

Nuevas estrategias terapeuticas en cancer infantil

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Definicion

- “un enfoque emergente que busca, mediante la consideración precisa de la variabilidad genética y ambiental individual, mejorar la práctica clínica en sus tres aspectos fundamentales: prevención, diagnóstico y tratamiento”

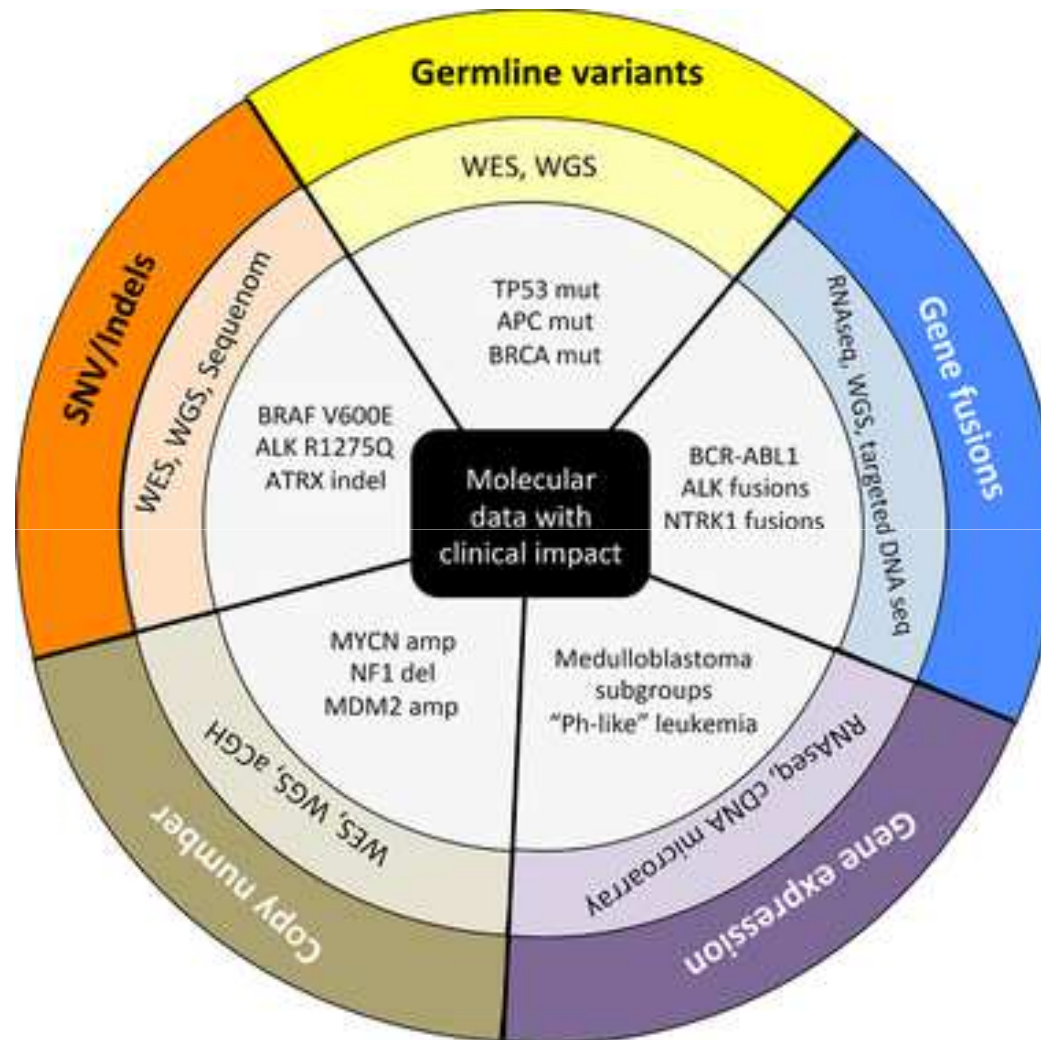
Biomarcadores

- De diagnostico: ej: Phi
- De pronostico (define grupos de riesgo): ej: Phi, amplificacion NMYC
- De respuesta a tratamiento (define tratamientos de precision): Phi, NPM-ALK

