An introduction to decentralized and virtual clinical trials

The Spiderweb Model

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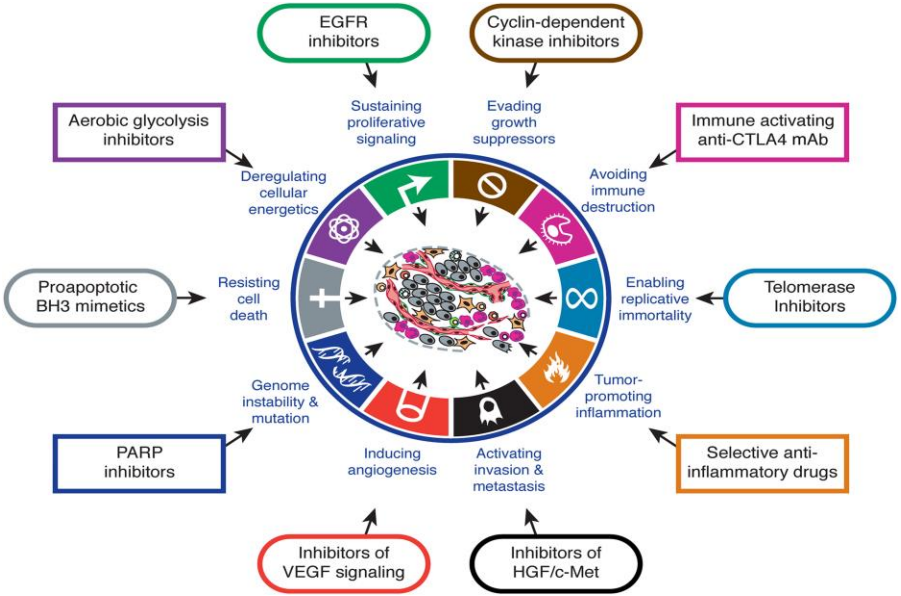
15th BSMO - 3/12/2021

Biology of cancer cells is better understood

Cancer care 15 years ago:

-Treatment based on histology, location and size
- Few biomarkers
- Basic treatment modalities

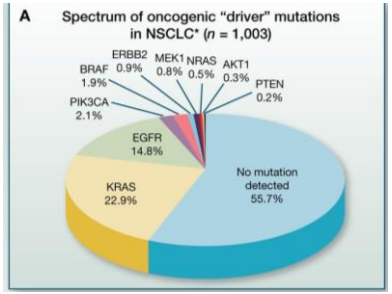


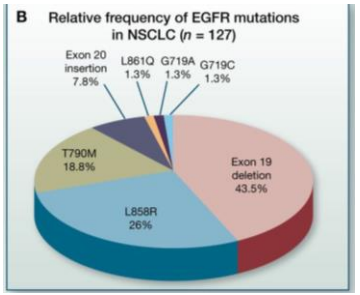
Hanahan et Weinberg, 2011

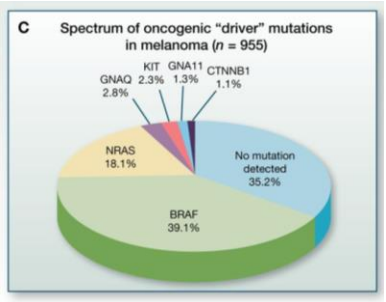
From empirical oncology to molecular and immunological therapeutic approaches

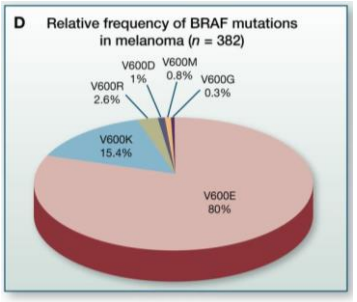
Common cancers now collections of rare cancers

Tumor types are divided in several cancer subtypes depending on molecular characteristics









Catherine B. Meador et al. Clin Cancer Res 2014;20:2264-2275

Precision medicine has proven to be efficacious

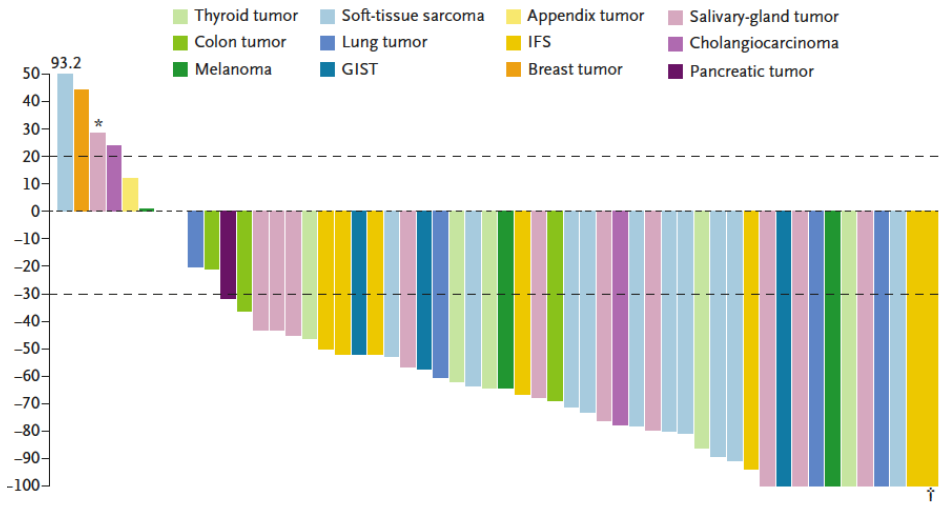
Example of TRK fusions

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of Larotrectinib in *TRK* Fusion–Positive Cancers in Adults and Children

