OMICS and AI TO NOVEL TRIAL ADDRESS

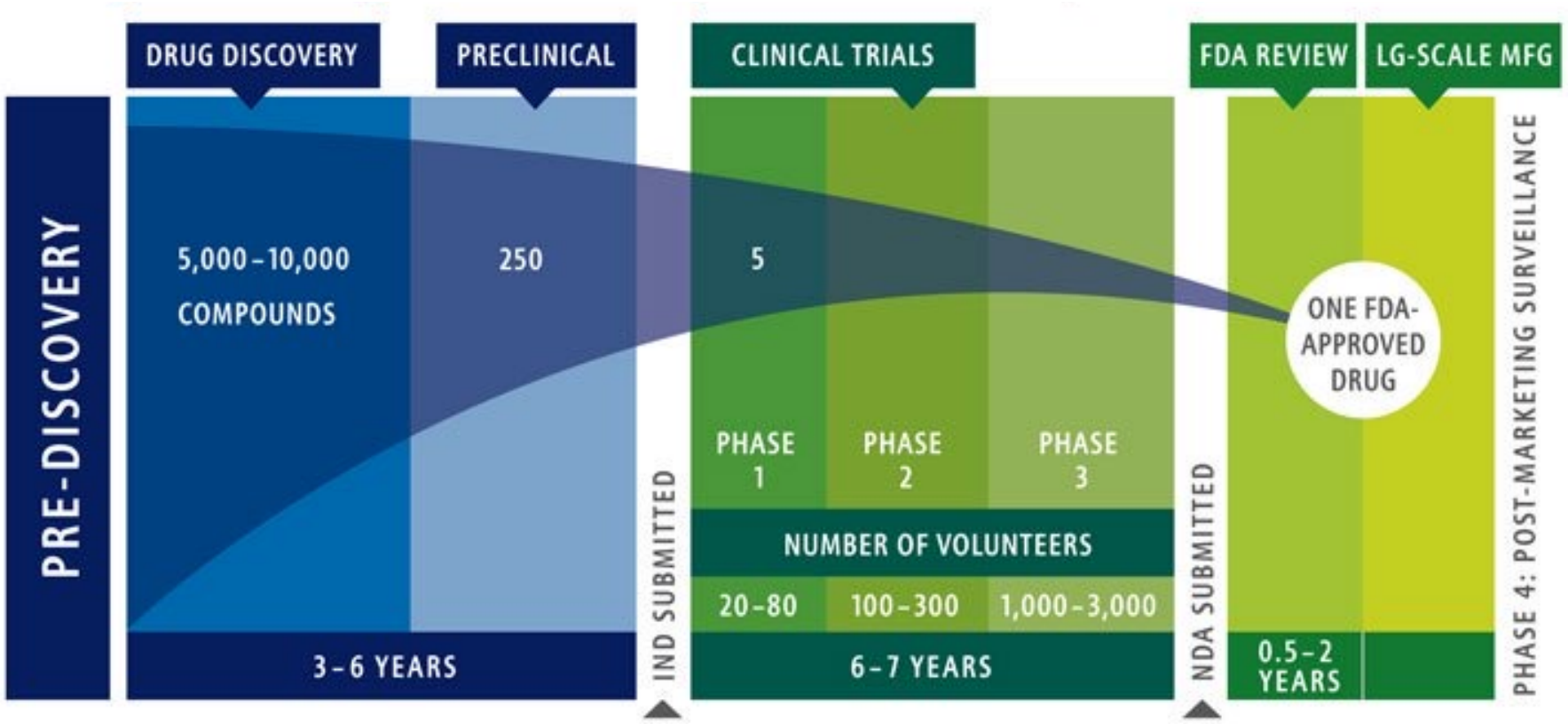
AI applications in modern oncology: What reliable supports for clinical decisions?

Camilla Nero

WHERE ARE WE NOW?

IMPRECISION MEDICINE

Slow, expensive, ineffective and wasteful



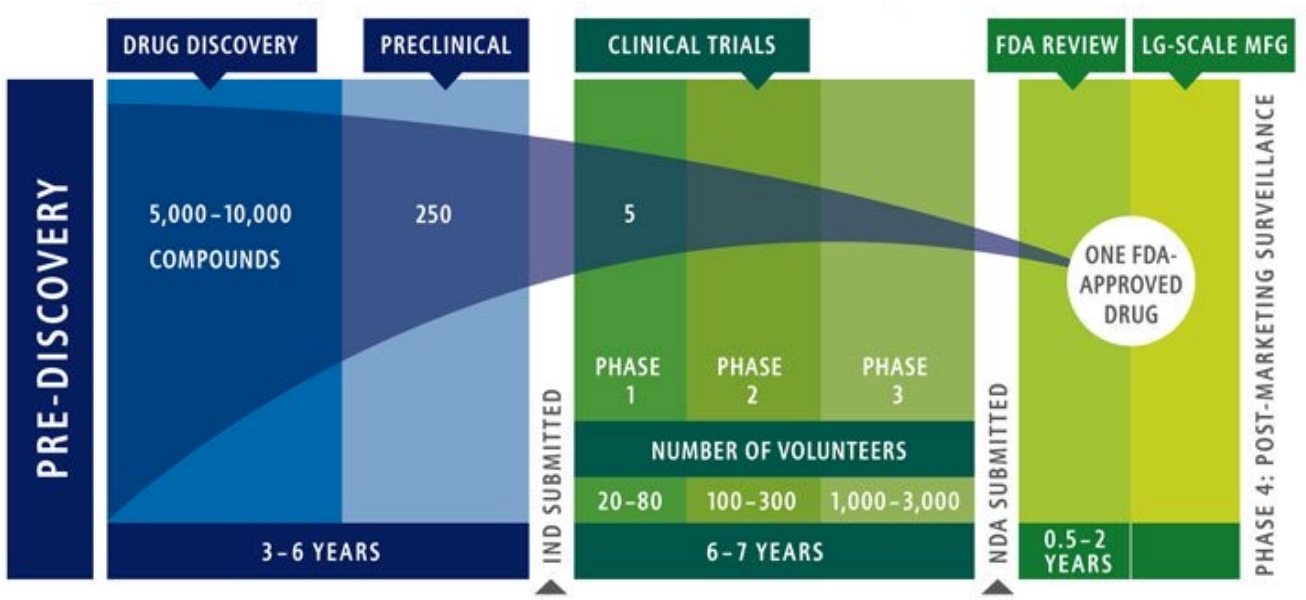
Drug Candidate Type	Approval Rate
Oncology (antiancer drugs)	3.4%
Endocrinology (hormones)	19.6%
Cardiovascular (heart/circulatory system)	25.5%
Central Nervous System (brain/spinal cord)	15.0%
Autoimmune and Inflammation	15.1%
Ophthalmology (eye disorders)	32.6%
Infectious disease (including vaccines)	25.2%
Other uncategorized	20.9%