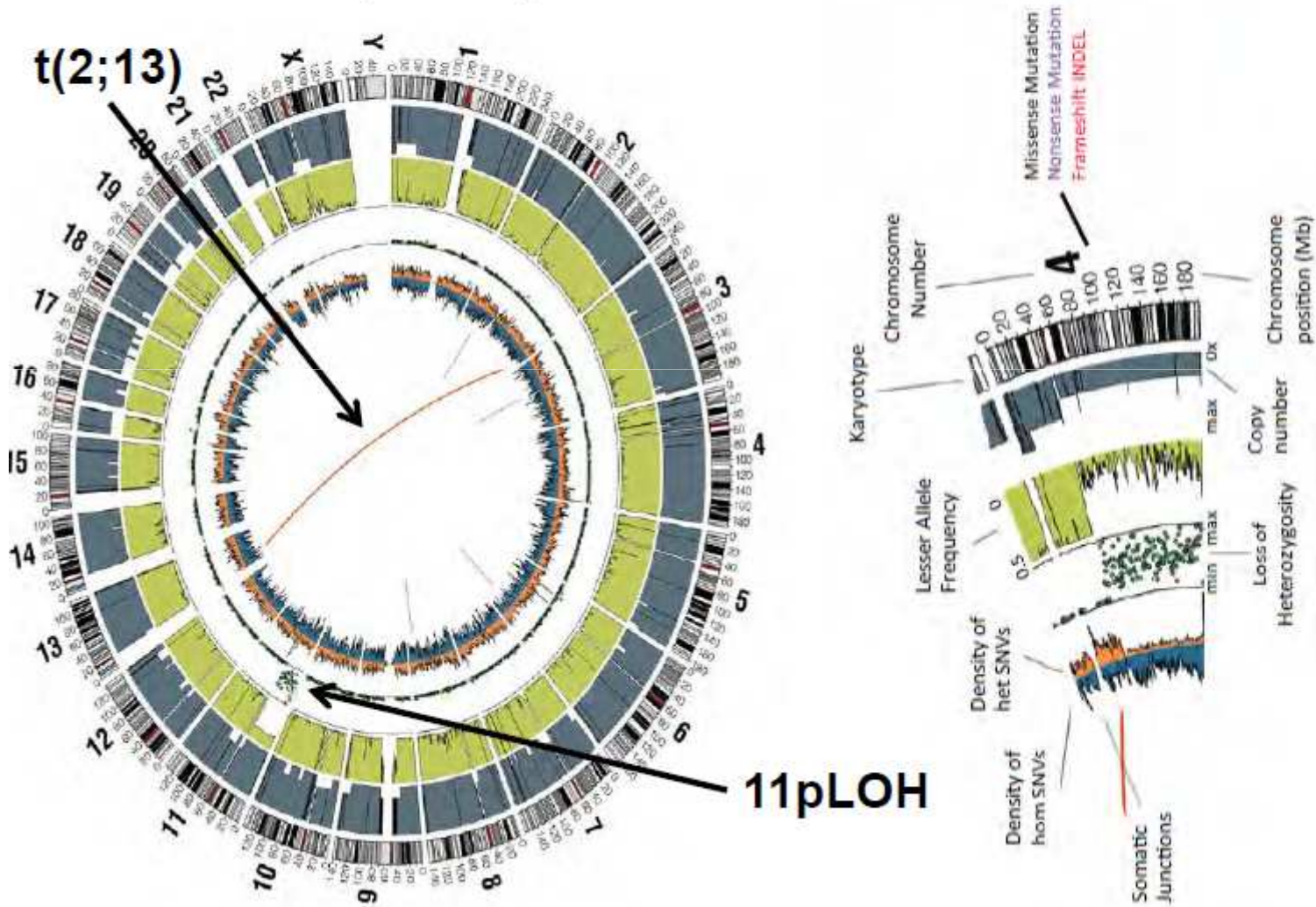
Estudios en Medicina de Precision

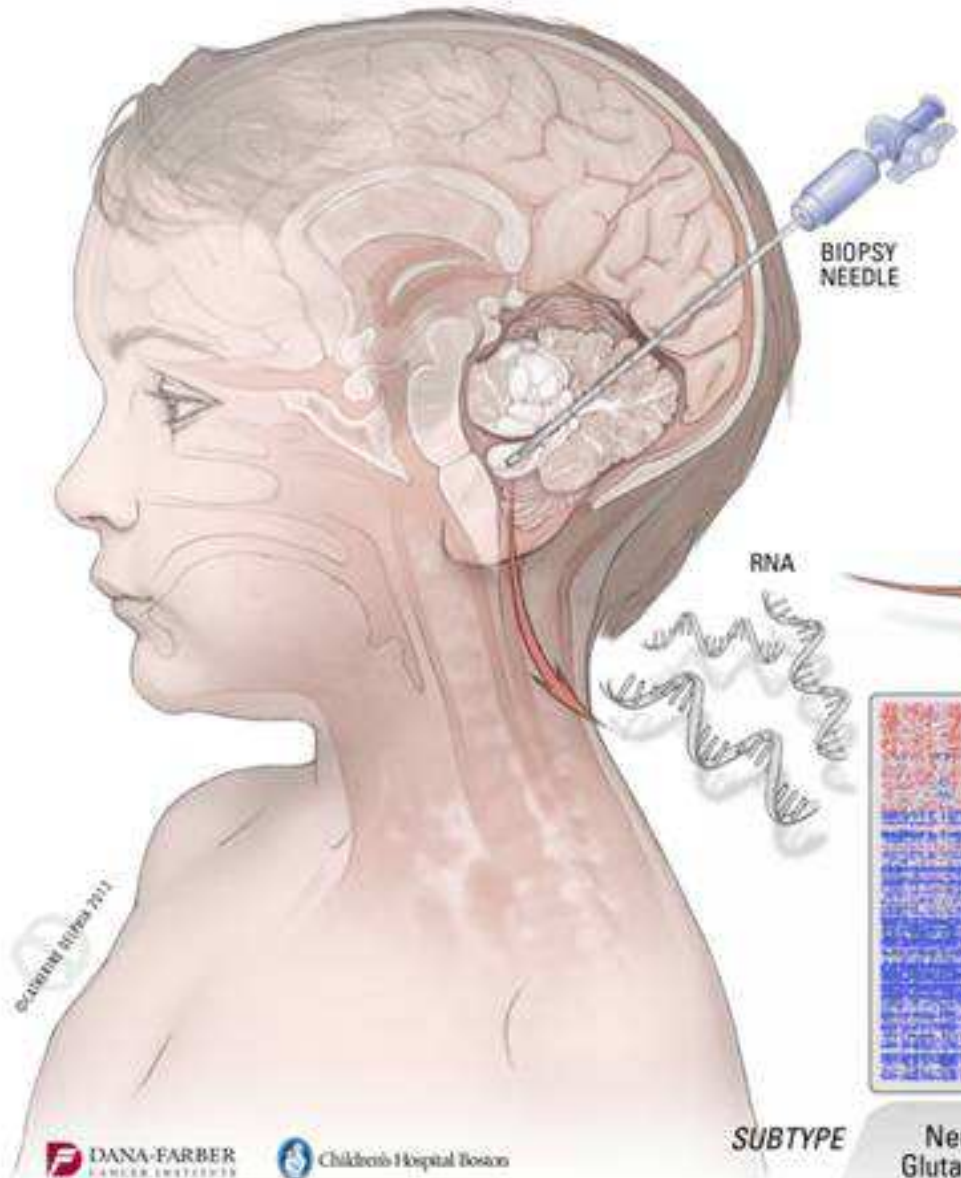
- Secuenciacion dirigida/paneles
- Secuenciacion de exoma
- Secuenciacion de genoma completo
- Arrays de expresion
- Secuenciacion de ARN