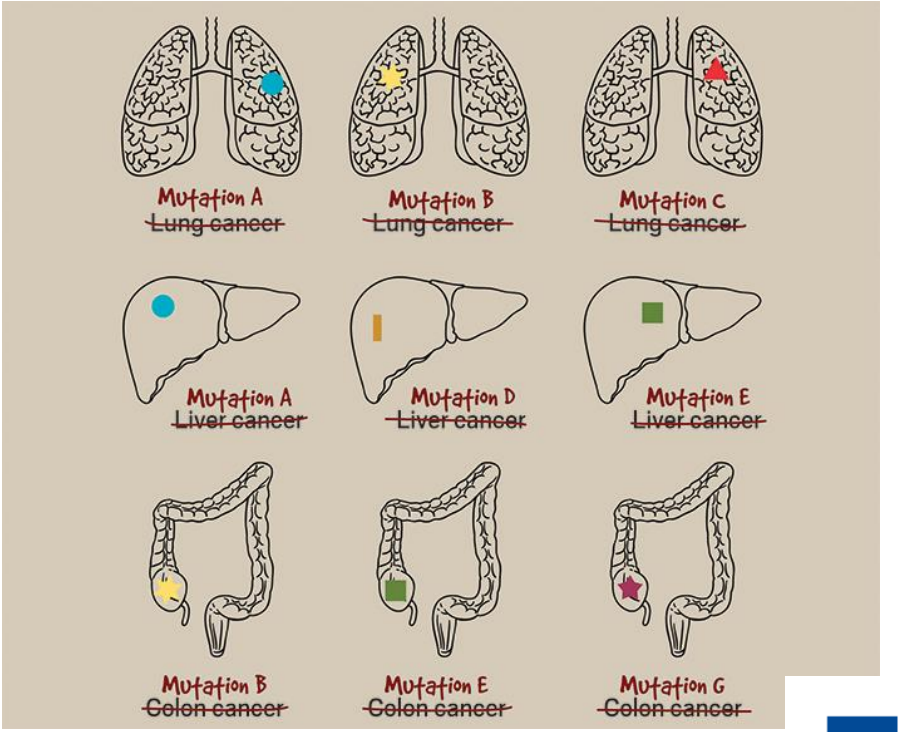
A. Drilon, T.W. Laetsch, S. Kummar, S.G. DuBois, U.N. Lassen, G.D. Demetri, M. Nathenson, R.C. Doebele, A.F. Farago, A.S. Pappo, B. Turpin, A. Dowlati, M.S. Brose, L. Mascarenhas, N. Federman, J. Berlin, W.S. El-Deiry, C. Baik, J. Deeken, V. Boni, R. Nagasubramanian, M. Taylor, E.R. Rudzinski, F. Meric-Bernstam, D.P.S. Sohal, P.C. Ma, L.E. Raez, J.F. Hechtman, R. Benayed, M. Ladanyi, B.B. Tuch, K. Ebata, S. Cruickshank, N.C. Ku, M.C. Cox, D.S. Hawkins, D.S. Hong, and D.M. Hyman



More and More « tumor-agnostic » treatment strategies

Treat patients based on cancer genetics and molecular features ..

