

OMICS and AI TO NOVEL TRIAL ADDRESS

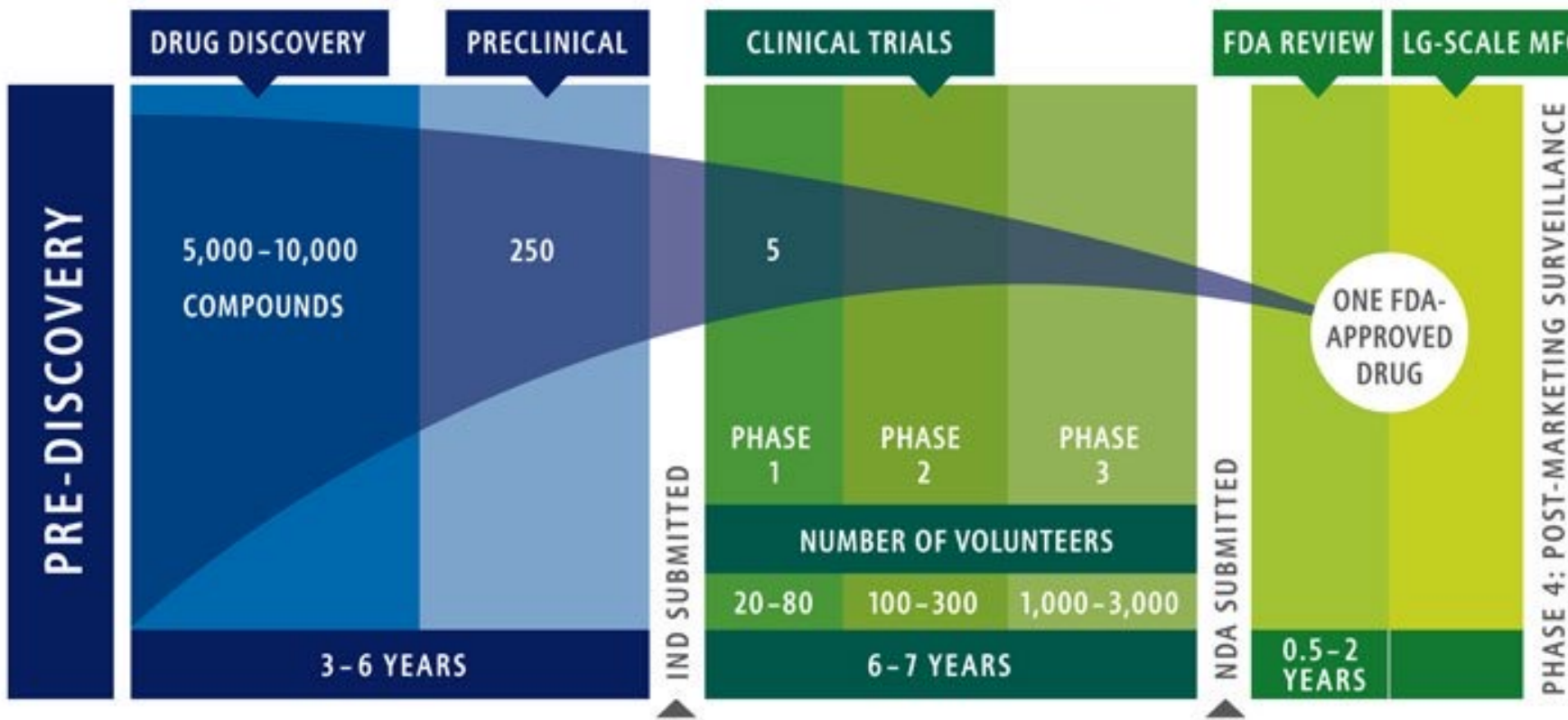
AI applications in modern oncology: What reliable supports for clinical decisions?

Camilla Nero

WHERE ARE WE NOW?