2009-2018

source: Pharmaceutical Research and Manufacturers of America

IMPRECISION MEDICINE

Slow, expensive, ineffective and wasteful



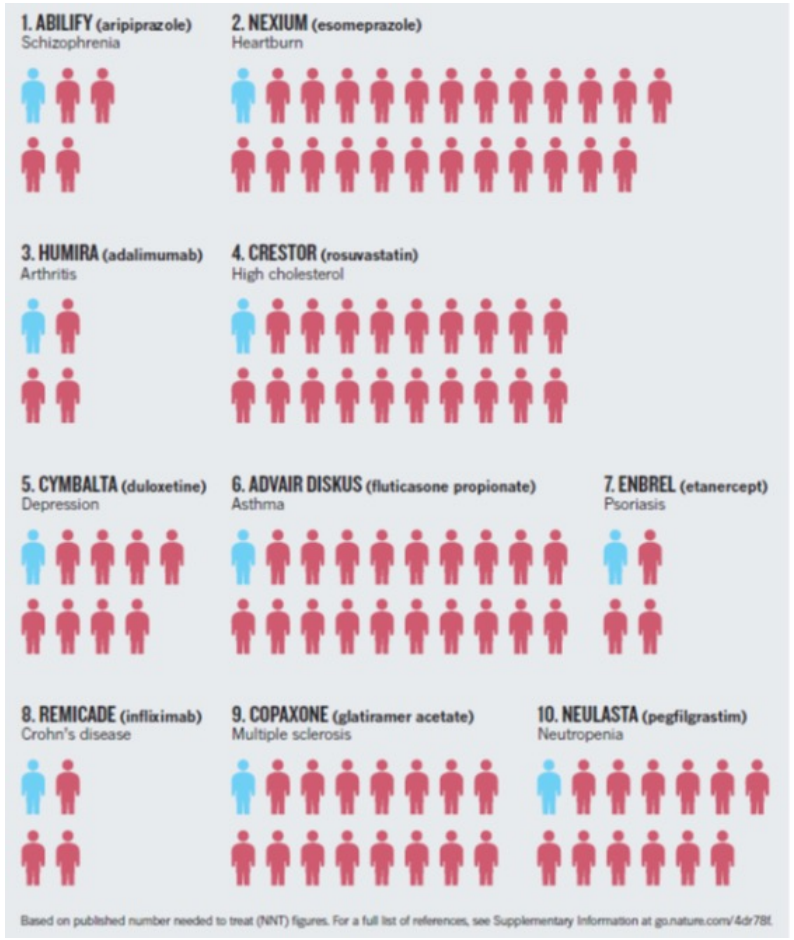
$1.8B

2018	**1,064** $ million	**446** $ million	**2** $ million
2022	**1,255** $ million	**526** $ million	**3** $ million

FTLO Science
Washington DC: Foundation For Biomedical Research
Wong, C. Biostatistics, 2018.
Mestre-Ferrandiz, J .2012
Paul S.M., et al, Nature reviews Drug discovery 2010

IMPRECISION MEDICINE

Slow, expensive, ineffective and wasteful



FAILURE TO IMPROVE THE CONDITION OF BETWEEN

3 TO 24

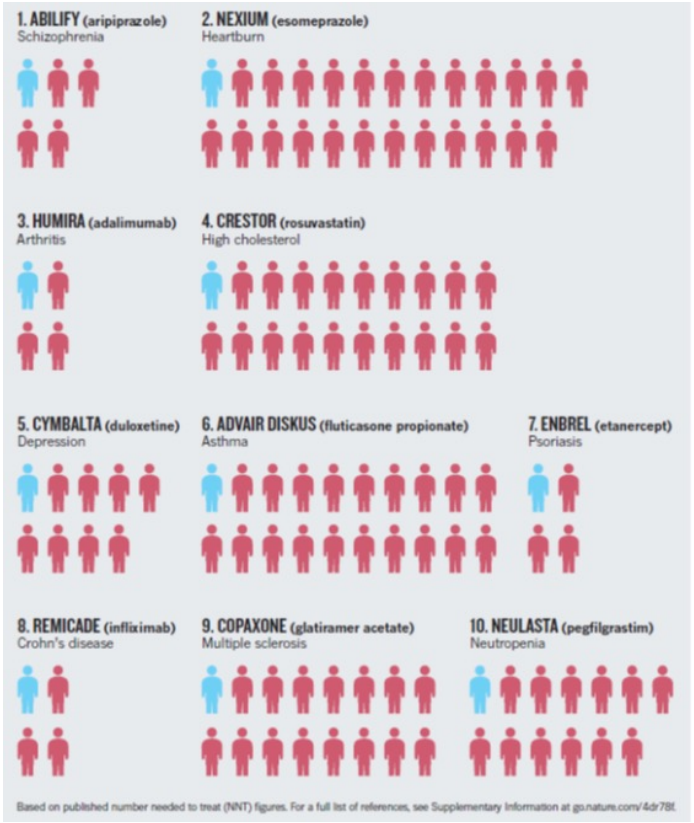
PEOPLE

Nature 2015

IMPRECISION MEDICINE

Slow, expensive, ineffective and wasteful

Response rate



Nature 2015

All costs incurred for top 10 drugs (billions)