- Metiloma

Precision medicine in pediatric oncology: Lessons learned and next steps



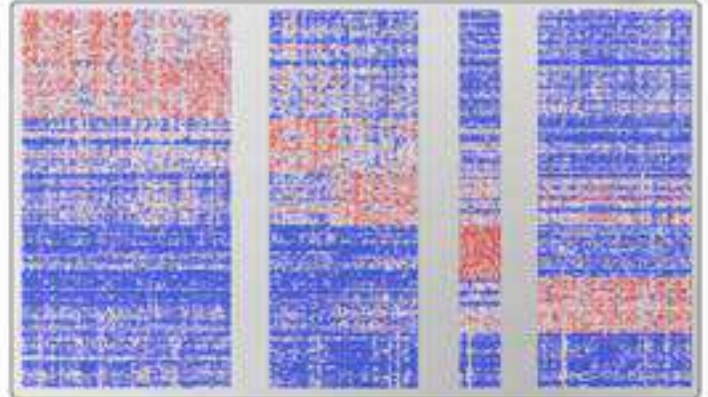
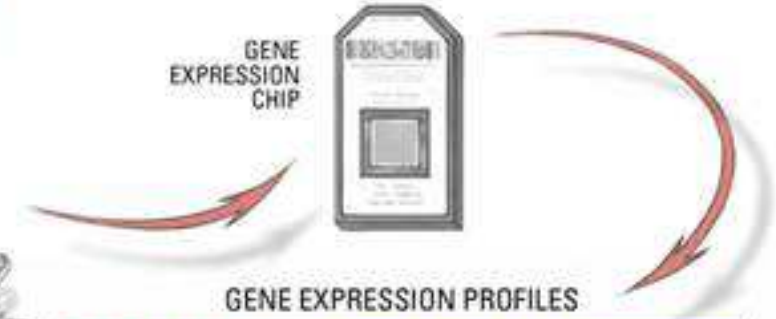
Typical Fusion Positive ARMS; Fusion Gene, Low Aneuploidy, Low Somatic Mutation rate





