Previsione del rischio di ripresa .....

I risultati della ricerca nel carcinoma mammario metastatico nei fenotipi HR+/HER2negativo, triplo negativo, HER2-positivo e nelle donne portatrici di VP BRCA1-2

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Roma

Gemelli

What more shocking change in metastatic BC?

ASCO Evolution

JOURNAL OF CLINICAL ONCOLOGY ASCO SPECIAL ARTICLE

Chemotherapy and Targeted Therapy for Women With Human Epidermal Growth Factor Receptor 2–Negative (or unknown) Advanced Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline

2014: OT over CT

Use of Biomarkers to Guide Decisions on Systemic Therapy for Women With Metastatic Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline

2015: rebiopsy and testing ER PR HER2

Endocrine Treatment and Targeted Therapy for Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer: ASCO Guideline Update

2021: PIK3CA, BRCA, no ESR1

Biomarkers for Systemic Therapy in Metastatic Breast Cancer: ASCO Guideline Update

2022: PIK3CA, BRCA, NTRK, no ESR1, no PALB2
PDL1 MMR/MSI TMB in TNBC

Having to Make a Selection .....

HER2 Low **The New Biomarker**

HER2 - **Resistence to IL CDK4/6i : this is the problem**

HER2 + **The Perfect Storm**

HR-/HER2- **no more Untargetable**

How to follow disease?

Having to Make a Selection:

HER2 Low **The New Biomarker**

HER2 - **Resistence to IL CDK4/6i : this is the problem**

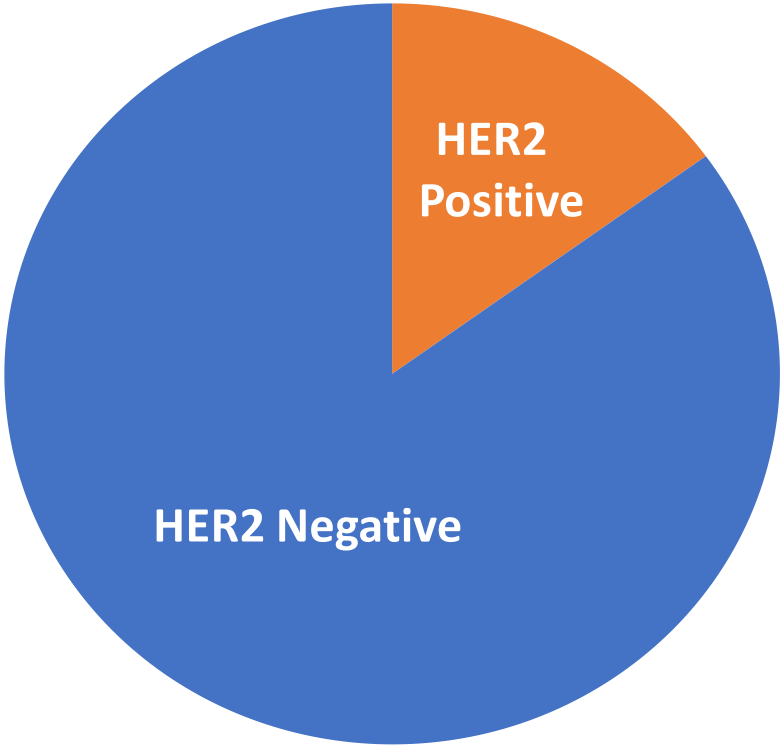
HER2 + **The Perfect Storm**

HR-/HER2- **no more Untargetable**

How to follow disease?

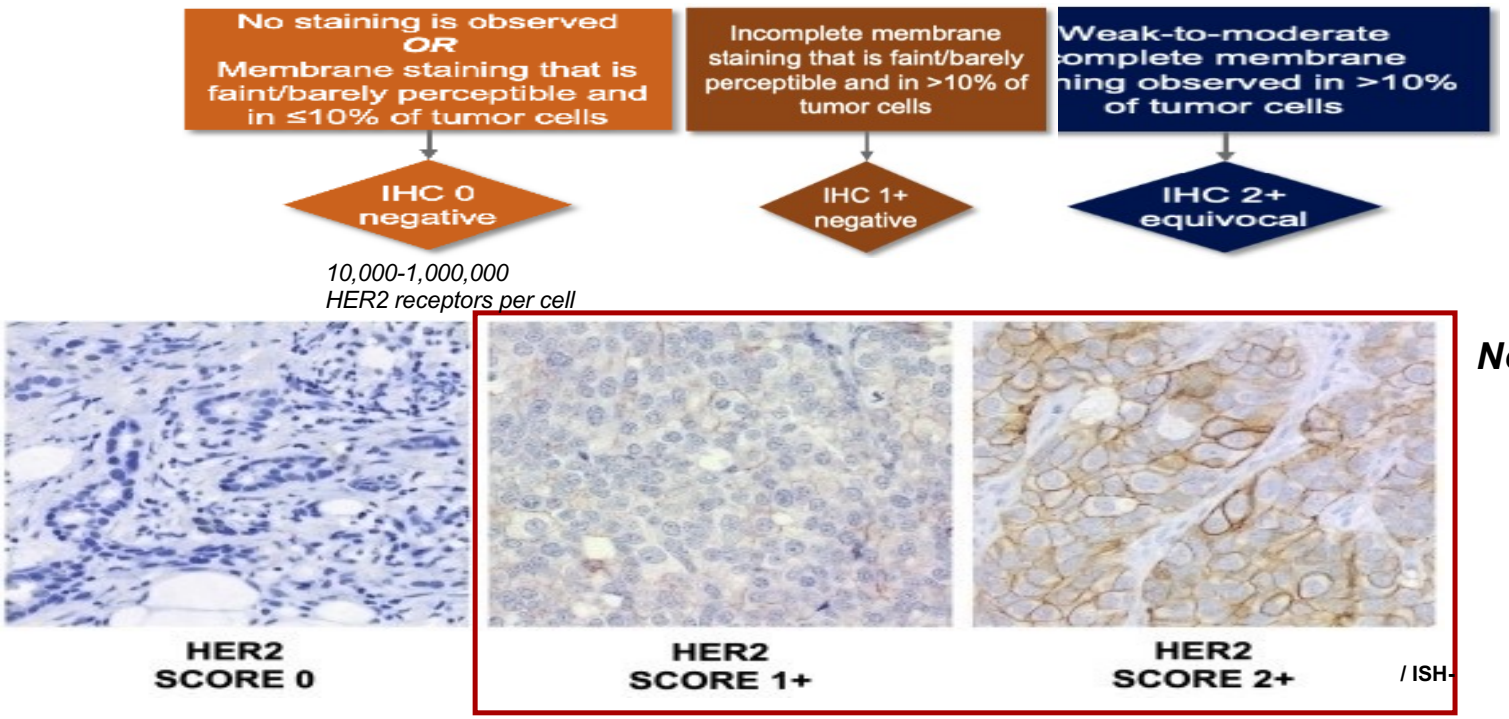
Traditional View of HER2-Positive Breast Cancer

- Tumors lacking *ERBB2* overexpression or amplification are collectively defined as HER2 negative



Wolff A et al. J Clin Oncol. 2018.

HER2 Negative: Composed of HER2-low & HER2 0

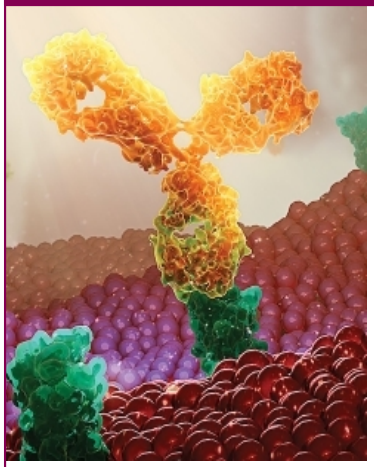


No approved anti-HER2 agent between 2000 and 2021

Marchiò C et al. Semin Cancer Biol. 2021

50 years in the making: Learning the right combinations for successful ADCs

1 TARGETS & ANTIBODIES

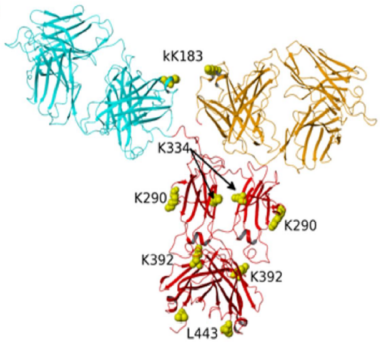


Optimal
Tumor:
Normal ratio
+ Internalization

Efficient delivery of ADC payload

2 CONJUGATION CHEMISTRY + LINKERS

Optimize conjugation chemistry

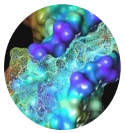


Overcome potential off-target tox

3 PAYLOADS

Match disease biology

TOPOISOMERASE
Inhibitors



DNA Intercalators
Crosslinkers

MICROTUBULE
Inhibitors

Enables biology-driven combinations, overcome resistance

DESTINY-Breast04: First Randomized Phase 3 Study of T-DXd vs Treatment of Physicians Choice for HER2-low MBC

- HER2-low (IHC 1+ vs IHC 2+/ISH-), unresectable, and/or MBC treated with 1-2 prior lines of chemotherapy in the metastatic setting
- HR+ disease considered endocrine refractory[a]

R 2:1

T-DXd
5.4 mg/kg Q3W (n = 373)

HR+ ≈ 480
HR− ≈ 60

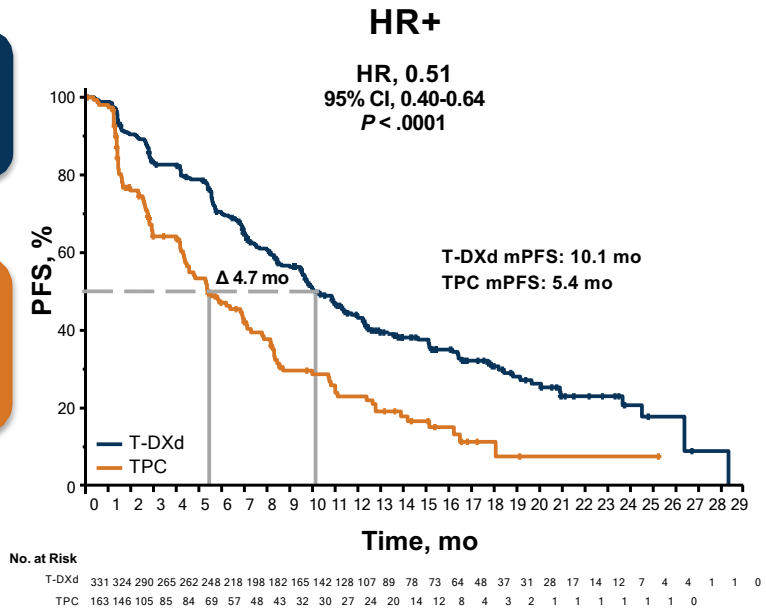
TPC
Capecitabine, eribulin, gemcitabine, paclitaxel, nab-paclitaxel[c] (n = 184)

Primary endpoint

- PFS by BICR (HR+)

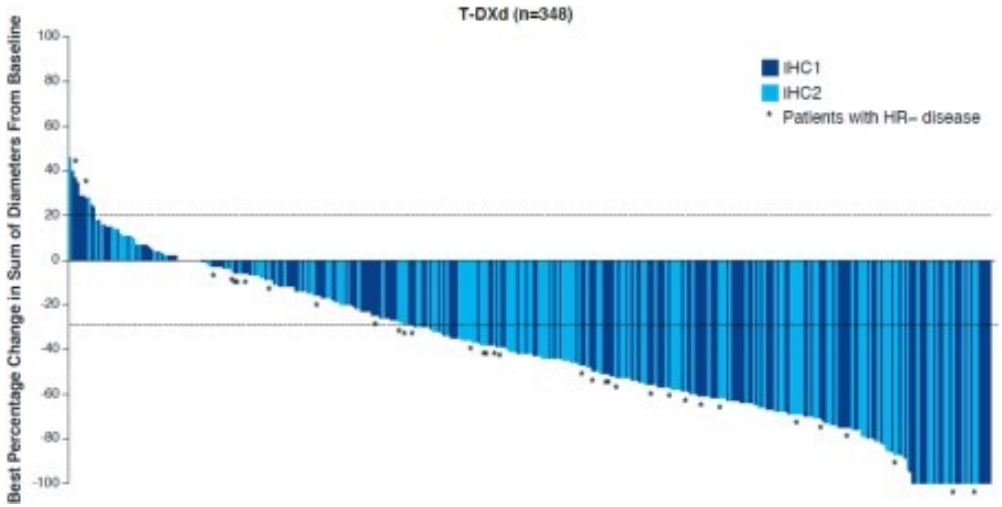
Key secondary endpoints[d]

- PFS by BICR (all patients)
- OS (HR+ and all patients)



Modi S et al. ASCO 2022
Modi S et al. *N Engl J Med*. 2022.