Estimated waste

Nexium	Heartburn	$25.3	$2.42
Advair Diskus	Asthma	22.6	2.15
Crestor	Cholesterol	22.2	2.10
Abilify	Antipsychotic	21.1	1.69
Cymbalta	Antidepressant	19.6	1.76
Spiriva	Asthma	19.6	1.37
Namenda	Dementia	15.6	1.56
Januvia	Diabetes	14.6	1.02
Lantus Solostar	Diabetes	13.7	.27
Revlimid	Cancer	13.5	.54
Source: Centers for Medicare and Medicaid Services		Total $18.8B	$14.9B

The Wall Street Journal

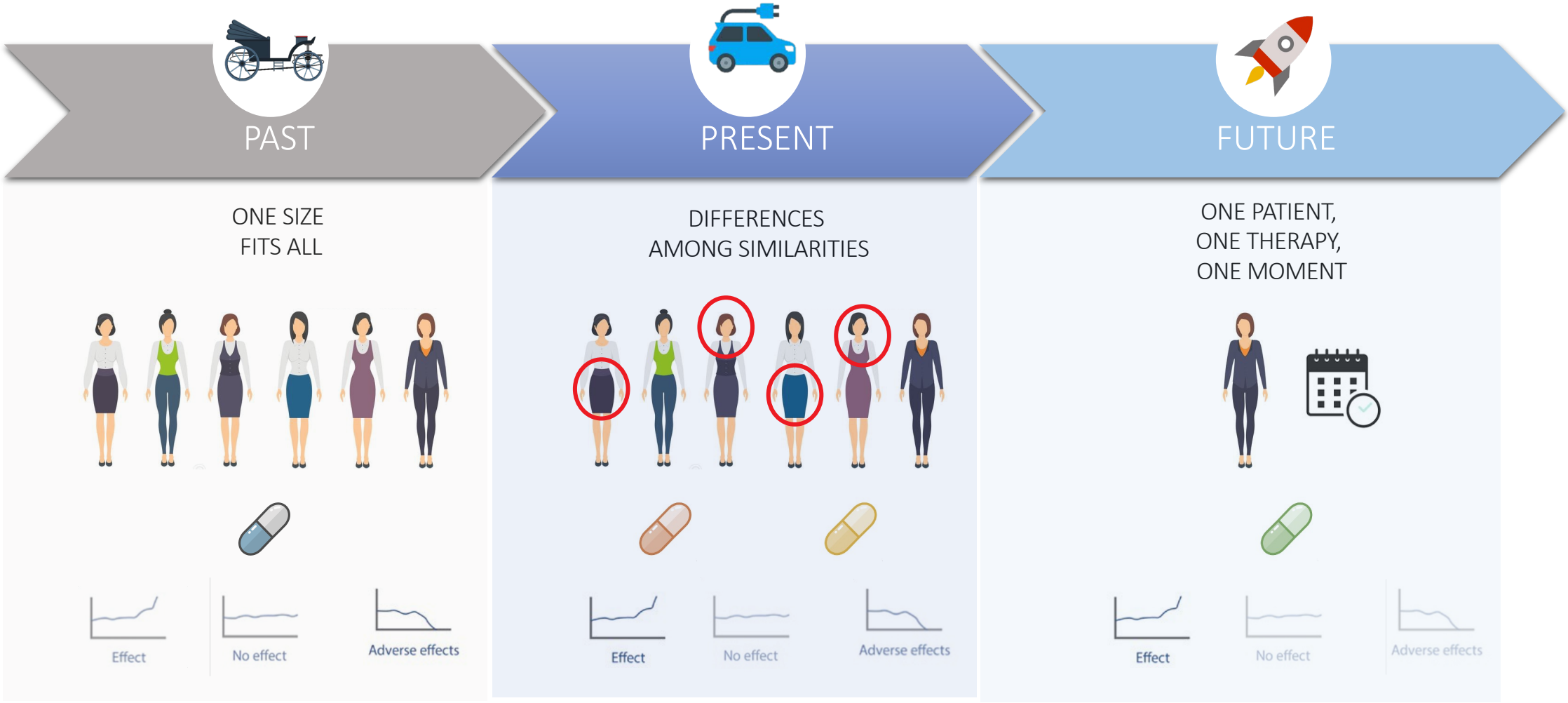
79%

WASTED

WHERE ARE WE GOING?

