

Giornate **AIEOP**

BOLOGNA

Zanhotel Europa

14-15 Aprile 2025

I TUMORI RENALI

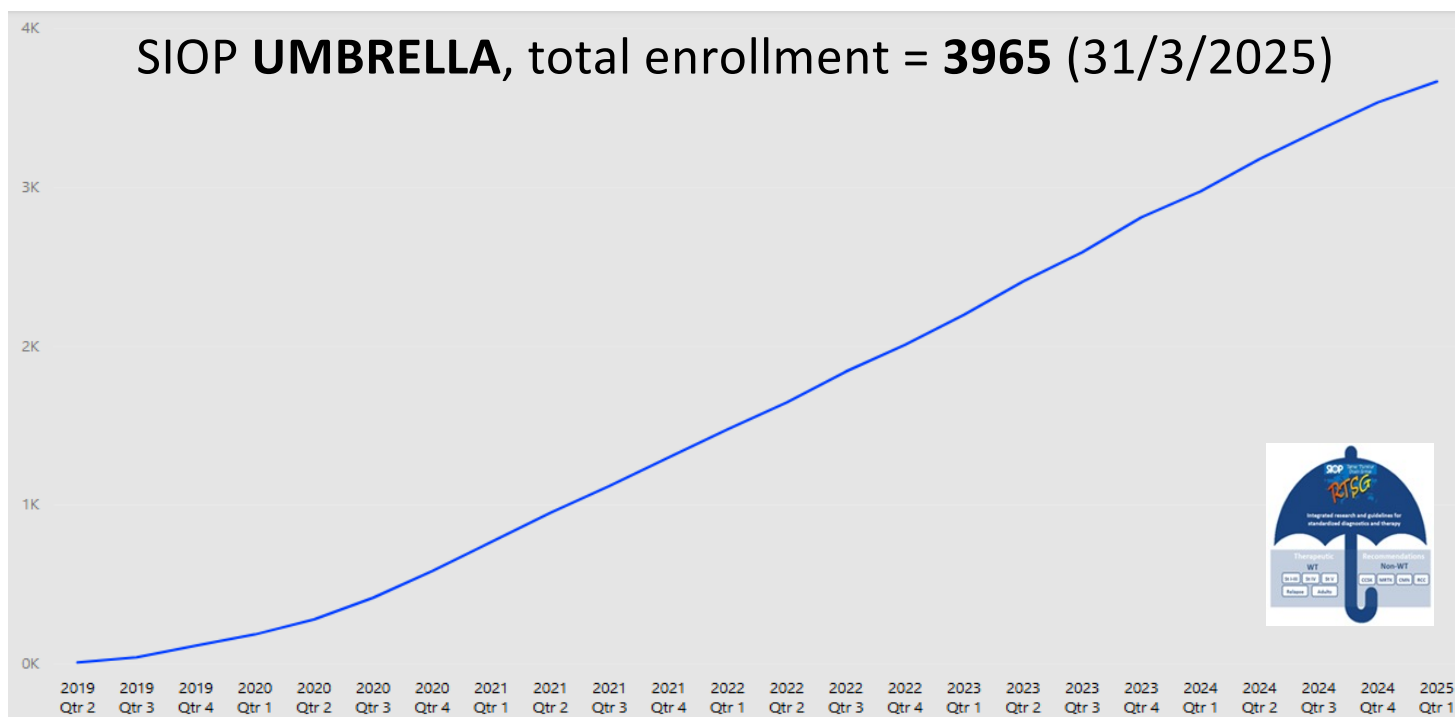
Filippo Spreafico

Fondazione IRCCS Istituto Nazionale dei Tumori
di Milano

I have no conflict of interest or competing interest to declare

Agenda

- SIOP-Umbrella
 - campionamento linfonodi
 - Backstage nuovo protocollo SIOP
 - Studi biologici
-

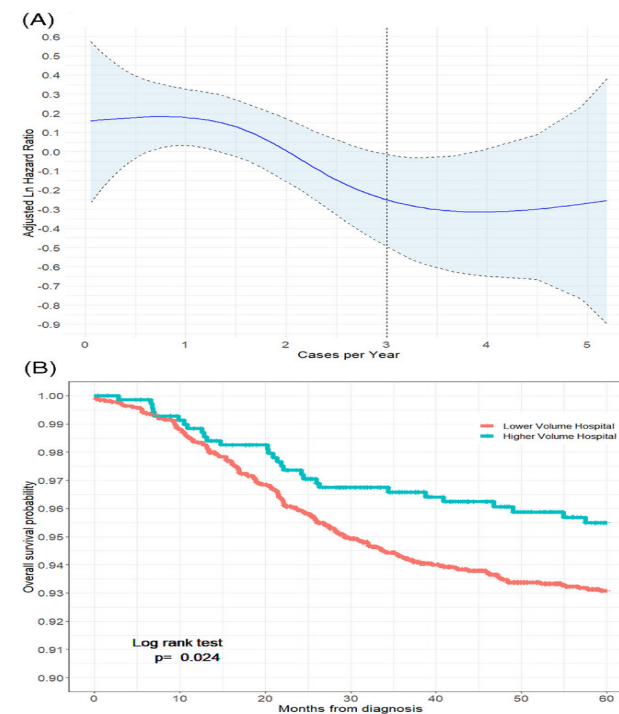


3 casi/anno

401 casi

	N TOT CASI		CASI/ANNO
ROMA (OPBG)	72	296 (74%)	≥ 5
INT MILANO	55		
TORINO	33		
NAPOLI	28		
PADOVA	28		3-4
BARI	23		
CATANIA	20		
FIRENZE	20		
BRESCIA	17	47 (12%)	< 2
PALERMO	11		
GENOVA	10		
ROMA (GEMELLI)	9		
BERGAMO	9		
ANCONA	8		
PERUGIA	6		
PESCARA	6	58 (14%)	≤ 1
TRIESTE	6		
VERONA	5		
BOLOGNA	5		
CAGLIARI	5		
MODENA	6		
PARMA	5		
PAVIA	4		
PISA	4		
RIMINI	3		
S. GIOVANNI ROTONDO	3		
Aviano, Catanzaro, Cosenza, Lecce, Roma Sapienza, Sassari	0		

Chidiac C *et al.* Impact of hospital volume on survival for pediatric Wilms tumor. *Pediatr Blood Cancer* 2025;72(3):e31503



