

VIII SIMPOSIO NACIONAL
de ONCOLOGÍA de PRECISIÓN

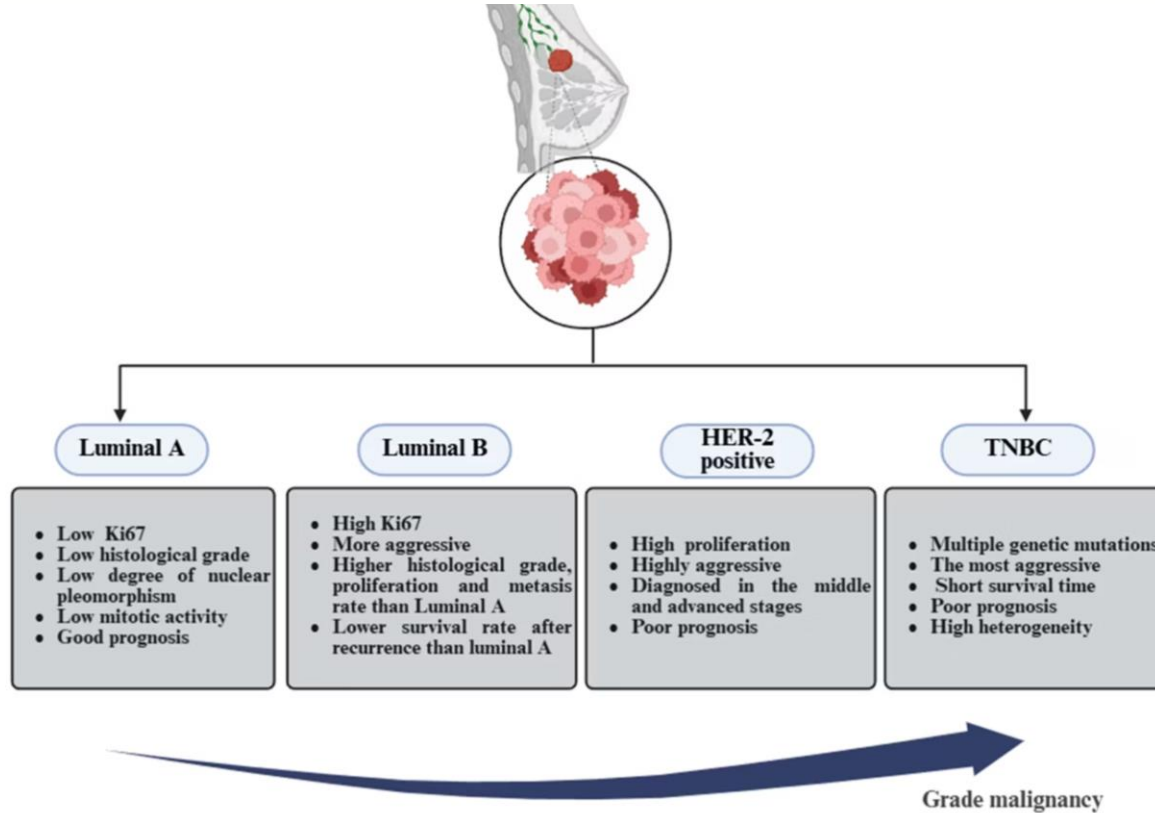
Vigo, 19 y 20 de febrero de 2026



CÁNCER DE MAMA: LO MEJOR DEL 2025 EN 20 DIAPOSITIVAS

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Oncología Médica

Hospital Universitario de A Coruña



FUNDAMENTOS MOLECULARES Y BIOLOGÍA COMPUTACIONAL

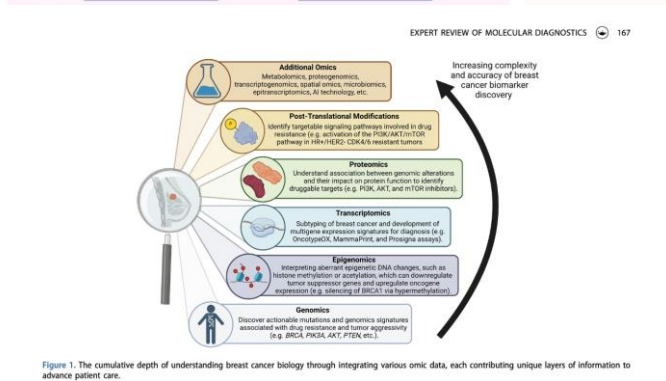
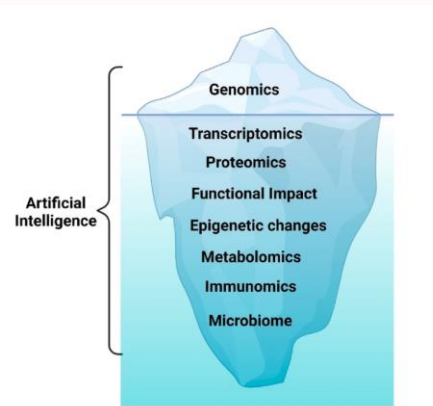
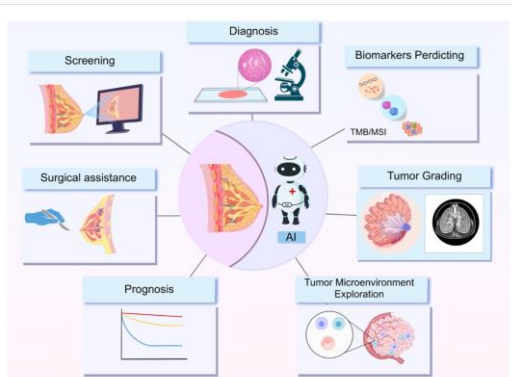
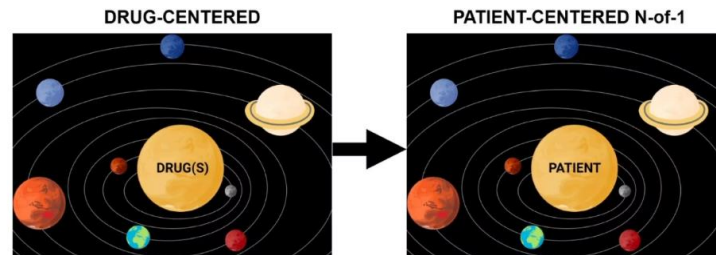
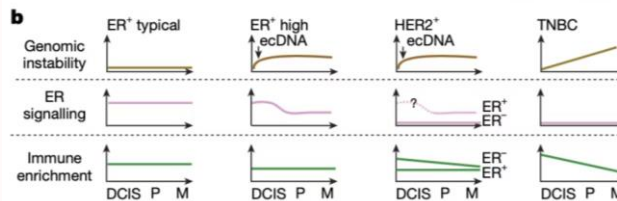
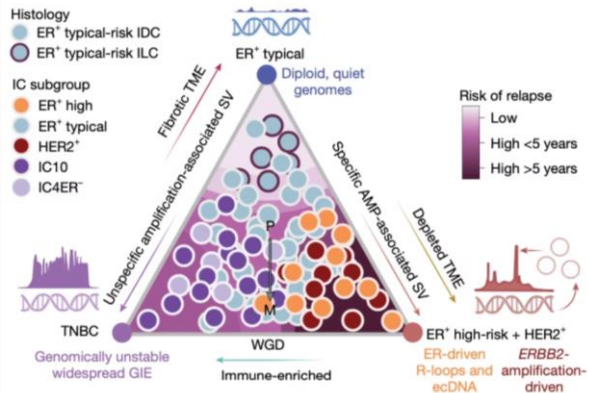
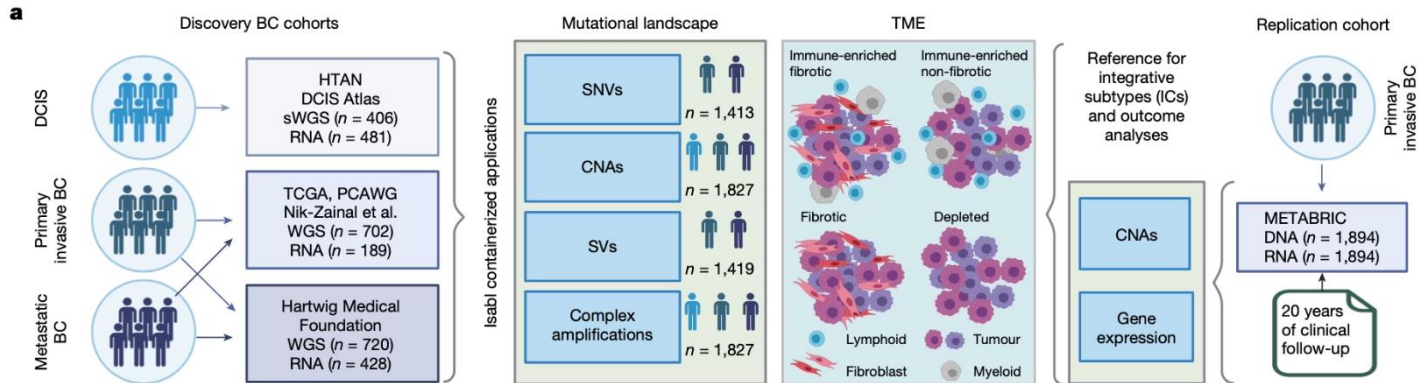