PRECISION AND PERSONALIZED MEDICINE

To the “one size fits all” approach to a N-of-1 trials

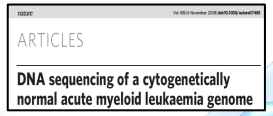


PRECISION MEDICINE

Technology evolution produced a paradigm shift

2000

First genome sequencing



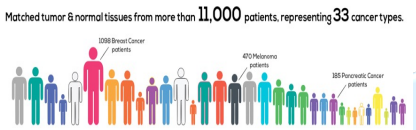
2008

First sequencing using Second-Generation-Technology

2012

Sequencing of 800 genomesfrom 25 different cancer types

TCGA



2015

More than 11.000 genoms from 33 different cancer types

2018

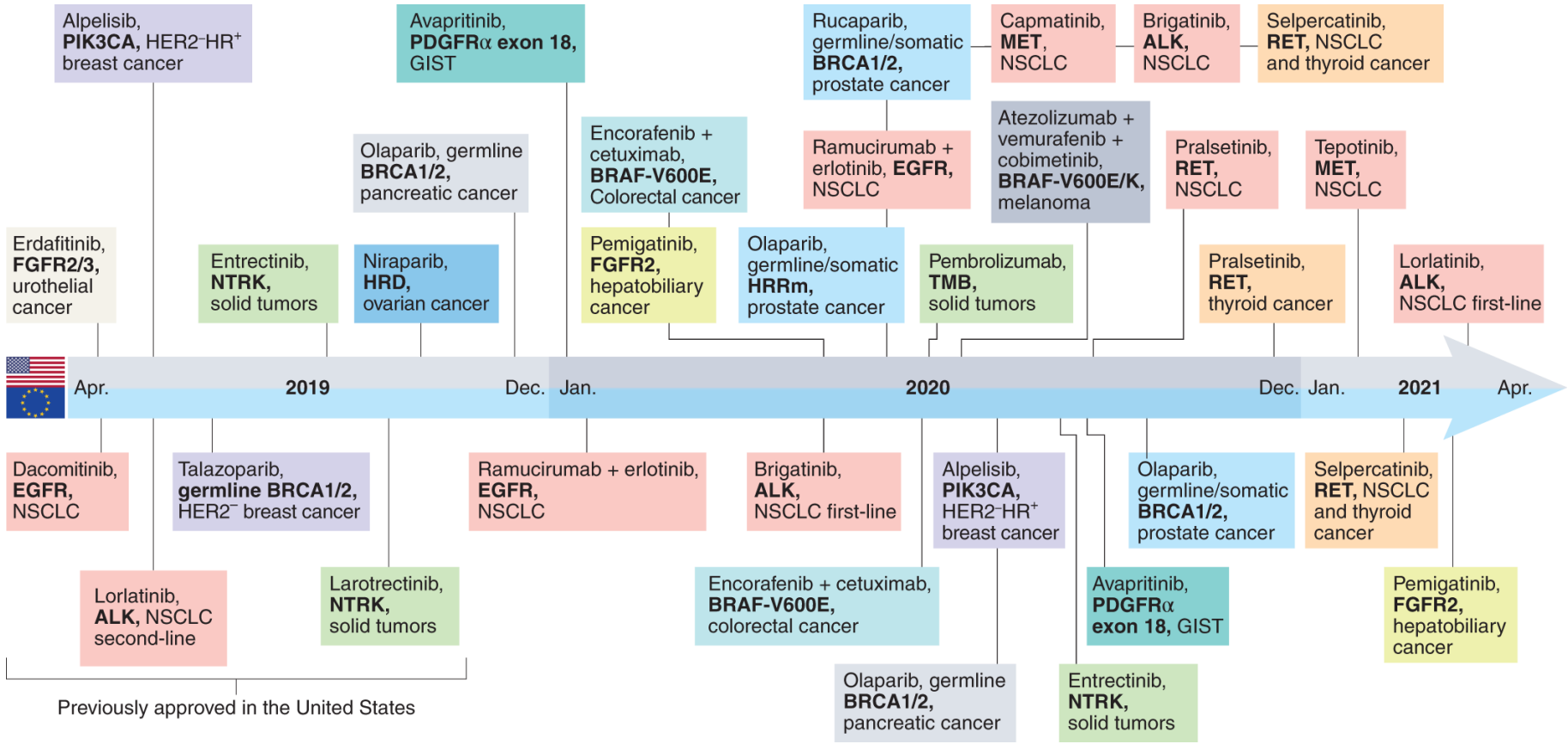
The Pan-Cancer Atlas

International project		One center
> 10 years		Few hours
3,8B US $		<1000 US $

18 YEARS

PRECISION MEDICINE

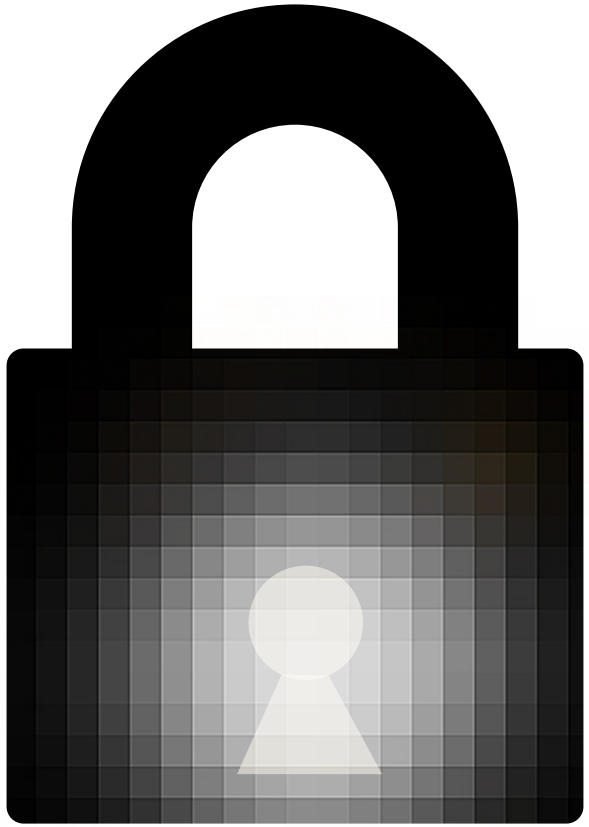
Target therapy in cancer: constant evolution