Mancato campionamento LN

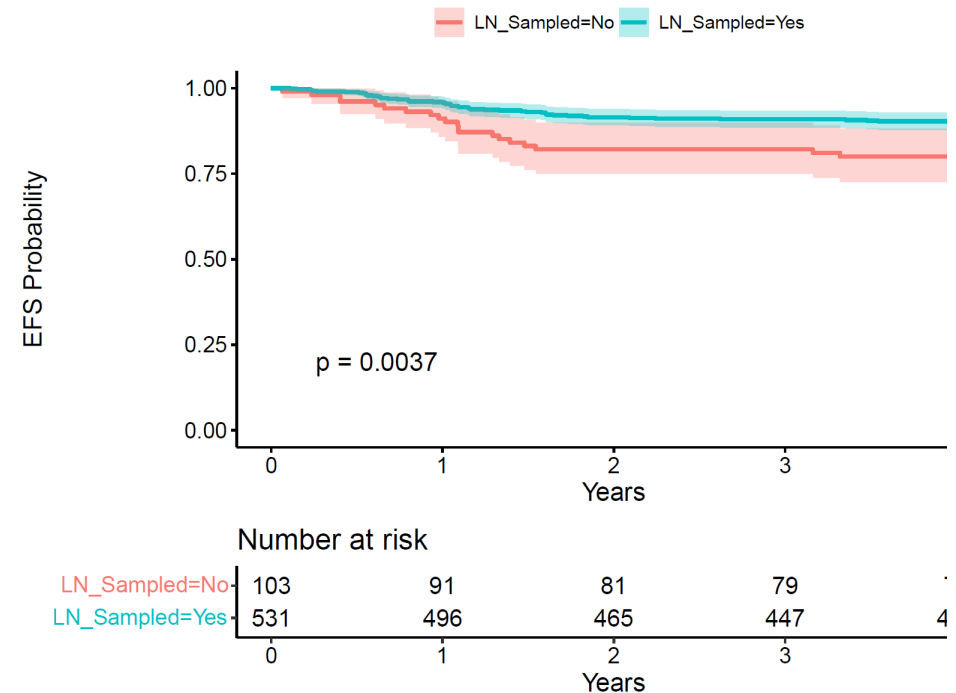
15.2%, COG

16%, SEER database (*real word*)

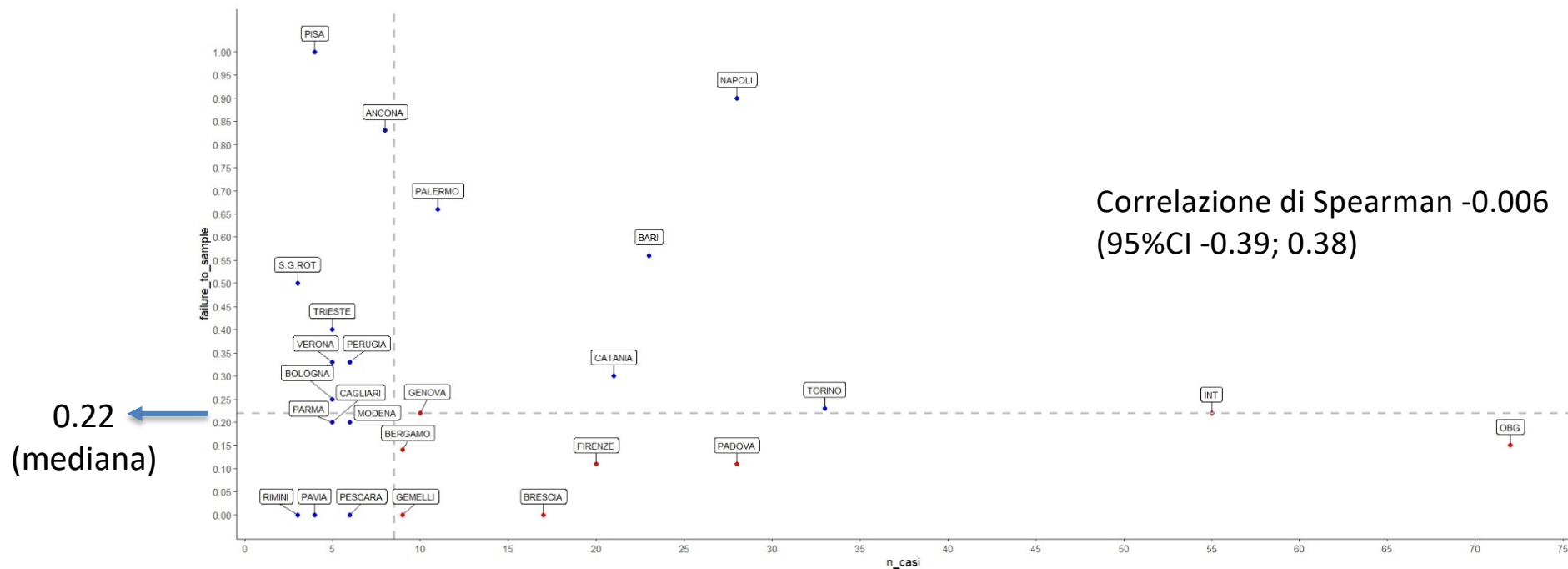
20%, Central America & Caribbean
(2020-24) vs 29% (2012-18)

22%, AIEOP (Umbrella)

26%, Wilms Africa II

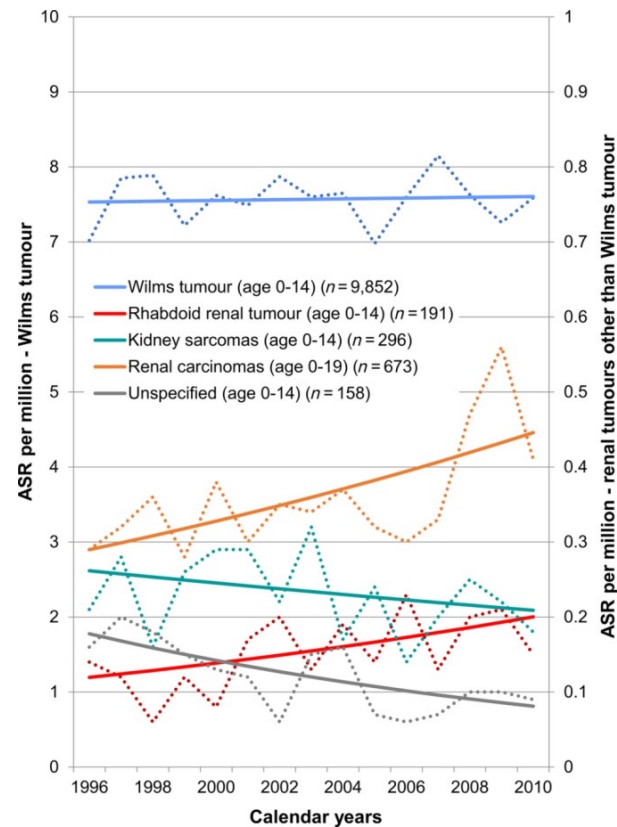


AIEOP, assenza di correlazione lineare tra volume del centro e mancato campionamento LN