Activity of T-DXd according to HER2 IHC levels from HER2-low



No differences in terms of ORR

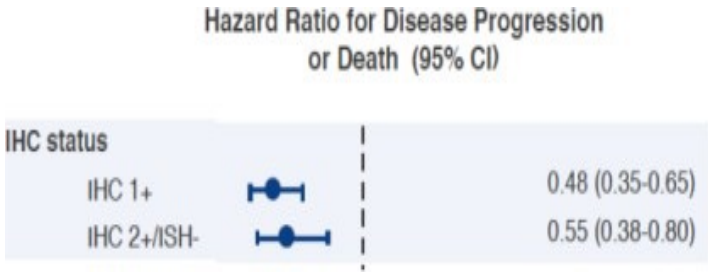


Figure modified from supplemental material

No differences in terms of PFS

Modi et al. NEJM 2022

Activity of T-DXd according to HR status from HER2-low

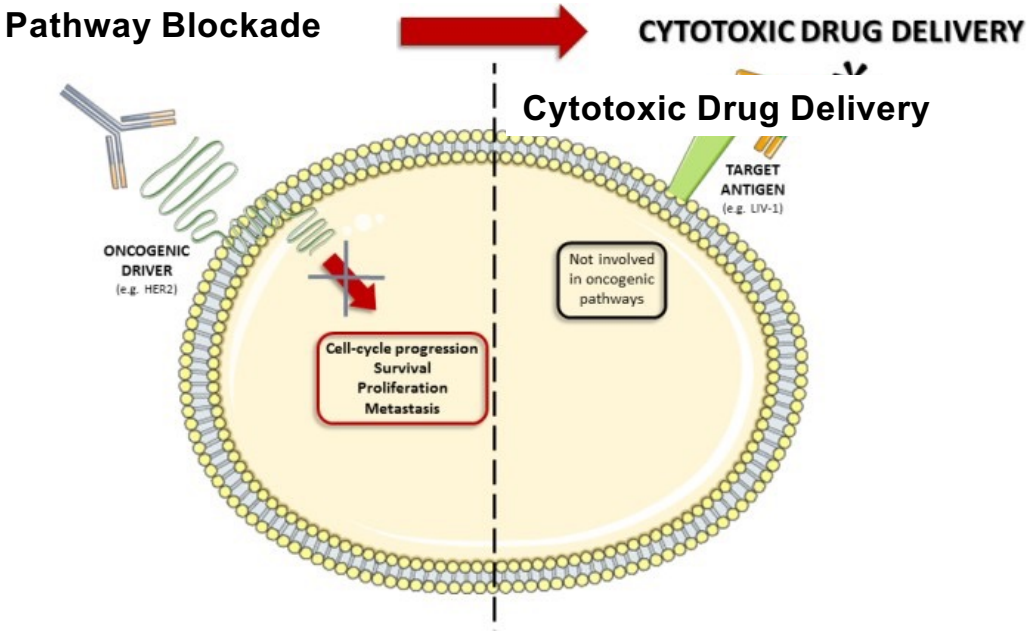
	HR-positive		HR-negative	
	T-DXd	Control	T-DXd	Control
ORR	52.6%		50.0%	
PFS	10.1	5.4	8.5	2.9
	0.51		0.64	
OS	23.9	17.5	18.2	8.3
	0.46		0.48	

No differences in terms of ORR and PFS/OS Hazard Ratio

Modi et al. NEJM 2022

HER2 Low: Activity of HER-directed ADCs not likely related to blockade of an oncogenic driver

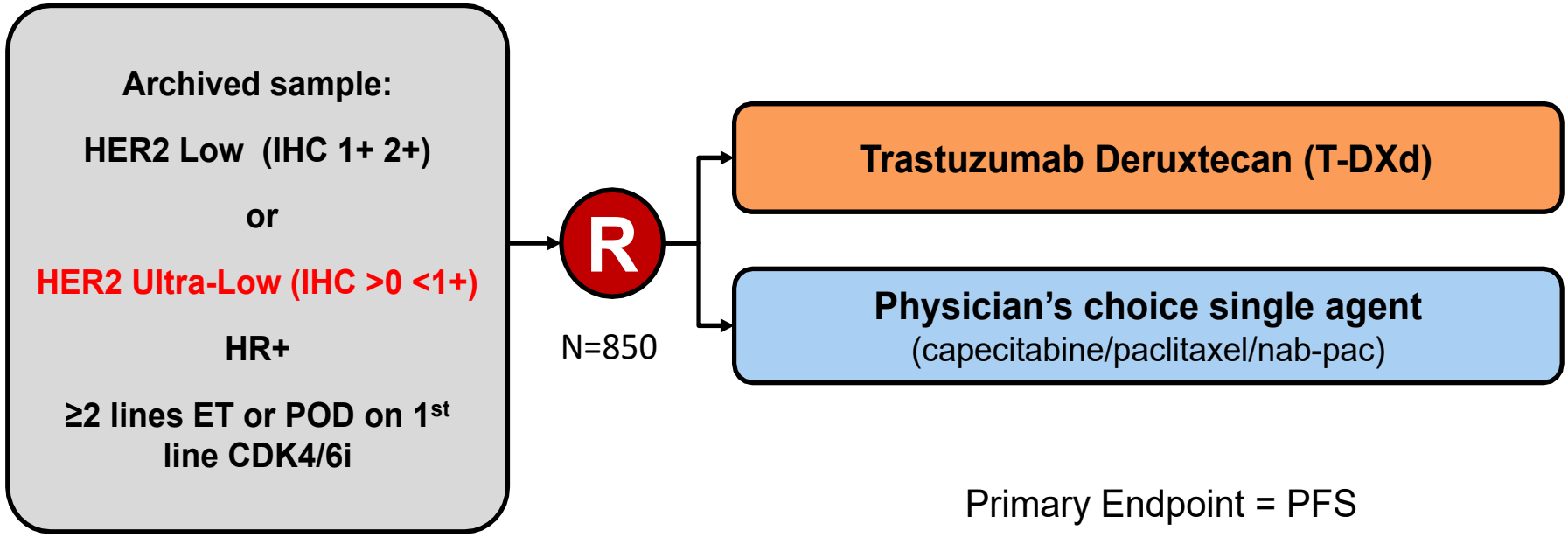
- **No benefit with HER2-blockade**
- Activity is not likely related to the blockade of an oncogenic pathway, but rather to the **targeted delivery of a highly potent payload**
- **HER2-low not a new subtype characterized by an oncogenic driver, but is rather a biomarker for benefit to ADCs targeting HER2**



Tarantino P et al. Expert Opin Biol Ther. 2020;20:1009-1024.

The Super New!!!

DESTINY Breast-06: Chemotherapy-naïve, HR+, HER2 LOW or HER2 Ultra-Low MBC



Primary Endpoint = PFS

Having to Make a Selection:

HER2 Low — The New Biomarker

HER2 - — Resistance to IL CDK4/6i : this is the problem

HER2 + — The Perfect Storm

HR-/HER2- — no more Untargetable

How to follow disease?

When do patients receive chemotherapy after CDK4/6i PD?

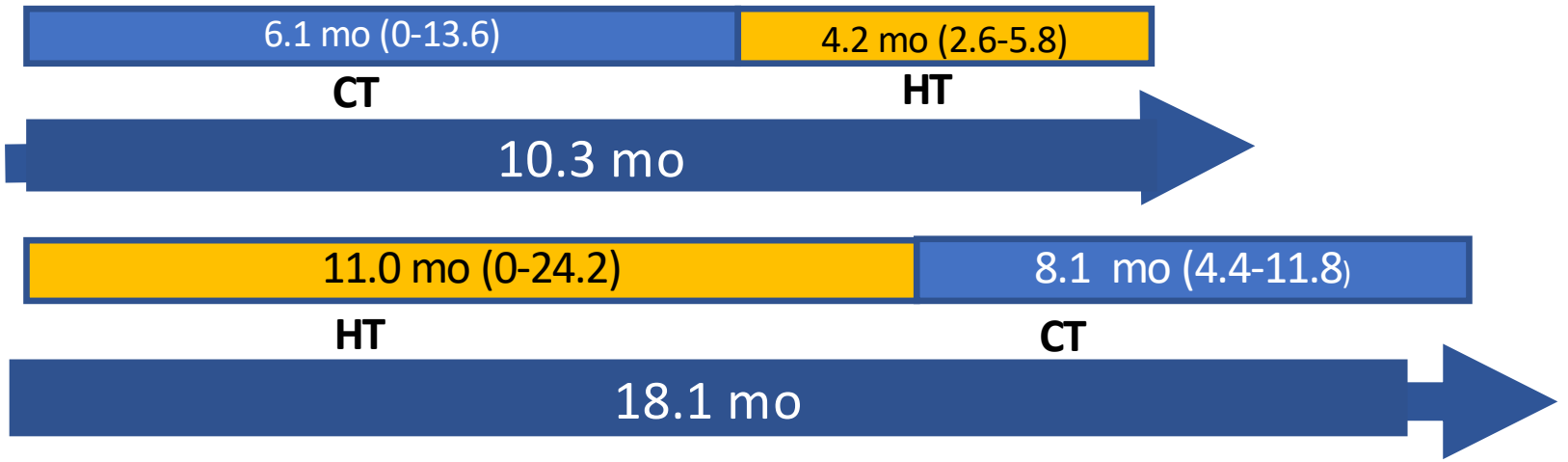
Table 2. First Subsequent Antineoplastic Therapy among Patients Who Discontinued the Trial Regimen.

Variable	Ribociclib Group (N=335)	Placebo Group (N=337)
No. of patients who discontinued the trial regimen	219	280
Patients who received any subsequent therapy — no. (%)	151 (68.9)	205 (73.2)
Chemotherapy alone	49 (22.4)	80 (28.6)
Chemotherapy plus hormone therapy or other therapy*	18 (8.2)	22 (7.9)
Hormone therapy alone	49 (22.4)	57 (20.4)
Hormone therapy plus other therapy†	31 (14.2)	41 (14.6)
Other	4 (1.8)	5 (1.8)

Im SA et al, NEJM 2019

Post-progression treatments after Palbociclib plus Endocrine Therapy in HR+/HER2- Metastatic Breast Cancer patients: which better choice?