IMPRECISION MEDICINE

Slow, expensive, ineffective and wasteful



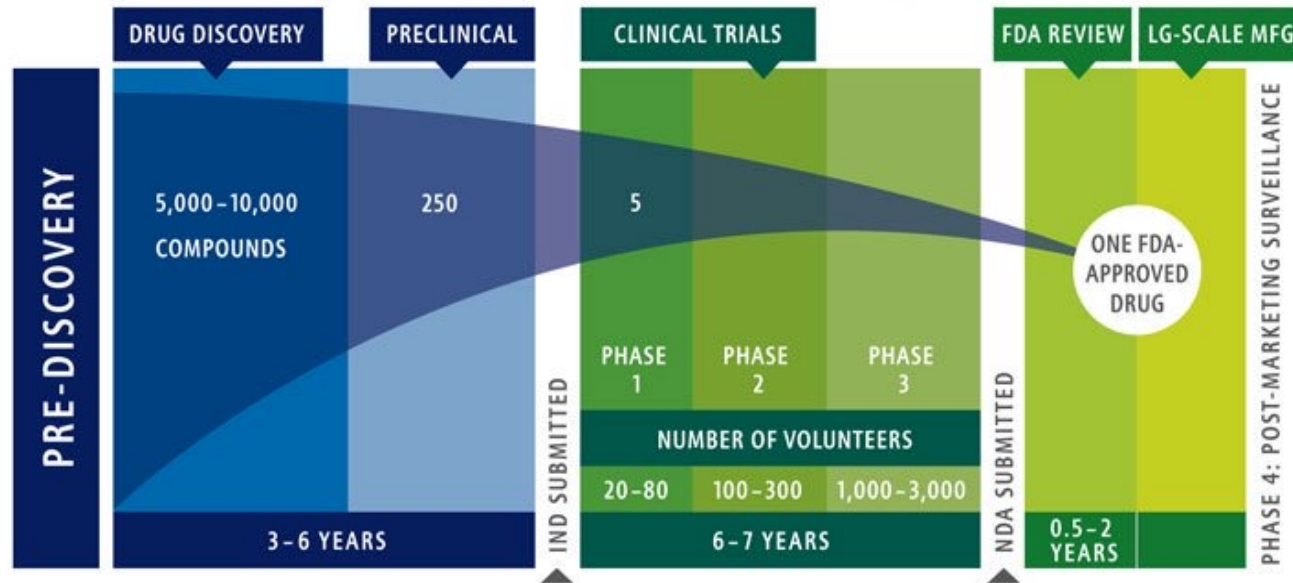
Drug Candidate Type	Approval Rate
Oncology (antiancer drugs)	3.4%
Endocrinology (hormones)	19.6%
Cardiovascular (heart/circulatory system)	25.5%
Central Nervous System (brain/spinal cord)	15.0%
Autoimmune and Inflammation	15.1%
Ophthalmology (eye disorders)	32.6%
Infectious disease (including vaccines)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

2009-2018

source: Pharmaceutical Research and Manufacturers of America

IMPRECISION MEDICINE

Slow, expensive, ineffective and wasteful



\$1.8B

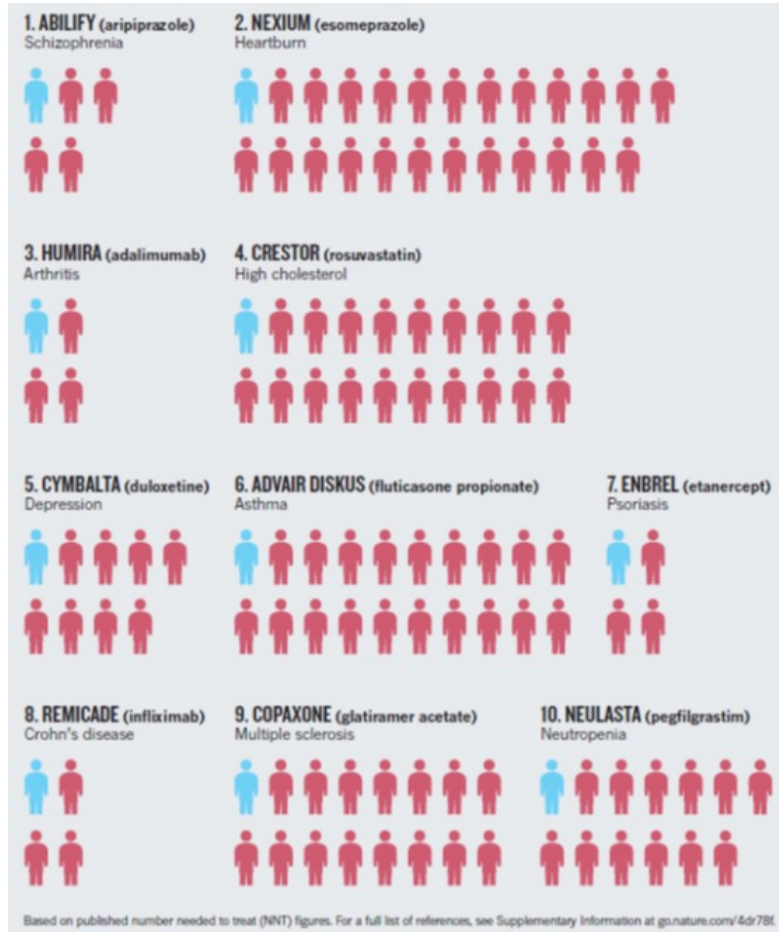
2018 **1,064** \$ million **446** \$ million **2** \$ million