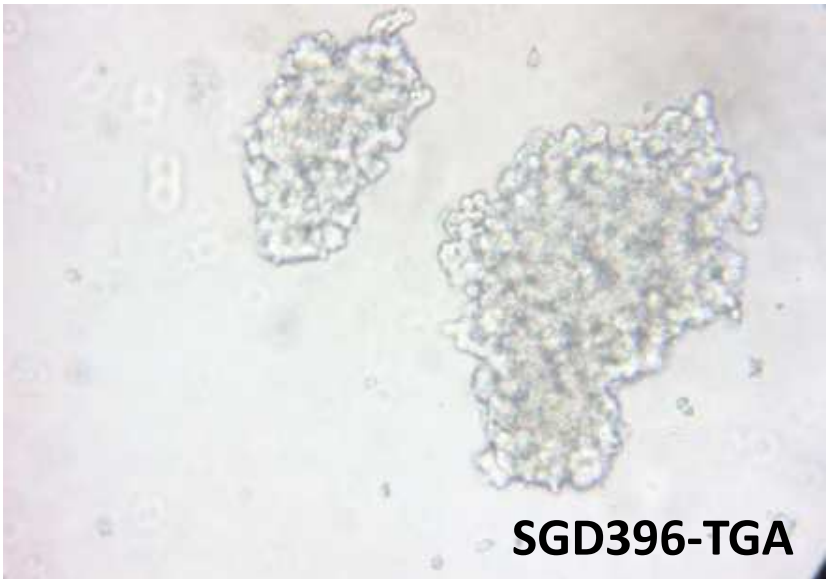
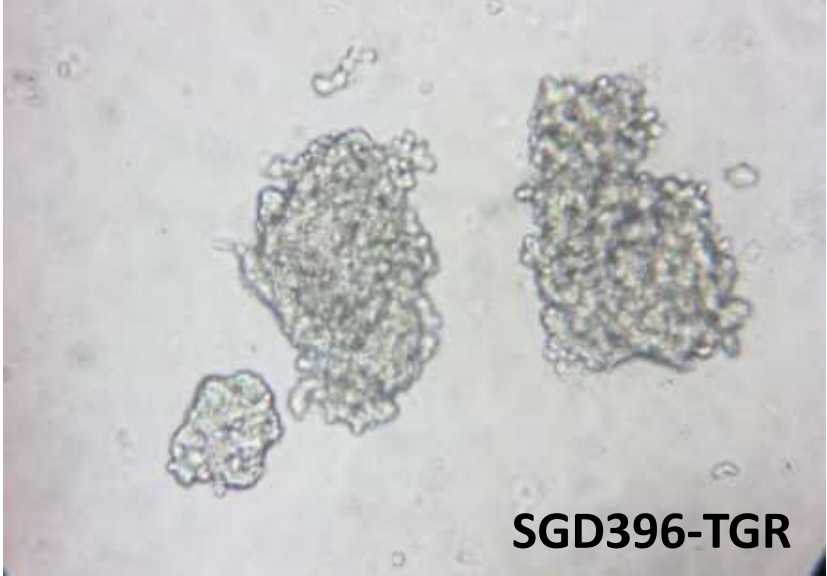
MEDULLOBLASTOMA

- 500 births / year in US
- 70% average survival
- Poor quality of life among survivors

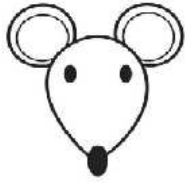


SUBTYPE	Neuronal/ Glutamatergic	Photoreceptor/ GABAergic	WNT	SHH
SURVIVAL RATE	87% / 95%	74% / 20%	90%	65%