without regards to the cancer type



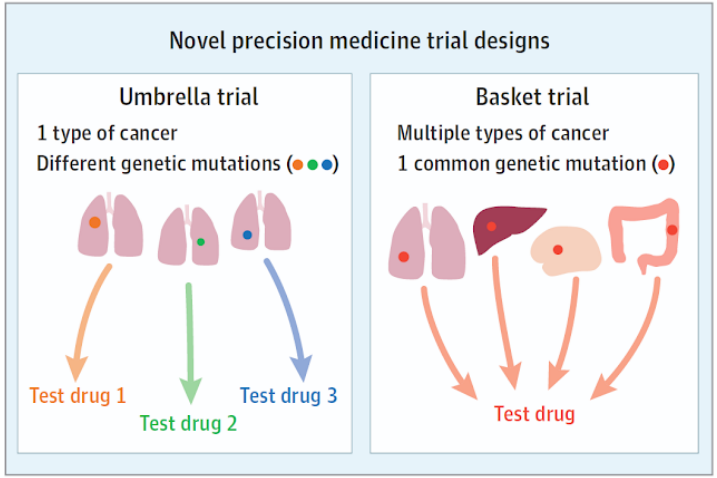
Credit: Yang H. Ku/C&EN/Shutterstock

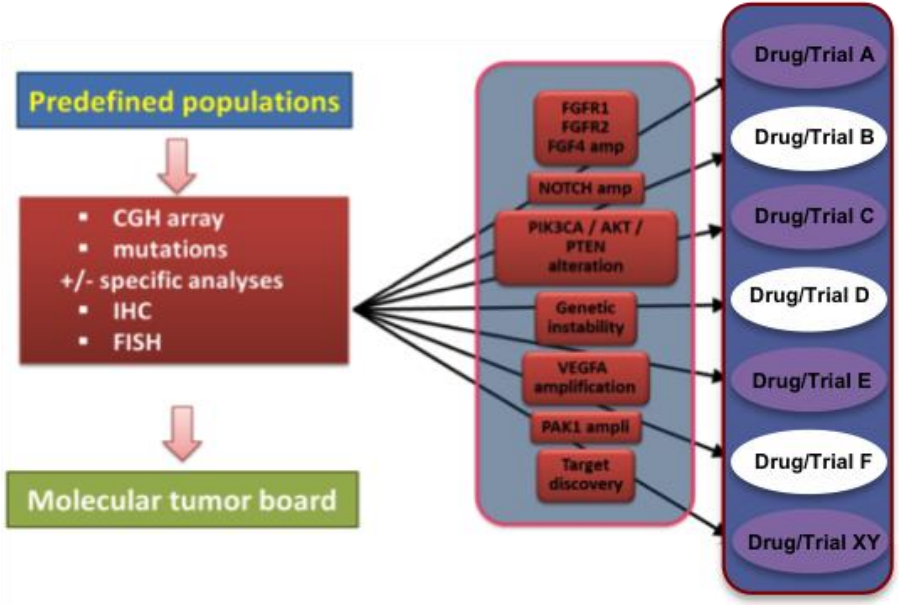
A lot of efforts at national and international levels are currently ongoing to implement NGS application in clinical practice

BALLETT

The Belgian Molecular Profiling Program of Metastatic Cancer for Clinical Decision and Treatment Assignment

From drug-oriented trials to target-oriented trials





Response rates in selected oncology Phase 1 trials

Series	Period covered	Trials included (*n*)	Patients (*n*)	Agents tested (*n*)	ORR	Grade 5 AEs at least possibly related to drug
Estey et al. (1986)	1974–1982	187	NR	54	4.2%	NR
Decoster et al. (1990)	1972–1987	211	6,639	87	4.5%	0.5%
Horstmann et al. (2005)	1991–2002	460	11,935	NR	10.6%	0.49%;
Roberts et al. (2004)	1991–2002	213	6,474	149	3.8%	0.54%
Schwaederle et al. (2016)	2011–2013	Biomarker-driven trials of targeted agents: 57	Biomarker-driven trials: 2,655	NR	31.1% (42% in the case of genomic biomarkers)	1.9%
		Non-biomarker-driven trials of targeted agents: *n* = 177	Non-biomarker-driven trials: *n* = 10,548		5.1%	NR
		Non-biomarker-driven trials of cytotoxic agents: *n* = 116			Non-biomarker-driven trials of cytotoxic agents: 4.7%	Non-biomarker-driven trials of cytotoxic agents: 2.2%
Waligora et al. (2018)	2004–2015	170	4,604	NR	10.29%	2.09%
Chakiba et al. (2018)	2014–2015	224	NR	224	19.8%	NR

AE, adverse event; NR, not reported; ORR, overall response rate

Adashek JJ et al; Nat Rev Clin Oncol. 2019 Dec

Challenges in “Biomarker-driven” clinical research

1. Tumor heterogeneity and **accumulation of rare genomic alterations**
   - Need for data sharing and molecular tumor boards to better orient patients

1. **Limited access** to marketed targeted agents or targeted-oriented clinical trials for cancer patients
   - High attrition rate
   - Ethical issues

2. Patients sometimes have **to travel even outside their home country and far from family** to access those specific clinical trials targeting a molecular abnormality.

3. Drug development is even more challenging that the molecular aberration targeted is rare
   - High number of patients to screen for 1 patient to be included in one clinical trial

1. **Administrative** burden and **financial** issues

Results of the ESMO survey on the administrative and bureaucratic burden in clinical research

Statement	Mean score (0=strongly disagree, 10=strongly agree) Overall score (n=940)	Research experience >5 years (n=690)
The current burden of administrative tasks in clinical research is excessive.	8.3	8.6
Current administrative and bureaucratic procedures in clinical research could be reduced without affecting the safety and rights of the patients and the quality of the data.	8.2	8.5
Current administrative and bureaucratic procedures represent an obstacle for the development of clinical research.	8.1	8.4
It is necessary to incorporate the feedback from physicians about the procedures related with clinical research.	8.6	8.8

JL Perez-Gracia et al., Esmo open 2021

There is an important medical need to:

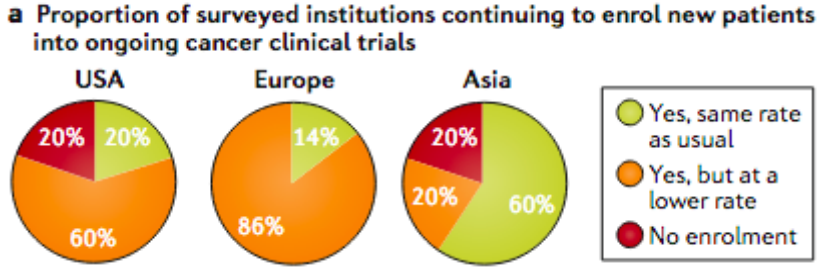
- Facilitate access to innovative targeted clinical trials for all cancer patients

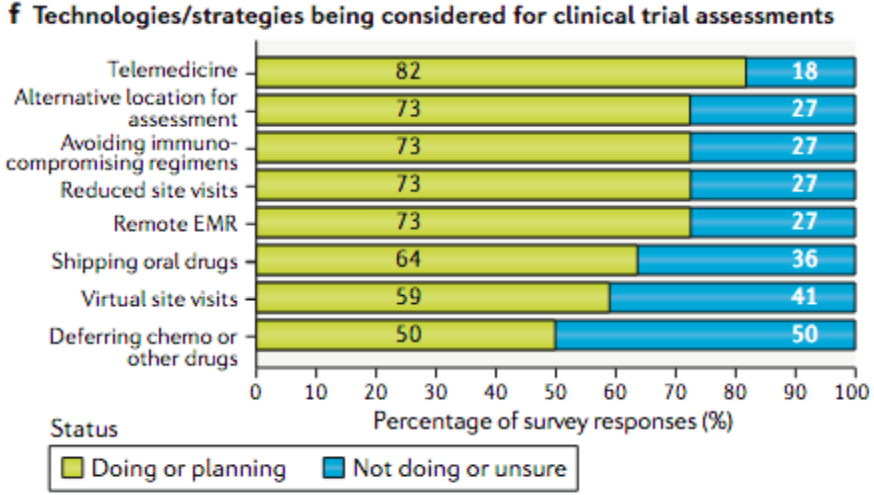
- Improve targeted drug development methodology in the era of precision medicine by building a network for innovative clinical trials in oncology

Impact of COVID-19 on oncology clinical trials

The COVID-19 pandemic has catalyzed the adoption of decentralized clinical trials.

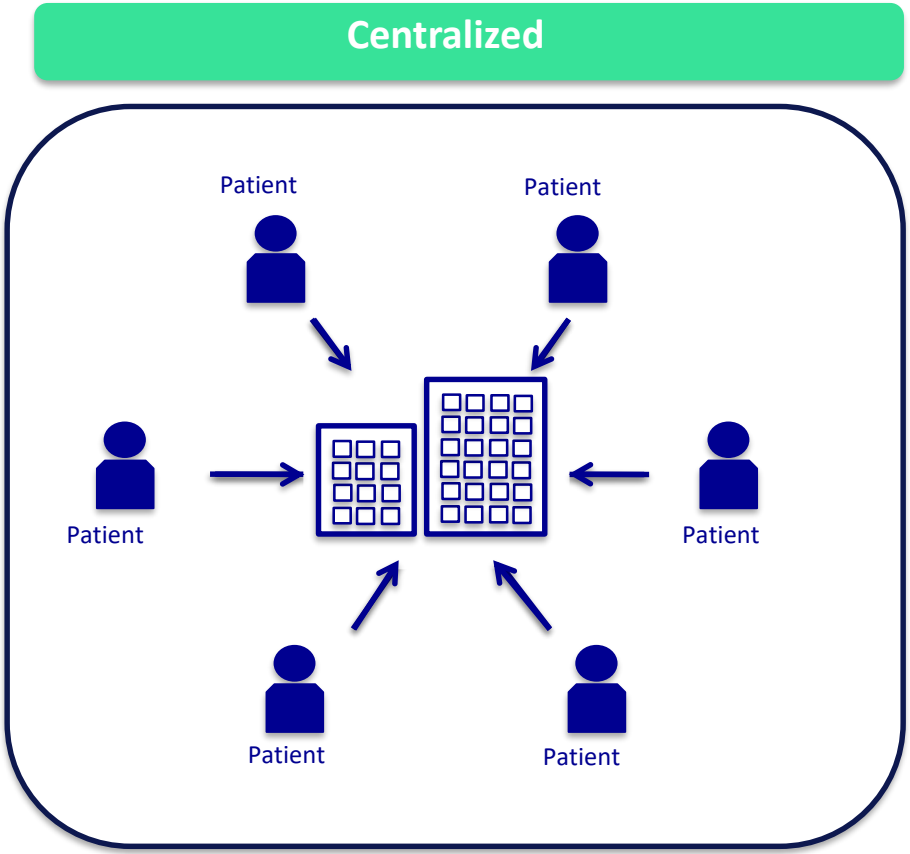
Bringing trial's activities to the patients rather than using the traditional paradigm of bringing patients to a trial site.





Upadhaya S,.Nat Rev Drug Discov. 18 mai 2020;19(6):376-7.