J. Mateu et al, Nature 2022

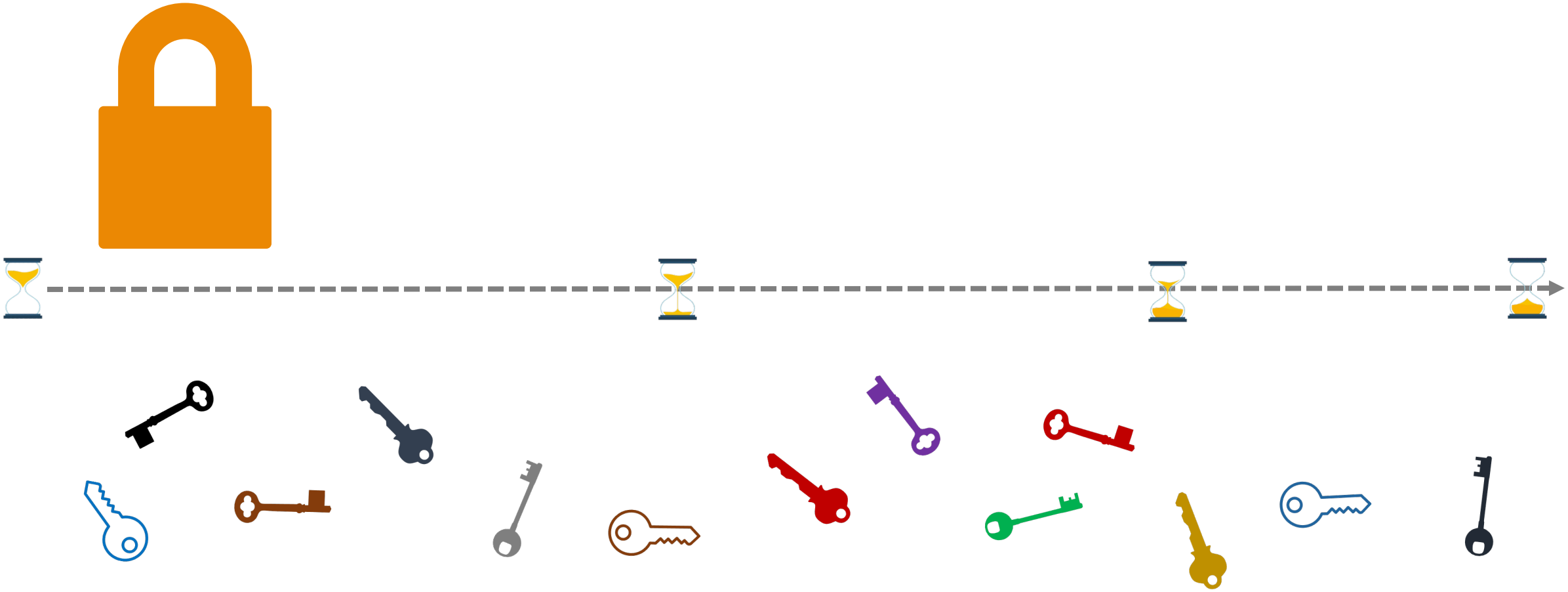
PRECISION MEDICINE

To win a war, you'd better know your enemy



PRECISION MEDICINE

To win a war, you'd better know your enemy

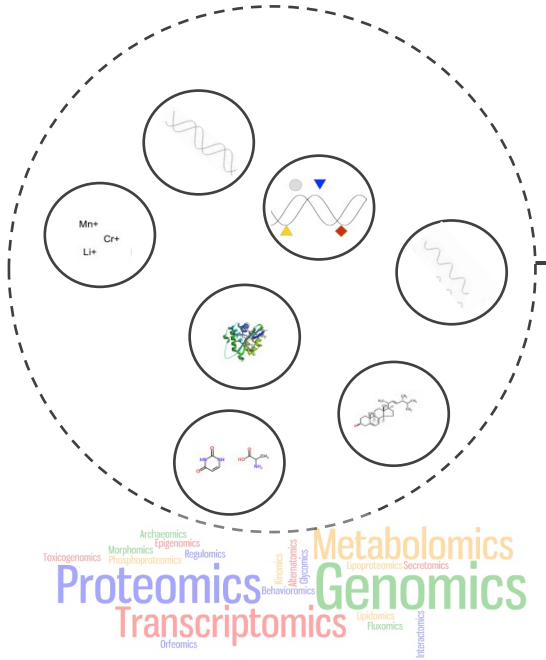


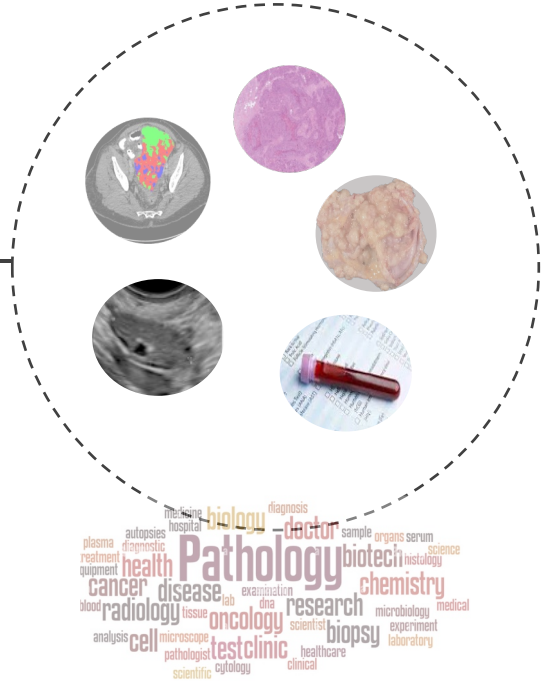
HOW CAN WE GO THERE?

