic *BRCA* 1/2 mutations	DNA sequencing
C-KIT, PDGFR	Imatinib	Gastrointestinal stromal tumor	*c-KIT* Exon 9 and 11 mutations, *PDGFR* mutations	IHC, DNA sequencing
PDGFRB	Imatinib	Myelodysplastic/ myeloproliferative syndromes	*PDGFRB* rearrangement	FISH
Estrogen/ progesterone receptors (ER/PR)	Tamoxifen, raloxifene, fulvestrant, toremifine	Breast cancer	ER/PR expression	IHC
erBB2/HER-2	Trastuzumab, pertuzumab, ado-trastuzumab, emtansine, neratinib	Breast cancer, gastric cancer	HER-2 protein expression, *HER-2* amplification	IHC, FISH
EGFR	Gefitinib, erlotinib, afatinib, dacomitinib	NSCLC	*EGFR* exon 19 deletion, exon 21 L858R mutation	DNA sequencing, PCR[1]
	Osimertinib		*EGFR* T790M mutation	
FGFR2/3	Erdafitinib	Bladder cancer	*FGFR3* mutations, *FGFR2/3* fusions	DNA sequencing, FISH
FLT3	Midostaurin, gilteritinib	Acute myeloid leukemia	*FLT3* mutations	DNA sequencing, PCR[1]
IDH1/2	Ivosidenib, enasidenib	Acute myeloid leukemia	*IDH1/2* mutations	IHC, DNA sequencing
MET	Crizotinib (breakthrough designation)	NSCLC	*MET* amplification, *MET* exon 14 alterations	FISH, DNA/RNA sequencing
MSI-H or dMMR	Pembrolizumab	MSI-H or dMMR solid tumors	MLH1, MSH2, MSH6, PMS2 protein expression, MSI high	IHC, DNA sequencing, PCR[1]
	Nivolumab and ipilimumab	Colorectal cancer		
NTRK	Larotrectinib, entrectinib	Solid tumors with NTRK fusions	*NTRK* protein expression, *NTRK* fusion	IHC, FISH, DNA/RNA sequencing
PI3KCA	Alpelisib	Breast cancer	*PI3KCA* mutation	DNA sequencing
PI3K (alpha and delta)	Copanlisib	Follicular lymphoma	*PI3K* mutation	DNA sequencing
PI3K (delta and gamma)	Duvelisib	Chronic lymphocytic leukemia, small lymphocytic lymphoma	*PI3K* mutation	DNA sequencing
RAS (negative predictor)	Cetuximab, panitumumab	Colorectal cancer	*KRAS/NRAS* wildtype	DNA sequencing
RET	LOXO-292 (breakthrough designation)	NSCLC, medullary thyroid cancer	*RET* fusion, *RET* mutation	FISH, DNA/RNA sequencing
ROS1	Crizotinib, entrectinib	NSCLC	*ROS* translocation	FISH, DNA/RNA sequencing

Malone et al. Genome Med 2020; 12 (8): 1-19

Acceso a medicamentos y biomarcadores oncológicos en España



Spain is different

Proposal for the creation of a national strategy for precision medicine in cancer: a position statement of SEOM, SEAP, and SEFH

MEDICINA DE PRECISIÓN: acceso emergente al tratamiento y prevención de la enfermedad que tiene en cuenta la variabilidad genética individual, el medio de desarrollo y el estilo de vida de cada persona

- Ha transformado la investigación biomédica

- Oportunidad de mejorar la salud pública y abaratar costes
- Se implantará, pero sin plan estratégico nacional se corre el riesgo de: NO FIABLE, NO IGUALITARIA, CARA, NO ACCESIBLE…..

Garrido P et al. Clin Trans Oncol 2018; 20 (4): 443-447

Study of the Spanish Society of Medical Oncology (SEOM) on the access to oncology drugs and predictive biomarkers in Spain

- 84 hospitales (17 CCAA), solo 4 privados, 58% contactados
- 42% decisión de la Comunidad Autónoma
- 60% decisiones Comisión Farmacia hospitalaria
- 84% centros no hay comisión de Biomarcadores

Lung cancer	PD-L1
	ALK
	ROS-1
Melanoma	BRAF
Ovarian cancer	BRCA1/BCRA2

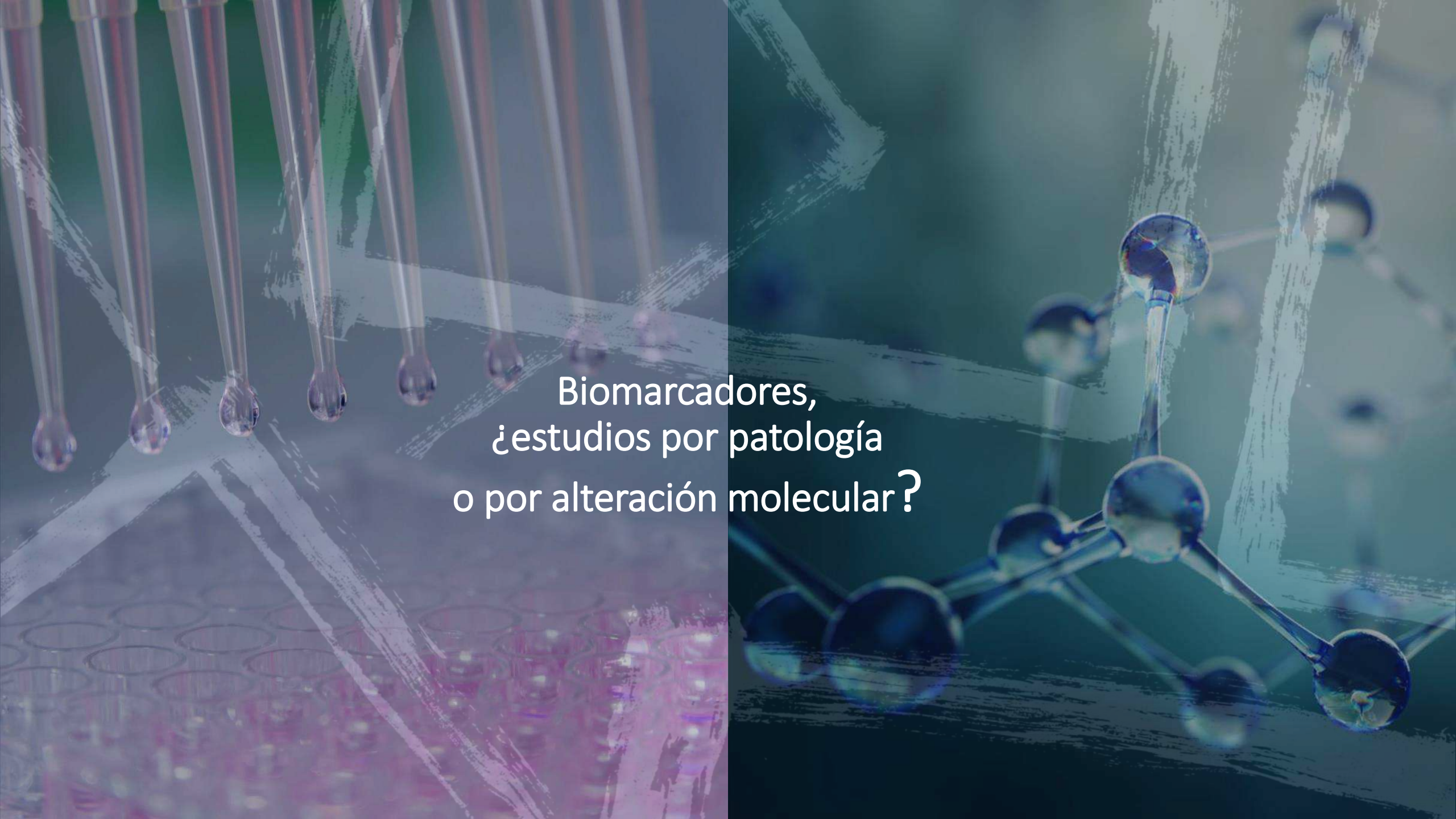
Results Results highlight the still existing differences in the access of oncology drugs, as well as the newly identified differences in the access to predictive biomarkers between Autonomous Communities (AACC) in Spain, as well as between different hospitals within the same Autonomous Community.