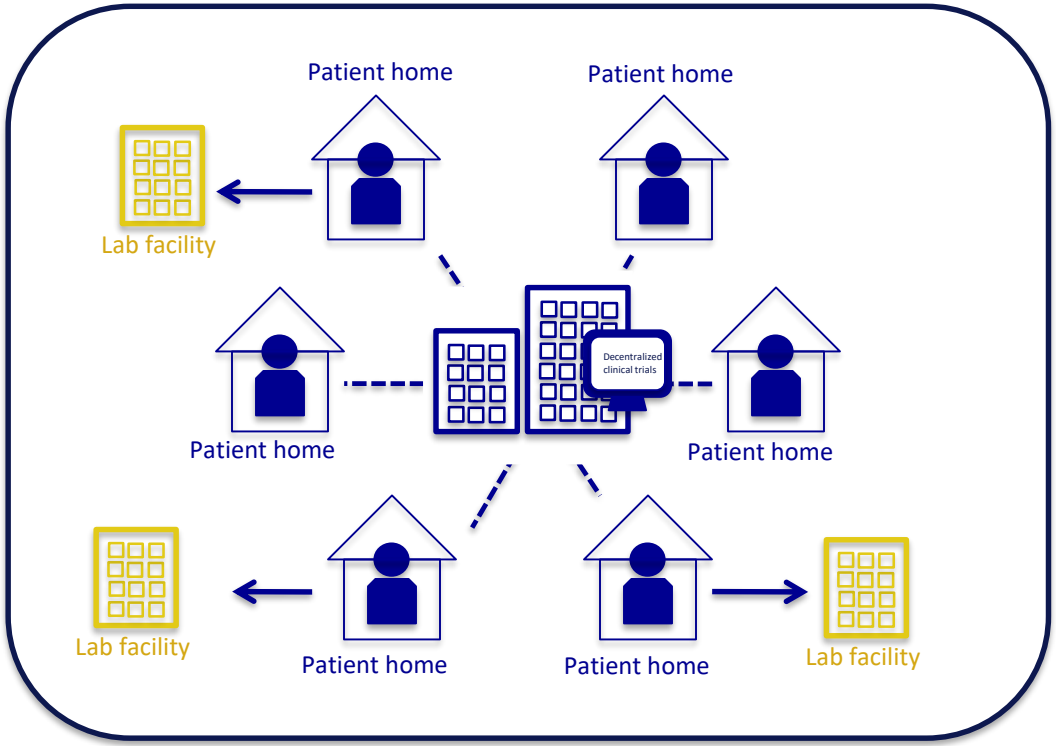
What are Centralized Clinical Trials ?



All trial procedures are conducted at a research site (eg: academic hospital)