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



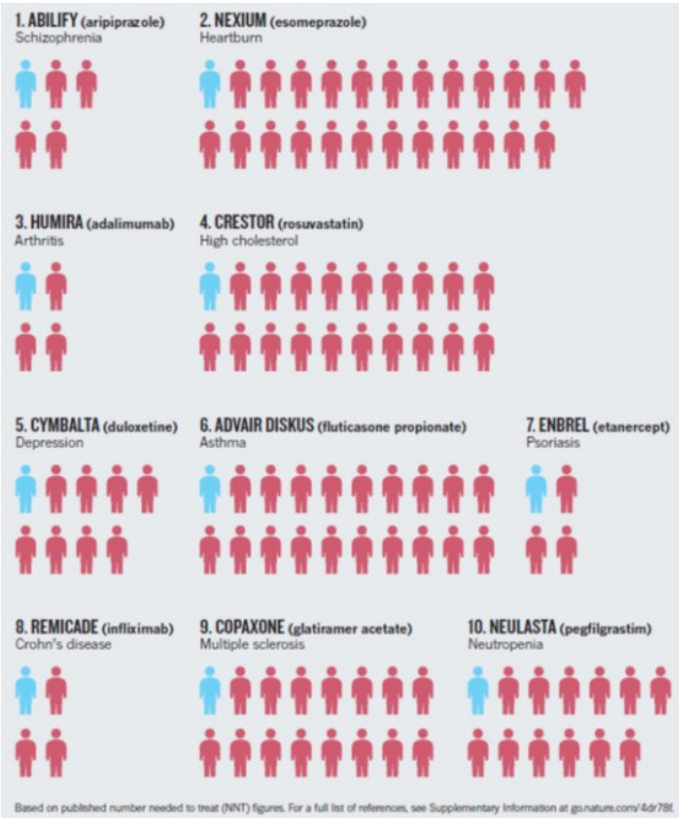
FAILURE TO IMPROVE
THE CONDITION OF
BETWEEN
3 TO 24
PEOPLE

Nature 2015

IMPRECISION MEDICINE

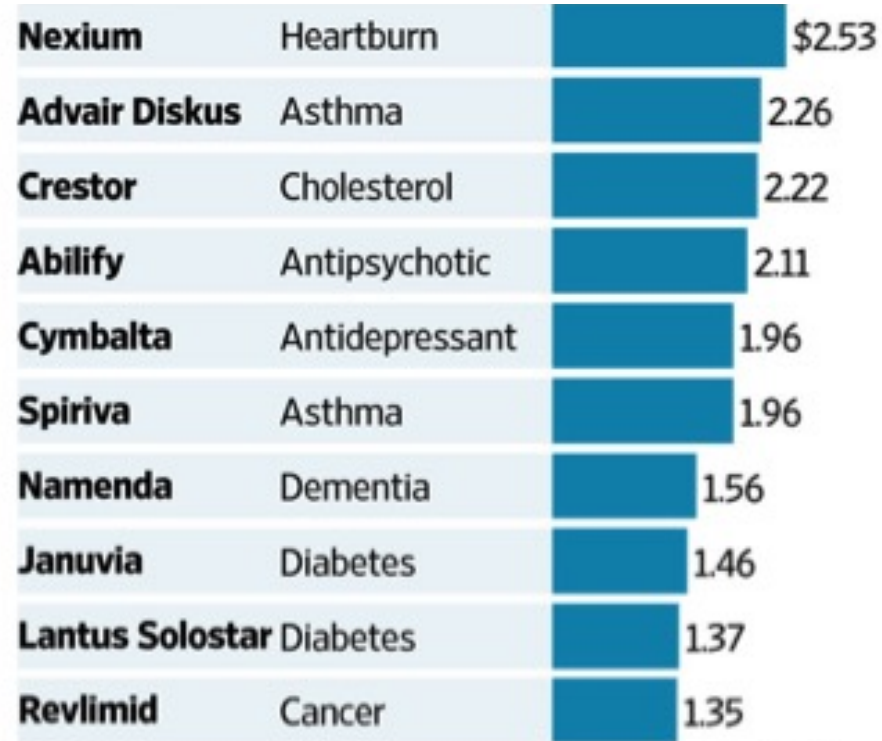
Slow, expensive, ineffective and wasteful

Response rate



Nature 2015

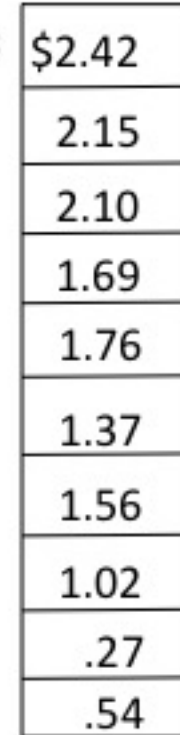
All costs incurred for top 10 drugs (billions)