Conclusions

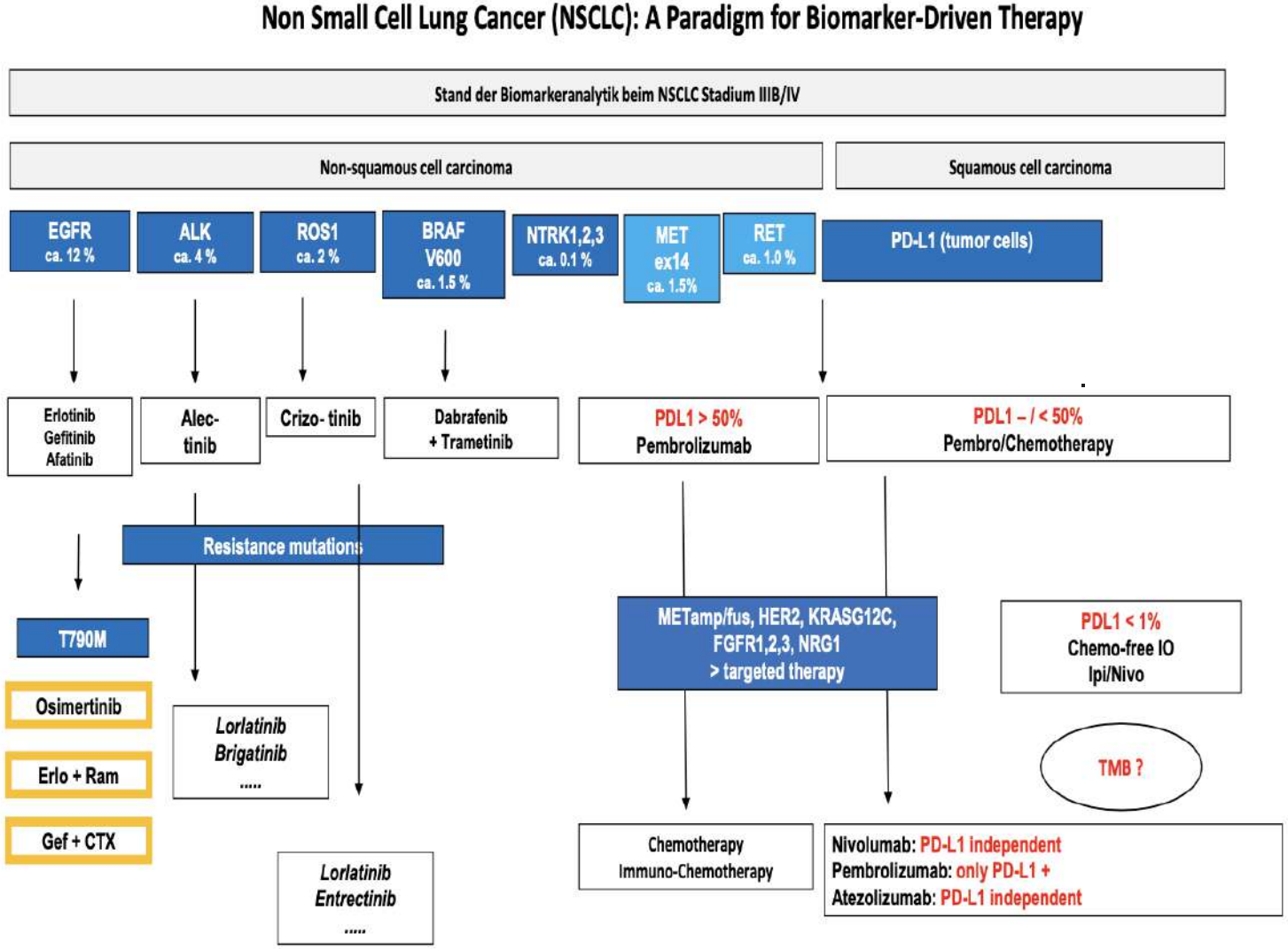
The SEOM considers it necessary to reduce the differences identified, increase homogeneity, and improve conditions of access to oncology drugs and biomarkers, and makes proposals to address these issues.

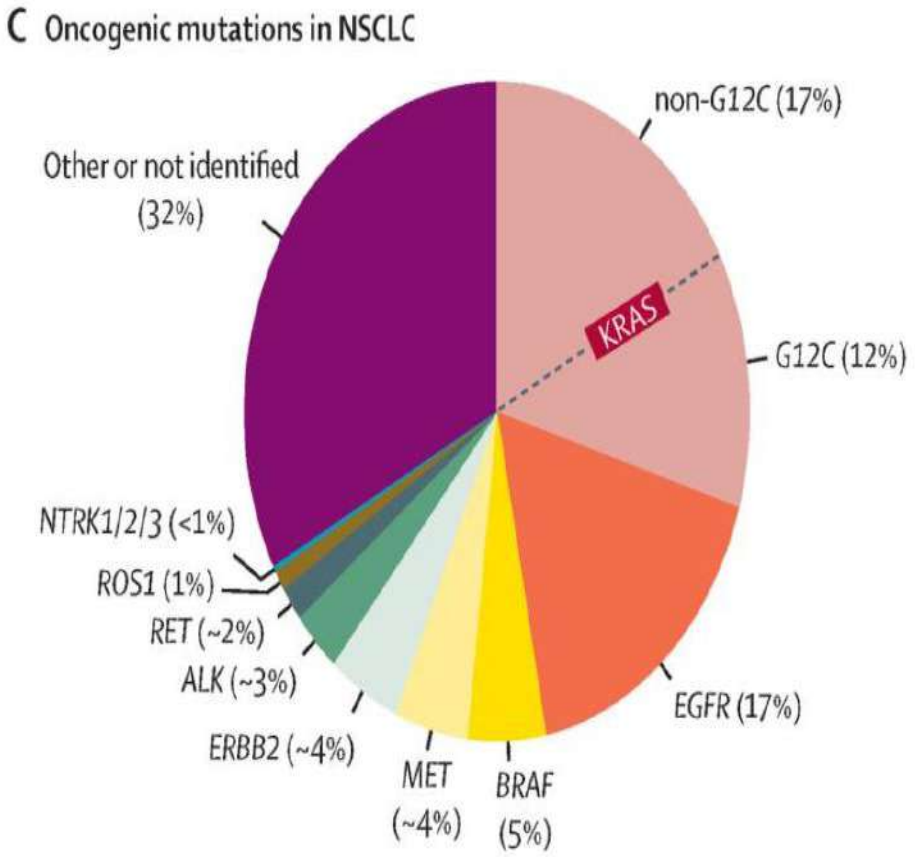
Lung cancer	Pembrolizumab
	Atezolizumab
	Nivolumab
Breast cancer	Ribociclib
	Palbociclib
Melanoma	Dabrafenib y Trametinib
	Cobimetinib y Vemurafenib
Ovarian cancer	OLAPARIB

Rguez-Lescure A al. Clin Trans Oncol 2020; 22 (12): 2253-2263


Biomarcadores,
¿estudios por patología
o por alteración molecular?