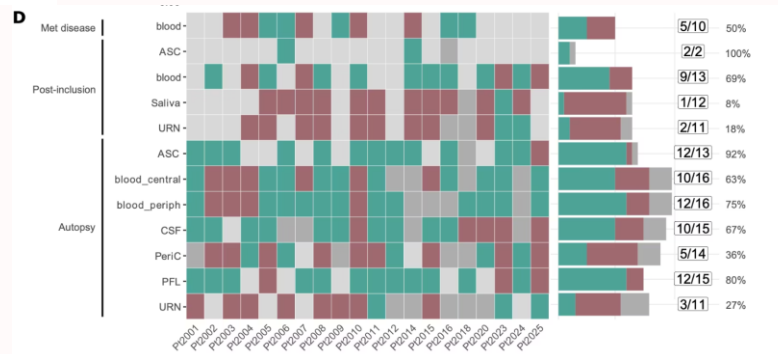
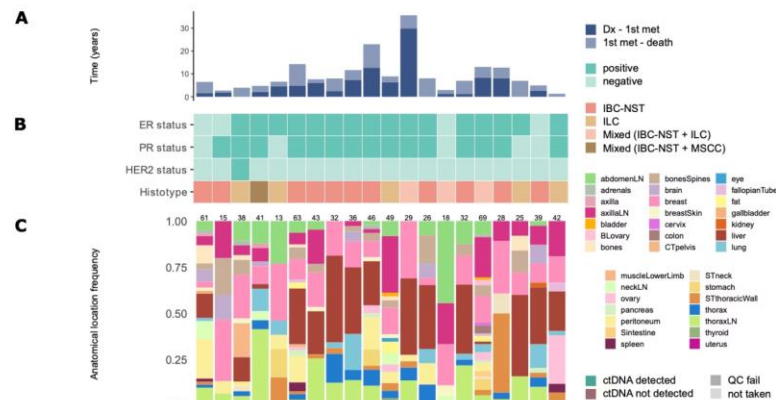
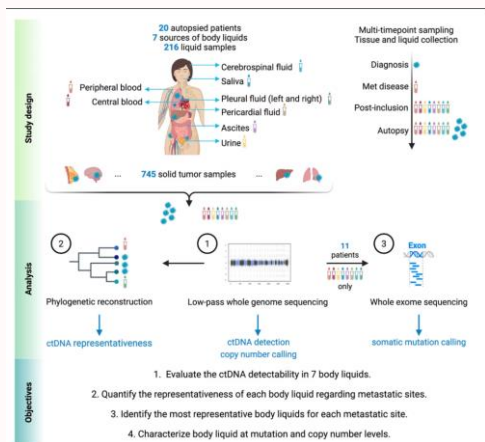
Figure 1. The cumulative depth of understanding breast cancer biology through integrating various omic data, each contributing unique layers of information to advance patient care.



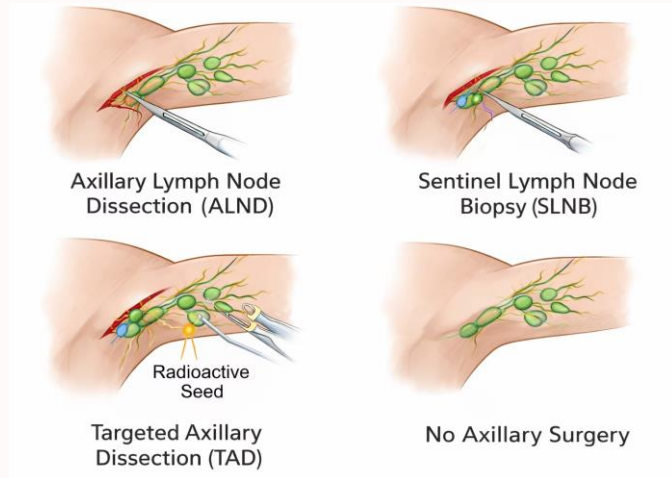
ARQUETIPOS GENÓMICOS DE CÁNCER DE MAMA



ctDNA EN 7 LÍQUIDOS CORPORALES



PRECISIÓN EN ENFERMEDAD PRECOZ: DE-ESCALADA QUIRÚRGICA



ASCO Guidelines 2025



May Omit SNB

- T1 with negative axillary ultrasound
- Postmenopausal and ≥ 50 years old
- Grade 1 or 2, HR+, HER2-
- Endocrine therapy planned
- BCT with whole breast RT