Source: Centers for Medicare and Medicaid Services Total \$18.8B

The Wall Street Journal

Estimated waste



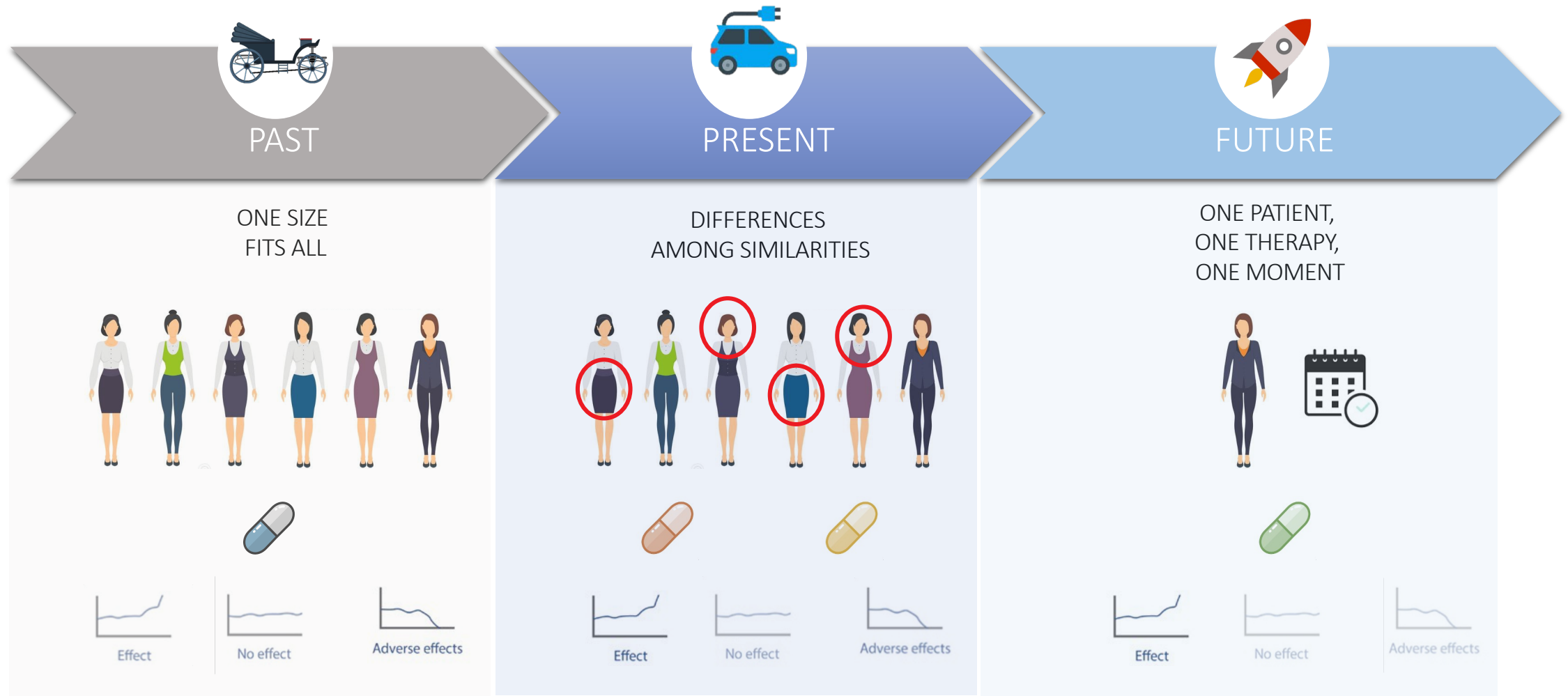
\$14.9B

79%
WASTED

WHERE ARE WE GOING?