RWE



Fabi et al. Oncology 2021

Mutations in Breast Cancer

P53: 37%

PI3K: 36% ➡ SOlar 1 study -> Alpelisib + FLV

GATA: 11%

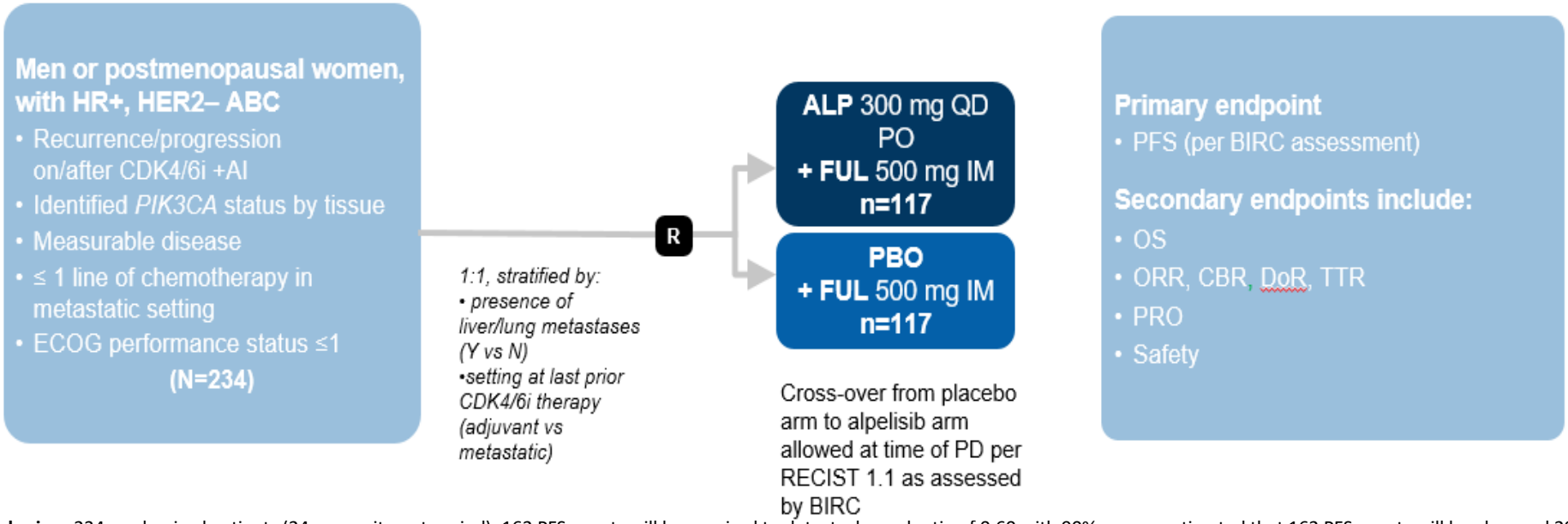
MAP3K1: 8%

MLL3: 7%

MAP2K4: 4%

CGAN Network, Nature 2012;490:61

EPIKB5: Phase III trial of alpelisib + fulvestrant in HR+, HER2- advanced breast cancer with a PIK3CA mutation who progressed on or after AI and a CDK4/6 inhibitor



.

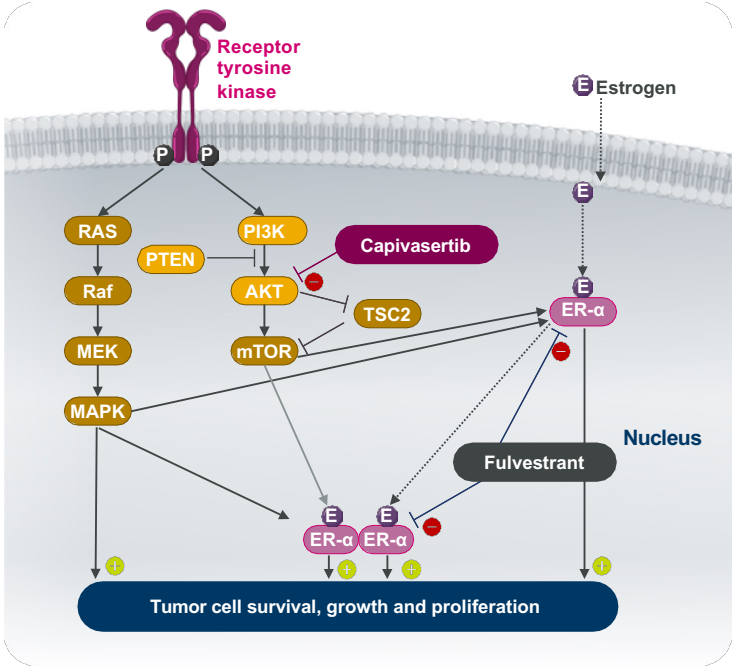
Sample size: 234 randomised patients (24m recruitment period); 162 PFS events will be required to detect a hazard ratio of 0.60 with 90% power, estimated that 162 PFS events will be observed 29 months after FPFV

But this is an ongoing Trial

Overcoming Resistence to HT

- AKT pathway activation occurs in many HR+/HER2- ABC through alterations in *PIK3CA, AKT1 and PTEN*, but may also occur in cancers without those genetic alterations.[1,2] AKT signalling is also implicated in the development of resistance to endocrine therapy[2]
- Capivasertib is a potent, selective inhibitor of all three AKT isoforms (AKT1/2/3)
- In the Phase II, placebocontrolled FAKTION trial[3]:

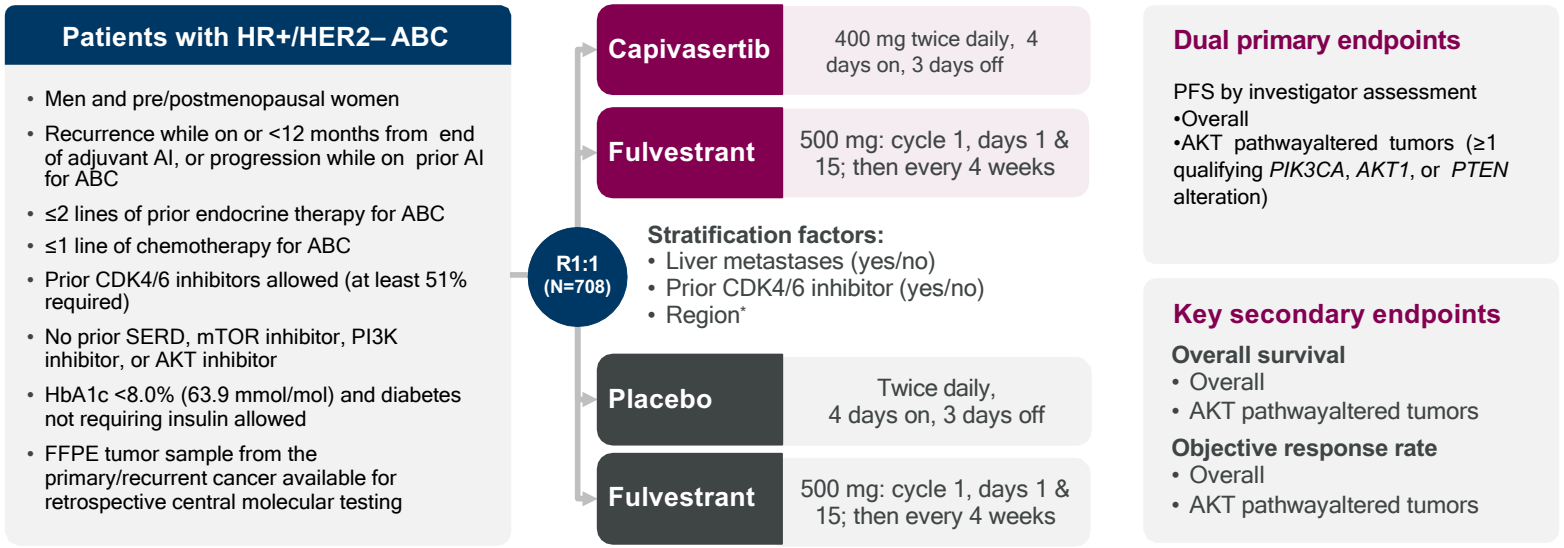
- The addition of capivasertib to fulvestrant significantly improved PFS and OS in postmenopausal women with AI-resistant HR+/HER2- ABC in the overall population, with a more pronounced benefit in pathway altered tumours
- No patients had received prior CDK4/6 inhibitors



1. Millis et al. *JAMA Oncol* 2016;2:15651573; 2. Toss et al. *Oncotarget*. 2018;9:3160631619; 3. Howell et al. *Lancet Oncol* 2022;23:851-64. ABC, advanced breast cancer.

CAPItello291: Study overview

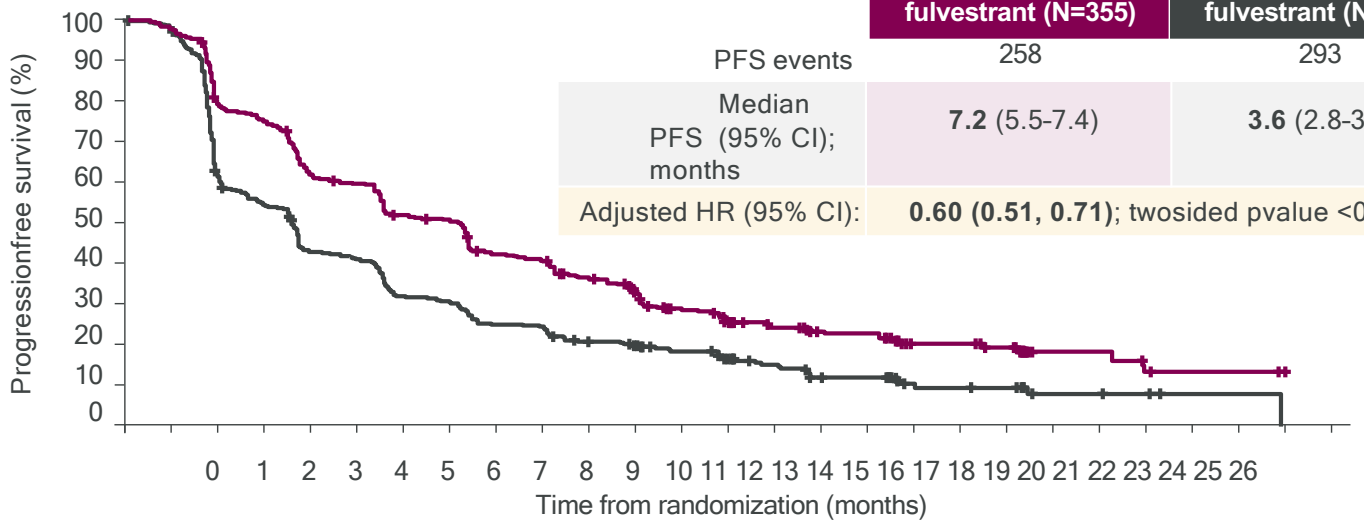
Phase III, randomized, double-blind, placebo-controlled study (NCT04305496)



HER2- was defined as IHC 0 or 1+, or IHC 2+/ISH-. *Region 1: United States, Canada, Western Europe, Australia, and Israel, Region 2: Latin America, Eastern Europe and Russia vs Region 3: Asia. ABC, advanced (locally advanced [inoperable] or metastatic) breast cancer.