Park, KU et al JCO June 2025

1

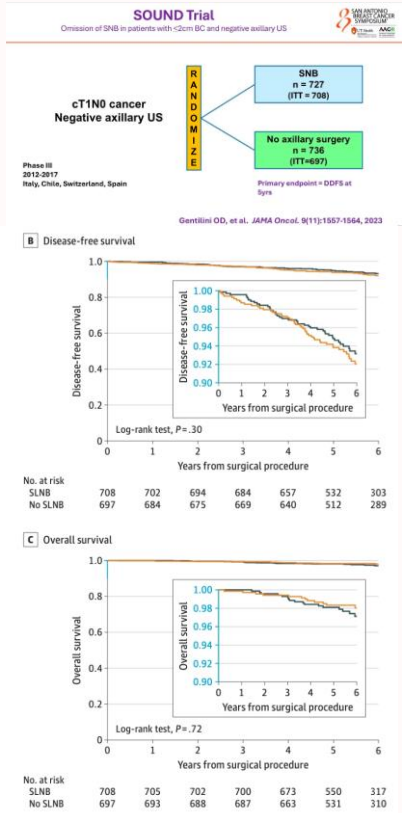
Ensayos SOUND e INSEMA

Demostraron que la omisión de la biopsia de ganglio centinela (SNB) es segura en subgrupos seleccionados de bajo riesgo: HR+/HER2-, posmenopáusicas con tumores T1/T2 y ultrasonido axilar negativo.

2

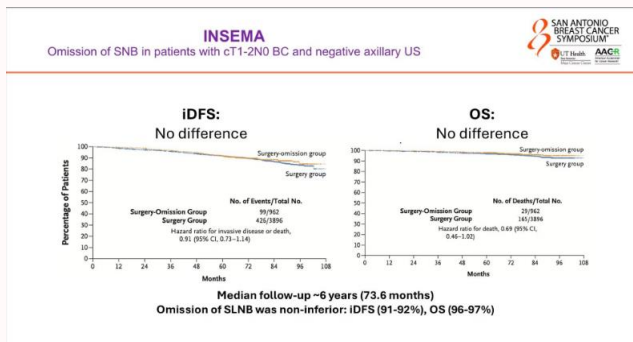
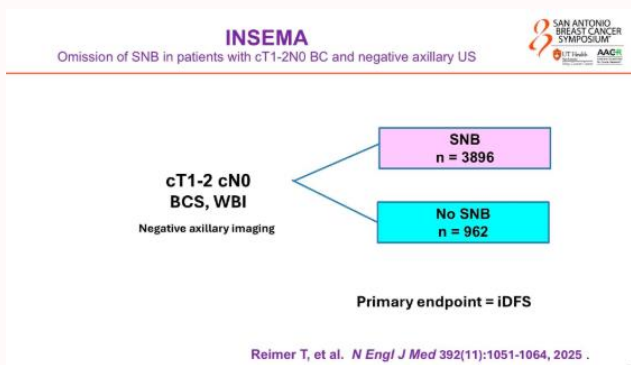
REDUCCIÓN DE MORBILIDAD