PERSONALIZED MEDICINE

Integrated Multi-omics longitudinal profiling

CLINICAL
DATA 2.0

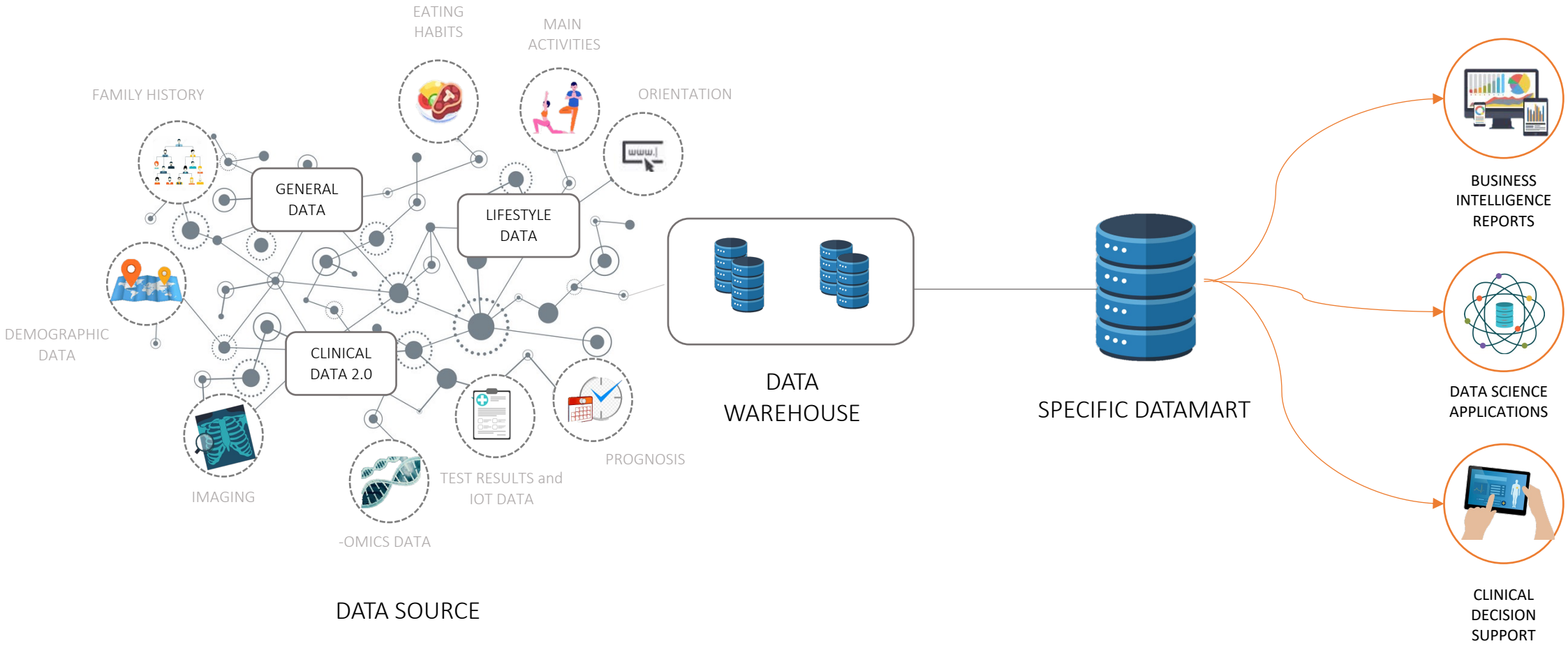




OVER TIME

TO PERSONALIZED MEDICINE

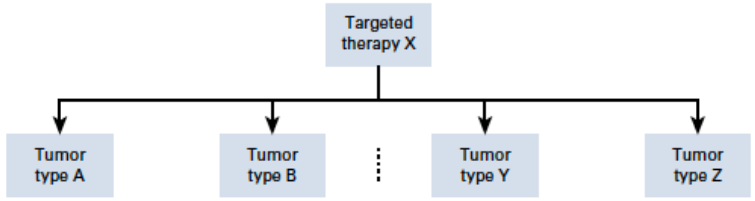
From data to information



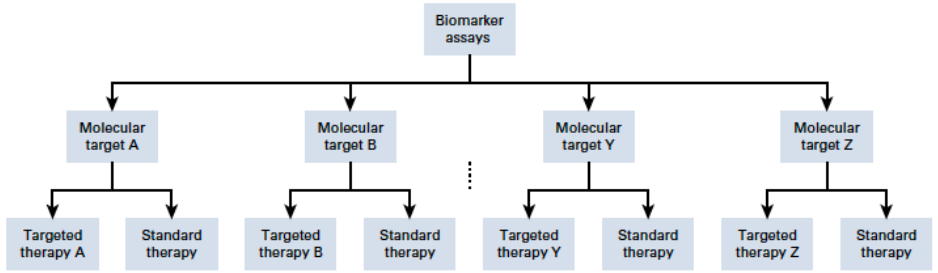
RE-DESIGNING CLINICAL TRIALS

Biomarker-driven oncology clinical trials

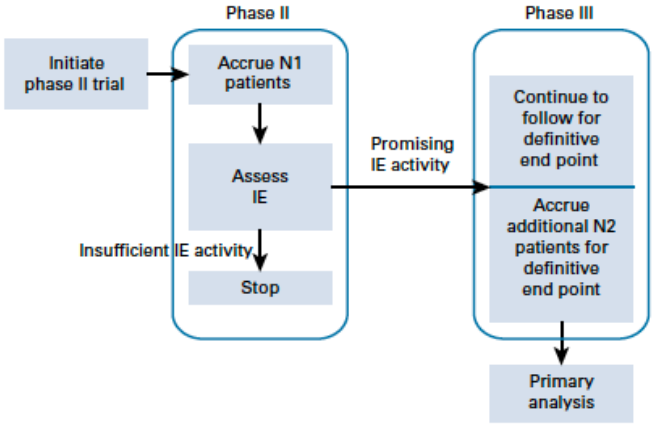