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Cortesia Paula Schaiquevich



Modelo tumoral ortotopico

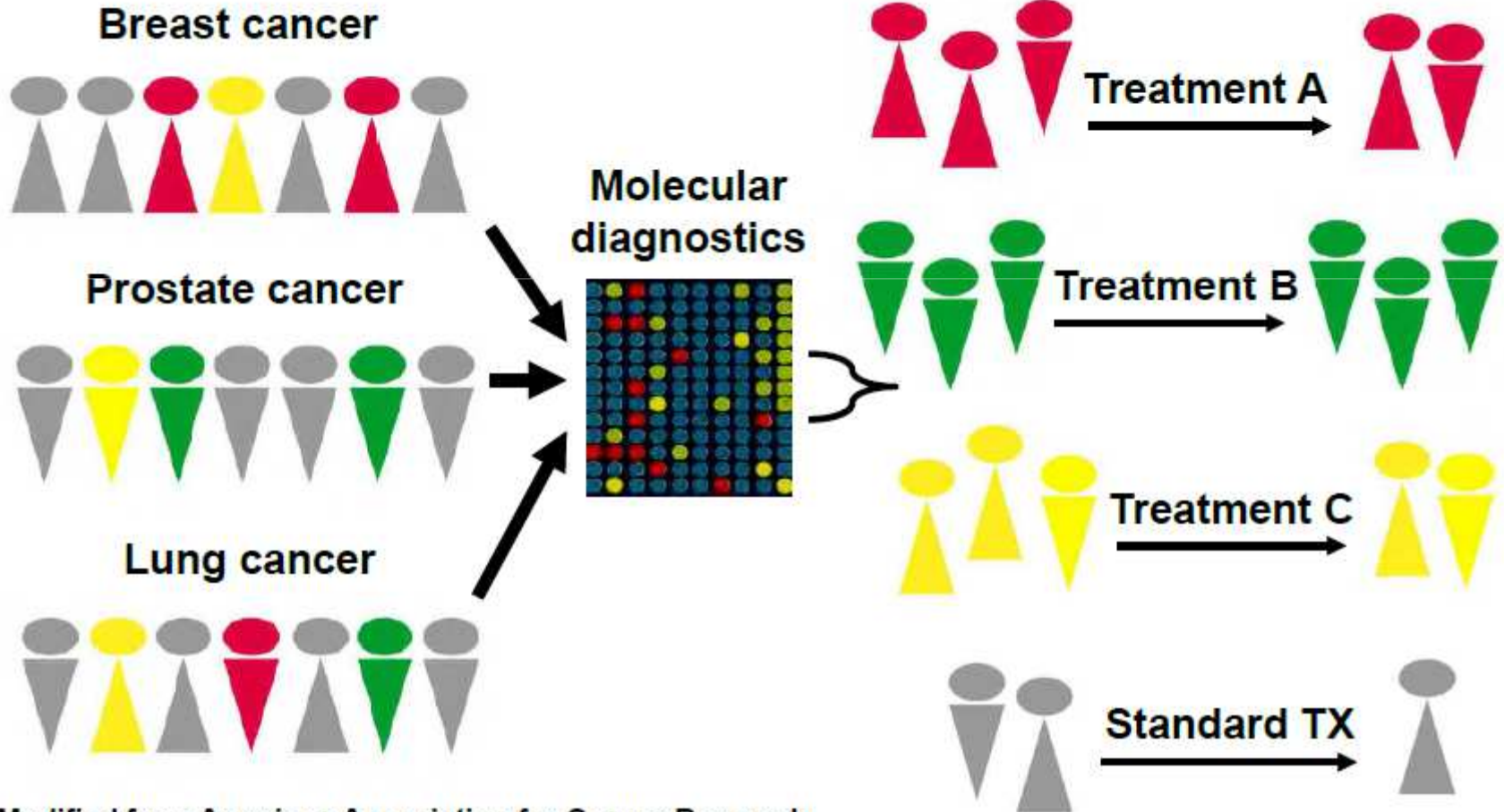


Biopsia liquida

- Busqueda de celulas tumorales aisladas o ADN tumoral en sangre periferica, efusiones u otros fluidos (humor acuoso)
- Facil acceso
- Permite monitoreo continuo
- Dificultades tecnicas en pediatria

¿Como se aplica en la clinica?