Decentralized clinical trials or « Patient-centered » clinical trials

Decentralized



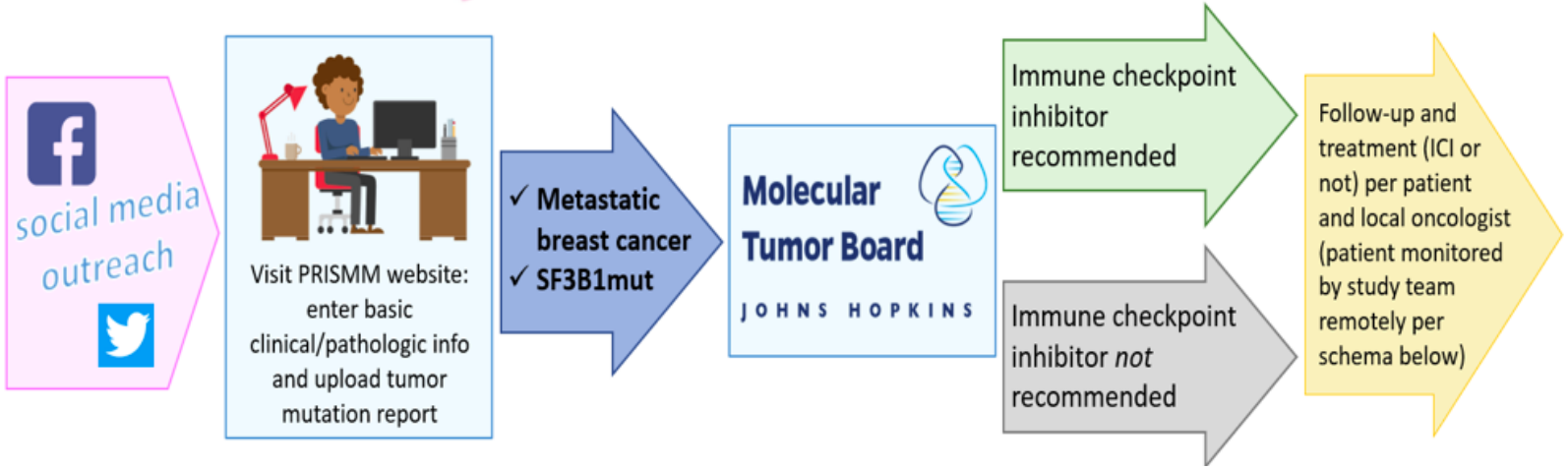
Hydrid

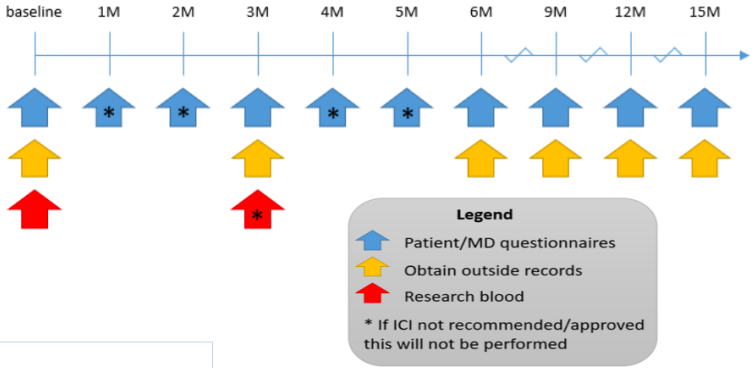
Complex trial procedures are conducted via research sites
Less complex trial procedures that don’t require in person visits are conducted via mobile clinicians, alternative sites, telehealthcare, remote data collection or direct to patient supply.

Virtual

All trial procedures are conducted virtually enabled by digital technology and supply delivery

PRISMM Design





Courtesy Cesar Santa-Maria

Hunter et al.,
SABCS Abstract OT-13-08 Dec 2020

Advantages for Decentralized clinical trials

- Improved logistics of conducting a clinical trial by improving recruitment and retention of patients

- Improved trial access for participant populations and recruitment times

- Reduced number of central research sites and the related administrative burden

- Improved compliance and potentially enhanced study safety.

- Reduced costs and workload for the coordinating site study team

- Outcomes that better reflect the safety and efficacy behavior of the study drug in a “real world” environment.

- Digitalized tools may allow more objective methods of measure.

Adapted from Van Norman GA. *JACC Basic Transl Sci*. 2021

Challenges for Decentralized clinical trials

- Logistics for drug distribution and management

- Local Health authorities laws may need to be addressed

- Greater complexity and risk in clinical trials, both to the subjects themselves and to the integrity of the trial

- Technological advances and devices requires clinical validation before being used

- Protecting patient privacy – stored on connected devices - and the information transmitted through connection services

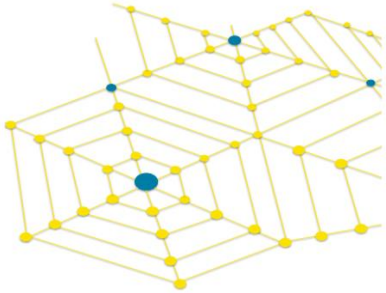
Adapted from Van Norman GA. *JACC Basic Transl Sci*. 2021

Spiderweb

A new model of “patient-centered” clinical research for biomarker-driven clinical trials called *“Spiderweb” model*.

- *« Bring the clinical trial to the patient »*
- *Master Agreement (MA) between sites which would allow a patient from a hospital to be treated on-site in a clinical trial opened at another hospital*

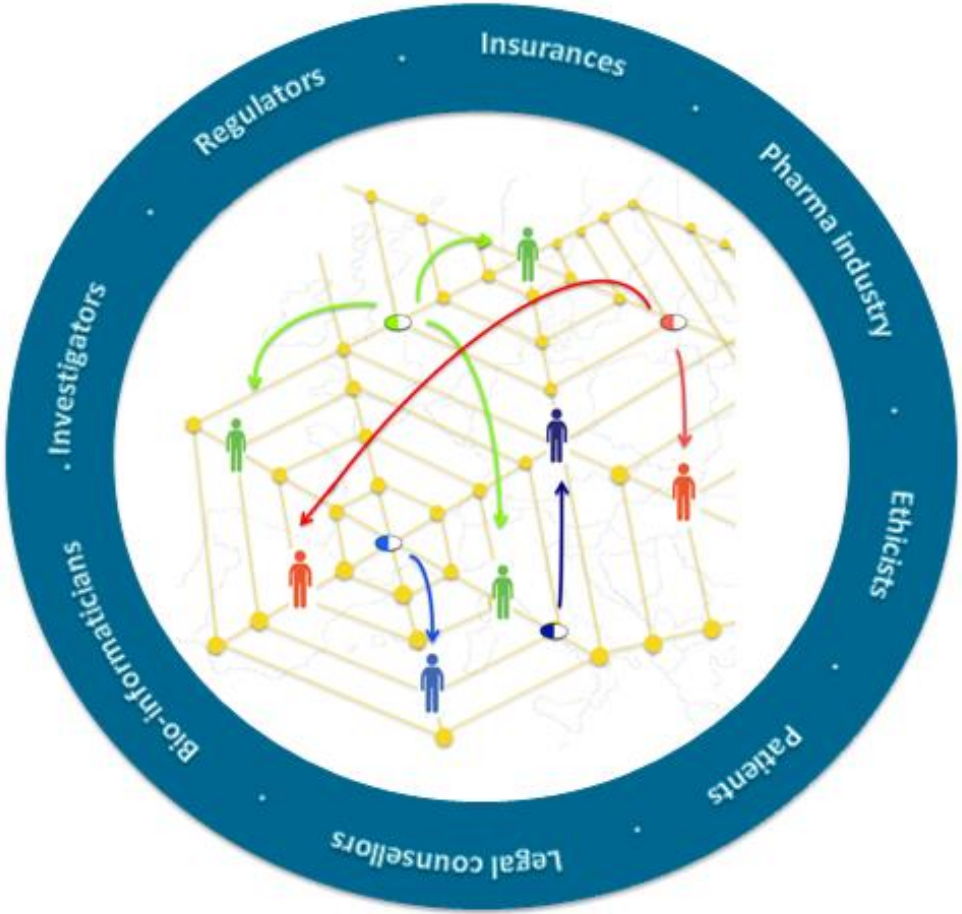
Panel of clinical trials covering as many targetable mutation as possible by working in close collaboration with pharma