MEDICINA DE PRECISIÓN: PULMÓN





La Vecchia 2019: Cancer Mortality in Europe

MEDICINA DE PRECISIÓN: MAMA

Tabla 2. Características de las cuatros pruebas genómicas incluidas en la revisión

	MammaPrint®	Oncotype DX®	EndoPredict	Prosigna
Empresa comercializadora	Agendia	Genomic Health TM	Sividon/Myriad	NanoString Technologies, Inc.
Genes analizados	70 genes implicados en todos los aspectos de la biología del tumor: proliferación, angiogénesis, invasión, trasvasación, adhesión a la matriz extracelular…	21 genes: ***16*** oncogenes y ***5*** genes de referencia	12 genes: 3 genes de ciclo de proliferación celular y 5 de señalización hormonal (uno de ellos relacionado con el síndrome metabólico); 4 genes control	50 genes para la identificación del subtipo molecular y 8 genes control
Técnica analítica	Micromatrices o Microarray	qRT-PCR	RT-PCR sondas taqman	Sondas que hibridan directamente con el ARNm en solución (*nCounter Analysis System*)
Tejido utilizado	Tejido tumoral fresco o congelado con hielo seco o nitrógeno líquido. Tejido tumoral incluido en parafina y fijado con formalina (Sapino *et al.*, 2013)	Tejido tumoral incluido en parafina y fijado con formalina	Pieza postquirúrgica en parafina	Pieza postquirúrgica en parafina
Laboratorios de referencia	Centralizado en Holanda	Centralizado en EEUU	laboratorios locales	laboratorios locales
Población diana	Mujeres menores de 61 años con cáncer de mama en estadios I/II tanto ER-positivo como ER-negativo sin afectación ganglionar y con tumores < 5 cm	Mujeres con cáncer de mama ER-positivo, HER-2-negativo y sin afectación de los ganglios linfáticos tratadas con tamoxifeno	Mujeres pre y postmenopáusicas con cáncer de mama ER+, HER2- en estadios tempranos con y sin afectación ganglionar	Mujeres postmenopáusicas con cáncer de mama y receptores hormonales positivos, en estadios tempranos con y sin afectación ganglionar
Medida de resultado	Metástasis a 10 años sin tratamiento adyuvante	Metástasis a 10 años tras 5 años de tratamiento con tamoxifeno	Metástasis a 10 años con tratamiento hormonal adyuvante	Metástasis a 10 años con tratamiento hormonal adyuvante.
Resultado prueba	Resultado dicotómico: buen pronóstico mal pronóstico	Resultado continuo **Índice RS**: (*Recurrence Score*)	Resultado continuo **Índice EP:** basado en los niveles de expresión génica **Índice EPclin:** algoritmo que combina datos genómicos con los clínicos (tamaño del tumor y estado de afectación ganglionar)	Resultado continuo Subtipos moleculares **Índice ROR**: algoritmo que combina datos genómicos con clínicos y está basado en el subtipo molecular (PAM50), tamaño del tumor, estado de proliferación del tumor y el estado de afectación ganglionar

Tabla 2. Características de las cuatros pruebas genómicas incluidas en la revisión

	MammaPrint®	Oncotype DX®	EndoPredict	Prosigna
Clasificación del riesgo de recurrencia de las pacientes según los índices	Riesgo bajo Riesgo alto	Riesgo bajo: RS < 18 Riesgo intermedio: RS = 18 – 31 Riesgo alto: RS > 18	**EP:** valor de 0 – 15. Clasifica en bajo y alto riesgo de recaída con un valor de corte igual a 5 **EPclin:** valor de 1 – 6,5. Clasifica en bajo y alto riesgo de recaída con hormonoterapia considerando un valor de corte igual a 3,3	Valor de 0 – 100 clasificado en tres categorías de riesgo: alto, bajo e intermedio Los puntos de corte entre los tres grupos de riesgo son diferentes en función de si hay o no afectación ganglionar
Aplicación clínica	Pronóstico	Pronóstico/Predictivo	Pronóstico	Pronóstico
FDA/CE	Aprobado/con CE	No presentado/con CE	–/con CE	Aprobado/con CE

Martínez-Férez IM et al. Plataformas genómicas de carácter pronóstico-predictivo en el cáncer de mama: Sevilla: Agencia de Evaluación de Tecnologías Sanitarias de Andalucía. Red Española de Agencias de Evaluación de Tecnologías Sanitarias y Prestaciones del SNS; 2018

Las dianas moleculares son ahora uno de los mayores puntos de interés en cáncer

ESMO ADVANCED COURSE ON BIOMARKERS FOR PRECISION MEDICINE:

NGS for tissue biopsies

Reinhard Buettner, Institute for Pathology and Center for Integrated Oncology (CIO) Cologne / Germany

Zürich, November 12th, 2020

Targeting KRAS: clinical relevance and therapeutic perspectives for non-G12C mutations

Chiara Ambrogio

2021 ESMO congress

'Opening New Horizons' RET, NTRK, MET, HER2 ...

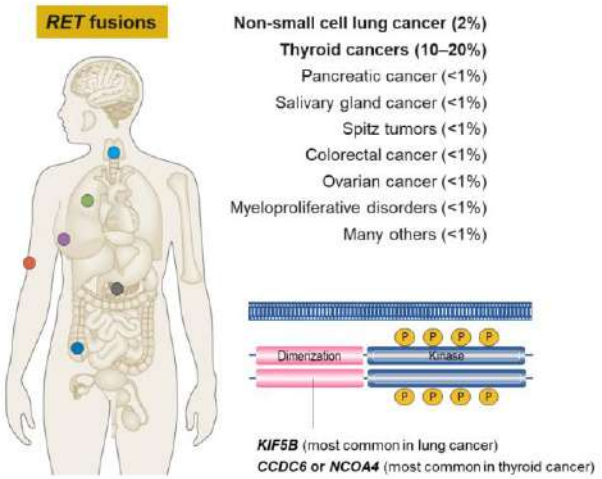
Educational Programme | ESMO Virtual Congress 2021

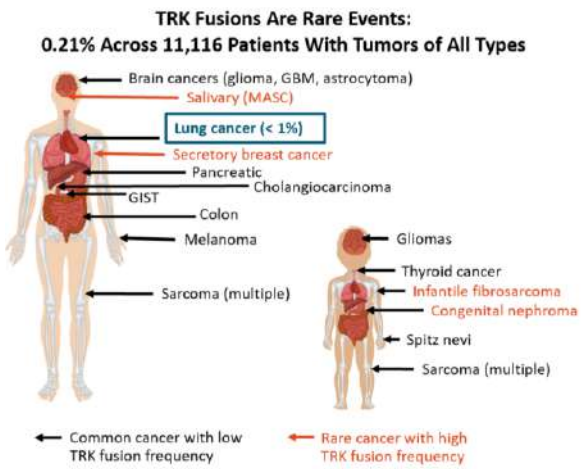
Dr. Herbert H. Loong
MBBS, PDipMDPath, MRCP(UK), FRCP Edin, FHKCP, FHKAM(Medicine)

Established and promising new gene fusion inhibitors and new drugs

Dr. Victor Moreno

Early Phase Clinical Trials Unit START Madrid-FJD
Hospital Fundación Jiménez Díaz, Madrid. Spain





New gene fusion inhibitors

ALK	Lorlatinib
ROS1	Lorlatinib, entrectinib, repotrectinib
NTRK	Entrectinib, Larotrectinib, selitrectinib
RET	Pralsetinib, sepercatinib, TPX-0046
FGFR	Erdafitinib
NRG1	Zenocutuzumab (MCLA-128)

