

Riunione Annuale

GIM GRUPPO
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HOTEL EXCELSIOR SAN MARCO

PIAZZA DELLA REPUBBLICA, 6

Disclosure:

- The author declares no conflicts of interest



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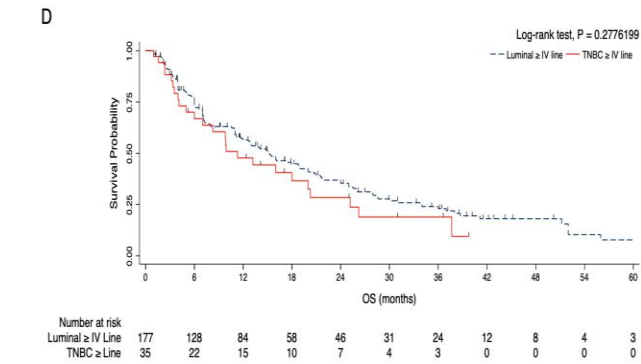
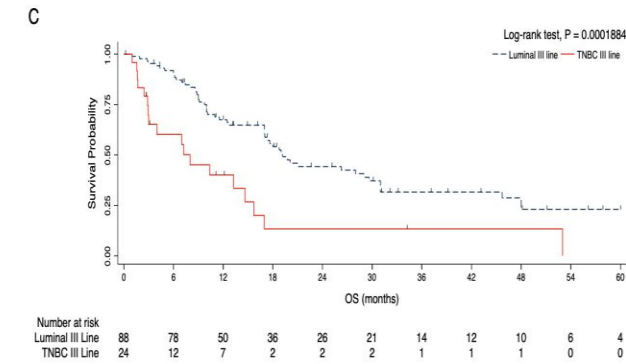
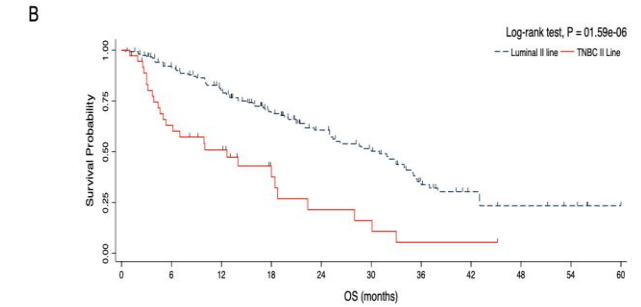
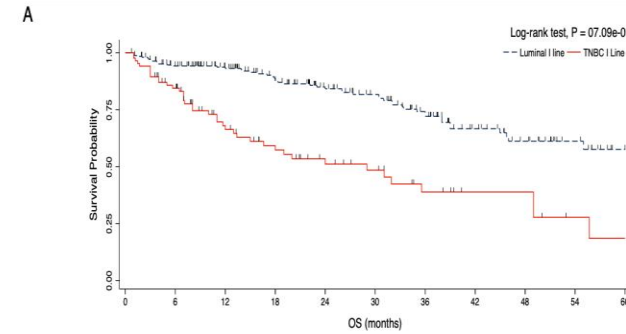
The interSWITCH Study

A Prospective Ancillary Analysis of the interSECT (GIM38) Study Evaluating the Clinical and Molecular Characteristics of HR-positive, HER2-negative (HR+/HER2-) Metastatic Breast Cancer (MBC) Undergoing Subtype Reassessment in Subsequent Lines of Therapy