ENSAYOS SOUND



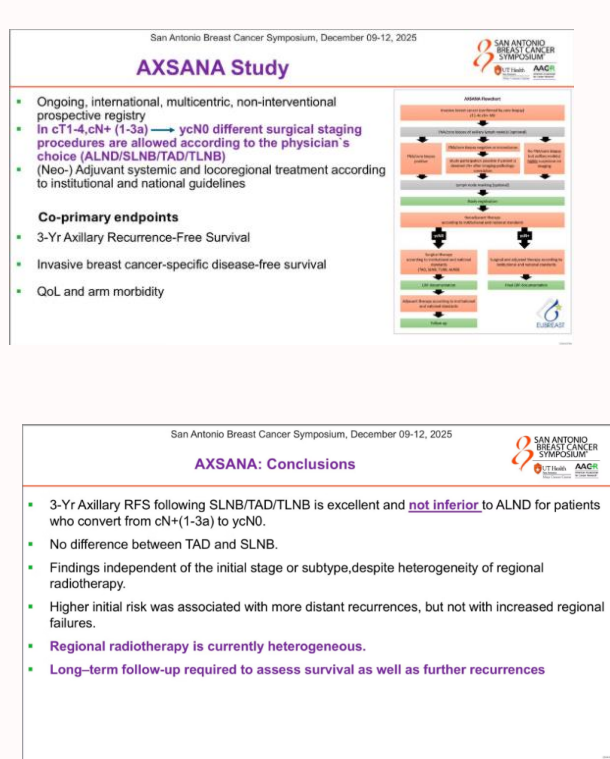
Gentilini, OD JAMA Oncol 2023

INSEMA



Reimer, T NEJ Med 2025

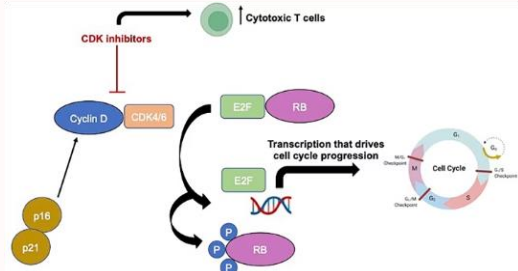
AXSANA



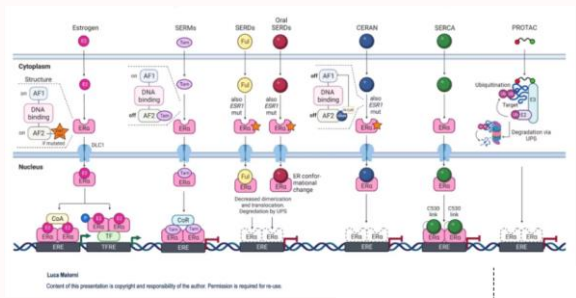
Kuhn, T SABCS 2025

ADYUVANCIA Y NEOADYUVANCIA BASADA EN RIESGO

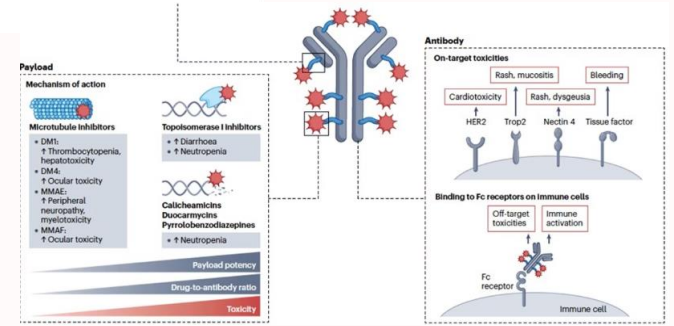
Inhibidores CDK4/6



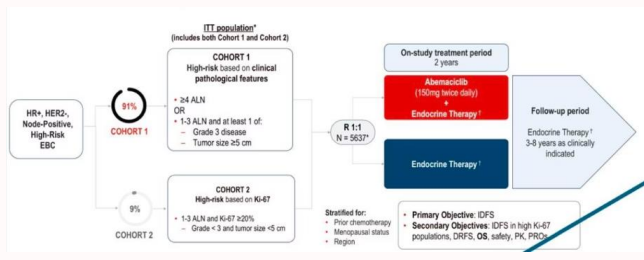
Nuevos SERDs Adyuvantes



TDx en Enfermedad precoz HER2 positiva

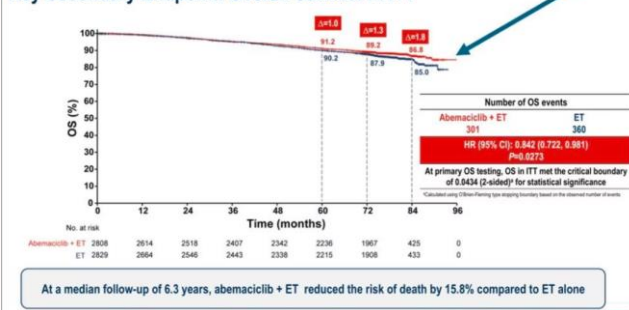


ENSAYOS MONARCHE Y NATALEE



1.8% = 15.8% Rel Risk Reduction

Key Secondary Endpoint: Overall Survival in ITT

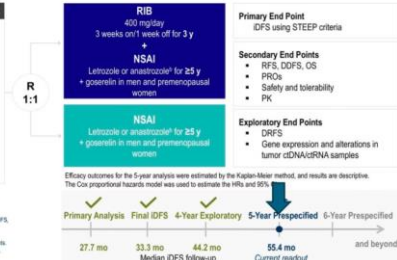


Study Design: NATALEE

An open-label, multicenter, randomized, phase 3 trial^{1,2}

Adult patients with stage II and III HR+/HER2- EBC

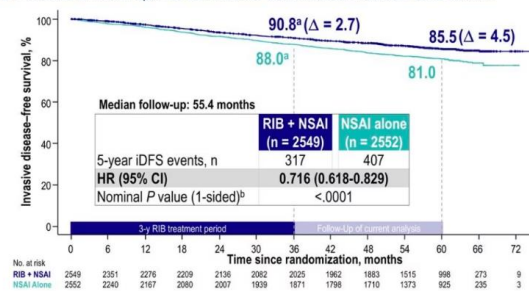
- Prior ET allowed up to 12 months
- **Anatomical stage IA***
- NO with:
 - Grade 2 and evidence of high risk:
 - Ki-67 $\geq 20\%$
 - Oncotype DX Breast Recurrence Score ≥ 26 or
 - High risk via genomic risk profiling
 - Grade 3
- **Anatomical stage IB***
- NO or N1
- **Anatomical stage III**
- NO, N1, N2, or N3



*Treatment of patients with stage III disease was stopped at 40%. The investigational drug ctDNA/sRNA, circulating tumor DNA/sRNA, iDFS, distant disease-free survival, DRFS, distant recurrence-free survival, EBC, early breast cancer, ET, endocrine therapy, ER, breast cancer, EFS, invasive disease-free survival, ITT, intention to treat, N, node, NSAI, nonsteroidal aromatase inhibitor, OS, overall survival, PK, pharmacokinetics, PRD, patient-reported outcomes, RFS, recurrence-free survival, STEEP, Standardized Definitions for Efficacy End Points. 1. Chakrabarti et al. *Nature Reviews Cancer* 2023; 23(10):615-30. 2. Slamon et al. *The Ash Met Disc*. 2023;15:1-16.

iDFS in the ITT Population

With 55.4 months of follow-up, RIB continues to demonstrate a durable iDFS benefit



ENSAYO LIDERA: GIREDESTRANT ADYUVANTE

lidERA Breast Cancer study design

A global, randomized, open-label, multicenter Phase III trial

- Key eligibility criteria**
- Participants with ER+, HER2- early breast cancer
 - Stage I-III disease
 - pN0 and pT > 1 cm with Grade 3, or Ki67 ≥ 20%, or high score on genomic assay*
 - Node-positive
 - Pre-/peri- or post-menopausal†
 - Prior surgery < 12 months
 - (Neo)adjuvant chemotherapy if indicated



Stratification factors

- Risk: Medium- vs high-risk‡ Stage I-III breast cancer
- Region: USA/Canada/Western Europe vs Asia-Pacific vs RoW
- Previous chemotherapy: No vs yes
- Menopausal status: Pre- or peri-menopausal vs post-menopausal

Primary endpoint

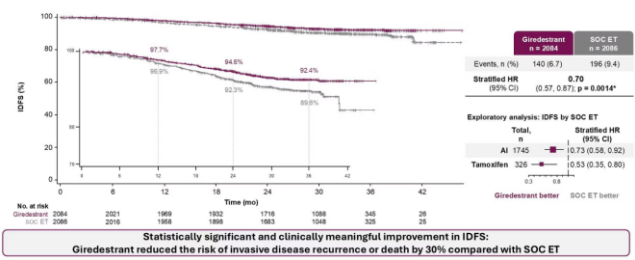
- IDFS (excluding second primary non-breast cancer)

Key secondary endpoints

- DFS, DRFI, IDFS (including second primary non-breast invasive cancer with exception of non-melanoma skin cancers and in situ carcinomas of any site), LRRFI, OS, safety

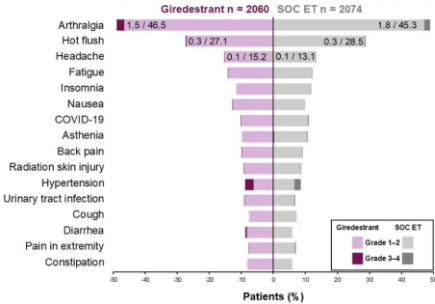
Giredestrant is currently also being investigated in combination with abemaciclib in the adjuvant setting (lidERA Breast Cancer substudy 1)