Basket trial



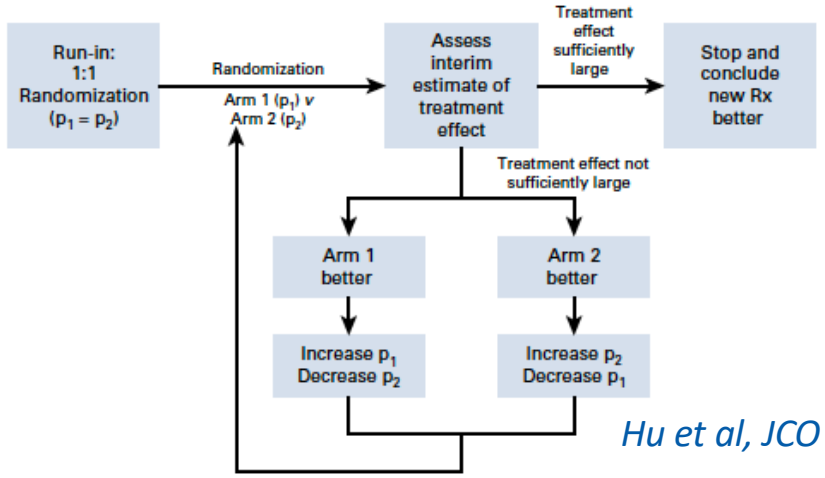
Umbrella trial



Seamless phase II/III design



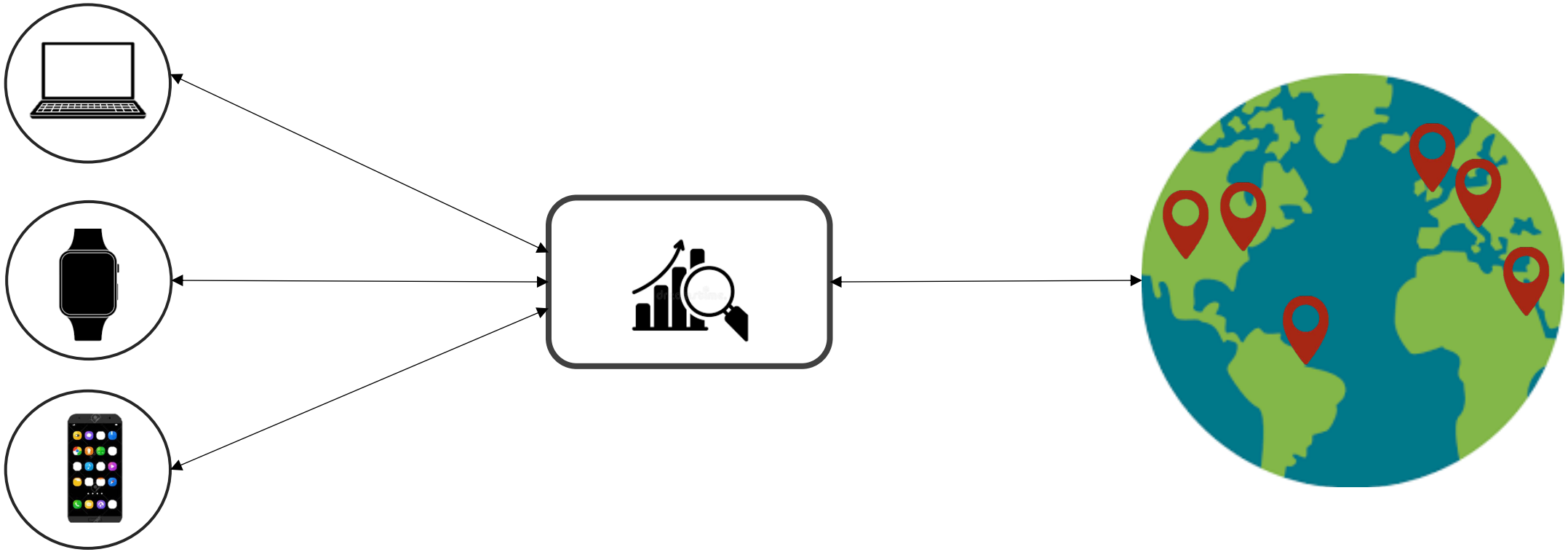
Outcome adaptive randomization



Hu et al, JCO Precision Oncology 2019

«DECENTRALIZED» CLINICAL TRIALS

Real time, world wide



Digital Technologies

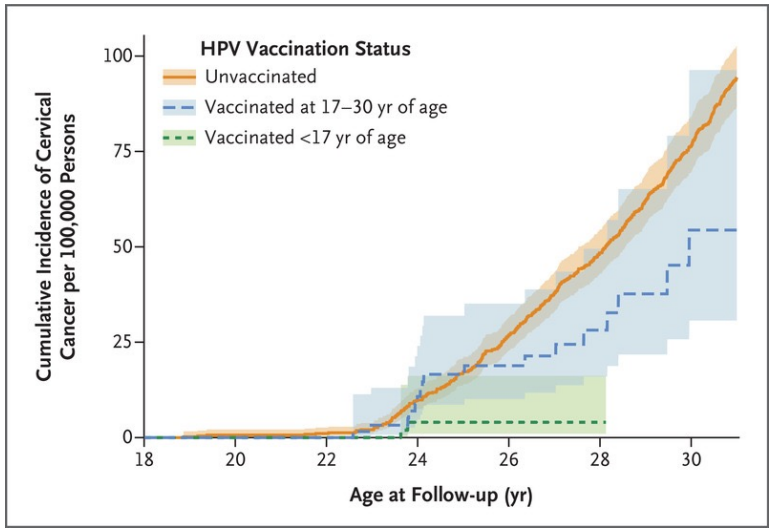
Data analytics

Global

WHY SHOULD WE PURSUE THIS STRATEGY?