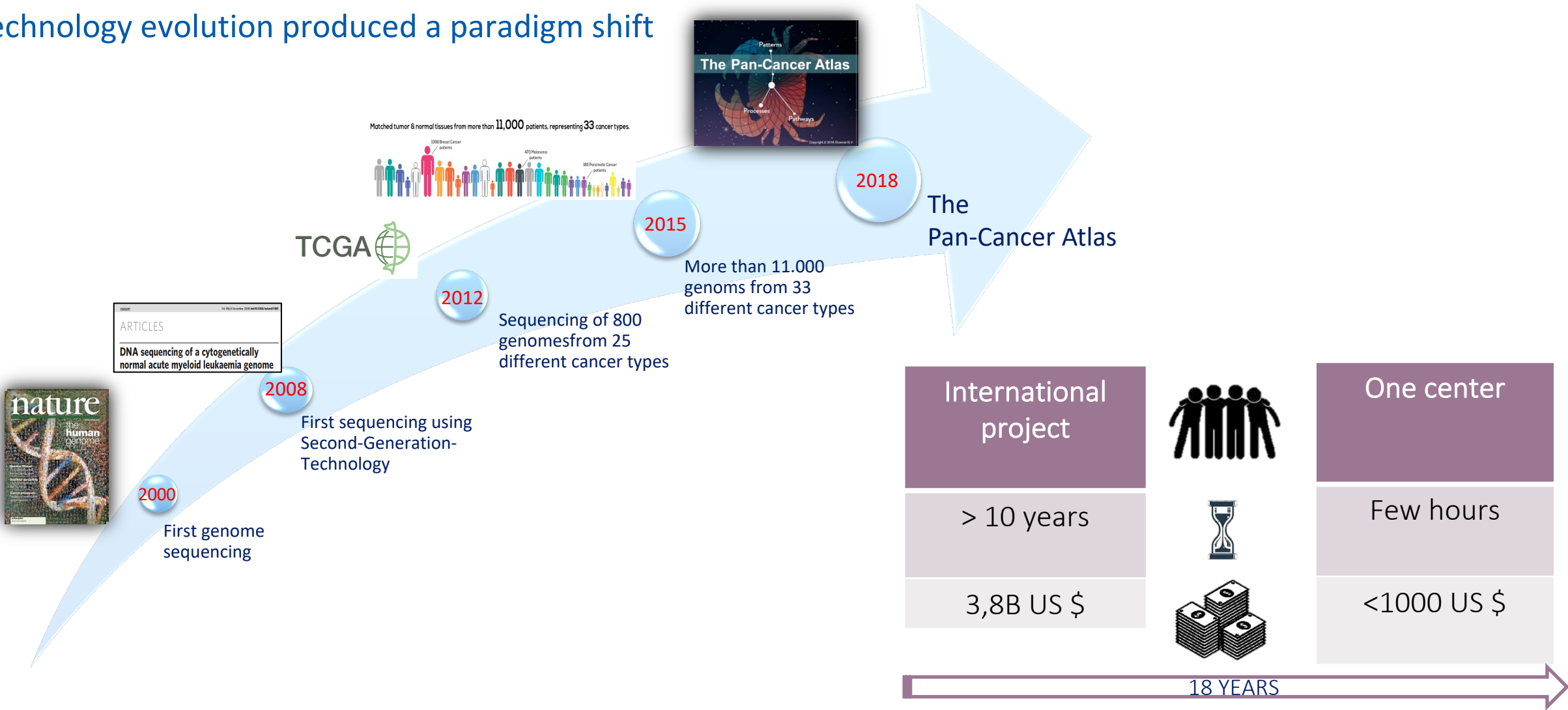
PRECISION AND PERSONALIZED MEDICINE

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

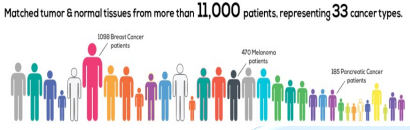


PRECISION MEDICINE

Technology evolution produced a paradigm shift