Spiderweb management team

Coordinating site (CS) for a clinical trial *
- Site staff: PI , +/- Sub investigators, Study coordinators/nurse, Data managers

Site with an eligible patient for the trial : Participating site
- Site staff: PI, Sub investigators, Study coordinators/nurses, Data managers


Insurances
Pharma industry
Ethicists
patients
Legal counsellors
Bio-informaticians
Investigators
Regulators

Process for initiating a clinical trial within Spiderweb

Contact the Spiderweb management team

Coordinating site selection process

Unique Site contract between the CS & Sponsor

PS are covered through the MA – using a common budget grid for academic & Pharma-sponsored

Study Insurance covering the CS

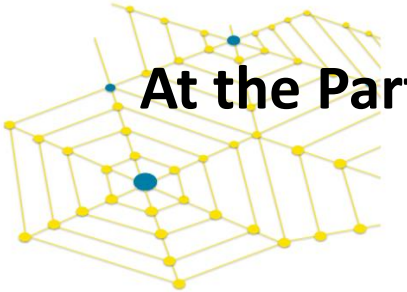
Extendable to PS whenever needed

Submit to CA/EC :

CS/PI and potential PS/PI delegate

Site initiation Visit at the CS

At the Participating Site level : *Process for study activation*



Contact the Spiderweb management team

Study specific Annex to the MA to be signed from both parties

Signed MA

identify Patient based on NGS tests at one site → Identify a clinical trial → Become a Participating Site → Inform patient in the Participating Site → Patient screening and treatment in the participating site

Remote SIV

Drug supply

Shared matched « Spiderweb » biomarker/clinical trial database

A new model of “patient-centered” clinical research for Biomarker-driven clinical trials: Spiderweb model, a proposition of the Oncodistinct Network

Partnering project

mypl
My Personal Lifescope

ONCODISTINCT NETWORK

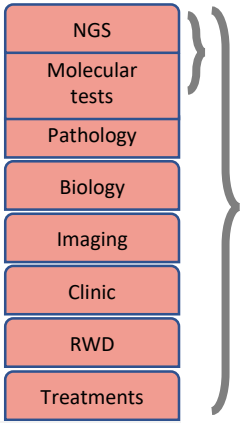
Christophe Vergne, CEO
Jean-Alexandre Kaminisky, COO
Justin Pariente, Project Manager

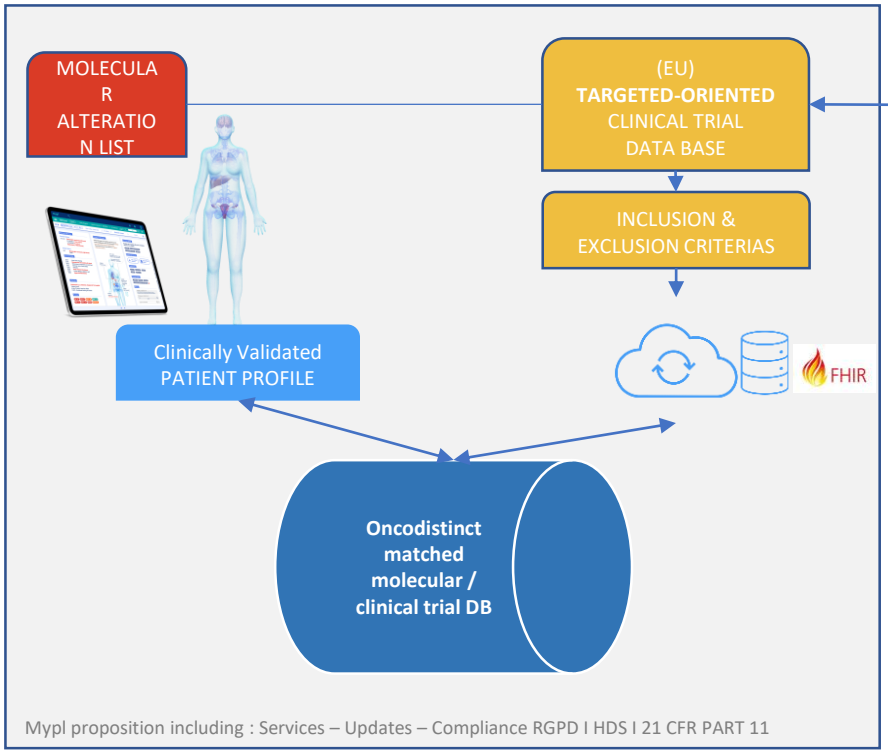
MYPL GATHERS, STRUCTURE & PRESENTS MEANINGFUL CANCER DATA TO SPEED **DECISION MAKING** FOR HEALTHCARE PROFESSIONALS & RESEARCH