Ringraziamenti, Dott.ssa C. Ciniselli

	PATOLOGIA	N. 85	
NON WILMS (21%)	CCSK	8	
	Nefroma mesoblastico	15	
	Nefroma cistico	6	
	Carcinoma del rene	18	
	RTK	4	
	T miofibroblastico infiammatorio	1	
	Neuroblastoma	4	
	Sarcoma di Ewing	3	
	Linfoma di Burkitt	3	
	Adenofibroma metanefrico	1	
	Sarcoma NAS	1	
	Spindle cell mesenchimal tumor TRK-r	1	
	T mesenchimale con fusione KIAA1549-BRAF	1	
	Sarcoma mixoide SMARC deleto	1	
	Sarcoma anaplastico	3	DICER1 sindrome
	Neoplasia maligna piccole cellule	1	
	T mesenchimale basso grado	1	
	Angiomiolipoma	6	
	T cellule oncocitiche	1	
	Altro (displasia renale cistica)	3	
	Non npl	2	

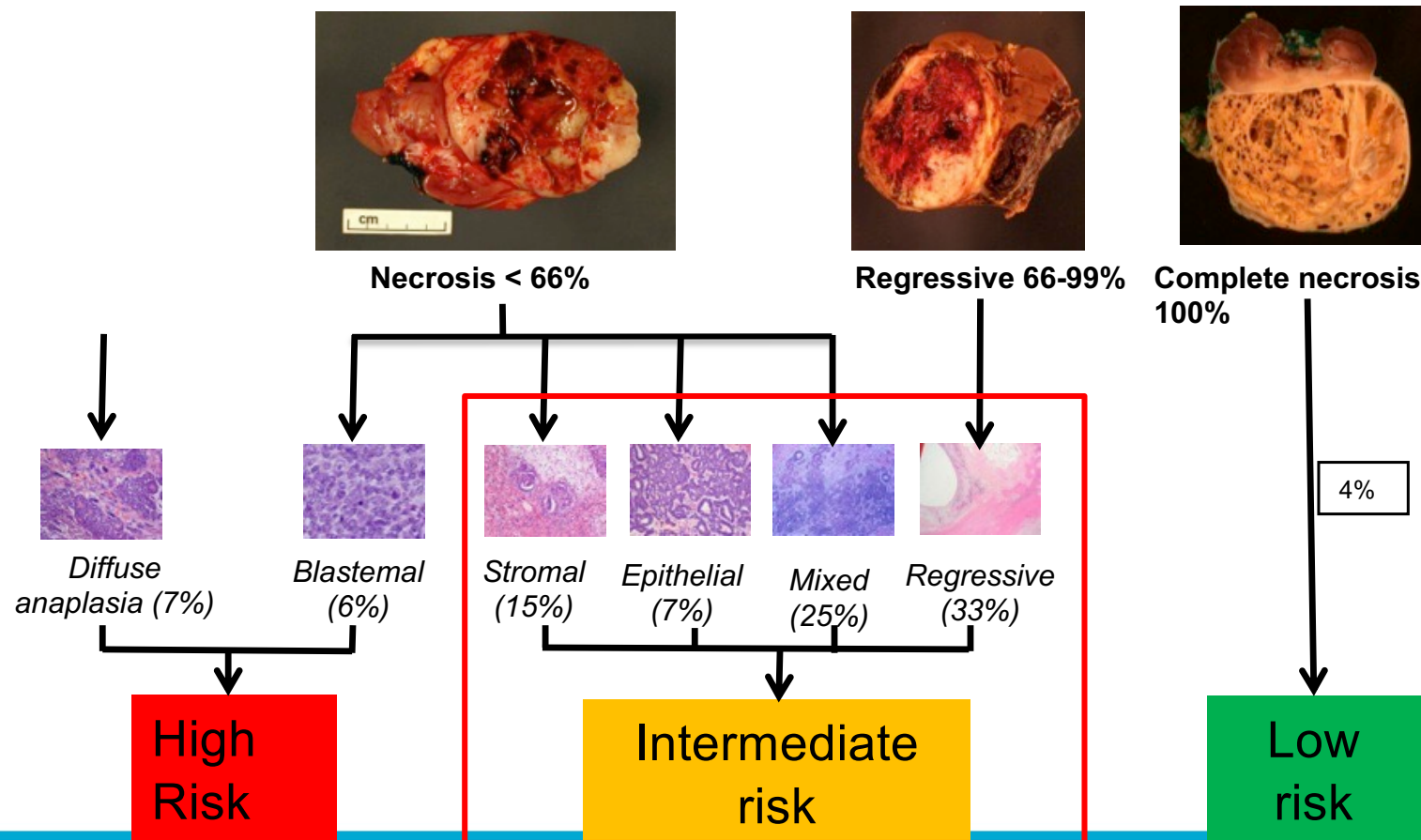


By the age of 14 yrs, RCC represent 50% of pediatric renal tumors

Increase may reflect growing exposure to dietary risk factors, **obesity** or medications (as a **second cancer** in childhood cancer survivors)