Genes relacionados con predisposición hereditaria al cáncer: CONSEJO GENÉTICO

La asignatura pendiente…

Síndromes hereditarios en cáncer más comunes y genes implicados

Cancer Syndrome	Site at High-Risk of Cancer	Gene Mutated
General Population	**Non Applicable**	
- Hereditary breast and ovarian cancer syndrome (HBOC)	Breast, Ovary Pancreas, Prostate	*BRCA1*
	Breast, Pancreas	*BRCA2*
	Breast	*PALB2*
	Ovary, Breast	*RAD51A*
	Breast	*RAD51C*
	Ovary, Breast	*BARD1*
		BRIP1
- Lynch syndrome	Ovary, Colon Rectum Endometrial Pancreas, Stomach	*MLH1*
		MSH2
	Ovary, Colon Rectum Endometrium	*MSH6*
		PMS2
- Ataxia-telangiectasia	Breast, Pancreas Risk of Leukaemia Risk of Lymphoma	*ATM*
- Hereditary breast and colorectal cancer	Breast, Colon Rectum	*CHEK2*
- Cowden syndrome - PTEN hammartoma tumour syndrome - Bannayan–Riley–Ruvalcaba syndrome	Breast, Colon Rectum Endometrium Other sites Risk of Melanoma	*PTEN*
- Familial adenomatousus polyposis - Syndrome attenuated familial - Adenomatous polyposis gardner syndrome	Colon, Rectum Pancreas, Stomach	*APC*
- Hereditary diffuse gastric cancer	Breast, Stomach	*CDH1*
- Juvenile polyposis syndrome	Colon, rectum Stomach	*BMPR1*
- Juvenile polyposis syndrome - Hereditary haemorrhagic telangiectasia	Colon, Rectum, Stomach, other sites	*SMAD4*
- Li Fraumeni syndrome	Overall cancer risk at young age	*TP53*
- Melanoma-pancreatic cancer syndrome - Melanoma cancer syndrome	Pancreas Risk of Melanoma	*CDKN2A*[1]
- MUTYH-associated polyposis syndrome - MUTYH-associated colon cancer risk	Colon, Rectum	*MUTHY*
- Peutz Jeghers syndromes	Breast, Colon Rectum Endometrium Pancreas, Stomach Ovary	*STK11*
- Retinoblastoma	Retinoblastoma	*RB*
- Hereditary mixed polyposis syndrome	Colon, Rectum	*SCG5 GREM1*
- Hereditary ovarian cancer risk	Ovary	*RAD51D*
- Melanoma-pancreatic cancer syndrome - Melanoma cancer syndrome	Pancreas, risk of Melanoma	*CDK4*
- Nijmegen breakage syndrome	Breast, Prostate	*NBN*
- Neurofibromatosis	Risk of sarcomas	*NF1*
- Oligodontia-colorectal cancer syndrome	Colon, rectum	*AXIN2*
- Multiple endocrine neoplasia	Parathyroid gland, Pancreas Pituitary gland	*MEN1*
- Polymerase proofreading-associated syndrome	Colon, Rectum	*POLE, POLD1*
- Von Hippel-Lindau syndrome	Kidney, Pancreas, Genital tract	*VHL*
- Turcot syndrome	Brain	*APC, MLH1, PMS2*

Van a ser hasta 8% genes relacionados en la secuenciación somática

Kamps et al. Int J Mol Sci 2017; 18:308-365

Germline-focussed analysis of tumour-only sequencing: recommendations from the ESMO Precision Medicine Working Group

LA IMPORTANCIA DEL CONSEJO GENÉTICO

- Excluir hipermutaciones
- Genes de alta penetrancia
- Ratio de conversión línea germinal > 10%
- Edad del portador: insistir en < 30 años
- Estudio normal o negativo: BRCA1/MSH/reevaluación bianual

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

SPECIAL ARTICLE

Box 1. Recommendations for genes to be included for germline-focussed analysis and triggering of germline sample laboratory confirmation

	Any tumour type		Associated tumour type only
Tumour arising any age	*BRCA1*	*RAD51C*	*FLCN*
	BRCA2	*RAD51D*	*FH*
	BRIP1	*RET*	*BAP1*
	MLH1	*SDHA*	*POLE*
	MSH2	*SDHAF2*	
	MSH6	*SDHB*	
	PALB2	*SDHC*	
	PMS2	*SDHD*	
	VHL[a]	*TSC2*	
		MUTYH[b]	
Tumour arising age <30 only	*RB1*		*TP53*[c]
	APC		*NF1*

[a]Renal tumours to be excluded.
[b]*MUTYH* should be included for germline-focussed tumour analysis but reporting and germline follow-up testing should only be performed on detection of two pathogenic variants.
[c]Brain tumours to be excluded.

Mandelker D et al. Anns Oncol 2019; 30:1221-1231

Sección SEOM
Cáncer Familiar y Hereditario

Beneficios

Los resultados de esta prueba genética le pueden ayudar a usted y a su médico en la toma de decisiones sobre su atención médica, en cuanto a la realización de pruebas de detección precoz, cirugías reductoras de riesgo y otras estrategias preventivas/curativas.

La detección de una variante patológica en una familia permite que otros miembros de la misma puedan conocer si han heredado o no la susceptibilidad genética haciéndose un estudio genético directo.

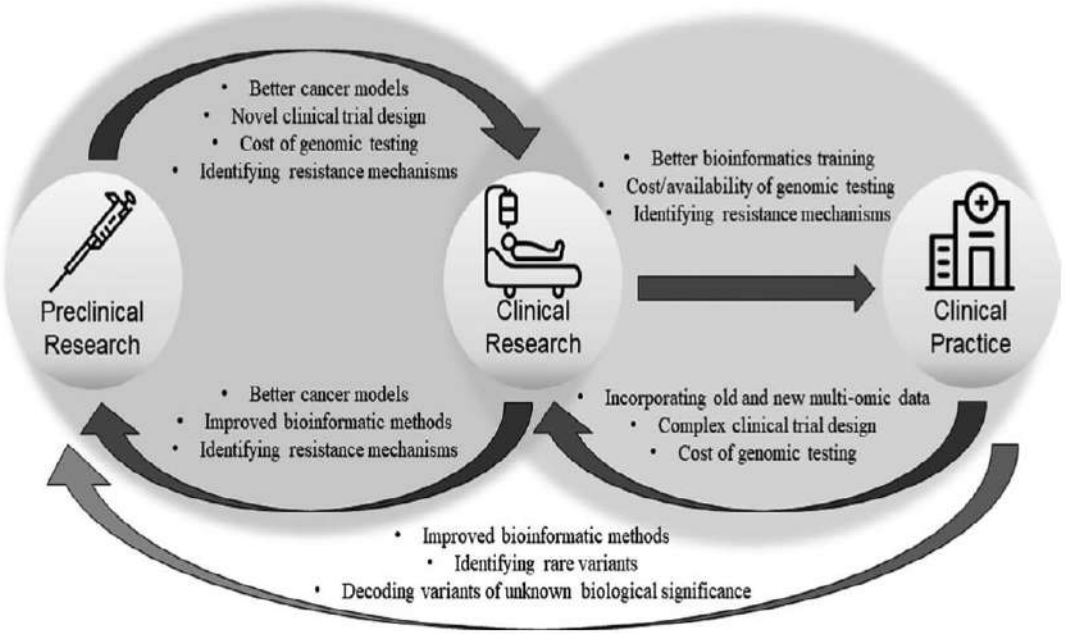
Riesgos asociados al estudio genético

El estudio de un número elevado de genes en el panel aumenta la probabilidad de tener un resultado no esperado, es decir que se identifique una variante patológica en un gen que no esté asociado con el/los tumor/es que se ha/n presentando en su familia. Este resultado puede tener o no implicaciones en el manejo clínico preventivo y para el asesoramiento de otros familiares.