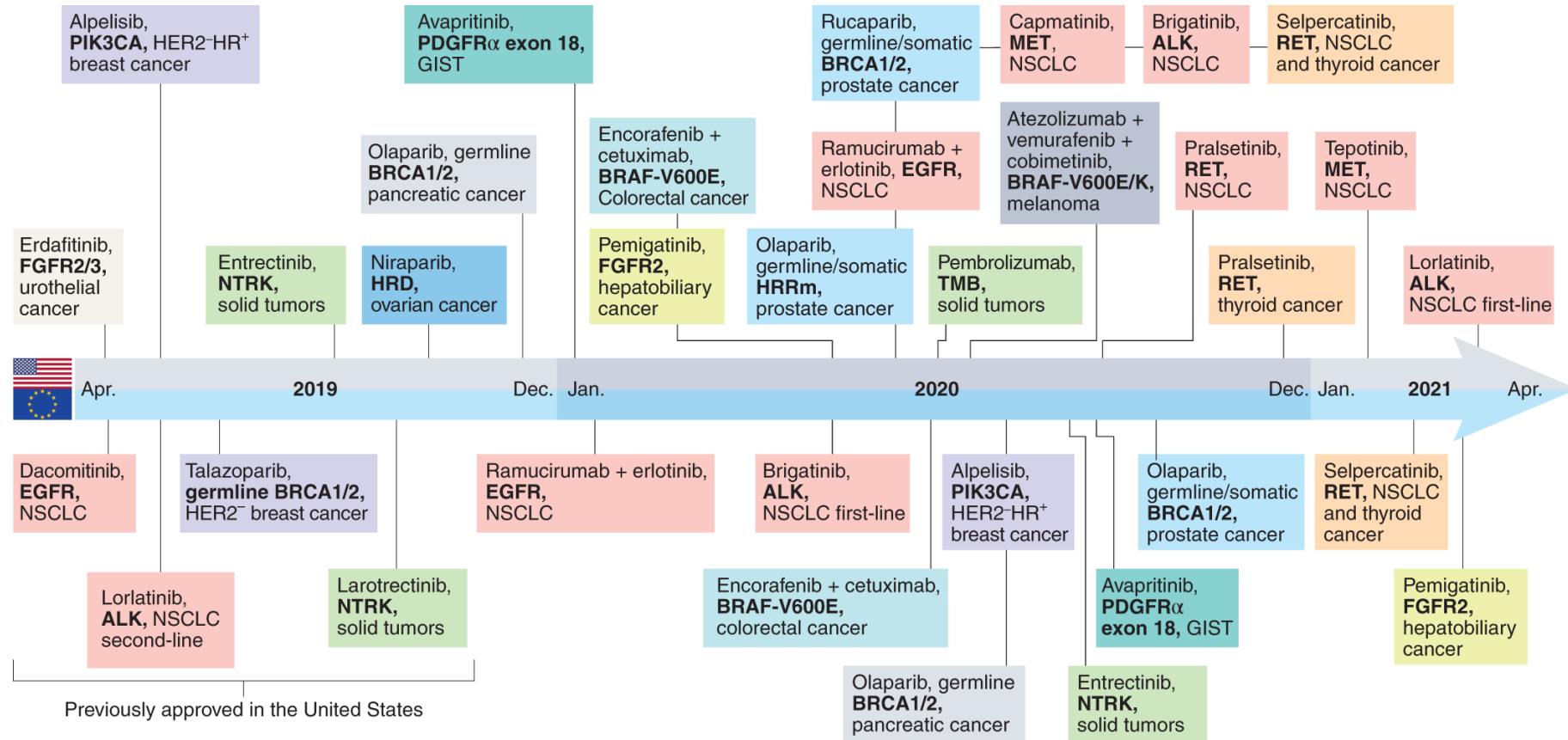


ARTICLES
DNA sequencing of a cytogenetically normal acute myeloid leukaemia genome



PRECISION MEDICINE

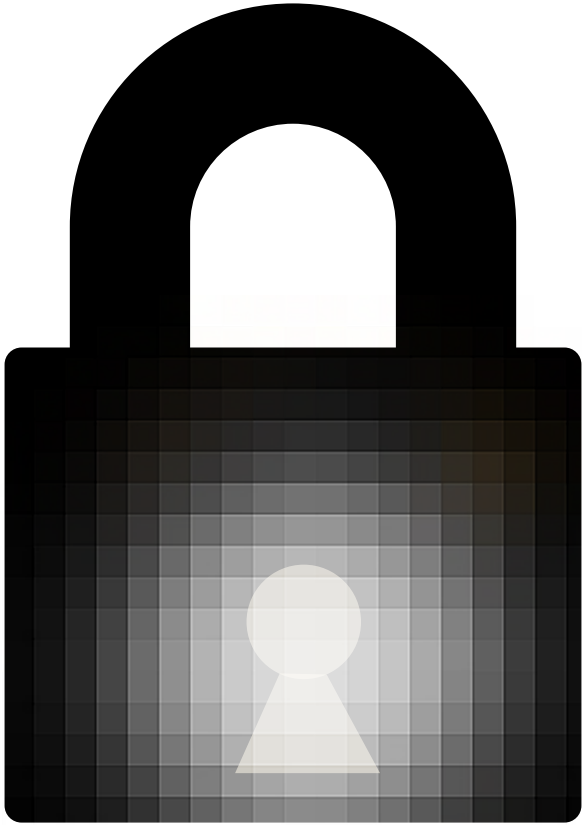
Target therapy in cancer: constant evolution