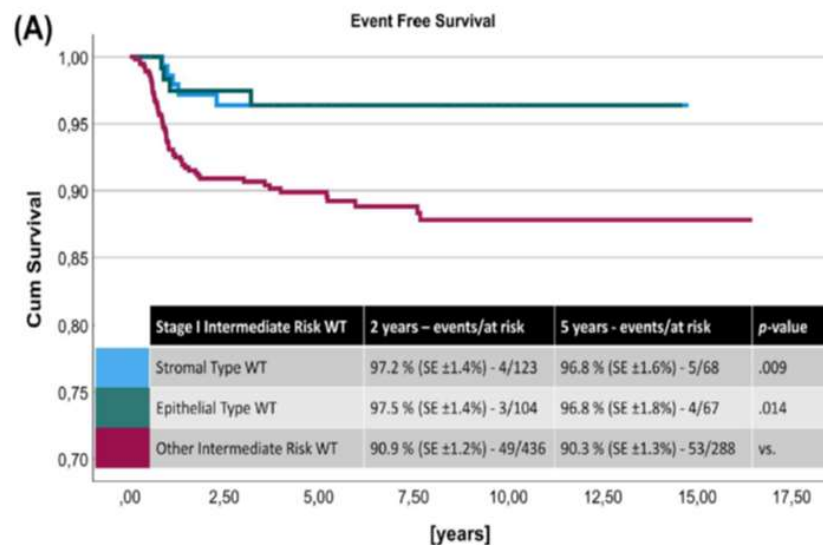
Prospettive nuovo protocollo SIOP

Sustainable personalized medicine through pre-op CT

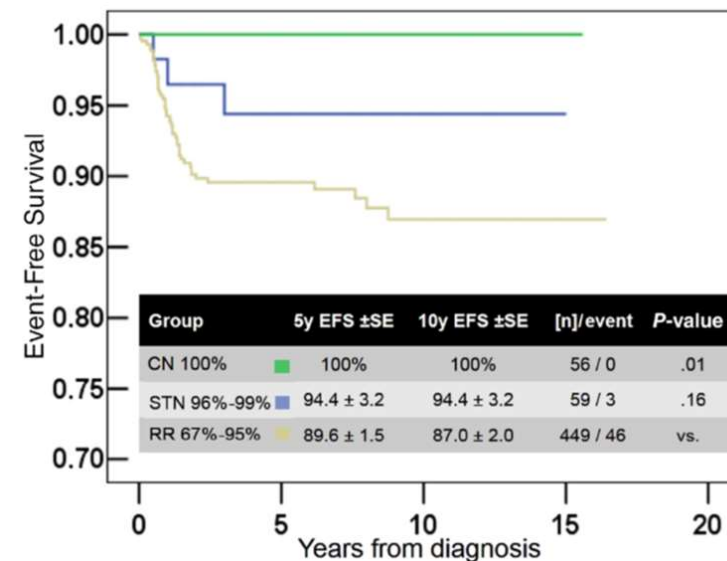


(1) To *dissect* the Intermediate-Risk group

Epithelial, Stromal types



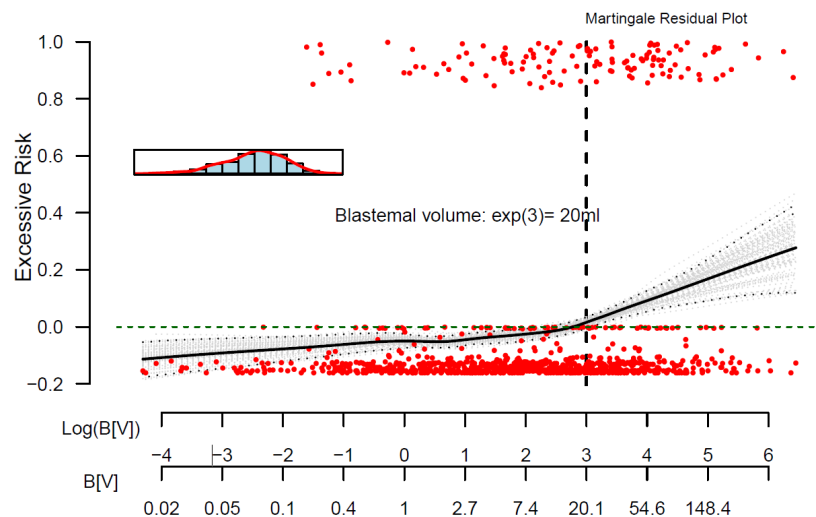
Subtotally Necrotic (STN)



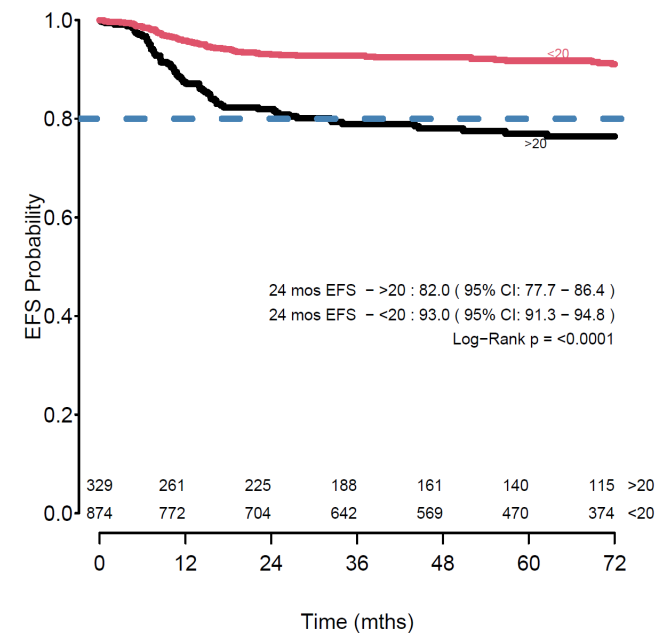
D'Hooghe et al. *Cancer* 2023

(2) Absolute Blastemal Volume

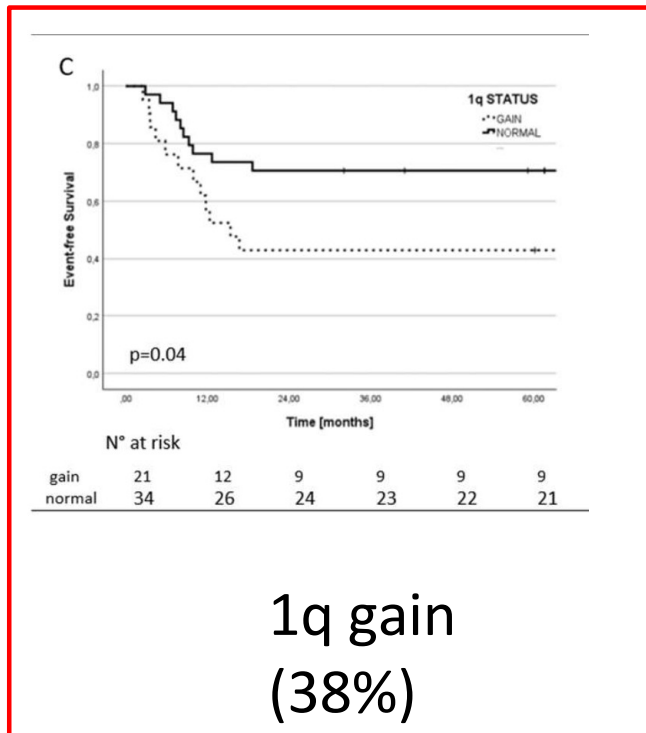
Martingale residual plot of blastemal volume and EFS