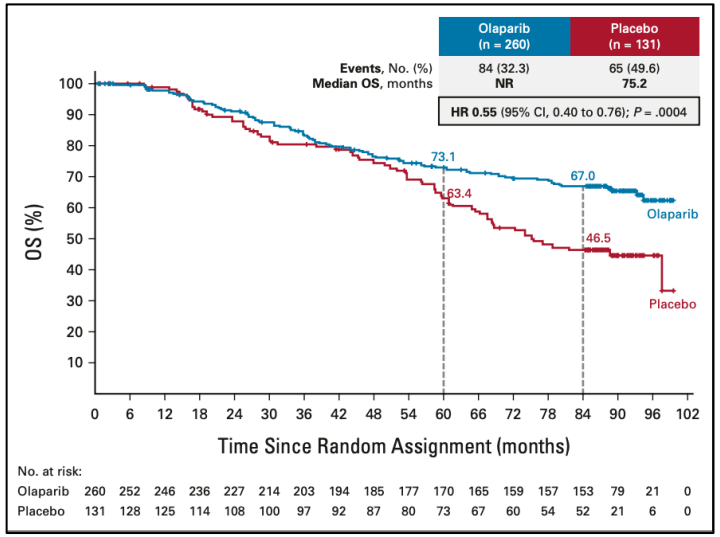
BECAUSE IT WORKS!!!

Closer to cure cancer



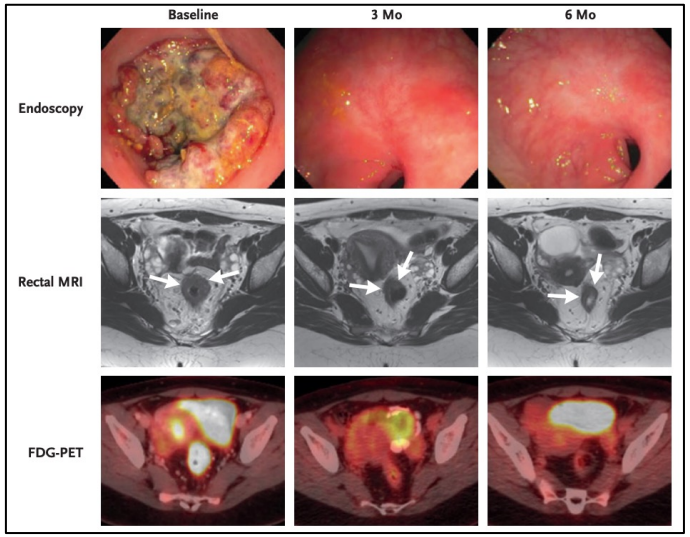
- Cervical cancer
- High risk HPV
- Vaccine

Jiayao Lei, NEJM 2020



- Advanced Ovarian cancer
- BRCA mut
- PARPi

DiSilvestro P et al, JCI 2022



- Locally Advanced Rectal Cancer
- Mismatch Repair–Deficient
- PD-1 Blockade

Cercek A et al, NEJM 2022

CONCLUSIONS

1. Traditional approach is not «cost-effective»

2. Precision and personalized medicine are enabled by –OMICS and AI implementation in clinical

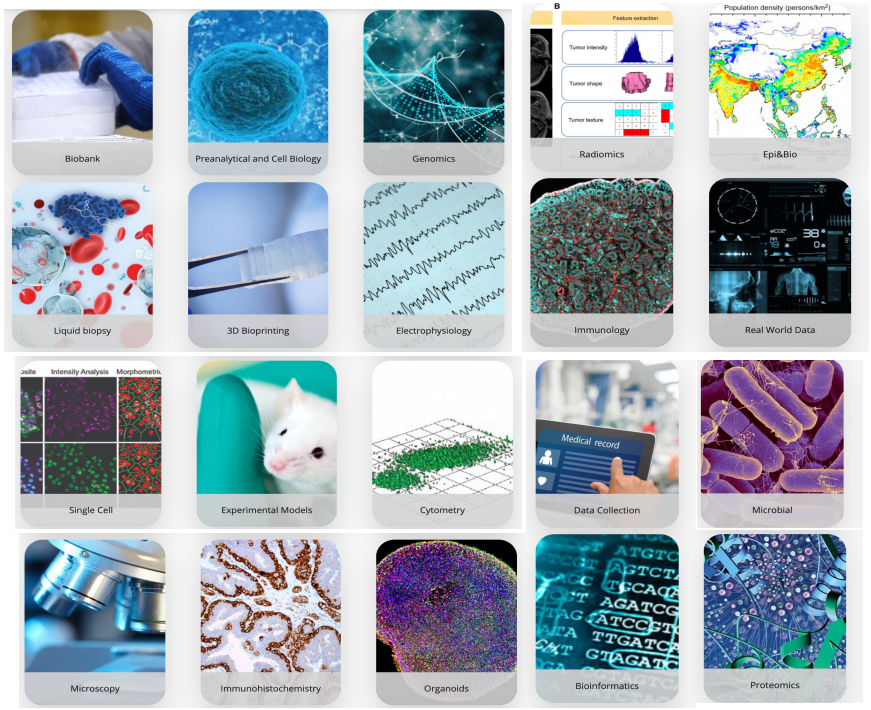
3. Biomarker-driven oncology trials and «decentralized trials» can speed up the process in a sustainable way

4. **Every contribution matters…**

CONCLUSIONS

Fondazione Policlinico Universitario Agostino Gemelli IRCCS experience

GSTeP
Gemelli Science and Technology Park



MRO.ART
MODERN RADIATION ONCOLOGY