Primary endpoint: IDFS



AE overview (safety-evaluable population)

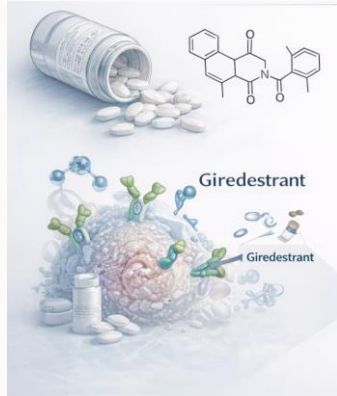
Common TEAEs (≥ 7.5% of patients in either arm at any grade)



Selected AEs

Patients, n (%) with selected AEs by medical concept†	Giredestrant n = 2060		SOC ET n = 2074	
	Grade 1-2	Grade 3-4	Grade 1-2	Grade 3-4
Bradycardia‡	232 (11.3)	0	66 (3.2)	0
Venous thromboembolic events	16 (0.8)	2 (< 0.1)‡	10 (0.5)	7 (0.3)
Patients, n (%) with treatment discontinuations due to AEs				
Musculoskeletal disorders (including arthralgia)	38 (1.8)		92 (4.4)	
Vascular disorders (including hot flush)	2 (< 0.1)		18 (0.9)	

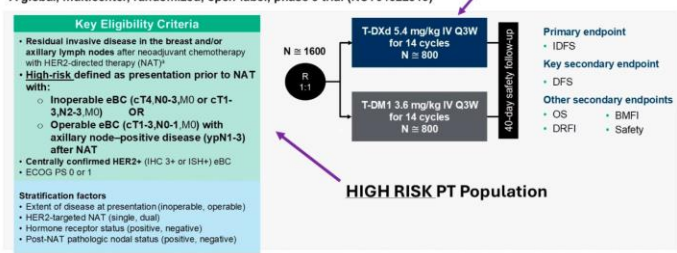
Giredestrant supone potencialmente el primer nuevo fármaco endocrino adyuvante en cáncer de mama en los últimos 20 años.



ENSAYOS DESTINY BREAST 05 Y 011

DESTINY-Breast05 study design

A global, multicenter, randomized, open-label, phase 3 trial (NCT04622319)



DESTINY Breast-05: Conclusions

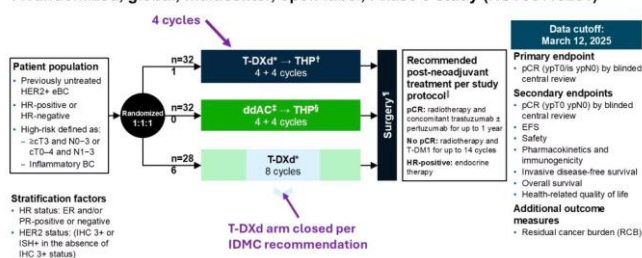
53% reduction in the risk of invasive disease recurrence or death

IDFS Benefit T-DXd versus T-DM1
 3-year IDFS rate
 92.4% versus 83.7%
 HR 0.47
 P value <0.0001

Adjuvant T-DXd demonstrated superior efficacy with manageable safety in patients with high-risk HER2+ eBC and residual invasive disease after NAT, representing a potential new standard of care in this post-neoadjuvant setting

DESTINY-Breast11 study design

A randomized, global, multicenter, open-label, Phase 3 study (NCT05113251)

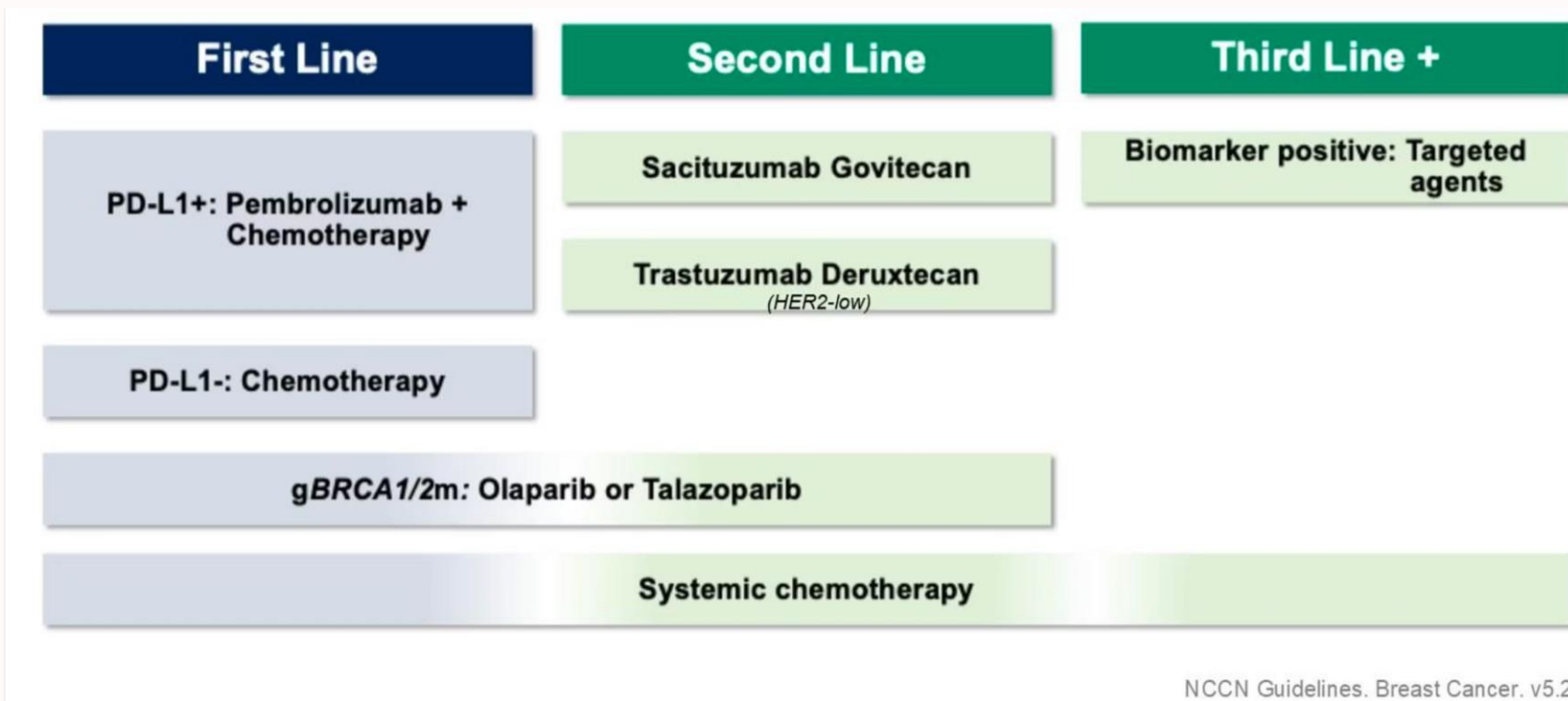


Conclusions

pCR rate 67.3%
 More than two thirds of patients in the T-DXd-THP arm had a pCR
 HR-positive: 61.4%
 HR-negative: 83.1%