EFS > vs < 20mL

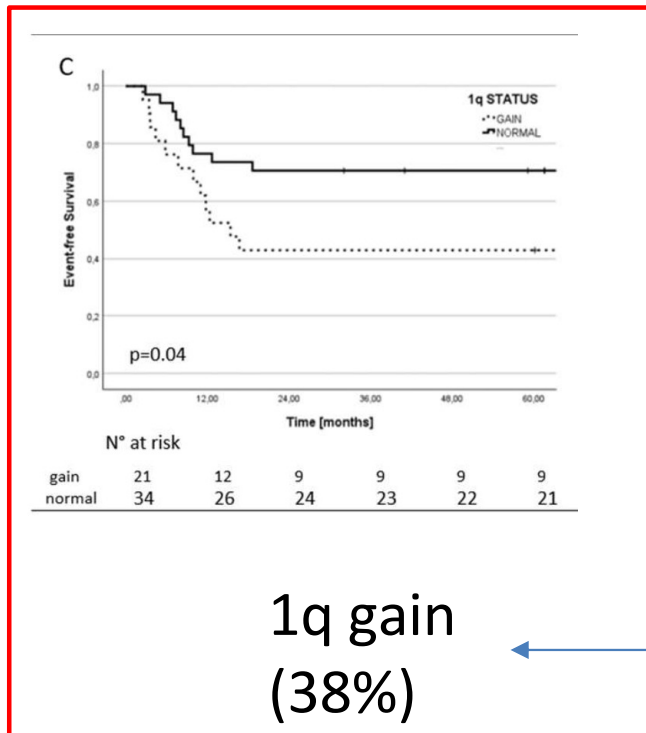


(3) Adverse molecular *biomarker*

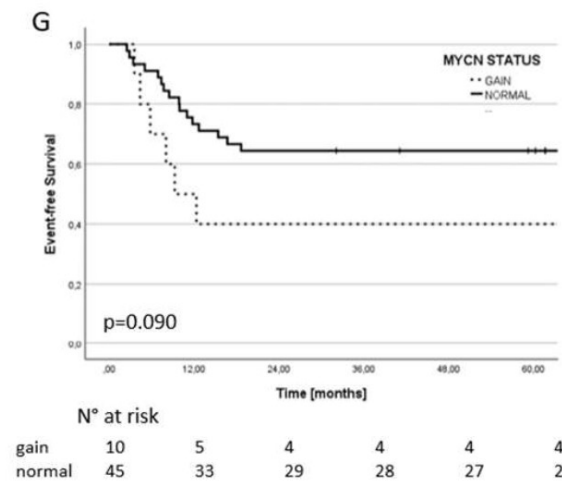


Welter et al. 2025

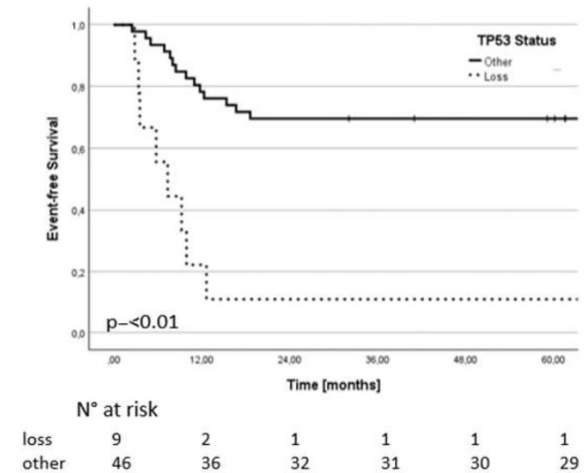
(3) Adverse molecular *signature*



1q gain
(38%)



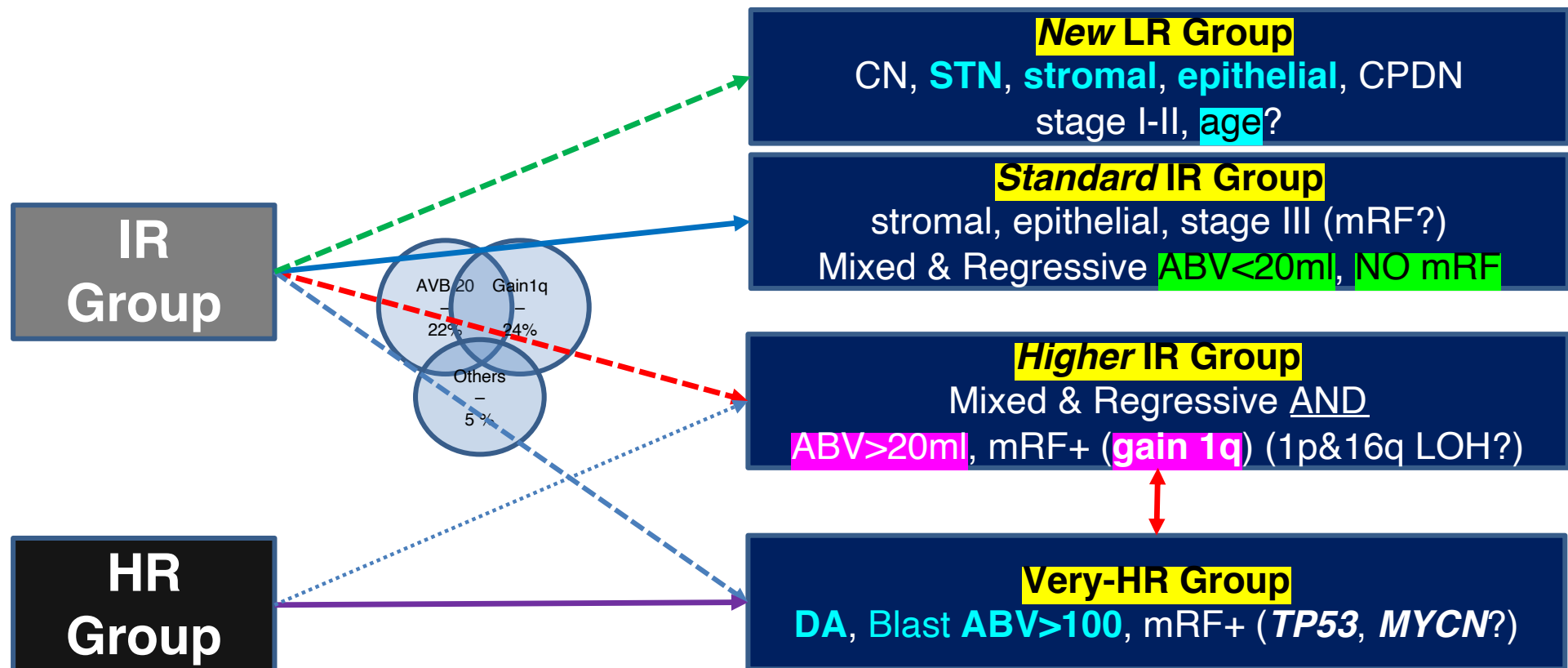
MYCN gain
(18%)



TP53 loss
(16%)

Welter et al. 2025

Williams et al. 2015



	Criteria	Preop. CT	Stage I	Stage II	Stage III
Infant LR	<12m, <400ml, noLN, no predisp	R: VCR vs AV	None/10w VCR?	«short» AV2?	AV2?
LR	Complete necrosis	all	None	«short» AV2?	AV2
Move to LR?	ET, ST, STN	all	None/10w VCR?	«short» AV2?	AV2 ± R-RT?
IR	Other IR (ABV<20ml)	all	AV1	AV2	AV2 + flank RT (dose?)
Higher IR*	ABV>20ml, mRR; TuVol >500ml	all	AV1 vs X?	R or HC? (AV2) AVD	R or HC? (AV2)AVD+ flank RT (dose?)
HR	BT-WT (or in HIR?)	all	AVD	HR-1	HR-1 + flank RT
	DA	all	AVD	HR-1 + flank RT	HR-1 + flank RT (dose?)
Highest HR	HR + TP53/MYCN?	all	?	New HR (taxane)?	New HR (taxane)?

mRF (1q gain? MYCN gain?)