Precision Medicine



Modified from American Association for Cancer Research



Diagnostico y estimacion de riesgo

- Tumores del SNC
- Neuroblastoma
- Sarcomas



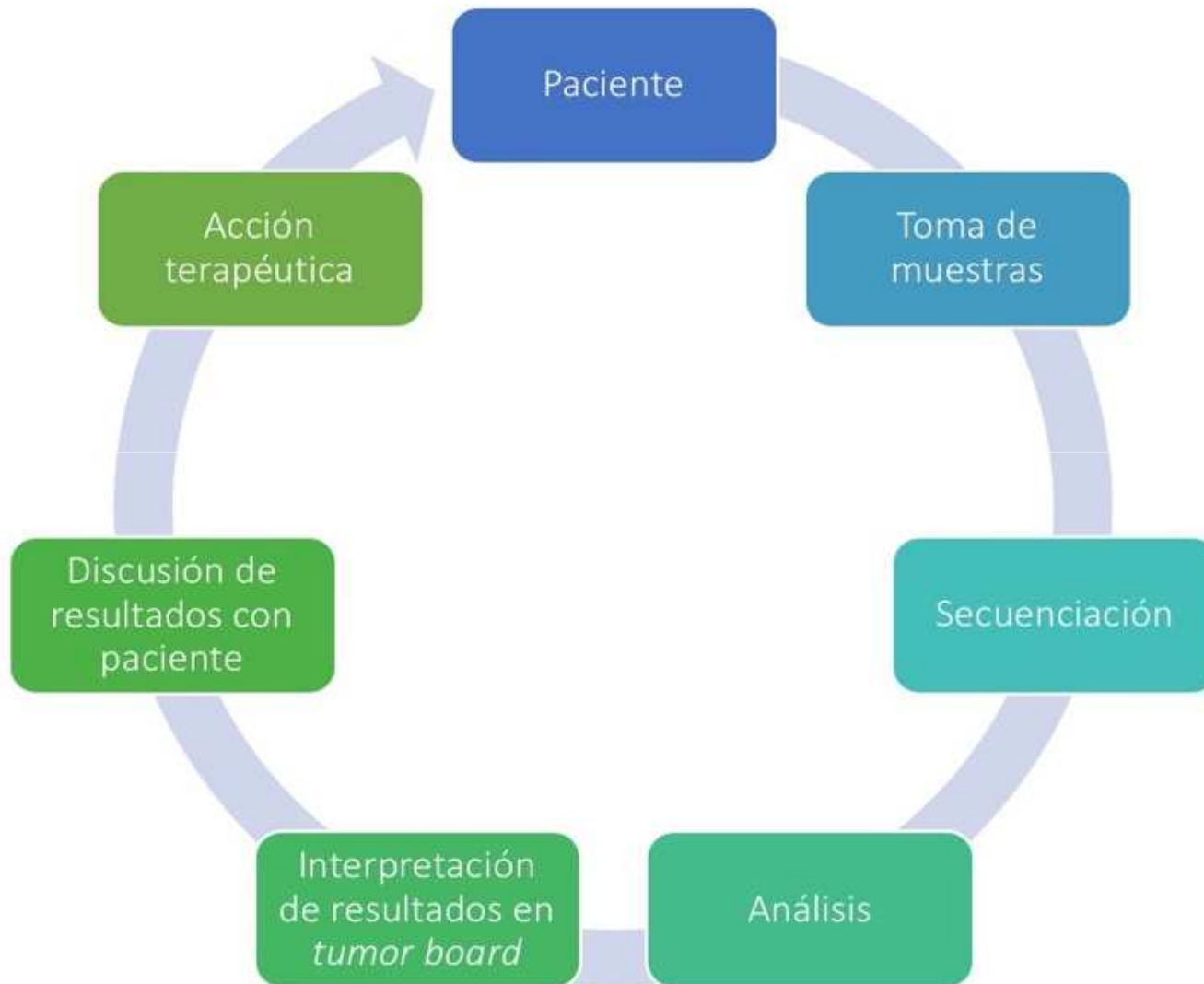
Variaciones epidemiologicas

- Neuroblastoma
- Ewing
- Retinoblastoma
- Tumores hepaticos



Tratamientos innovadores

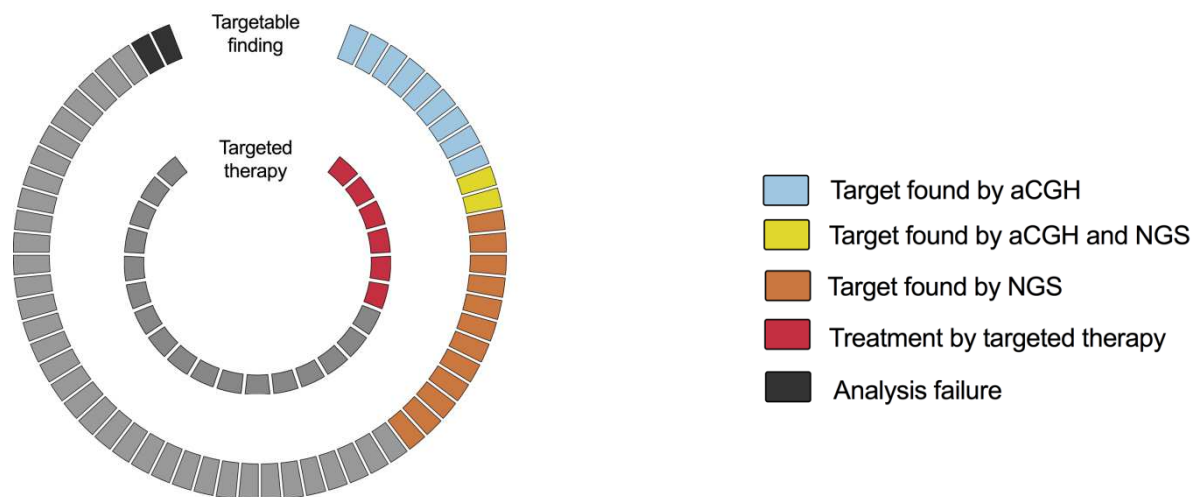
- Blancos moleculares alternativos con drogas conocidas
- Desarrollos propios de terapias dirigidas