- An early positive trend in EFS was observed, favoring T-DXd-THP vs ddAC-THP
 - Hazard ratio: 0.56 (95% CI 0.26, 1.17)
- The safety profile of T-DXd-THP was favorable vs ddAC-THP
 - Lower rates of Grade ≥3 AEs, serious AEs, and AEs leading to dose interruptions
 - Lower rates of hematological AEs, left-ventricular dysfunction, and fatigue
 - ILD rates were low and similar between arms

ESCENARIOS Y TRATAMIENTO EN CÁNCER DE MAMA MTS TRIPLE NEGATIVO



ADCs TARGETING TROP2 EN CÁNCER DE MAMA



Antibody Drug Conjugate

	ADC Attributes	Sacituzumab govitecan (SG) ¹⁻⁴	Datopotamab deruxtecan (Dato-DXd) ^{4,5}	SKB264(MK-3876) ^{1,4}
Antibody	Target	TROP2	TROP2	TROP2
	Antibody	hRS7 IgG1k	Datopotamab	hRS7 IgG1
Linker	DAR	~7.6	~4	~7.4
	Linker	CL2A	Tetrapeptide-based	2-methylsulfonyl pyrimidine
	Cleavable linker?	Yes	Yes	Yes
Payload	Payload	SN-38	DXd	KL610023 (T030)
	Payload MoA	Topoisomerase I inhibitor	Topoisomerase I inhibitor	Topoisomerase I inhibitor
	Membrane permeable?	Yes	Yes	Yes

1. Trail PA, et al. *Pharmacol Ther.* 2018; 2. Bardia A, et al. Presented at ASCO Annual Meeting, 2022. Poster 1071; 3. Kopp A, et al. *Mol Cancer Ther.* 2023; 4. Shastry M, et al. *The Breast.* 2022; 5. Lombardi P, et al. *Cancers (Basel).* 2023; 6. Cheng Y, et al. *Front Oncol.* 2022



PRIMERA LÍNEA EN CÁNCER DE MAMA MTS TRIPLE NEGATIVO

PD-L1+:

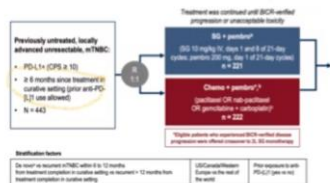
N ENGL J MED 394:4 NEJM.ORG JANUARY 22, 2026

ORIGINAL ARTICLE

Sacituzumab Govitecan plus Pembrolizumab for Advanced Triple-Negative Breast Cancer

S.M. Tolaney, E. de Azavedo, K. Kalinsky, S. Liu, S.B. Kim, C. Yam, et al.

ASCENT-04/KEYNOTE-D19: Study Design



N ENGL J MED 394:4 NEJM.ORG JANUARY 22, 2026

Daiichi-Sankyo AstraZeneca

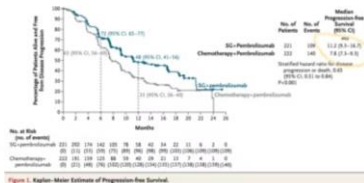
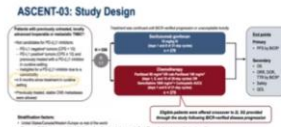


Figure 1. Kaplan-Meier Estimate of Progression-Free Survival.

Variable	Sacituzumab Govitecan plus Pembrolizumab (n=443)	Chemotherapy plus Pembrolizumab (n=443)
Median overall survival (95% CI) - mo	14.2 (13.4-15.0)	10.2 (9.4-11.0)
Median progression-free survival (95% CI) - mo	11.2 (10.4-12.0)	7.2 (6.4-8.0)
Median time to next anticancer therapy (95% CI) - mo	11.2 (10.4-12.0)	7.2 (6.4-8.0)
Median time to death (95% CI) - mo	14.2 (13.4-15.0)	10.2 (9.4-11.0)

PD-L1-:

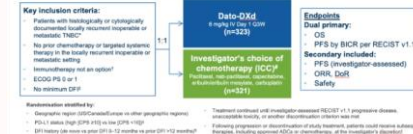
Primary Results From ASCENT-03: A Randomized Phase 3 Study of Sacituzumab Govitecan vs Chemotherapy in Patients With Previously Untreated Metastatic Triple-Negative Breast Cancer Who Are Unable to Receive PD-L1 Inhibitors



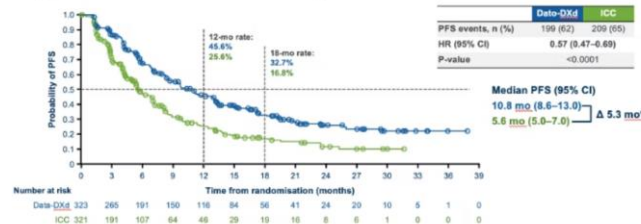
Javier Cortés, ESMO 2025

PD-L1-:

TROPION-Breast02: Study Design
Randomised, phase 3, open-label, global study (NCT05374512)



Progression-Free Survival by BICR



Dato-DXd demonstrated a statistically significant and clinically meaningful improvement in PFS compared with ICC, reducing the risk of progression or death by 43%

Not FDA Approved

mTNBC *Potential* Treatment Landscape (2025)



First Line

PD-L1+:

**Pembrolizumab
+
Sacituzumab Govitecan**
(ASCENT-04)

PD-L1-:

Sacituzumab Govitecan
(ASCENT-03)
Datopotamab Deruxtecan
(TROPION Breast-02)