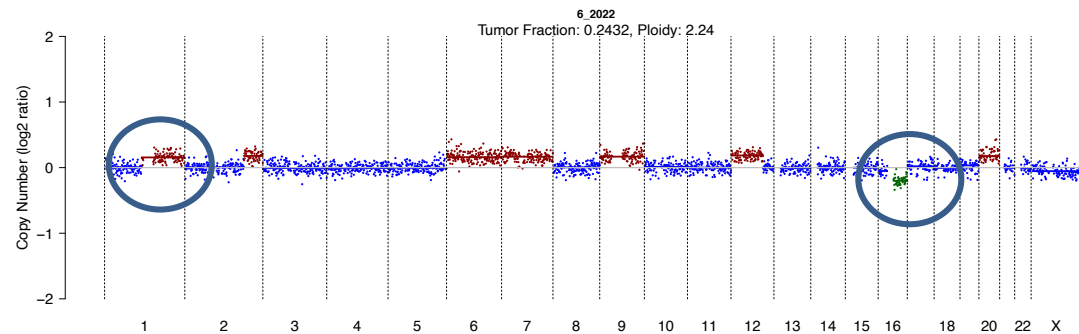
Relapse.new

	Initial tumor	CT received	EFS?	Proposed treatment?	Notes
Low-AA	stage I, LR-IR (metach. WT) relapse>6 mos age <2 yrs?	VA x 4, none	80%	VAD & stage IV-like approach Response-guided RT (to lung) Always local RT Surgery after VAD	
AA		VA27 (±RT?)	70%	CyD/CarbETO (AA regimen)	
BB		VAD + RT	68%	ICE/CyCE + HDT (BB regimen)	To extend to stage II-III HR upfront?
CC	stage II HR, stage IV IR slow-resp	HR (no Iri)	10-20%	VITB vs ICE	
High-CC	stage III-IV, DA, AVB-100+, 1q+?	HR + Iri	10%	Taxane/Gem (+ TMZ?) Early-phase new drug? SFOP Metro-Wilms?	RCT? (To extend to stage IV HR upfront? Window?)

F Spreafico

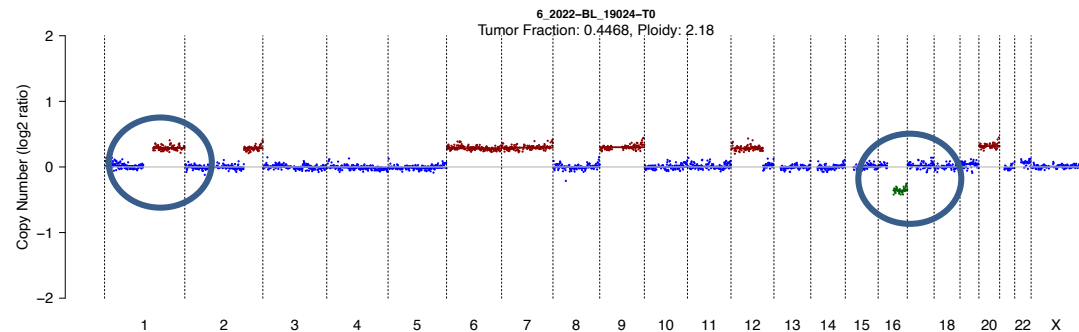
Ipotesi: ctDNA e tumore hanno identiche CNAs

TUMORE PRIMITIVO



BIOPSIA LIQUIDA

ctDNA (esordio)



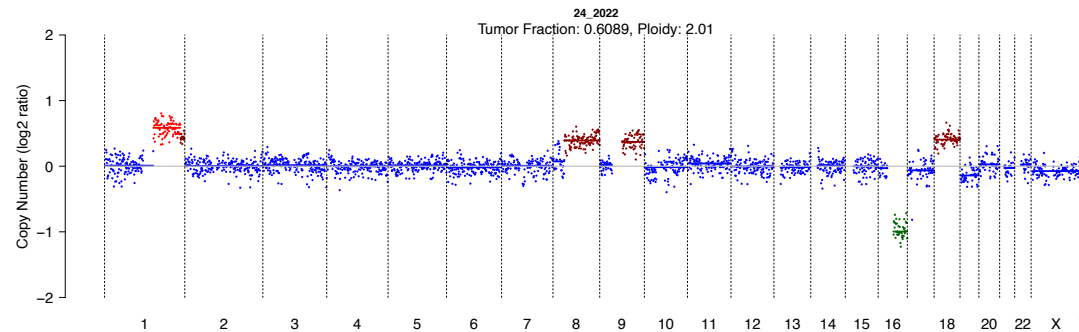
1q gain

17p loss

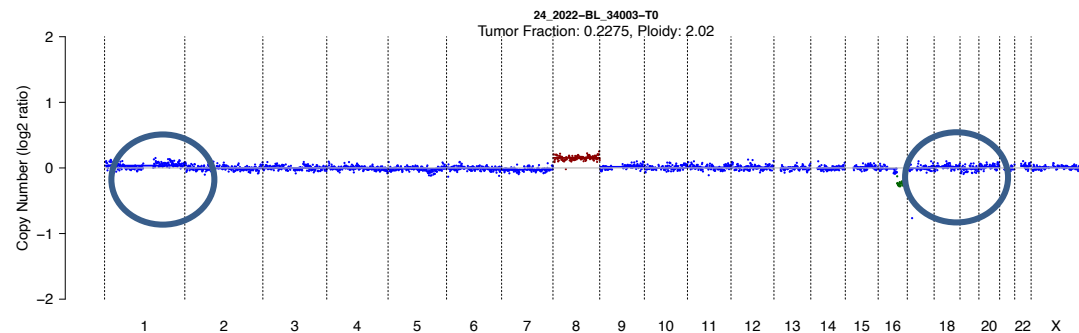
Courtesy, D. Perotti

ctDNA ha meno CNAs del tumore

TUMORE PRIMITIVO



ctDNA (esordio)