Pre or perimenopausal women also received a luteinizing hormonereleasing hormone agonist for the duration of the study treatment

Dualprimary endpoint: PFS in the overall population



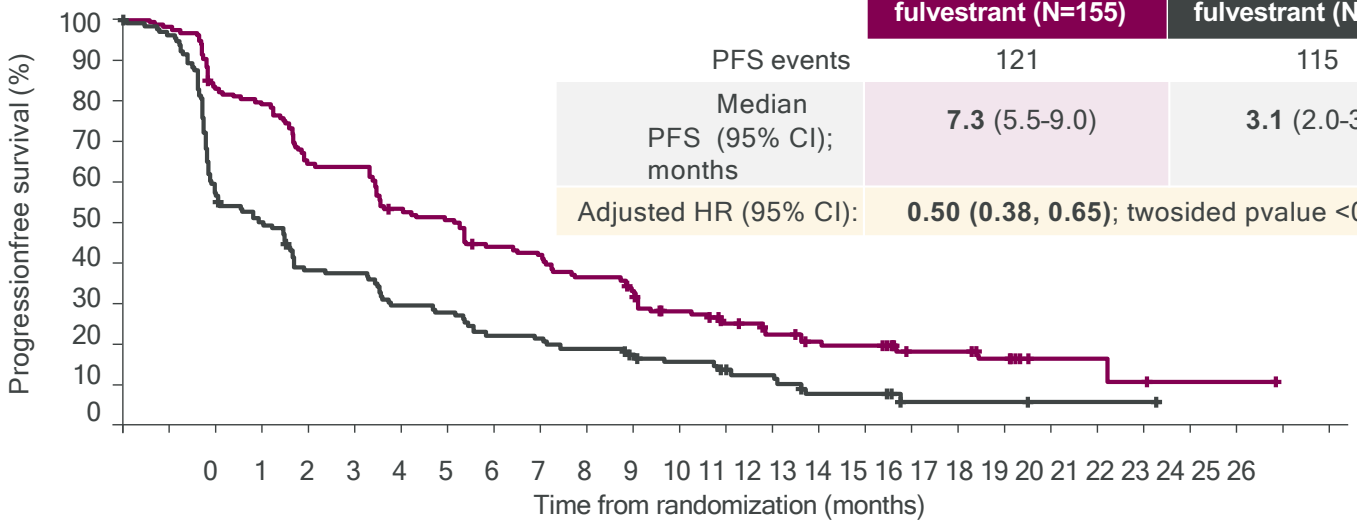
	Capivasertib + fulvestrant (N=355)	Placebo + fulvestrant (N=353)
PFS events	258	293
Median PFS (95% CI); months	**7.2** (5.5-7.4)	**3.6** (2.8-3.7)
Adjusted HR (95% CI):	**0.60 (0.51, 0.71)**; twosided pvalue <0.001	

Number of patients at risk

Capivasertib + fulvestrant	355	330	266	252	207	199	172	166	138	133	115	98	78	64	55	44	43	25	25	21	8	8	5	2	2	1	0
Placebo + fulvestrant	353	329	207	182	142	136	106	100	83	81	66	59	51	41	33	24	23	12	11	10	4	4	3	1	1	0	0

+ indicates a censored observation. HR was estimated using the Cox proportional hazard model stratified by the presence of liver metastases, prior use of CDK4/6 inhibitor, and geographic region.

Dualprimary endpoint: Investigator assessed PFS in the AKT pathway altered population



	Capivasertib + fulvestrant (N=155)	Placebo + fulvestrant (N=134)
PFS events	121	115
Median PFS (95% CI); months	**7.3** (5.5-9.0)	**3.1** (2.0-3.7)
Adjusted HR (95% CI):	**0.50 (0.38, 0.65)**; twosided pvalue <0.001	

Number of patients at risk

Capivasertib + fulvestrant	155	150	127	121	99	97	80	76	65	62	54	49	38	31	26	22	21	12	12	9	3	3	2	1	1	0	0
Placebo + fulvestrant	134	124	77	64	48	47	37	35	28	27	24	20	17	14	11	6	6	2	2	2	1	1	1	0	0	0	0

+ indicates a censored observation. HR was estimated using the Cox proportional hazard model stratified by the presence of liver metastases and prior use of CDK4/6 inhibitor.

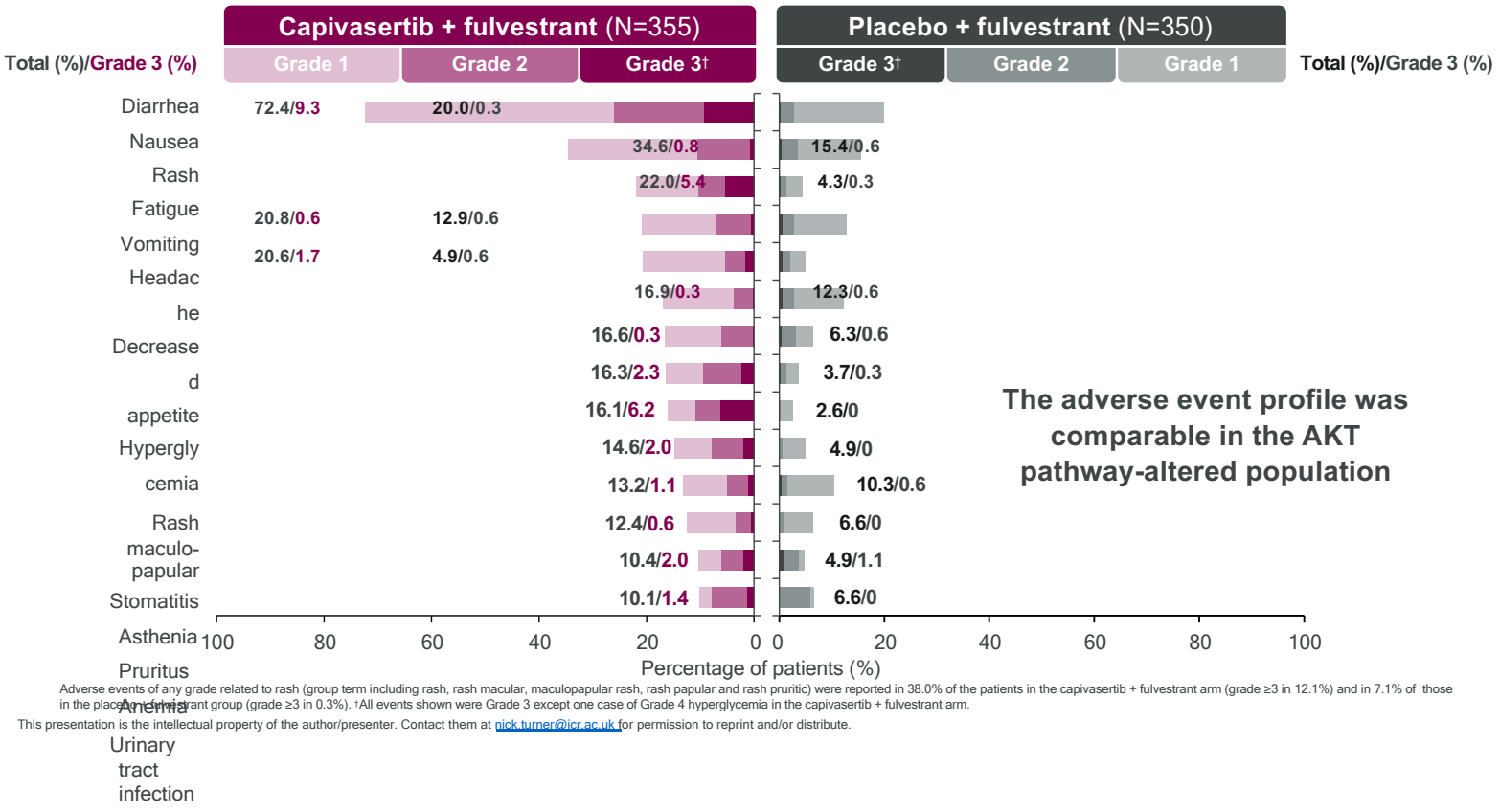
Response per investigator assessment

	Overall population		AKT pathway-altered population	
	Capivasertib + fulvestrant	Placebo + fulvestrant	Capivasertib + fulvestrant	Placebo + fulvestrant
Patients with measurable disease at baseline	310	320	132	124
Objective response rate; n (%)	71 (22.9)	39 (12.2)	38 (28.8)	12 (9.7)
Odds ratio (95% CI)*	2.19 (1.42, 3.36)		3.93 (1.93, 8.04)	
Best objective response in all patients; n (%)	355	353	155	134
Complete response Partial response Stable disease (≥ 8 weeks) Progressive disease Non evaluable	4 (1.1) 68 (19.2) 187 (52.7) 83 (23.4) 13 (3.7)	1 (0.3) 38 (10.8) 152 (43.1) 149 (42.2) 13 (3.7)	3 (1.9) 35 (22.6) 84 (54.2) 31 (20.0) 2 (1.3)	0 12 (9.0) 55 (41.0) 62 (46.3) 5 (3.7)

As per the multiple testing procedure, formal comparison of ORR will only be conducted if overall survival is significant in both populations.
Objective response rates were assessed in patients with measurable disease at baseline.

*Analysis was performed using logistic regression adjusted for stratification factors. Odds ratio >1 favors capivasertib + fulvestrant.

Adverse events (>10% of patients) – overall population



Adverse events of any grade related to rash (group term including rash, rash macular, maculopapular rash, rash papular and rash pruritic) were reported in 38.0% of the patients in the capivasertib + fulvestrant arm (grade ≥3 in 12.1%) and in 7.1% of those in the placebo + fulvestrant group (grade ≥3 in 0.3%). †All events shown were Grade 3 except one case of Grade 4 hyperglycemia in the capivasertib + fulvestrant arm.

Liquid Biopsy for ctDNA ESR1m

SERENA 6

Ongoing study

Eligibility Criteria

- Pre [a] - and postmenopausal women and men [a] with HR+/HER2- locally advanced inoperable or MBC
- Currently under treatment with CDK4/6 inhibitor (PAL or ABE) + AI (LET or ANA)+/- LHRHa as their 1L MBC treatment per CDK4/6 inhibitor approved local label indication
- AND have been on treatment for ≥ 6 months
- *ESR1m* positive detected by a prespecified ctDNA assay at central laboratories
- No evidence of disease progression per investigator assessment
- Willing to provide archival tumor assessment scan images before the detection of *ESR1m+*

1:1

Randomisation

Arm A
AZD9833 (75 mg once daily)
+ CDK4/6 inhibitor [b]
+ Placebo for AI

Arm B
Continue on
AI [c]
+ CDK4/6 inhibitor [b]
+ Placebo for AZD9833

N=300 patients

Primary Endpoint

- PFS by investigator assessment (blinded independent review will also be performed)

Secondary endpoints

- PFS2 by investigator assessment
- Chemotherapy-free survival
- ORR in patients with measurable disease
- CBR at 24 weeks
- OS
- OS at 2 and 3 years
- TFST
- TSST
- TTD
- Safety

Having to Make a Selection:

HER2 Low The New Biomarker

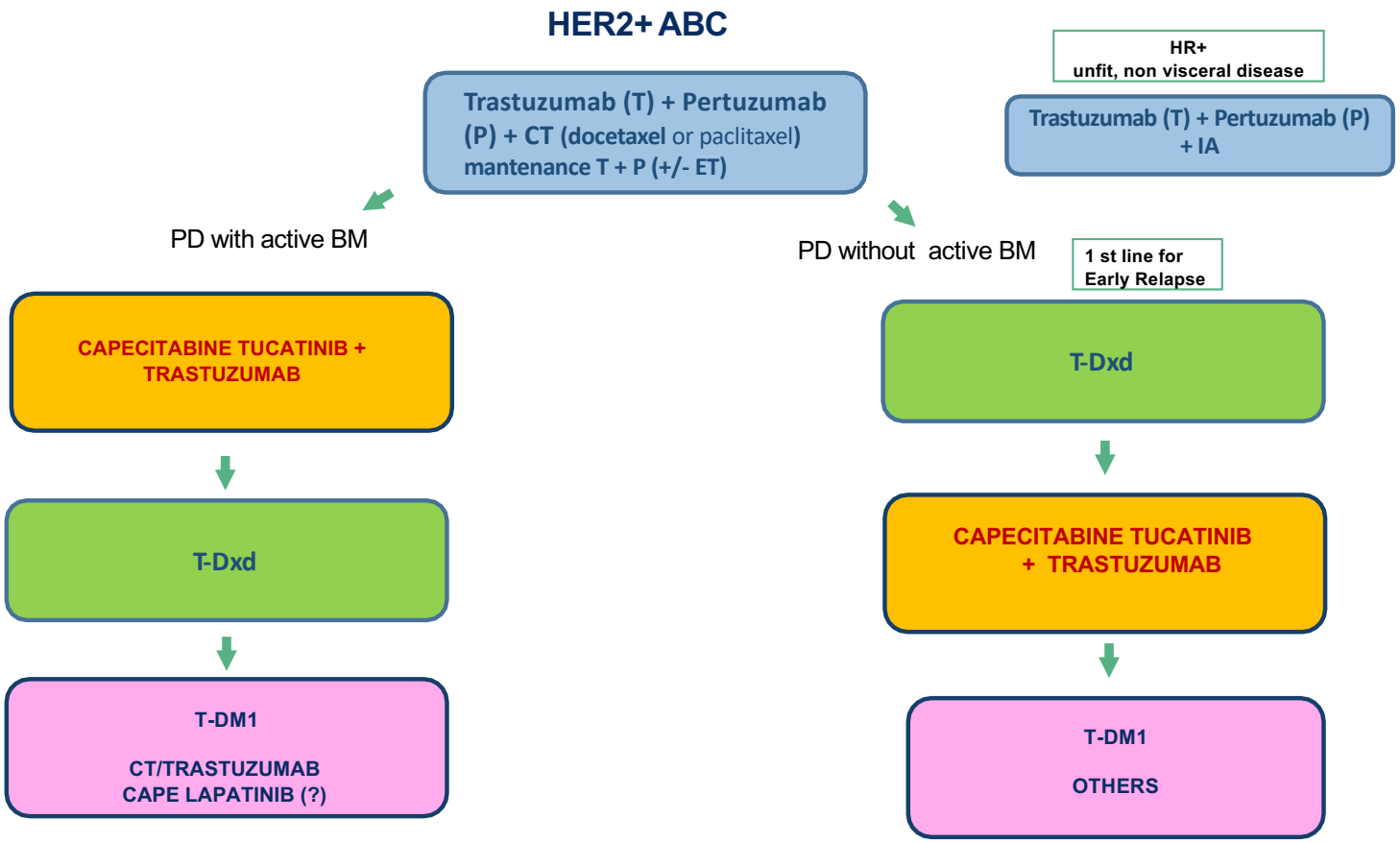
HER2 - Resistance to IL CDK4/6i : this is the problem

HER2 + The Perfect Storm

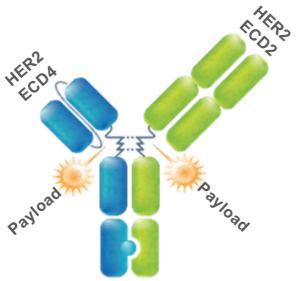
HR-/HER2- no more Untargetable

How to follow disease?

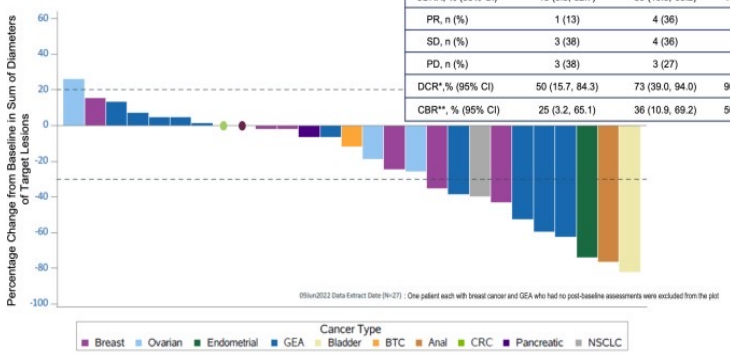
HER2 MBC: possible future treatment alghoritm



Zanidatamab Zovodotin (ZW49): Anti-HER2 Bispecific ADC



	Breast (n=8)	GEA (n=11)	All Other (n=10)	Total (N=29)[a]
cORR, % (95% CI)	13 (0.3, 52.7)	36 (10.9, 69.2)	40 (12.2, 73.8)	31 (15.3, 50.8)
PR, n (%)	1 (13)	4 (36)	4 (40)	9 (31)
SD, n (%)	3 (38)	4 (36)	5 (50)	12 (41)
PD, n (%)	3 (38)	3 (27)	1 (10)	7 (24)
DCR*,% (95% CI)	50 (15.7, 84.3)	73 (39.0, 94.0)	90 (55.5, 99.7)	72 (52.8, 87.3)
CBR**, % (95% CI)	25 (3.2, 65.1)	36 (10.9, 69.2)	50 (18.7, 81.3)	38 (20.7, 57.7)



[a]One patient of the 30 treated at 2.5 mg/kg Q3W was HER2 negative per central review and not included. *DCR = CR, PR, or SD. **CBR = SD ≥ 24 weeks or best overall response of CR or PR.
BTC = biliary tract cancer; CBR = clinical benefit rate; cORR = confirmed objective response rate; CRC = colorectal cancer; DCR = disease control rate; DE = dose escalation; DX = dose expansion; GEA = gastroesophageal adenocarcinoma; NSCLC = non-small cell lung cancer; PD = progressive disease; PR = partial response; Q3W = once every 3 weeks; SD = stable disease

- Immunoglobulin 1-like antibody backbone directed against extracellular domain 4 (ECD4) & ECD2 of HER2
- Auristatin payload (tubulin targeting) covalently linked via a protease cleavable valine-citruline linker ; (DAR) = 2
- Antibody-induced internalization with increased toxin-mediated cytotoxicity and immunogenic cell death

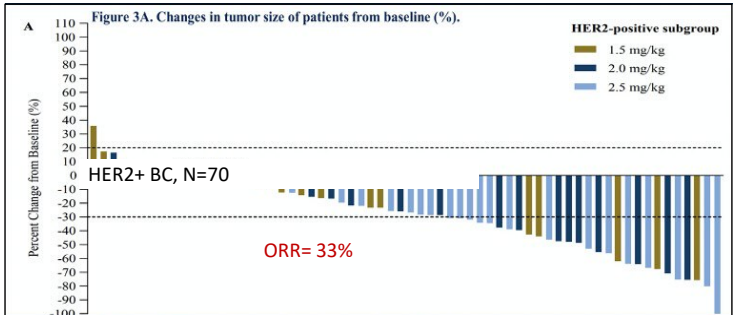
Jhaveri K et al, ESMO 2022

Disitamab Vedotin (RC-48): HER2 ADC for HER2+/Low BC

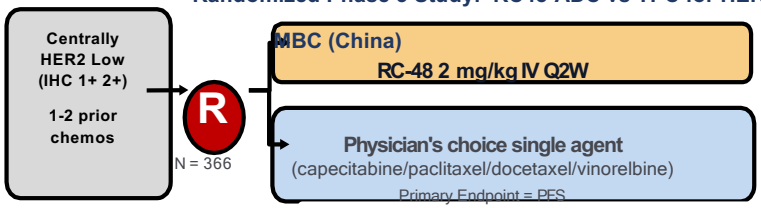
- HER2 Antibody:
- Hertuzumab
- different antigen recognition regions v Tras
- Preferable affinity v Tras

Linker:
- Cleavable
- Bystander Effect

Payload:
- MMAE
- Blocks polymerization of tubulin



Randomized Phase 3 Study: RC48-ADC vs TPC for HER2-Low



Wang J et al, ASCO 2021

Having to Make a Selection:

HER2 Low The New Biomarker

HER2 - Resistance to IL CDK4/6i : this is the problem

HER2 + The Perfect Storm

HR-/HER2- No more Untargetable

How to follow disease?

Triple Negative…….ER- PGR- HER2-

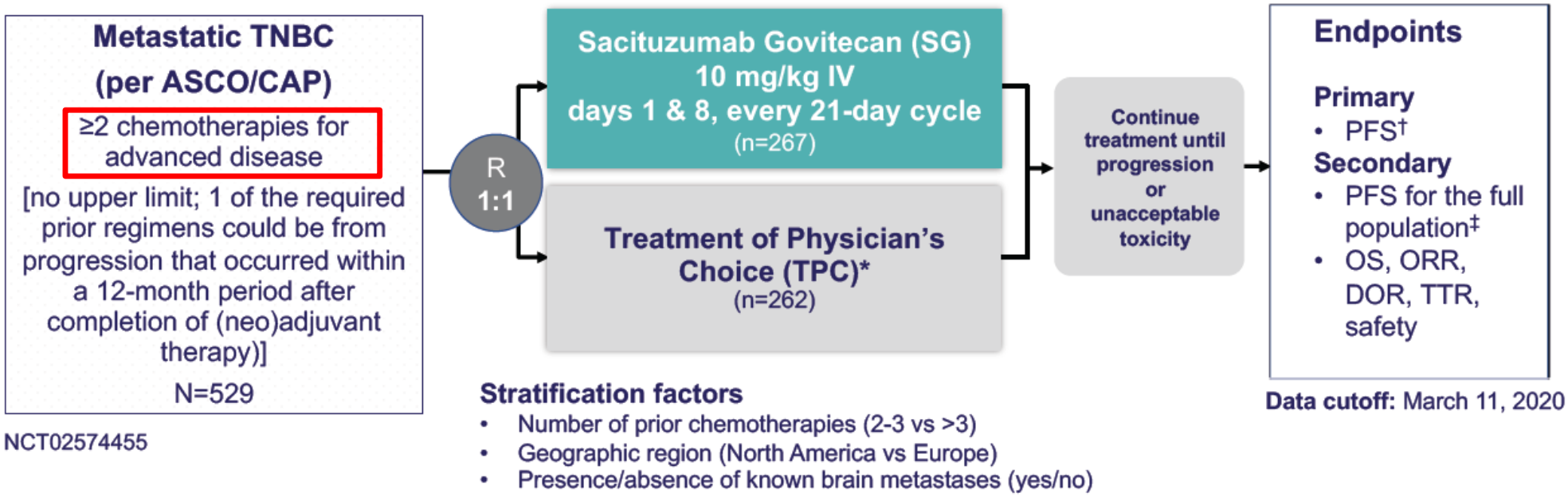
HER2
Classical and Actual Definition
HER0, 1+, 2+ FISH/SISH NA

……Looking for the Target !

PDL1
+ / -

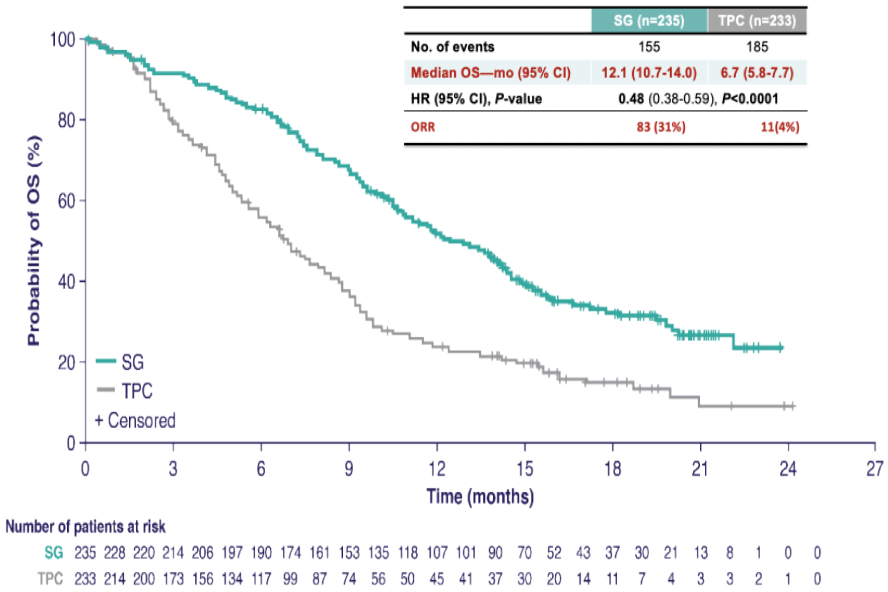
BRCA
m / wt

Phase 3 ASCENT Trial: Sacituzumab Govitecan vs TPC in mTNBC



* TPC options: capecitabine, eribulin, gemcitabine, vinorelbine

ASCENT: Sacituzumab Associated With 52% Increase in OS!