**ADC → ADC
Sequencing**

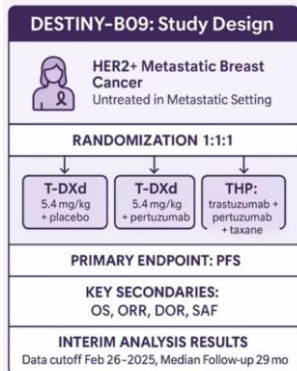
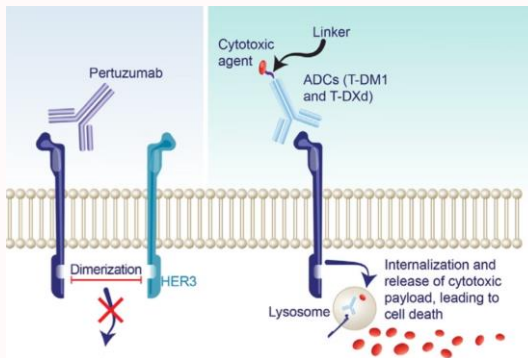
Second Line +

Trastuzumab Deruxtecan
(HER2-low)

Chemotherapy

gBRCA1/2m: Olaparib or Talazoparib

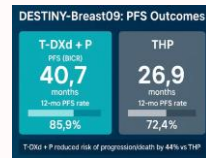
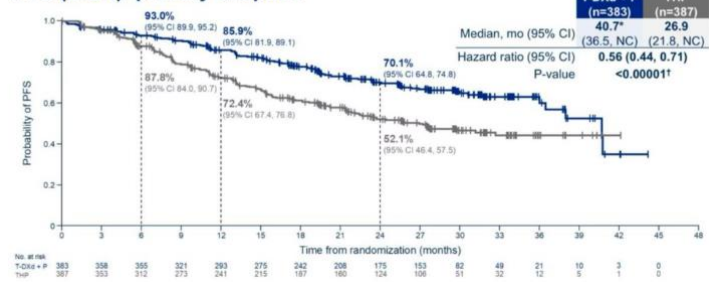
PRIMERA LÍNEA EN CÁNCER DE MAMA MTS HER2 POSITIVO



Evolution of T-DXd in HER2+ a/mBC

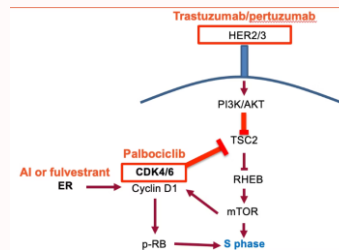
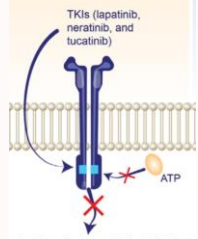


PFS (BICR): primary endpoint



PRIMERA LÍNEA EN CÁNCER DE MAMA MTS HER2 POSITIVO

Ensayos de mantenimiento



HER2CLIMB-05 is a randomized, double-blind, placebo-controlled, international, phase 3 trial (NCT05132582)

Key Eligibility Criteria

- Centrally confirmed HER2+ MBC
- No evidence of progression after THP (4 to 8 cycles)
- ECOG PS of 0 or 1
- No or asymptomatic BM confirmed by contrast-enhanced MRI at screening

Randomization was stratified by:

- Diagnosis: de novo or recurrent
- HR status: positive or negative
- Presence or history of BM: yes or no

R 1:1

1L Maintenance Therapy

- TUC 300 mg PO BID + HP***
Once every 21 days ± ET (n = 326)
- PBO PO BID + HP***
Once every 21 days ± ET (n = 328)

Study treatment continues until unacceptable toxicity, disease progression, consent withdrawal, or study closure. No crossover from PBO to TUC was allowed.

Endpoints

- Primary**
 - Investigator-assessed PFS per RECIST v1.1
- Secondary**
 - OS (key secondary)
 - PFS per BICR
 - CNS-PFS
 - Safety
 - HRQoL
 - Pharmacokinetics

Registration

- Historically confirmed HR+, HER2+ mBC
- No prior treatment in the advanced setting beyond induction treatment
- 6-8 cycles of treatment, including trastuzumab ± pertuzumab and taxane/vinorelbine

- ### Key eligibility criteria
- Completion of induction chemotherapy and no evidence of disease progression (i.e., CR, PR, or SD)

N=518

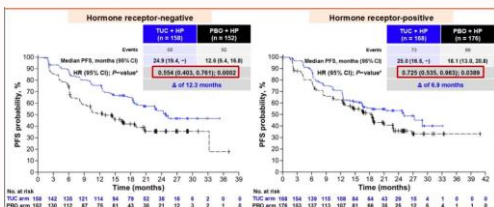
R 1:1

- Palbociclib (125 mg PO QD D1-D21)
Trastuzumab ± pertuzumab + endocrine therapy*

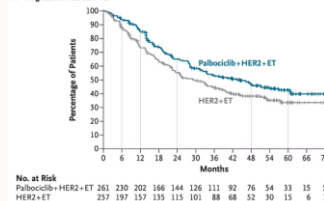
- Trastuzumab ± pertuzumab + endocrine therapy*

Until PD or toxicity

SURVIVAL FOLLOW-UP



A Progression-free Survival



Group	No. of Events/Total No. of Patients	Median Progression-free Survival (95% CI)
Palbociclib+HER2+ET	127/261	44.3 (32.4–58.8)
HER2-ET	135/257	29.1 (23.3–38.6)

Hazard ratio for disease progression or death, 0.75 (95% CI, 0.59–0.96)
Two-sided unstratified P=0.02 by log-rank test

No. at Risk	0	6	12	18	24	30	36	42	48	54	60	66	72
Palbociclib+HER2+ET	261	230	202	166	144	126	111	92	76	54	33	15	5
HER2-ET	257	197	157	135	115	101	88	68	52	30	15	6	1

POTENCIAL PRIMERA LÍNEA EN CÁNCER DE MAMA MTS HER2 POSITIVO

First Line

**T-DXd + Pertuzumab
(DESTINY Breast09)**

Maintenance ?

vs.