Molecular Tumor Board (Jan – Dec 2015): Molecular analysis to search for targetable genes (DOPAJA, I Curie)

Analyses for 67 patients
Median age: 11, range: 0 – 21 years

⇒ 22 patients with alterations of targetable genes
⇒ ie 34 % of the patients



Cortesia F Doz

Programa HUA-HSJD

- 5 pacientes estudiados
- Secuenciación en HSJD
- Interpretación en panel multidisciplinario
- Futura expansión a PDX

Problemas

- Disponibilidad de drogas para blancos accionables
- Costo
- Incidentalomas. Desafios eticos
- Material tumoral representativo (heterogeneidad tumoral, estroma)
- Necesidad de multiples agentes en pacientes refractarios-recaidos

Molecularly targeted therapy based on tumour molecular profiling versus conventional therapy for advanced cancer (SHIVA): a multicentre, open-label, proof-of-concept, randomised, controlled phase 2 trial

Lancet Oncol 2015

Published Online

September 3, 2015

[http://dx.doi.org/10.1016/S1470-2045\(15\)00188-6](http://dx.doi.org/10.1016/S1470-2045(15)00188-6)

51470-2045(15)00188-6

Christophe Le Tourneau, Jean-Pierre Delord, Anthony Gonçalves, Céline Gavoille, Coraline Dubot, Nicolas Isambert, Mario Campone, Olivier Trédan, Marie-Ange Massiani, Cécile Mauborgne, Sébastien Armanet, Nicolas Servant, Ivan Bièche, Virginie Bernard, David Gentien, Pascal Jezequel, Valéry Attignon, Sandrine Boyault, Anne Vincent-Salomon, Vincent Servois, Marie-Paule Sablin, Maud Kamal, Xavier Paoletti, for the SHIVA investigators