J. Mateu et al, Nature 2022

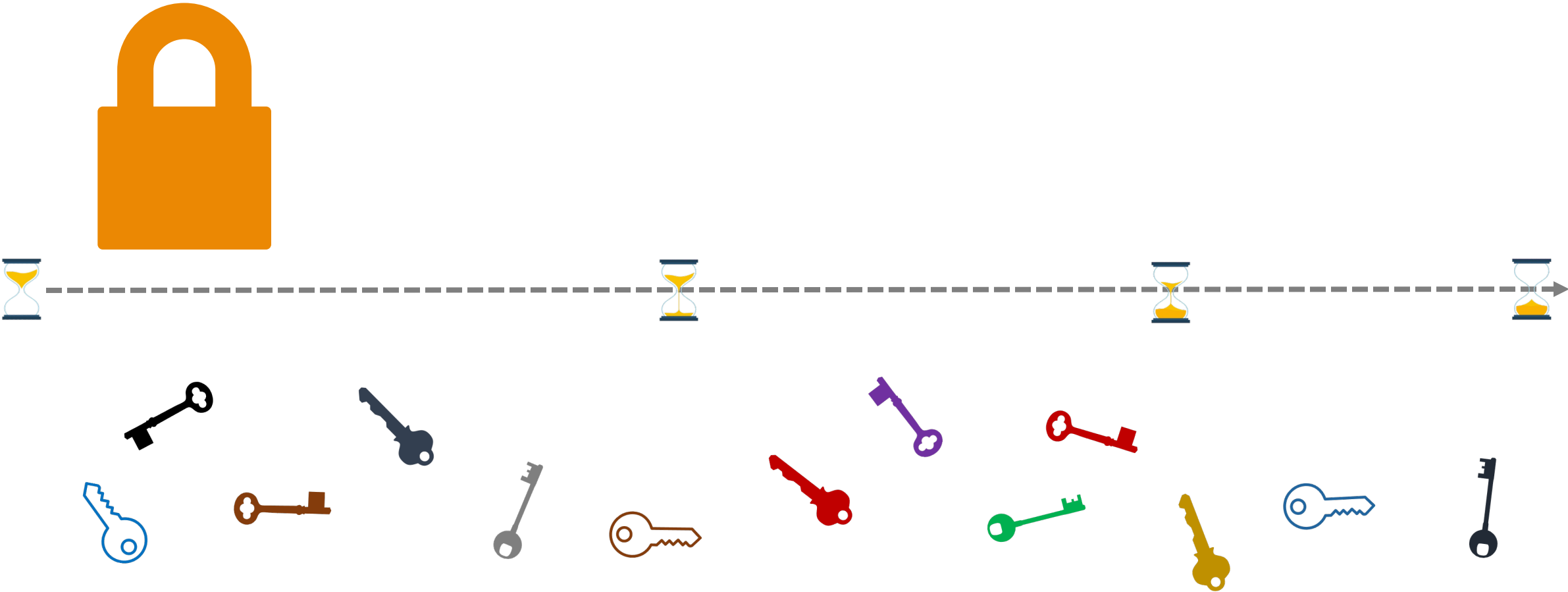
PRECISION MEDICINE

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



PRECISION MEDICINE

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

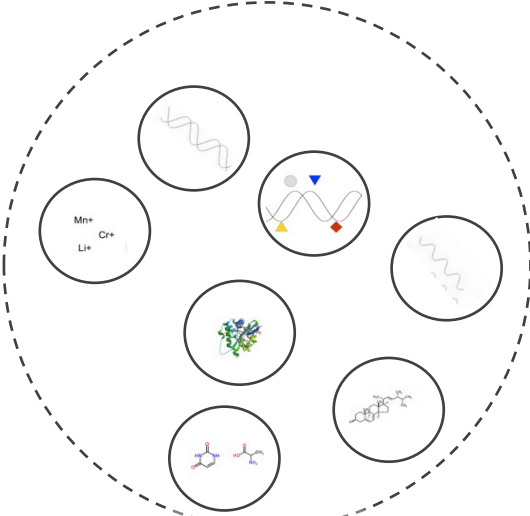


HOW CAN WE GO THERE?

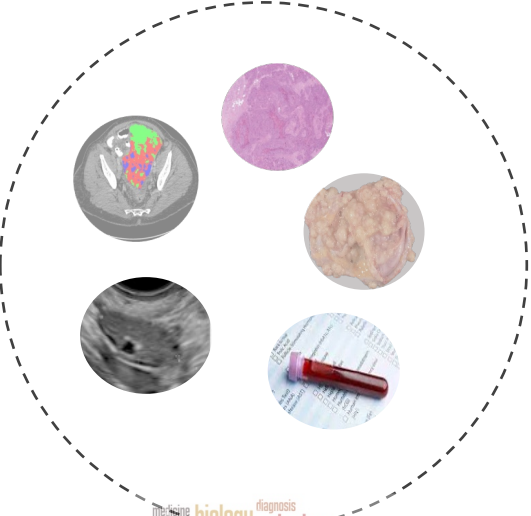
PERSONALIZED MEDICINE

Integrated Multi-omics longitudinal profiling

CLINICAL
DATA 2.0



Archaeogenomics
Epigenomics
Morphogenomics
Phylogenomics
Regulomics
Toxicogenomics
Proteomics
Metabolomics
Genomics
Transcriptomics
Fluorimetrics
Interactomics
Behavioromics
Lipidomics
Serotonomics