Además hay que estar preparado para un resultado incierto y para la posibilidad de que el resultado no cambie su manejo clínico.

La información masiva tiene implicaciones en el paciente y su descendencia…

Integración de las plataformas de caracterización genética en la práctica habitual oncológica



¿A quién y cuándo? Posibles soluciones

Las revolución terapéutica debería ser para todos…


Guías clínicas sobre
plataformas genéticas
en práctica oncológica

Medida del impacto clínico de la alteración molecular

A framework to rank genomic alterations as targets for cancer precision medicine: the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT)

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESCAT I	• Improved outcome in clinical trials	**READY FOR ROUTINE USE**
ESCAT II	• Antitumour activity but unknown magnitude of benefit	**INVESTIGATIONAL**
ESCAT III	• Suspected to improve outcome based on clinical trial data in other tumor- type	**HYPOTHETICAL TARGET**
ESCAT IV	• Pre-clinical evidence of actionability	**HYPOTHETICAL TARGET**
ESCAT V	• Objective response, but without clinically meaningful benefit	**COMBINATION DEVELOPMENT**
ESCAT X	• Lack of evidence for actionability	

Mateo et al. Anns Oncol 2018; 29: 1895-1902

Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group

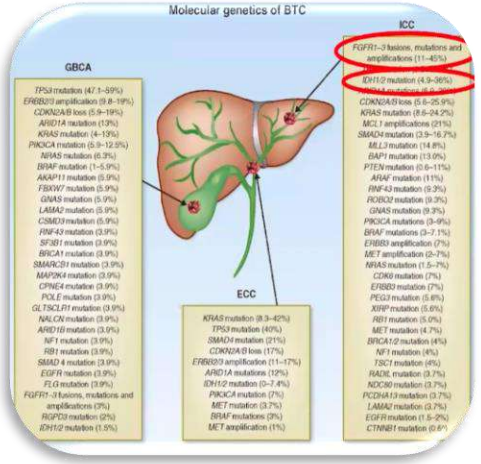
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

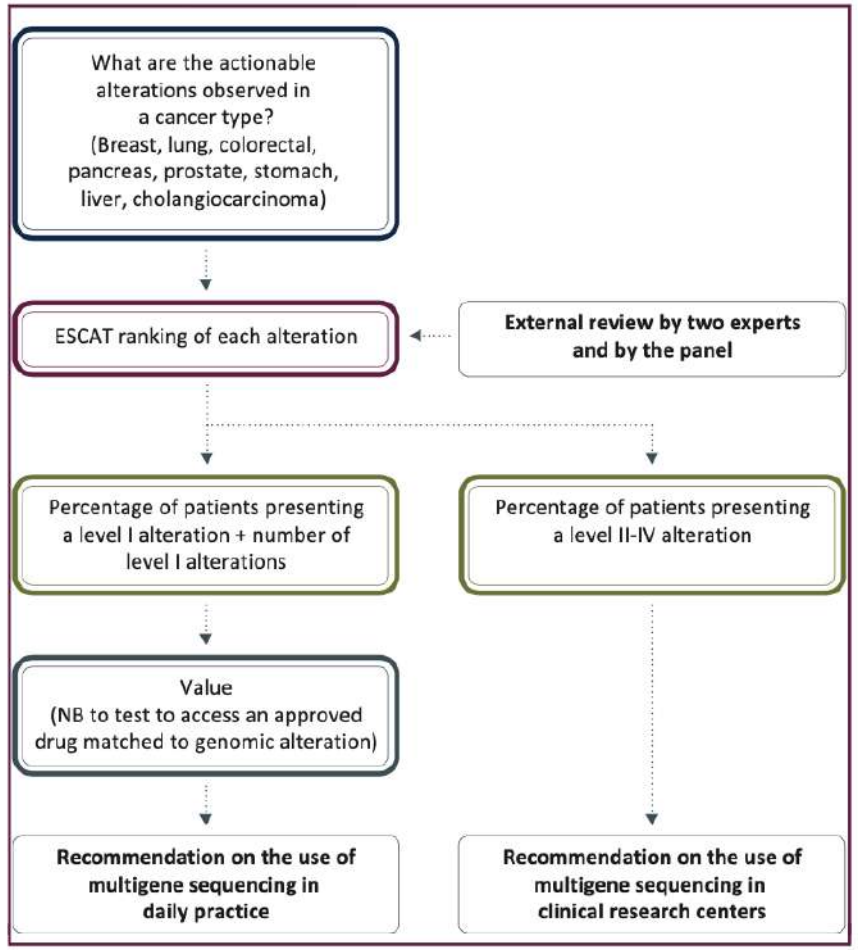
NGS USO RUTINA:
adenocarcinoma pulmón , próstata, ovario y colangiocarcinoma

TMB (KN-158 study): cérvix, TNE G1/2, gl salivares, vulva

- ❑ Ordenar paneles extensos si bajo/ningún coste (incluyendo terapia)
- ❑ Fomentar que se haga desde centros de investigación clínica
- ❑ Acelerar el desarrollo y acceso a terapias más eficaces
- ❑ Innovación para los pacientes y recogida de datos

Desde perspectiva pública y académica…





Mosele et al. Anns Oncol 2020; 31 811): 1491-1902

Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group

	ESCAT I	ESCAT II	ESCAT III
NSCLC	**EGFR** 15% del 19, L858R 60% EGFR mutant: acquired T790M exon 20 2-10% uncommon EGFR mutations (exon 18,20,21) 5% **ALK** 3% **MET** ex skipping 2% **BRAF**^{V600E} 1-2% **ROS1** 0.2-3% **NTRK** fusions 1-2% **RET** fusions	3% **MET** focal amplifications 12% **KRAS**^{G12C} 2-5% **ERBB2**	1.2% **BRCA** 1/2 1.2-7% **PI3K** 1.7% **NRG1**
CRC CANCER	44% **KRAS** 4% **NRAS** 8.5% **BRAF**^{V600E} 4-5% **MSI-H** 0.5% **NKTR1**	2% **ERBB2**	17% **PI3K** hotspot mutations 5% **ATM** mutations 1.7% **MET** amplifications 1% **AKT1**^{E17K} 1% **TMB-High** in MSS 0.3% **RET** fusions 0.2% **ALK** fusions
PROSTATE CANCER	9% **BRCA1/2** somatic mutations/deletions 1% **MSI-H**	40%**PTEN** 5% **ATM** 1% **PALB2**	3% **PI3K** 1% **AKT1**^{E17K}
ENDOMETRIAL CANCER*	2-5% **MSI-H**, PMS2	**ESR1**	**POLE**-aberrant **BRAF** **KRAS** **PIK3CA** **PTEN**?
OVARIAN*	**BRCA 1/2** germline, somatic		**ATM, BRIP1, CHEK2, PALB2, RAD51C, RAD 51B**
CHOLANGIOCARCINOMA	20% **IDH1** mutations 15% **FGFR2** mutations 2% **MSI-H** 2% **NKTR** fusions	5% **BRAF**^{V600E} mutations	10% **ERBB** Amplifications 2% **ERBB2** mutations 7% **PI3CA** hotspot mutations 3% **BRCA1/2** mutations 2% **MET** amplifications
BREAST CANCER	15-20% **ERBB2** amplification **ER, PR** 30-40% **PI3K** 1% **MSI-H**	4% **ERBB2** hotspot mutation 3% BRCA 1/2 somatic mutation	6% **NF1**??? 1% **MDM2** 2% **ERBB3**
	1% **NTRK** fusions 4% **BRCA** 1/2 germline mutation **androgen receptor** and **PDL-1** (Triple negative BC)	10% **ESR1**(mutation mechanism resistance) 7% **PTEN** 5% **AKT1**^{E17K}	