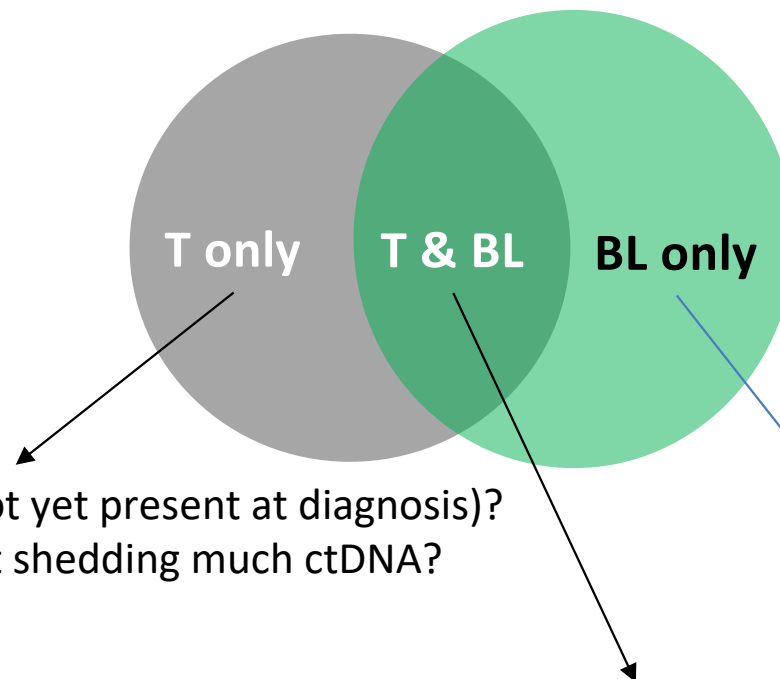


1q gain

17p loss

Courtesy, D. Perotti

Significato biologico del valore predittivo della biopsia liquida (discrepanze, CNAs)



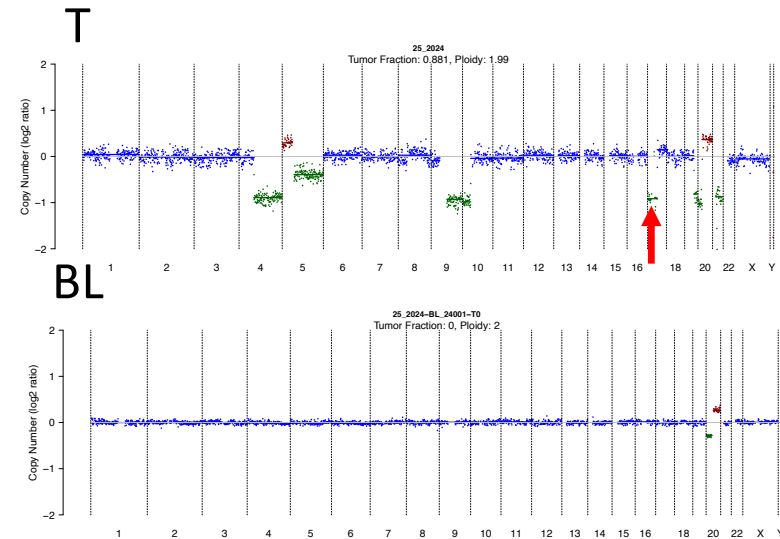
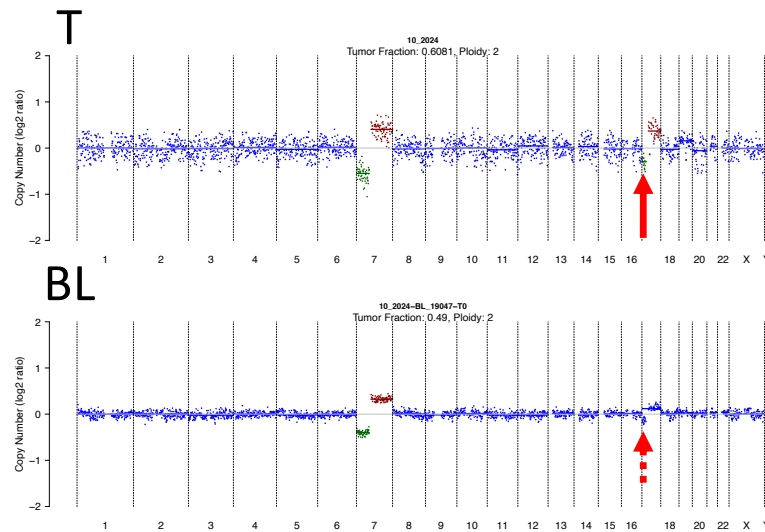
- Late occurring event (not yet present at diagnosis)?
- Small volume tumor not shedding much ctDNA?
- FAILED (no ctDNA)

importance of knowing ctDNA fraction!

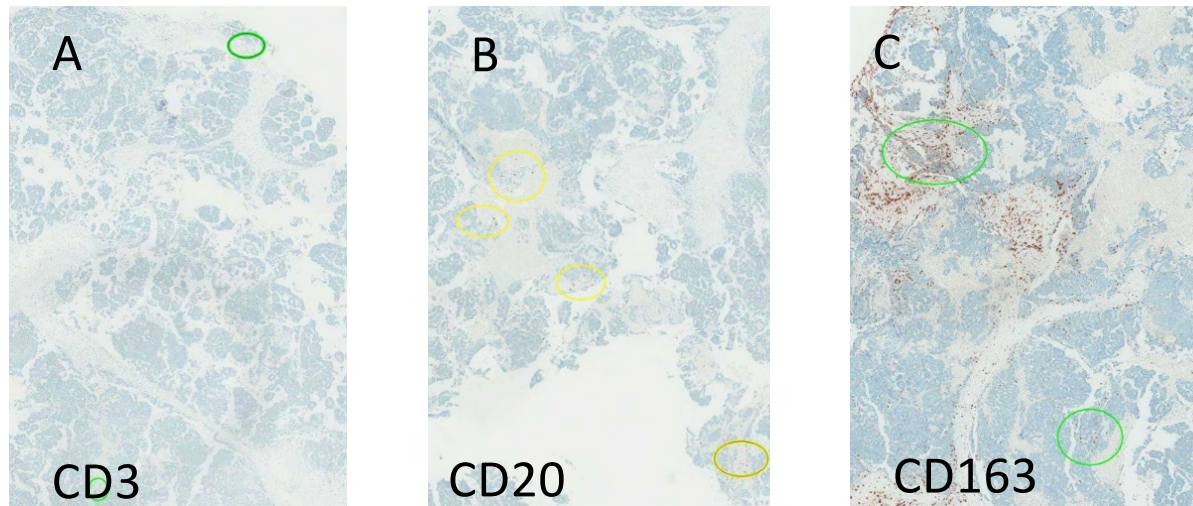
Bingo!