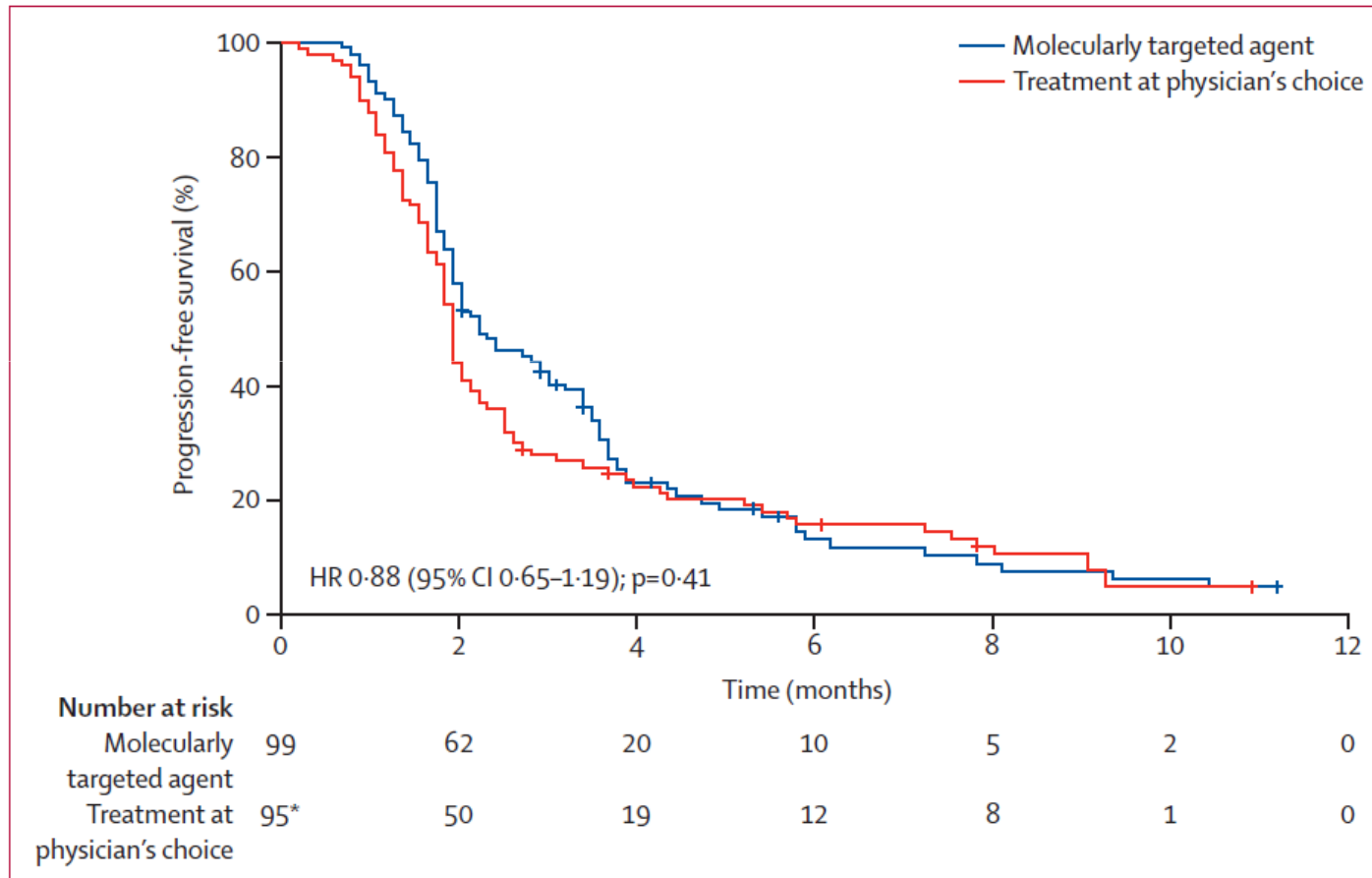


Figure 3: Progression-free survival

*One patient had a follow-up of zero days so is not shown here.

Original Investigation

September 2017

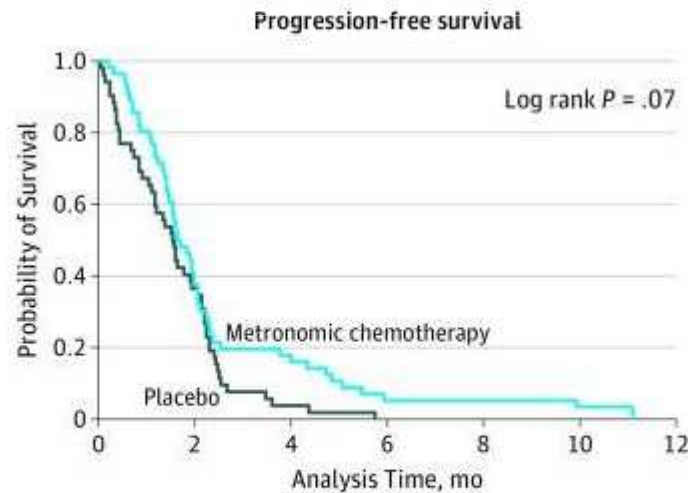
Metronomic Chemotherapy vs Best Supportive Care in Progressive Pediatric Solid Malignant Tumors

A Randomized Clinical Trial

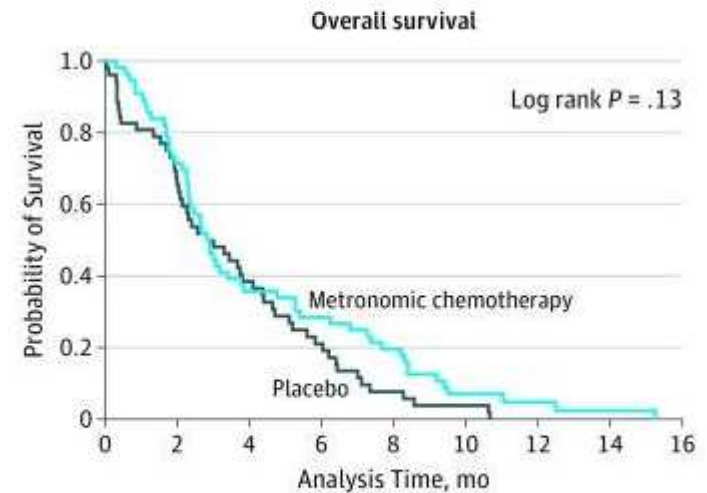
Raja Pramanik, DM¹; Sandeep Agarwala, MCh²; Yogendra Kumar Gupta, MD³; et al

> Author Affiliations

JAMA Oncol. 2017;3(9):1222-1227. doi:10.1001/jamaoncol.2017.0324



No. at risk	0	2	4	6	8	10	12
Placebo	52	19	2	0	0	0	0
Metronomic chemotherapy	56	21	10	3	3	1	0



No. at risk	0	2	4	6	8	10	12	14	16
Placebo	52	35	20	11	4	2	0		
Metronomic chemotherapy	56	40	20	16	11	3	2		

Conclusiones

- La medicina de precision provee un nuevo paradigma en el manejo de pacientes con cancer pediatrico
- Probablemente su uso sea mas efectivo en una mejor asignacion de tratamiento y diagnostico
- Nuevos desafios: farmacos dirigidos, costos, calidad de vida