GIST	**KIT, PDGFRA**		
PANCREATIC CANCER	1-4% **BRCA1/2** germline mutation 1-3% **MSI -H** <1% **NTRK**		3% **BRCA 1/2** somatic mutations 90% **KRAS** mutations 3% **PI3CA** 3% **BRAF**^{V600E} 2% **MDM2** amplifications 1-2%**ERBB2** amplifications/mutations 1% **NRG1** fusions <1% **ALK** fusions <1% **RET** fusions <1% **ROS1** fusions
GASTROESOPHAGEAL ADENOCARCINOMA	16% **ERBB2** amplifications 8% **MSI-H** 2% **NTRK** fusions	6% **EGFR** amplifications 3% **MET** amplifications	3%**ERBB2** hotspots mutations 1.3% **MET** Mutations 7% **PI3KCA** hotspot mutations 4% **FGFR2** amplifications 3% **ATM** mutations 1-5% **BRCA 1/2** mutations <1% **ROS 1** fusions <1% **RET** fusions 3% **ERBB3** hotspot mutations
MELANOMAS	50% **BRAF**^{V600E}		**KIT**
HEPATOCELLULAR CARCINOMA	1% **NTRK** fusions 1% **MSI- H**		4% **PI3CA** hotspot mutations 4% **MET** amplifications 2% RAS mutations

Mosele et al. Anns Oncol 2020; 31 811): 1491-1902

Clinical practice guidance for next-generation sequencing in cancer diagnosis and treatment (edition 2.1)

Japanese Society Medical Oncology: promover la medicina de precisión

- ❑ TIMING: tumores sólidos cuando no hay estándar
- ❑ A decisión del clínico: pacientes adecuados para terapias sistémicas tras test estado general, función analítica…fit para tratamiento, guías clínicas de sociedades académicas

2 Major cancer genomic medicine classifications	Estimate range	Number of patients to undergo genomic analysis	Number of patients subject to treatment or prevention based on genomic diagnosis
Somatic genomic medicine	(1) Low estimate	164,000	77,000 (treatment)
	(2) High estimate	400,000	150,000 (treatment)
(3) Germline genomic medicine		280,000	8000 (prevention)

"the right drug for the right patient at the right time,"

Naito Y et al. Int J Clin Oncol 2021 26:233-283

Optimal timing molecular tumour characterization: Is the earliest always the best?

Benedikt Westphalen, MD Comprehensive Cancer Center, University of Munich

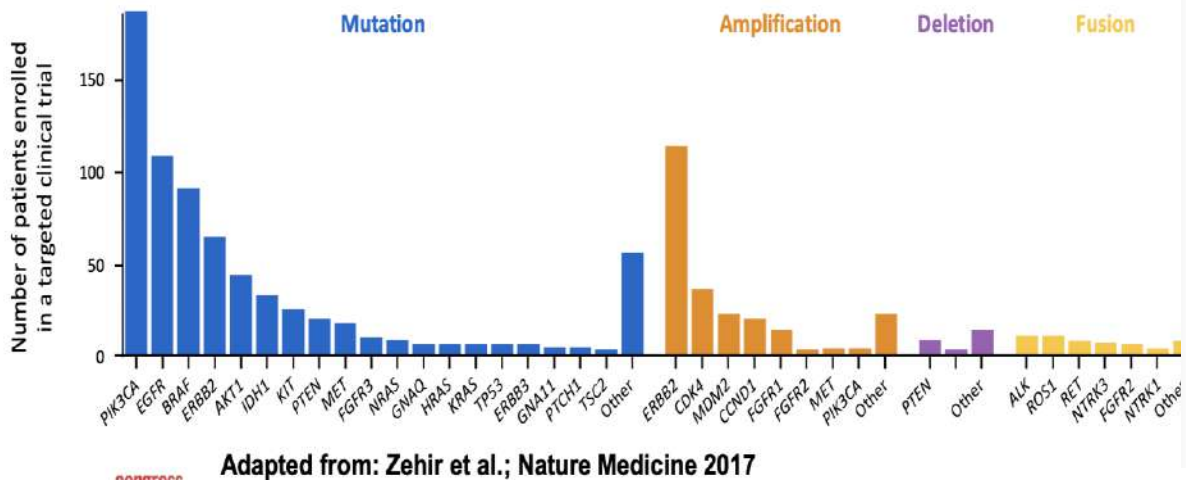
DKH Arbeitsgruppe
Molekulare Diagnostik & Therapie

ESMO Translational Research and Precision Medicine Working Group

Tumour profiling driving innovation…

> 10,000 patients screened using CGP

11% of patients enrolled in molecularly-guided clinical trials



Adapted from: Zehir et al.; Nature Medicine 2017

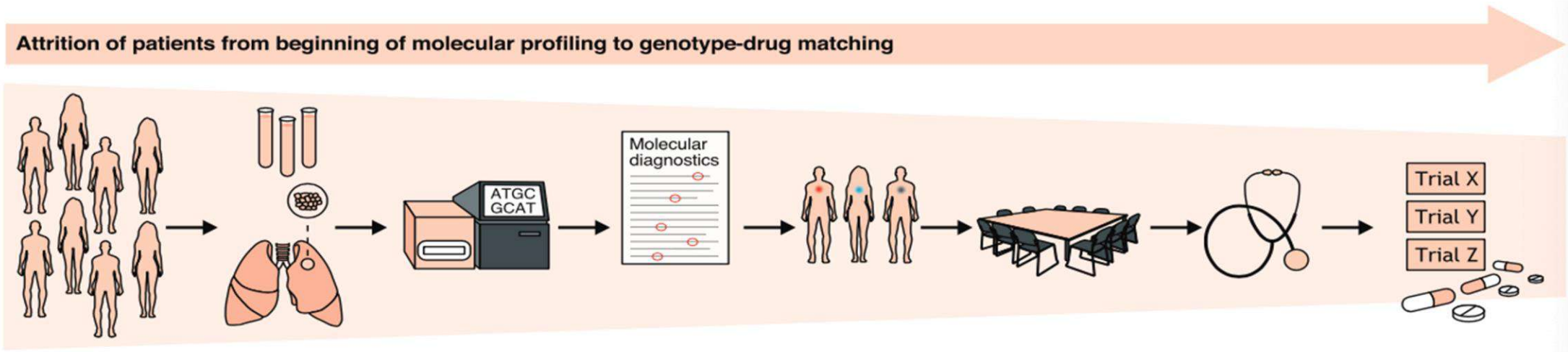
Rapidly increasing number of molecular agents

So why should we consider early tumour profiling?