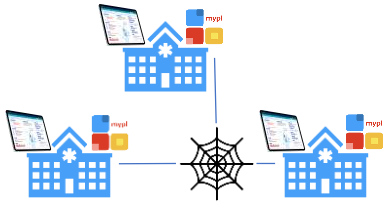
Shared matched molecular alteration/clinical trial database *(covering a large panel of targetable mutations)*

- *Foster access to innovative clinical trials for patients*
- *Encourage Pharma industry to participate to the Spiderweb model*
- *Create a shared academic database*

Building a data base of patient profile and biomarker-driven clinical trial– *(Pilot phase 4 sites)*







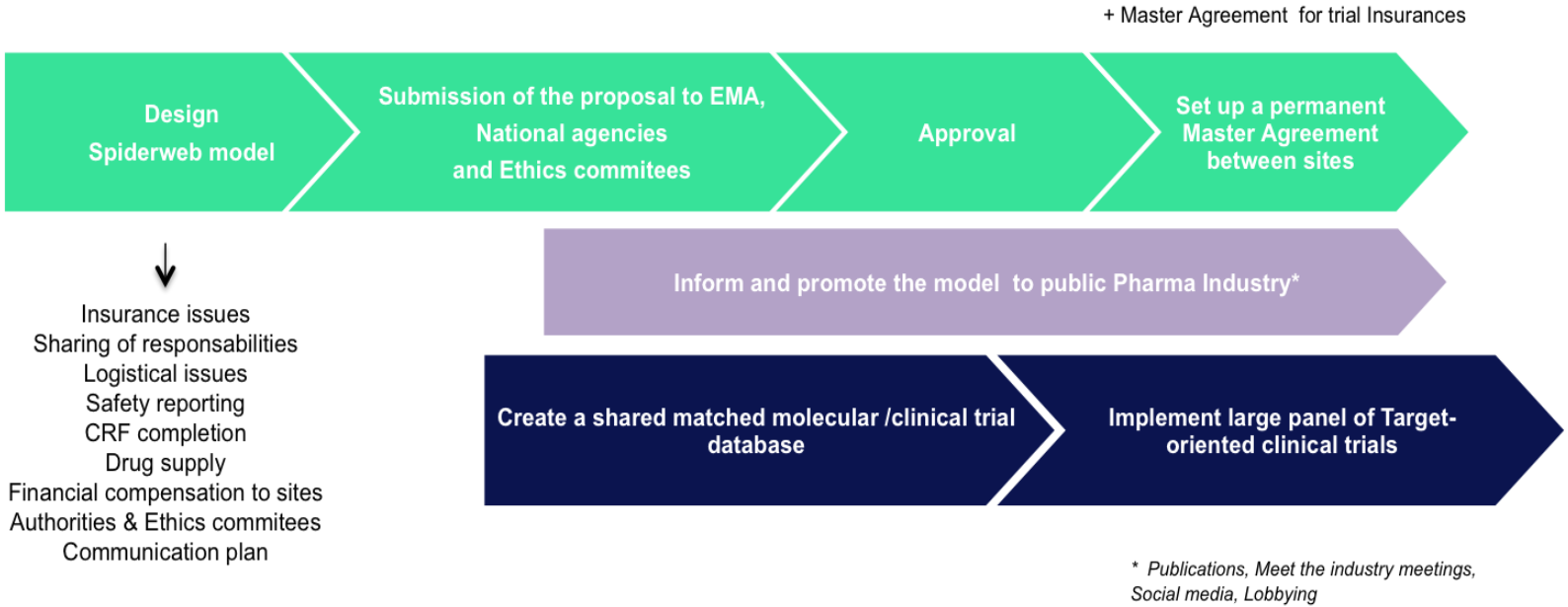
Data loading
Two complemenary solutions :

- **Full mypl solution** sites : automatic data gathering
- **mypl DB** sites : manual data gathering by an onsite person (Clinical Research Associate)

Somatic genomic events include fewer mutations, alterations in the number of copies and structural variants

"Spiderweb" model Workflow and next steps

Work package 1: Spiderweb Model Master Agreement
Work package 2: Communication plan and lobbying
Work package 3: Shared matched molecular clinical trial database



* *Publications, Meet the industry meetings, Social media, Lobbying*

"Accelerating Oncology drug Development and Innovative strategies in Clinical Trials"

@oncodistinct

Contact: nuria.kotecki@bordet.be