Sampling error?
Inratumor heterogeneity?
OK

17p loss, late occurring event



Infiltrato immune (IHC) in WT relapse

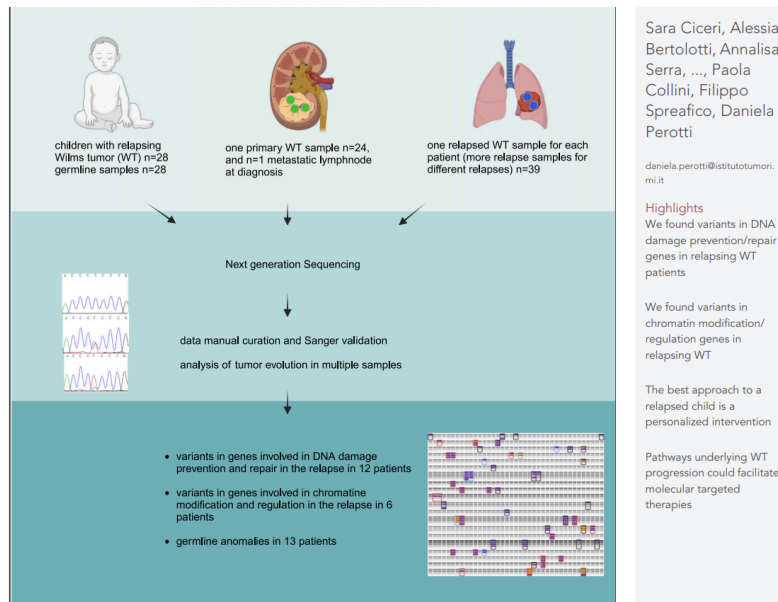


Esempio di selezione degli hotspots in IHC. Caso 10-10

Article

Widening the spectrum of players affected by genetic changes in Wilms tumor relapse

Sara Ciceri,¹ Alessia Bertolotti,² Annalisa Serra,³ Giovanna Gattuso,⁴ Luna Boschetti,⁴ Maria Capasso,⁵ Cecilia Cecchi,⁶ Stefania Sorrentino,⁷ Paola Quarello,^{8,9} Chiara Maura Ciniselli,¹⁰ Paolo Verderio,¹⁰ Loris De Cecco,¹¹ Giacomo Manenti,¹² Francesca Diomedì Camassei,¹³ Paola Collini,¹⁴ Filippo Spreafico,^{4,15} and Daniela Perotti^{1,15,16,*}



Sara Ciceri, Alessia Bertolotti, Annalisa Serra, ..., Paola Collini, Filippo Spreafico, Daniela Perotti

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Highlights

We found variants in DNA damage prevention/repair genes in relapsing WT patients

We found variants in chromatin modification/regulation genes in relapsing WT

The best approach to a relapsed child is a personalized intervention

Pathways underlying WT progression could facilitate molecular targeted therapies

Germline anomalies (mostly affecting DNA damage prevention & repair genes) identified in **46%** of patients

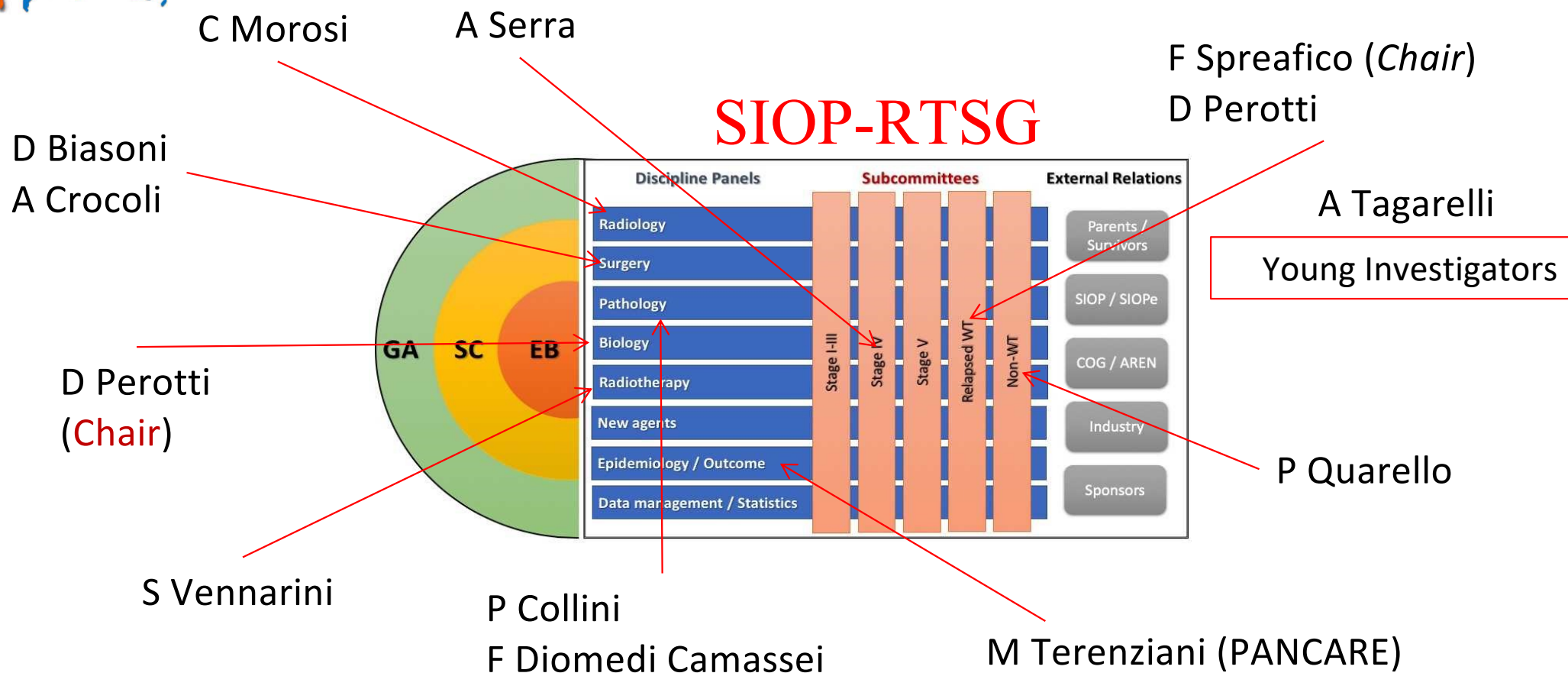
Giornate AIEOP

BOLOGNA 14-15 APRILE 2025



SECRETARY GENERAL: F. Spreafico (application for vice-Chair 2025-2028)

SIOP-RTSG





GDL AIEOP Tumori del Rene

A Di Cataldo (CT)

G Gattuso (MI)

F Melchionda (BO)

P Quarello (TO)

A Serra (Roma)

F Spreafico (MI)

A Tagarelli (TO)

A Guarina (PA, *Discovery*)

Consulenti

- P Collini (Anat Patologica)
- A Crocoli (chirurgia)
- C Morosi (radiologia)
- D Perotti (Biologia)

Collaboratori

- D Biasoni (chirurgia)
- F Diomedi Camassei (Anat Patologica)
- S Vennarini (radioterapia)
- P D'Angelo (oncologia)