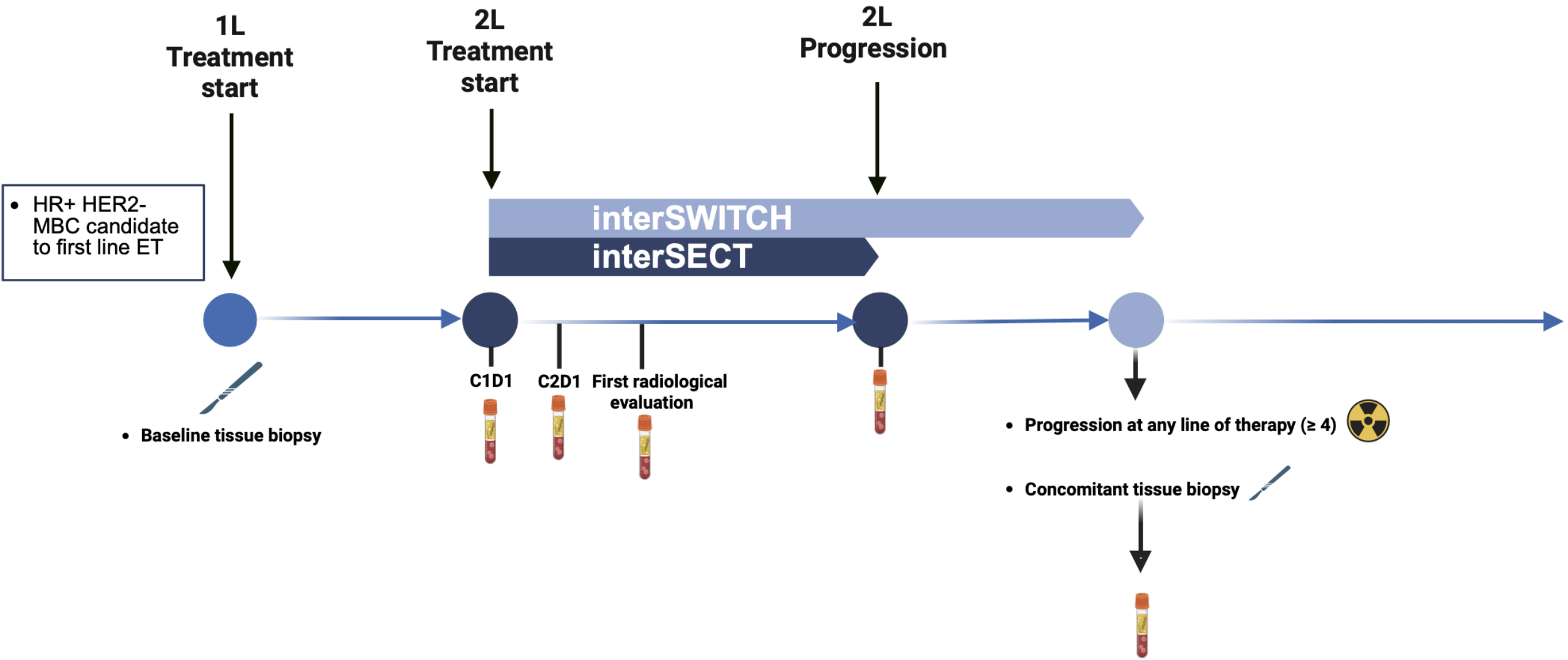
Background

The molecular and prognostic convergence of HR+/HER2- MBC to a TNBC profile

	RRR	[95% conf.interval]	P> z	
Luminal I line (reference group)				
Luminal ≥ IV line				
Visceral involvement	4	2.42	6.62	<0.001
Bone involvement				
Yes	2.41	1.25	4.61	0.008
Node involvement				
Yes	0.67	0.4	1.11	0.121
Soft tissue involvement				
Yes	2.46	1.21	5	0.013
MAF ≥ 3.3%	1.37	0.8	2.33	0.254
TP53 SNVs	1.81	1.09	3.01	0.022
PIK3CA SNVs	1	0.59	1.69	0.992
ESR1 SNVs	8.09	4.29	15.26	<0.001
PTEN SNVs	2.67	0.57	12.54	0.215
TNBC ≥ IV line				
Visceral involvement	3.46	1.43	8.35	0.006
Bone involvement				
Yes	0.89	0.36	2.23	0.802
Node involvement				
Yes	1.35	0.57	3.21	0.492
Soft tissue involvement				
Yes	4.3	1.46	12.7	0.008
MAF ≥ 3.3 %	1.15	0.43	3.03	0.785
TP53 SNVs	10.43	4.15	26.2	<0.001
PIK3CA SNVs	0.06	0.01	0.35	0.001
ESR1 SNVs	NA			
PTEN SNVs	33.4	4.71	237.13	<0.001



STUDY DESIGN



PROJECT PLAN

OBJECTIVES

Primary objective:

- To characterize the clinical and molecular landscape of subtype conversion from HR+/HER2- to HER2-positive or TNBC in patients enrolled in the interSECT study, integrating histological reassessment with liquid biopsy analyses

Secondary objectives:

- To compare newly detected genomic and epigenomic alterations at the time of re-sampling between patients with molecular subtype conversion and those with luminal subtype persistence, relative to baseline profiles
- To evaluate the association between previous therapies and the landscape of genomic and epigenomic alterations detected at the time of histological re-characterization
- To evaluate the association between subtype conversion and the choice and outcomes of post-second-line ($\geq 2L$) therapies
- To explore the development of a predictive machine learning algorithm for molecular subtype conversion, integrating clinical features with ctDNA-derived genomic and epigenomic profiles obtained through liquid biopsy

IMPACT

This study will provide a real-world characterization of ctDNA dynamics across treatment lines, with a specific focus on molecular subtype conversion in HR+/HER2- MBC, aiming to enable earlier detection of resistance mechanisms and to support real-time treatment decisions