Treatment-related discontinuation rates: Sacituzumab 4.7%, TPC 5.4%

TRAEs (All Grade, >20%; Grade 3/4, >5% of Patients)

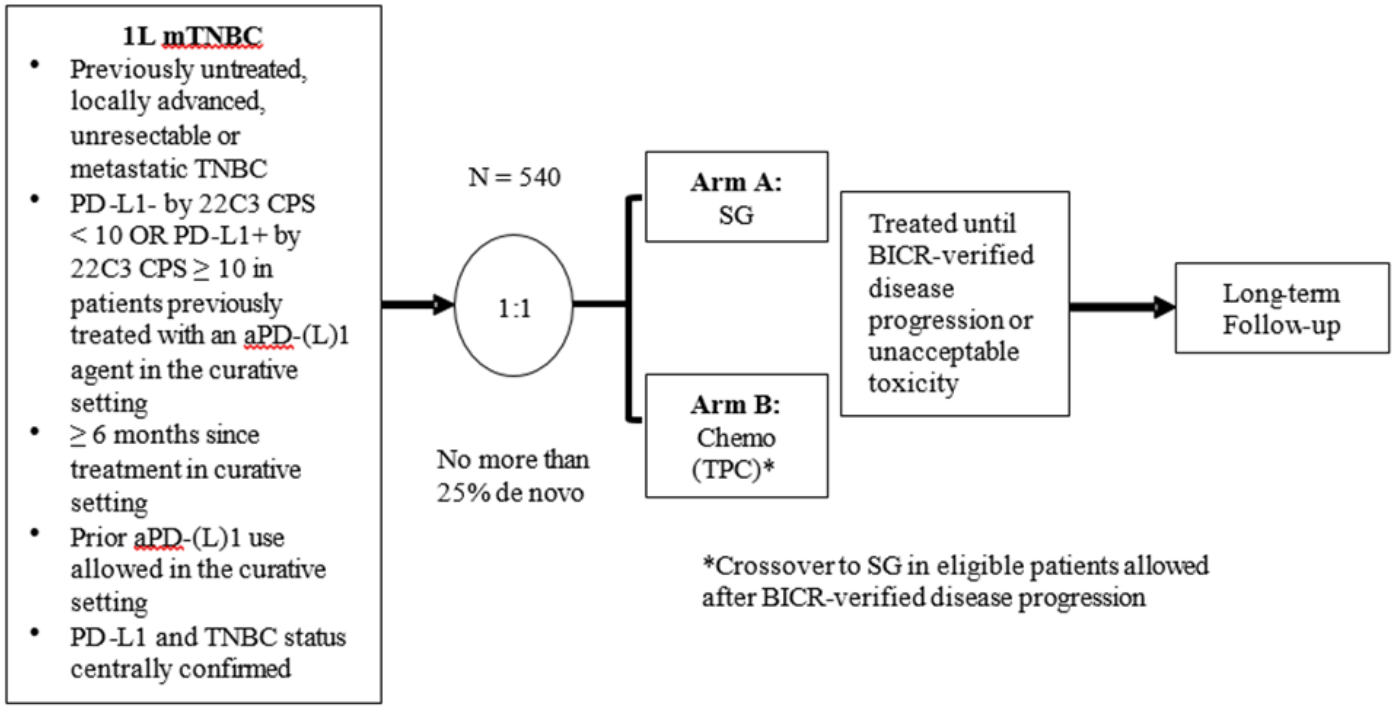
		SG (n=258)			TPC (n=224)		
	TRAE*	All grade %	Grade 3, %	Grade 4, %	All grade, %	Grade 3, %	Grade 4, %
Hematologic	Neutropenia†	63	46	17	43	27	13
	Anemia‡	34	8	0	24	5	0
	Leukopenia§	16	10	1	11	5	1
	Febrile neutropenia	6	5	1	2	2	<1
Gastrointestinal	Diarrhea	59	10	0	12	<1	0
	Nausea	57	2	<1	26	<1	0
	Vomiting	29	1	<1	10	<1	0
Other	Fatigue	45	3	0	30	5	0
	Alopecia	46	0	0	16	0	0

Sacituzumab approved for metastatic TNBC with at least one line of prior Tx

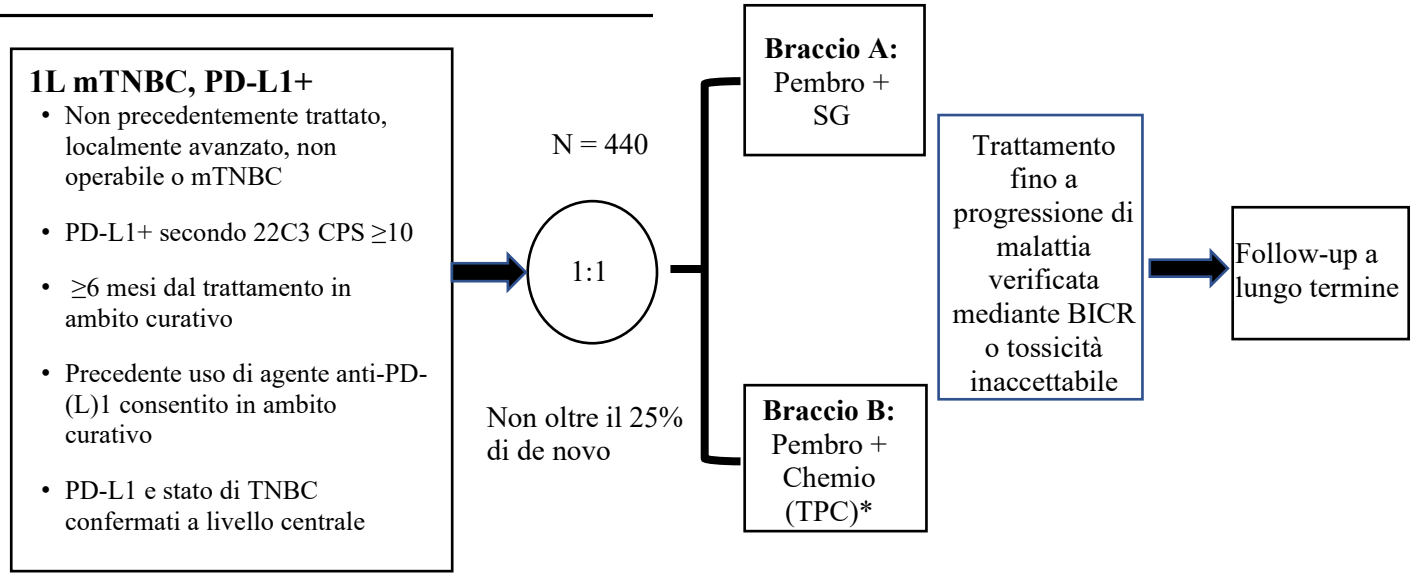
Bardia A, et al. *N Engl J Med*. 2021;384:1529-1541.

Figure 1. Study Schema

ASCENT 03



ASCENT 04



*Crossover a SG per pazienti eleggibili consentito dopo la progressione verificata mediante BICR

Fattori di stratificazione

- Malattia de novo rispetto a recidivante tra i 6 e 12 mesi dal completamento del trattamento in ambito curativo rispetto a malattia recidivante che si manifesta >12 mesi dal completamento del trattamento in ambito curativo**

Endpoint primario: PFS in popolazione ITT
Principali endpoint secondari: OS
Altri endpoint secondari: ORR, PRO e sicurezza

OlympiAD: Phase III study of olaparib vs. TPC in gBRCAm HER2- mBC

Study design

- **gBRCAm mBC**
- **TNBC or HER2-negative, ER/PR positive**
- **≤2 prior chemotherapy lines for mBC**
- **Previous treatment with anthracycline and taxane in either the (neo)adjuvant or metastatic setting**
- **Hormone receptor positive (HR+) disease progressed on ≥1 endocrine therapy, or not suitable**
- If patients have received platinum therapy there should be:
  - No evidence of progression during treatment in the advanced setting
  - At least 12 months since (neo)adjuvant treatment and randomisation
- ECOG PS 0-1
- At least one lesion that can be assessed by RECIST v1.1

FSI May 2014:[3]

Global Study in 19 countries and approximately 141 sites[1]

Randomise 2:1
n=302[4]

Stratification by:[2]

- *Prior chemotherapy regimens for metastatic breast cancer*
- *Hormonal receptor (HR) status*
- *Prior platinum therapy*

Olaparib
300mg**po* bid

Treatment of Physician's Choice
(TPC)

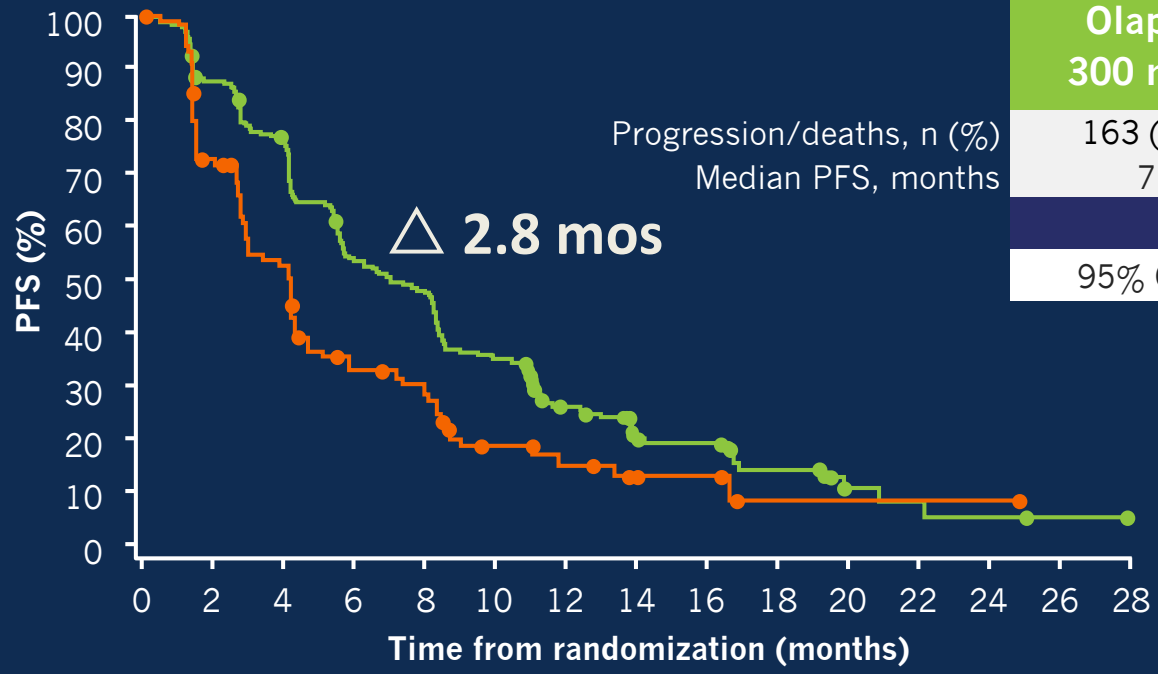
Primary endpoint
- PFS (RECIST 1.1, Independent Review)