- **Allows to cover all relevant biomarkers at once**
  - **Standard of care treatment**
  - **Screening for innovative clinical trials**
- **Allows to identify (ultra) rare alterations missed by single-gene testing**
- **Can save time, resources & tissue**
- **Patients benefit from personalized treatment at initial diagnosis**
- **Change of management only effective in 1st & 2nd line**

2021 ESMO congress

Identificación de problemas y soluciones

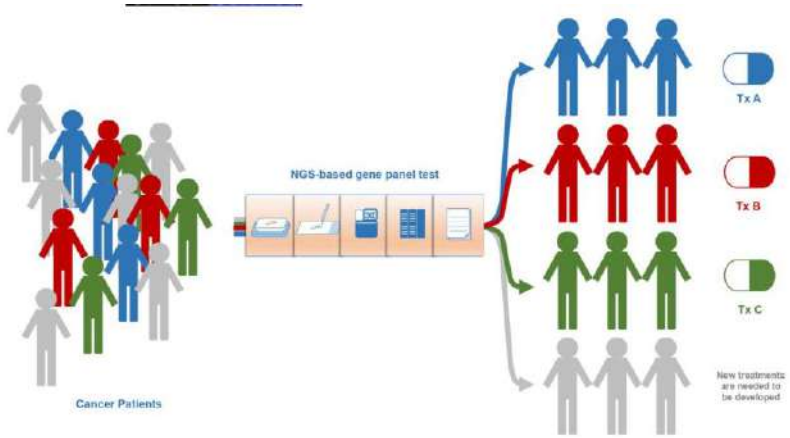


	Patient accrual	Sample collection	Laboratory operations	Variant interpretation	Clinical utility	Decision	Clinical interpretation	Trial matching
Examples of challenges	Patient factors: medical, logistics	Inadequacy of samples for profiling	Technical issues of NGS and other assays	Challenges with variant interpretation	Low rate of actionable results	Lack of access to MTB	Physician factors: busy clinics, lack of genomic understanding	Lack of access to drugs or clinical trials
Possible solutions	Appropriate patient selection, navigators, efficient consent and IRB aprocesses	Improvement in sample collection and processing, liquid biopsies	Advances in technology including limits of detection and coverage depth	Integrated knowledge bases, artificial intelligence tools for automation	Expansion of target identification beyond genomics	Increase availability to MTB e.g. virtual MTB	Navigators and tools to help physicians manage profiling results	Increase number and access to precision medicine trials; easier access to approved drugs

Fig. 1 The process from genetic sequencing of patients to enrollment on genotype-matched clinical trials. MTB, molecular tumor board; IRB, institutional review board; NGS, next-generation sequencing

Malone et al. Genome Med 2020; 12 (8): 1-19

Clinical Outcomes of Molecular Tumor Boards: A Systematic Review



MOLECULAR TUMOR BOARDS: Herramienta para incorporar uso de la medicina de precisión

Equipo multidisciplinar, órgano de consulta para pacientes con cáncer

DIAGNÓSTICO DE CERTEZA

DIANAS POTENCIALES

ENSAYOS CLÍNICOS

CONSEJO GENÉTICO

- 3328 pacientes de 14 ensayos para pacientes refractarios a la terapia estándar que aportaban resultados
- Ausencia de randomizados, realización NGS (paneles de > 300 genes)
- Tasa de respuestas: 0-67%

CONCLUSION Although data quality is limited by a lack of prospective randomized controlled trials, MTBs appear to improve clinical outcomes for patients with cancer. Future research should concentrate on prospective trials and standardization of approach and outcomes.

Larson et al. JCO Precis Oncol 2021; 5: 1122-32

Cancer core Europe Molecular Tumor Board Portal

https://www.mtbp.org/

On target

Multidisciplinary Tumour Boards in harmony: mission possible?

05 / 10 / 2021

La medicina de precisión va a depender de la experiencia del centro…acercarnos a los centros de excelencia

Las guías de tratamiento por patología son ahora insuficientes

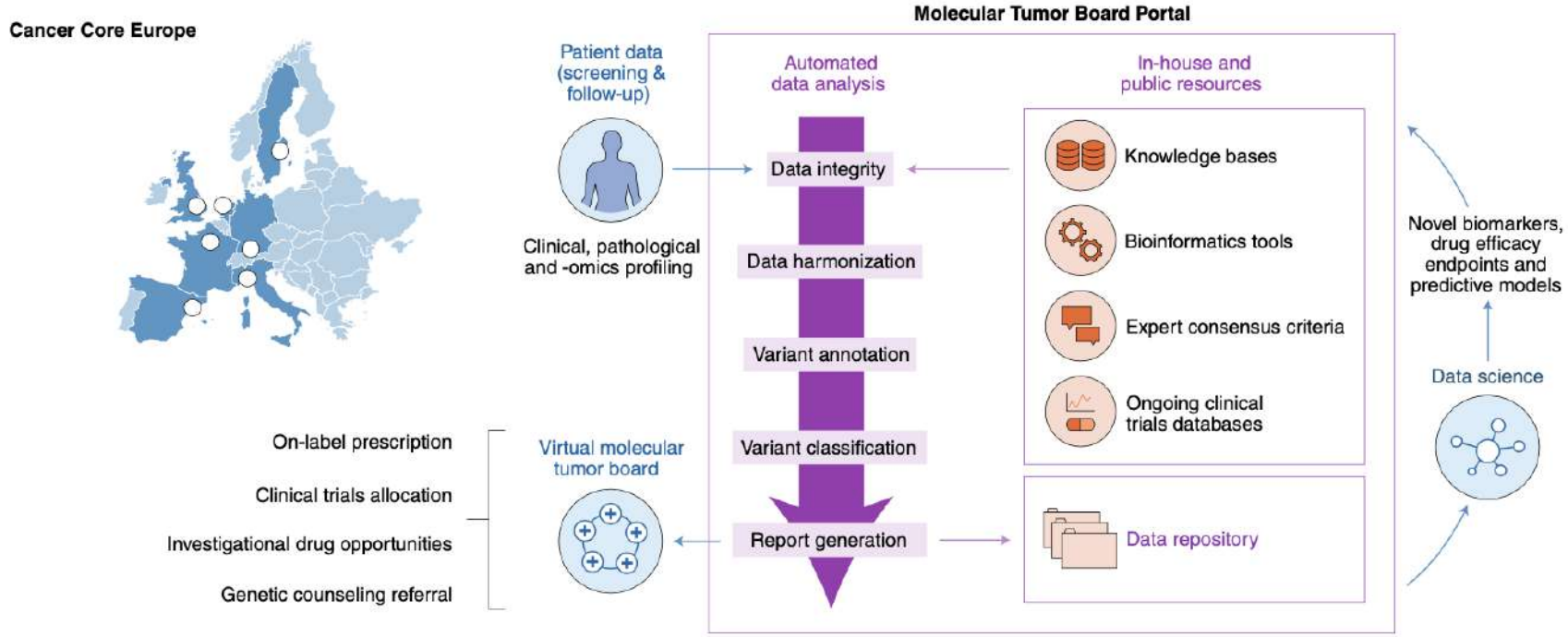
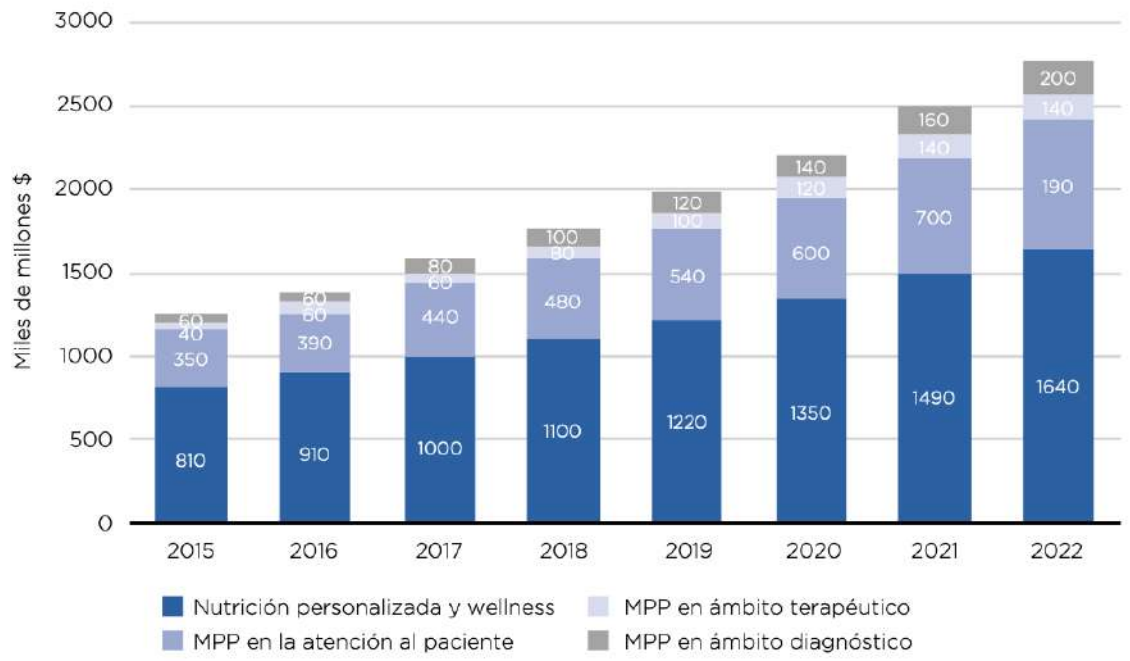