HR-

THP → HP maintenance

+ Tucatinib (HER2CLIMB-05)

HR+

THP → HP maintenance + ET

+ Palbociclib (PATINA)

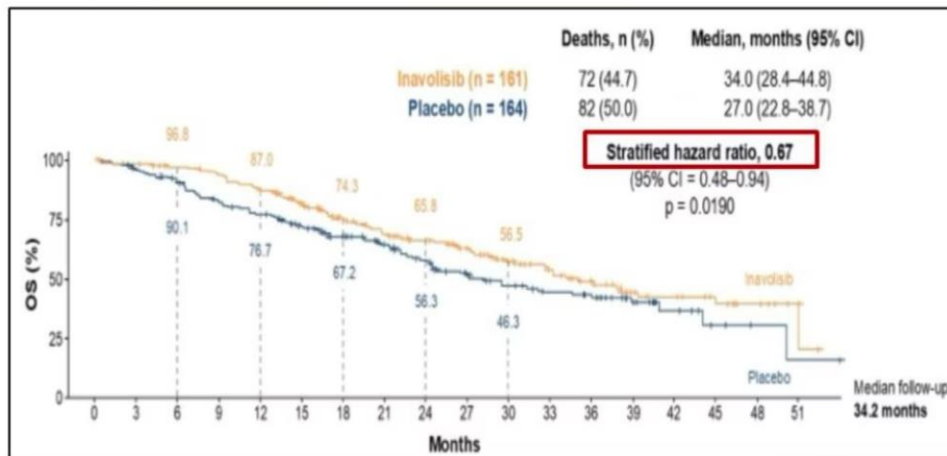
+ Tucatinib (HER2CLIMB-05)

1. Swain et al. Lancet 2020; 2. Hurvitz et al. Lancet 2023

PRIMERA LÍNEA EN CÁNCER DE MAMA MTS LUMINAL

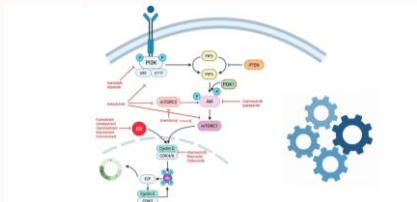
Line of therapy	Treatment	mPFS (mo)
1L	ET + CDK4/6i ET + CDK4/6i + Inavolisib* (High-risk, <i>PIK3CA</i> m)	24.8 – 28.2 15.0

Overall Survival (ASCO 2025)

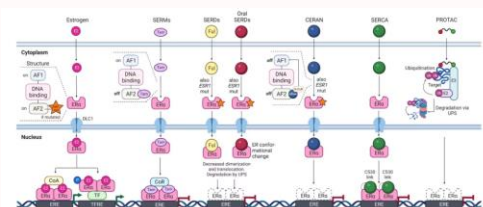


MAMA MTS LUMINAL: NUEVAS TERAPIAS Y SERDS ORALES EN SEGUNDA LÍNEA

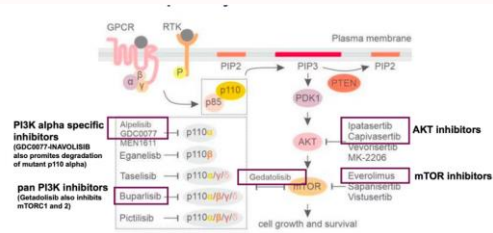
CROSS TALK ENTRE VÍAS PI3K-CDK4/6 Y RE



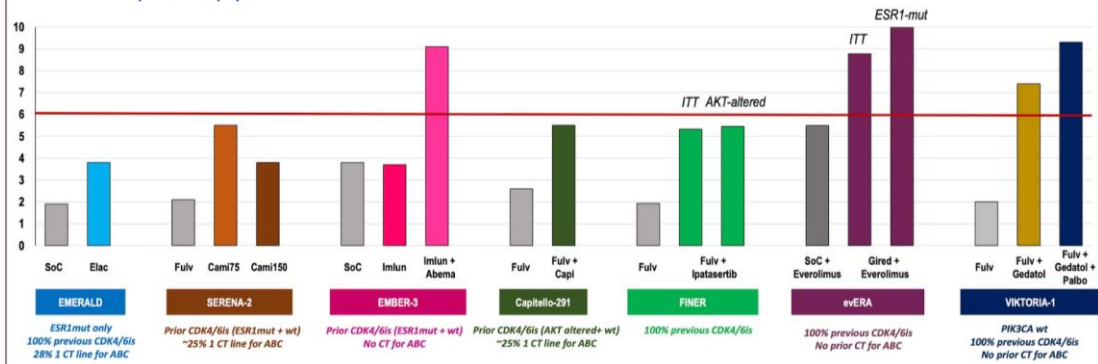
NUEVOS SERDS





INHIBIDORES DE PI3K-AKT-MTOR



Combination of SERDS/SERM with targeted therapies including PI3Ki and CDK4/6i represents the future of ET-based treatment in CDK4/6i-pretreated population



ESCENARIOS Y TRATAMIENTO EN CÁNCER DE MAMA MTS LUMINAL

First Line	Second Line	Third Line +
ET + CDK4/6i	<i>PIK3CA_{mut}</i> Fulvestrant + Alpelisib	T-DXd (HER2-low or ultralow)
	<i>PIK3CA_{mut}</i> Fulvestrant + Capivasertib	Sacituzumab Govitecan
ET + CDK4/6i + Inavolisib (High risk, <i>PIK3CA_{mut}</i>)	<i>AKT1/PTEN_{alt}</i> Fulvestrant + Capivasertib	Dato-DXd 
	<i>ESR1_{mut}</i> Elacestrant; Imlunestrant 	Chemotherapy
	<i>gBRCA_{mut}</i> Olaparib; Talazoparib	

	No targetable mutation	
		Switch CDK4/6i + ET
		Everolimus + ET
		Chemotherapy
		T-DXd (HER2-low or ultralow)

ONCOLOGÍA DE PRECISIÓN EN CÁNCER DE MAMA EN 2025

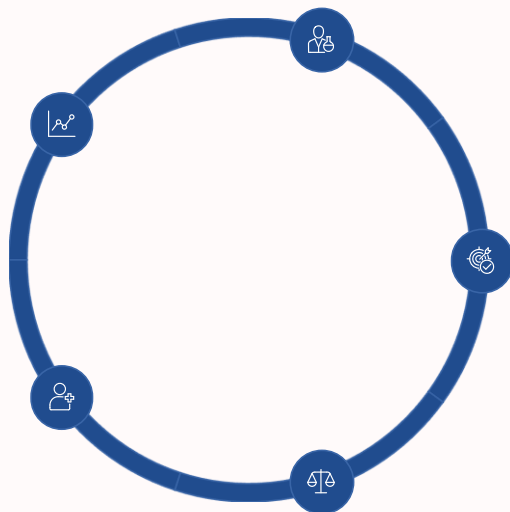
Ha trascendido la simple secuenciación de genes para convertirse en una estrategia multimodal que integra múltiples dimensiones del cuidado del paciente.

OMNICS + IA PARA DIAGNÓSTICO

Modelos avanzados mejoran la precisión diagnóstica y pronóstica

CENTRADO EN EL PACIENTE

Decisiones personalizadas según perfil molecular único



MONITOREO MOLECULAR

ctDNA en diferentes líquidos biológicos

TERAPIAS DIRIGIDAS

Fármacos específicos para alteraciones genéticas

DE-ESCALAMIENTO TERAPÉUTICO

De-escalada y escalada basada en evidencia molecular