Secondary endpoints
- OS
- PFS2
- ORR
- PFS, PFS2 and OS based on Myriad gBRCAm status
- HRQoL (EORTC-QLQ-C30)
- Safety and tolerability

* Tablet formulation (2 tablets twice daily)

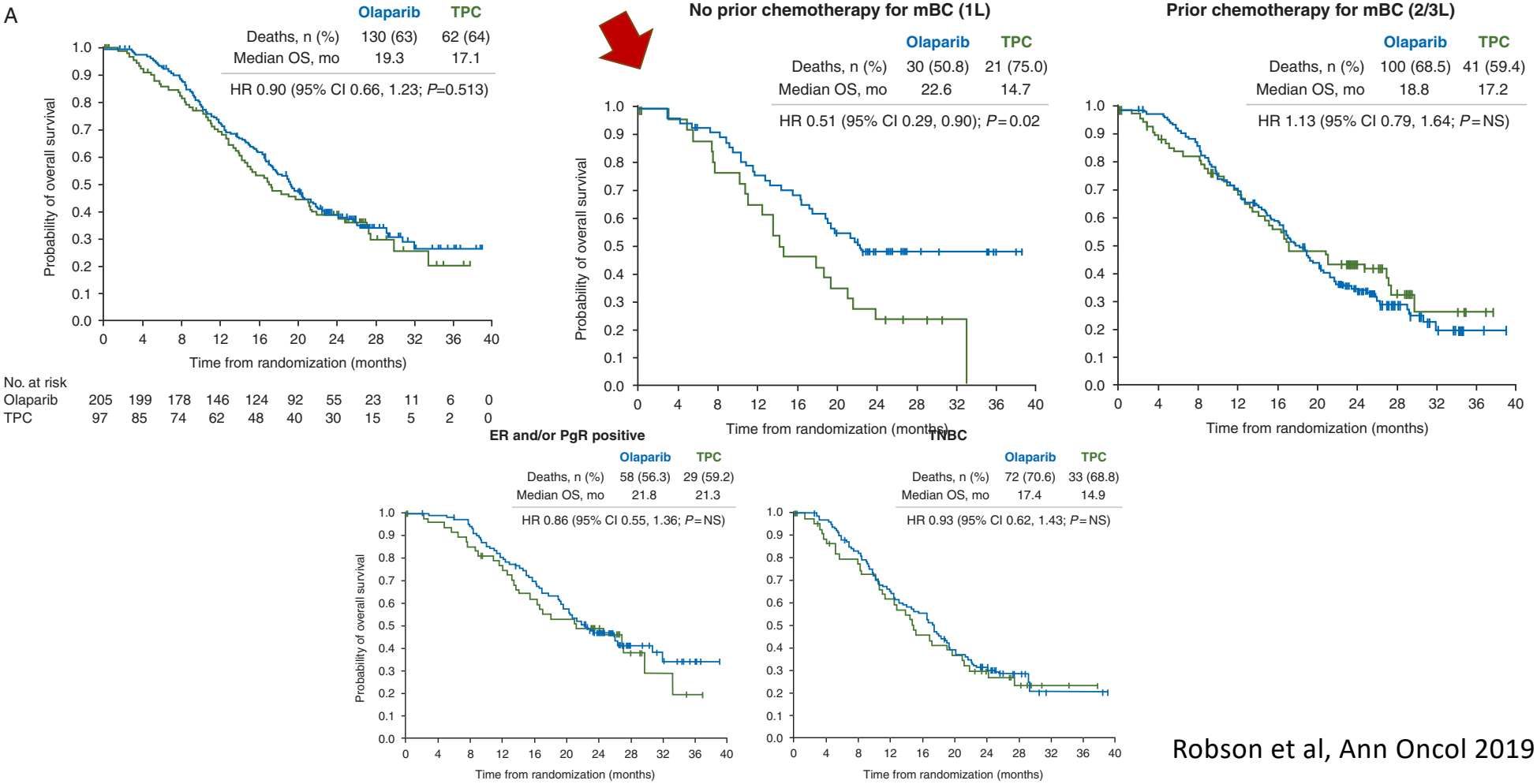
Robson et al. N Engl J Med. 2017; 377:523-533

Primary endpoint: progression-free survival by BICR



	Olaparib 300 mg bd	Chemotherapy TPC
Progression/deaths, n (%)	163 (79.5)	71 (73.2)
Median PFS, months	7.0	4.2
HR 0.58		
95% CI 0.43 to 0.80; *P*=0.0009		

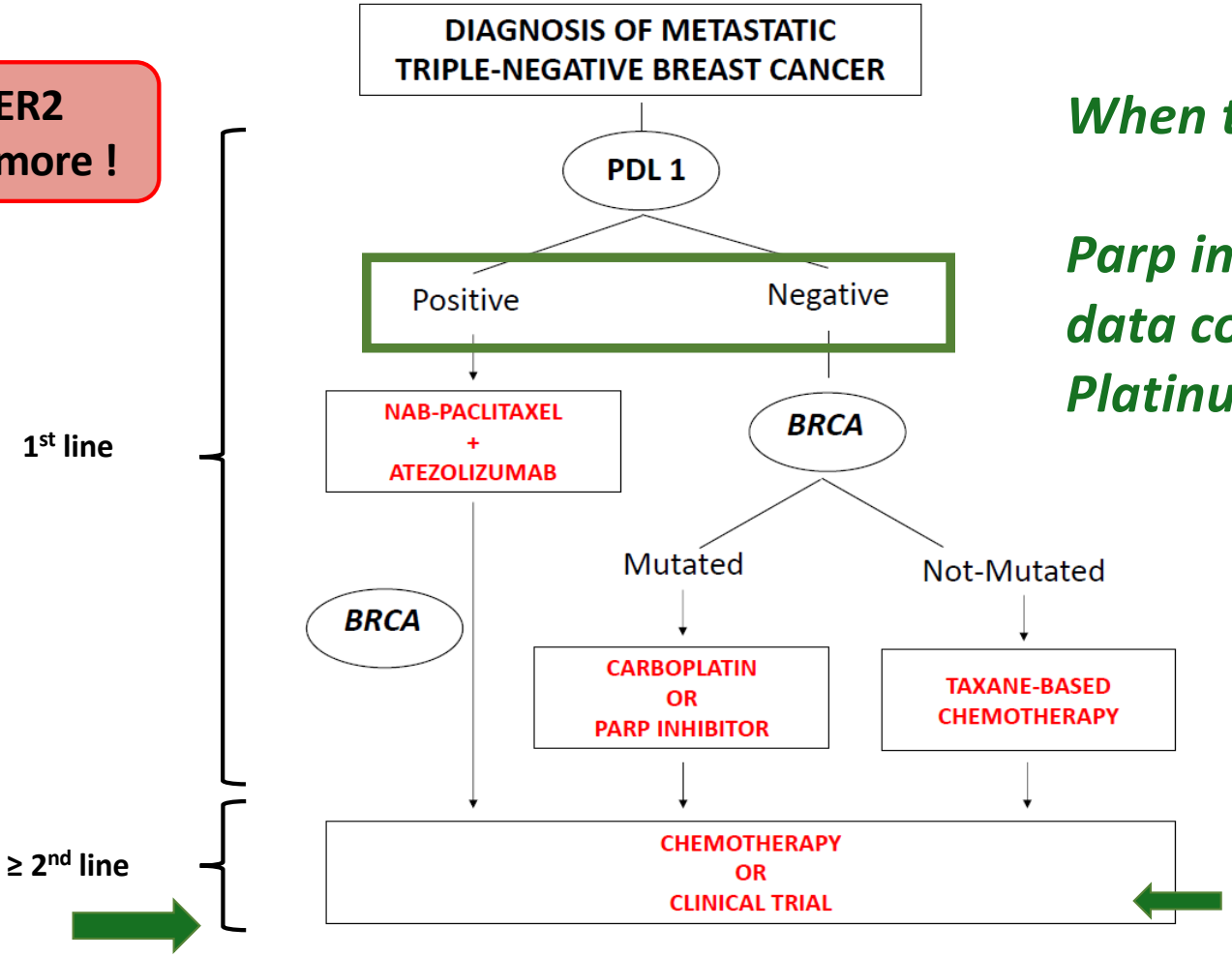
The Aim of the Survival



Robson et al, Ann Oncol 2019

Secondo lo scenario terapeutico in evoluzione in TNBC
……alla luce di nuovi marcatori biologici e nuovi farmaci

ER, PR and HER2 not enough anymore !



When to test BRCA???

Parp in first Line? No data comparing to Platinum!!

Sacituzumab

Having to Make a Selection:

HER2 Low	The New Biomarker
HER2 -	Resistance to IL CDK4/6i : this is the problem
HER2 +	The Perfect Storm
HR-/HER2-	No more Untargetable

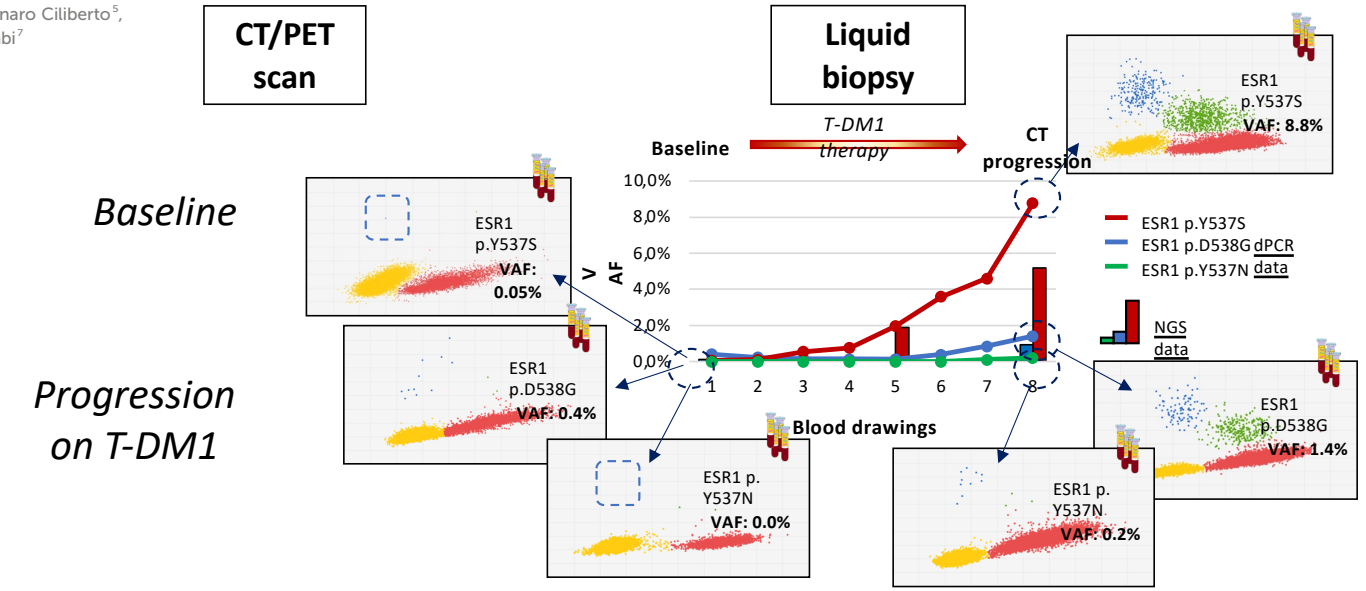
How to follow disease?