Fig. 1 | The Molecular Tumor Board Portal. MTBP automates a common process for the capture, interpretation and reporting of next-generation sequencing data across CCE centers, currently formed by the Cancer Research UK Cambridge Centre (Cambridge), German Cancer Research Center & National Center for Tumor Diseases (Heidelberg), Institut Gustave Roussy (Paris), Karolinska Institutet (Stockholm), National Cancer Institute (Milan), Netherlands Cancer Institute (Amsterdam) and Vall d'Hebron Institute of Oncology (Barcelona).

Tamborero et al. Nat Med 2020; 26: 990-994

Medicina de precisión, un valor en auge

Figura 3. Tamaño estimado del mercado mundial para la MPP del 2015 al 2022.



Fuente: *Dossier on Personalized Medicine* (2018) www.Statista.com. MPP en la atención al paciente incluye la atención médica, e-salud y telemedicina en el ámbito de la MPP; MPP en el ámbito diagnóstico incluye la venta directa de test diagnósticos al consumidor, test y servicios realizados por laboratorios privados; MPP en el ámbito terapéutico incluye medicina genómica, dispositivos médicos y medicamentos.

NCCN Biomarkers Compendium

1 year/1 user subscription

$249

Number of Users

1

ADD TO CART

Users	Price
1-3	$249 per user
4-6	$239 per user
7-10	$229 per user
11-24	$219 per user
25-50	$199 per user
51-100	$179 per user
101-249	$149 per user
250-499	$149 per user
500+	**For groups of 500 or more, please contact us**

Description

Contains information designed to support decision-making around the use of biomarker testing in patients with cancer. The NCCN Biomarkers Compendium® is updated in conjunction with the NCCN Guidelines on a continual basis.

Includes Tests that measure changes in genes or gene products and which are used for:

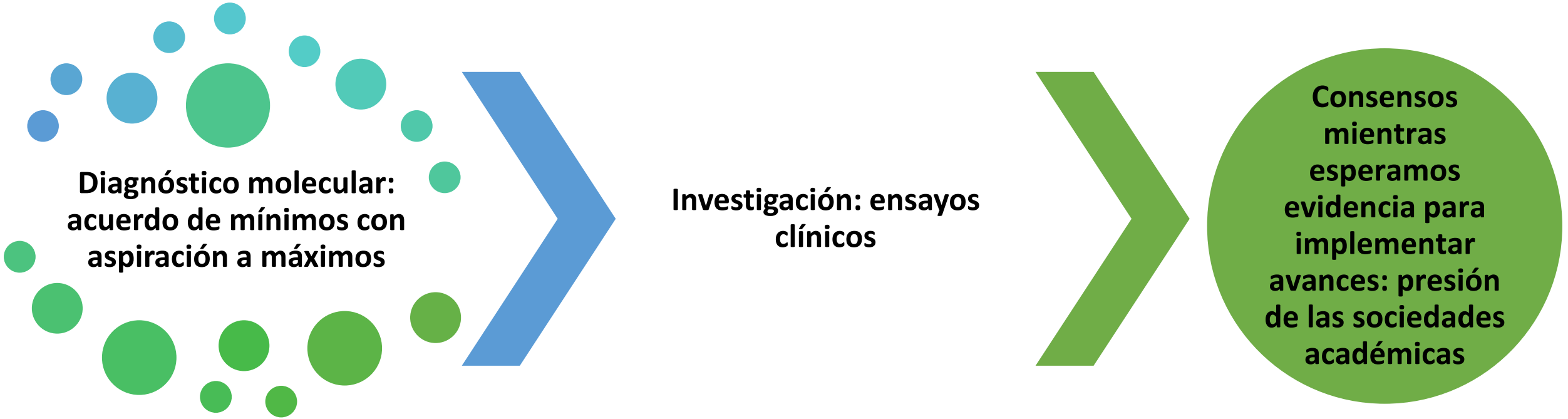
- Diagnosis
- Screening
- Monitoring
- Surveillance
- Prediction
- Prognostication

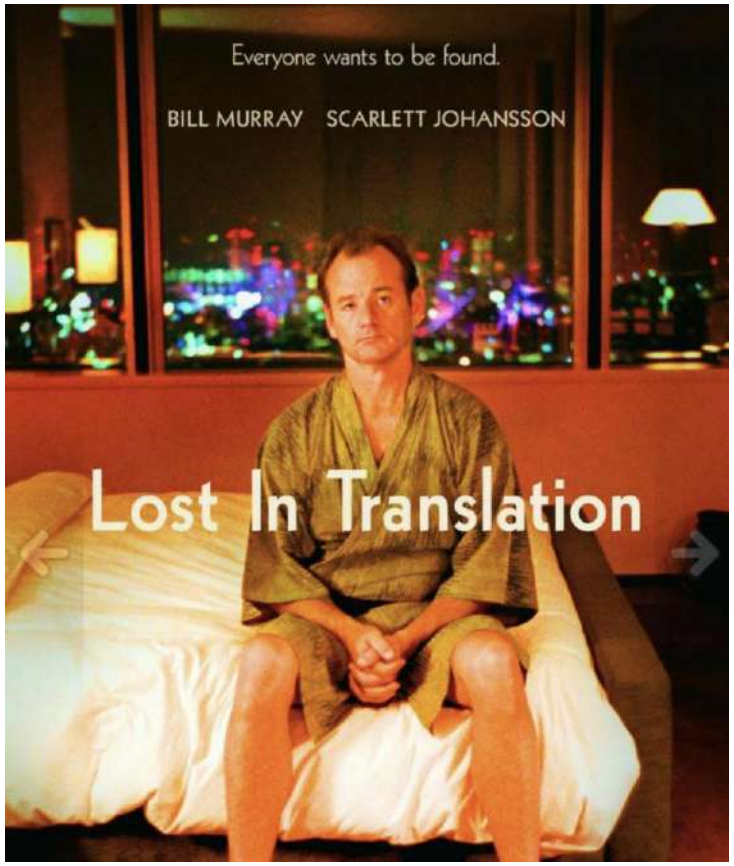
VIEW A SAMPLE

Porque la información es cara y difícil de interpretar

VII SIMPOSIO GETTHI

Integración de las plataformas de caracterización genética en la práctica habitual oncológica. CONCLUSIONES:





Muchas gracias por la atención

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