Unusual phylogenetic tree and circulating actionable ESR1 mutations in an aggressive luminal/HER2-low breast cancer: Case report

Matteo Allegretti[1], Vittoria Barberi[2], Cristiana Ercolani[3], Antonello Vidiri[4], Elena Giordani[1], Gennaro Ciliberto[5], Patrizio Giacomini[6*] and Alessandra Fabi[7]

Disclosure of Tumor Vulnerability

The Tumor Movie

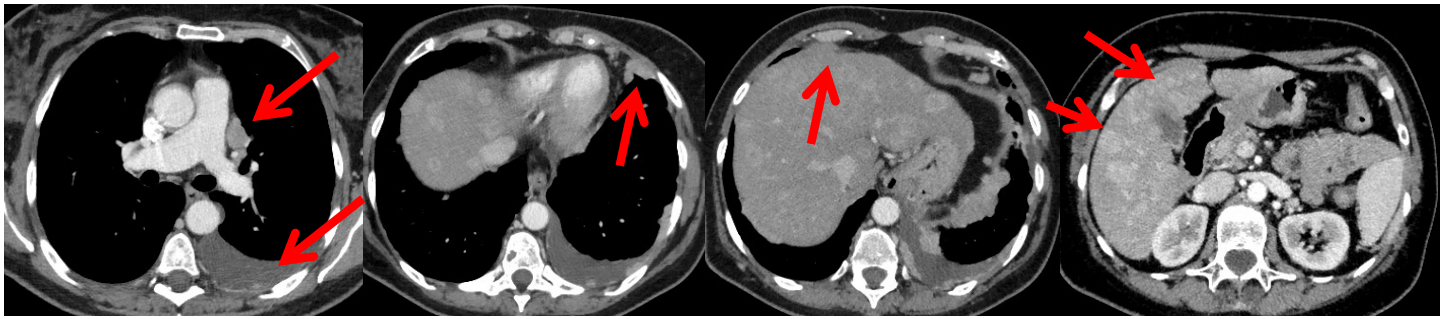


The patient story from 2016 to 2020

Front Oncol 2022

LiqBreastTrack: response to NON-SOC therapy

June 2019



HER2+ (tissue) -> ESR1m (blood) :

From the **Molecular Tumor Board:** anti HER2 targets to Fulvestrant

LB anticipates the imaging outcome by about 3.5 months

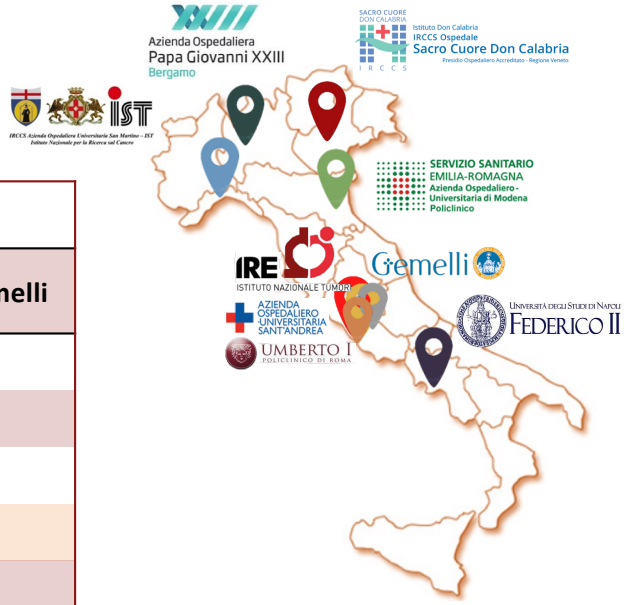
Liquid biopsy identifies actionable dynamic predictors of resistance to Trastuzumab Emtansine (T-DM1) in advanced HER2-positive breast cancer

Matteo Allegretti[1†], Alessandra Fabi[2,3†], Elena Giordani[1], Cristiana Ercolani[4], Paolo Romania[1], Cecilia Nisticò[2], Simona Gasparro[2], Vittoria Barberi[5], Maria Ciolina[6], Edoardo Pescarmona[4], Diana Giannarelli[7], Gennaro Ciliberto[8], Francesco Cognetti[9] and Patrizio Giacomini[1*]

Allegretti *et al. Mol Cancer*
https://doi.org/10.1186/s12943-021-01438-z

Moving forward: from LiqBreasTrack to GIM21

PI	*Center*
Study Coordinator: A. Fabi	**IRCSS Regina Elena/Policlinico Gemelli**
Tondini C	Papa Giovanni XXIII Hospital
Moscetti L	Modena University Hospital
Del Mastro L	IRCSS San Martino IST
Marchetti P	Umberto I University Hospital
De Placido D	Federico II University
Gori S	Sacro Cuore – Don Calabria Hospital
Fabi A	IRCCS Policlinico Gemelli
Bria E	IRCCS Policlinico Gemelli



AIRC id. 19503

https://www.oncotech.org/gim21

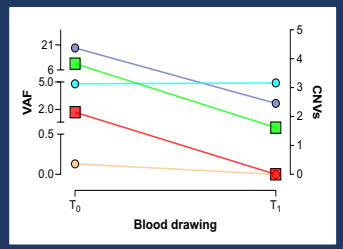
Dynamic circulating tumor DNA (ctDNA) in monitoring trastuzumab deruxtecan (TDXd) activity for patients (pts) with advanced breast cancer (BC): Preliminary results of a feasibility study.

Giordani E*, Palazzo A, Minucci A, Pavese F, Paris I, De Paolis E, Ricciardi E*, Orlandi A, Pannunzio S, Tiberi G, Carbognin L, Bria E, Giannarelli D, Scambia G, Giacomini P*, Fabi A
Fondazione Policlinico Gemelli, University Cattolica Del Sacro Cuore, Rome, Italy; *Regina Elena National Cancer Institute, Rome, Italy

Discovery of new mutational patterns

Marked clonal complexity, and variable clonal response to TDXd can be found in pretreated HER2 positive patients.

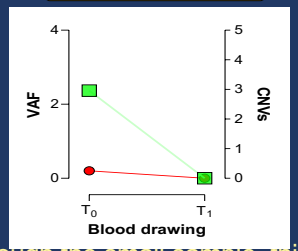
Fig. 1: Pts. N. 7 **T-DXd infusion**



SNPs
ERBB2 p.V777L
TP53 p.H179Y
CNVs
CCND3 CNV gain
ERBB2 CNV gain
INDEL
TP53 indel p.W146S

Best response after 6 TDxd cycles: stable disease

Fig. 2: Pts. N. 8 **T-DXd infusion**



SNPs
ERBB2 p.G309E
CNVs
ERBB2 CNV gain

Best response after 6 TDxd cycles: Partial response

Although the small sample, this complex tumor evolution is surprising in light of the bystander payload effect of T-DXd and suggest a correlation with disease response.

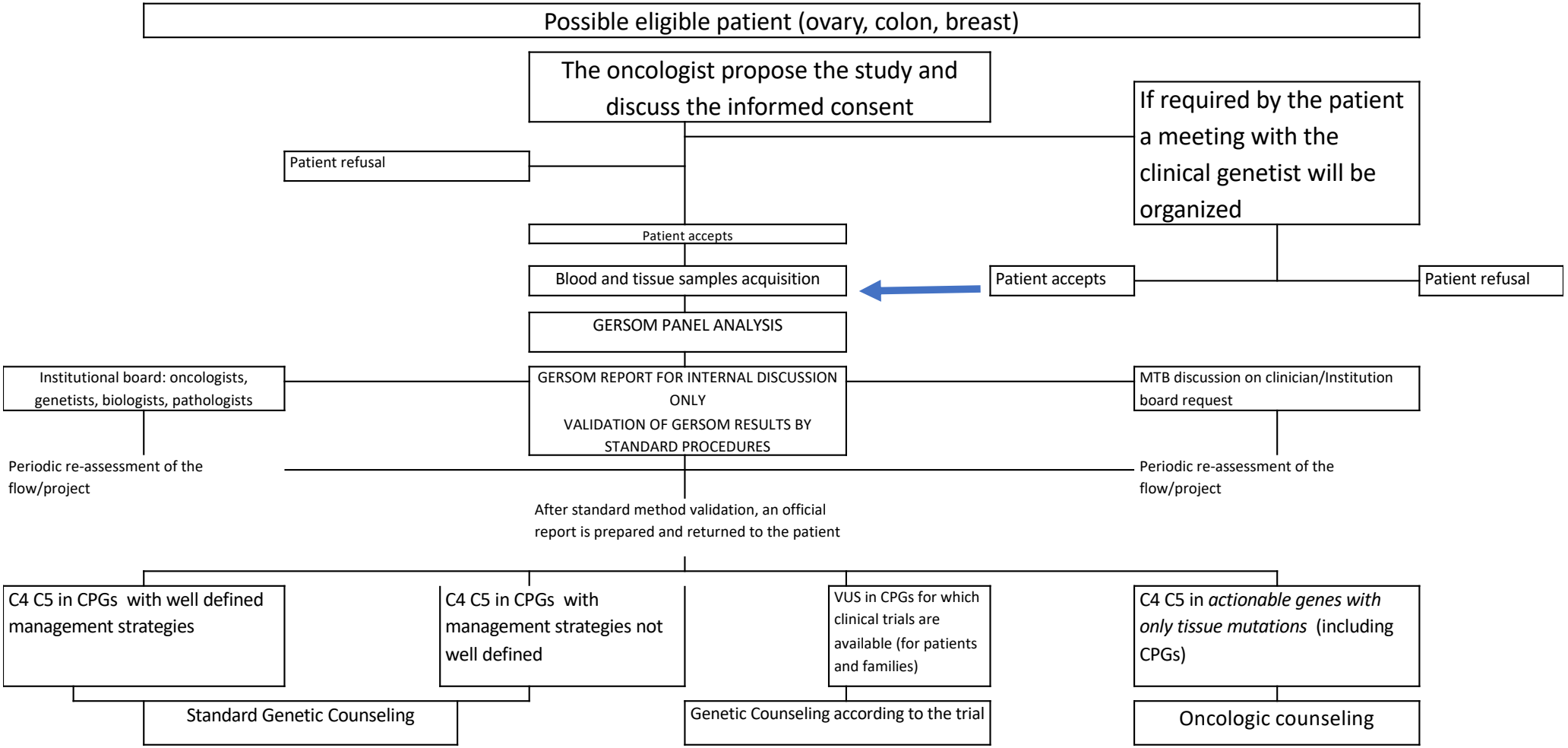
Patients	Number of Previous Tx'Lines	ctDNA			Timepoint		Trend	Radiological Best response
		SNPs	INDEL	CNVs	T_0	T_1		
#1	3	PIK3CA p.E542K TP53 p.K139N	TP53 indel p.W146S	FGFR3 loss	3,28% 0,17% 0,48	0,50%	↓ ↓ ↑ ↓	PR
#2	2		TP53 indel p.W146S		NF	0,60%	↑	PR
#3	5		EGFR indel p.P753E TP53 indel p.N29R		NF	0,10% 0,30%	↑ ↑	PR
#4	4	TP53 p.R248P		FGFR3 loss	0,48 0,20%	NA		NA
#6	6		TP53 indel p.N29R		NF	0,30%	↑	PR
#7	10	ERBB2 p.V777L TP53 p.H179Y	TP53 indel p.W146S	CCND3 gain ERBB2 gain	2,15 3,83 4,80% 19,13% 0,13%	1,62 4,90% 2,66%	↓ ↓ ↗ ↓ ↓	SD
#8	4	ERBB2 p.G309E		ERBB2 gain	0,20% 2,37%		↓ ↓	PR
#9	5	PIK3CA p.H1047R ESR1 p.D538G FGFR2 p.N549K TP53 p.R283C ERBB2 p.V777L			39,02% 48,38% 11,08% 68,94% 1,29%	NA		PR

Presented at ASCO 2022

Yesterday, Anne the Patients:
Dr., how do we understand if there is an onset of disease ?

The Microscopic Disease

GERSOM Project (ACC) - The patient journey



Cosa la Profilazione Genica può Aggiungere alla Clinica

Anticipare.....

Approfondire.....

Prevedere.....

Donare.....

....e Sognare!!!!