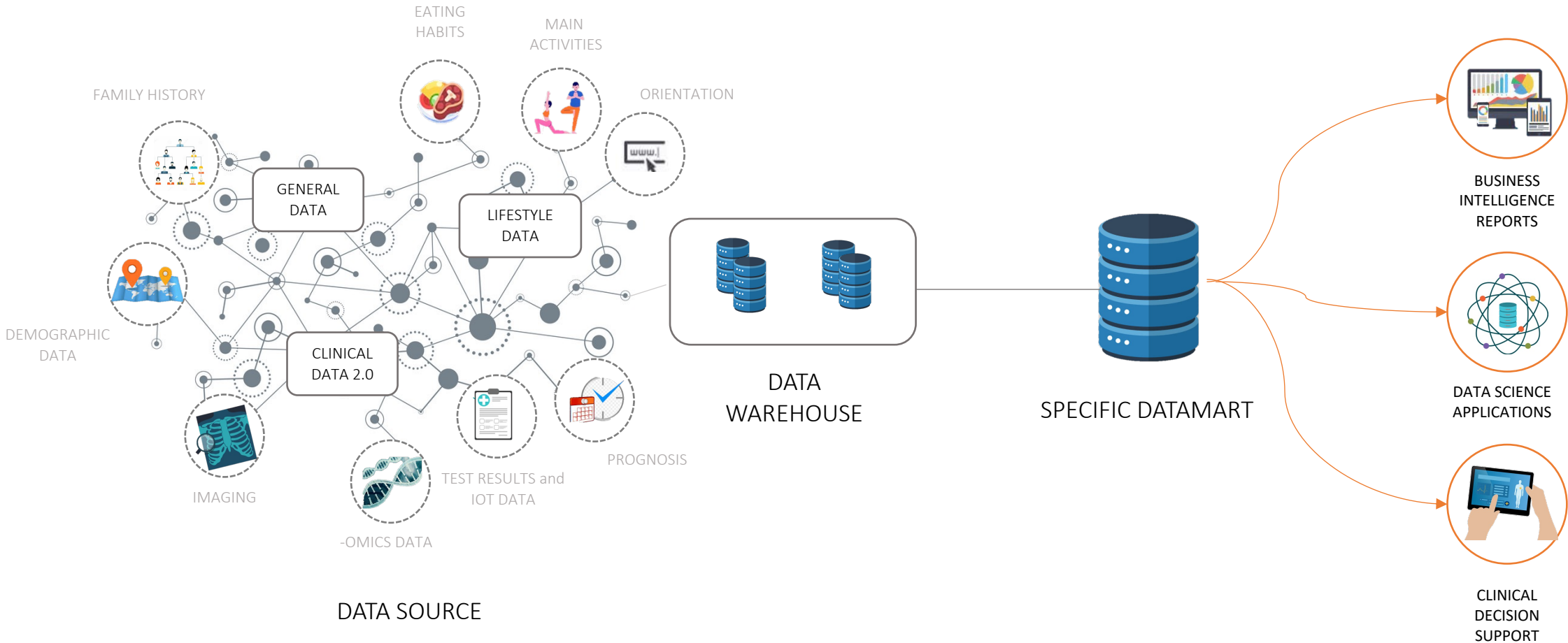


medicine
hospital
biology
diagnosis
doctor
sample
organs
serum
science
plasma
autopsies
health
disease
cancer
radiology
tissue
lab
dna
research
microbiology
medical
analysis
cell
microscope
pathologist
testclinic
healthcare
clinical
equipment
blood
radiology
tissue
lab
dna
research
microbiology
medical
analysis
cell
microscope
pathologist
testclinic
healthcare
clinical
scientific
cytology

OVER TIME

TO PERSONALIZED MEDICINE

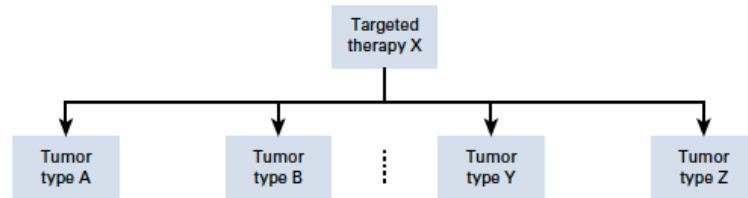
From data to information



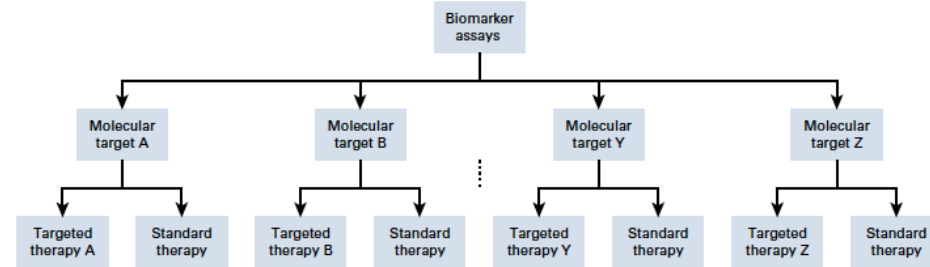
RE-DESIGNING CLINICAL TRIALS

Biomarker-driven oncology clinical trials

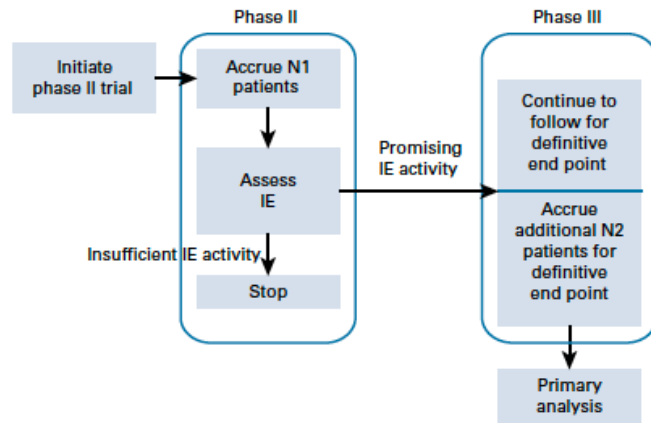
Basket trial



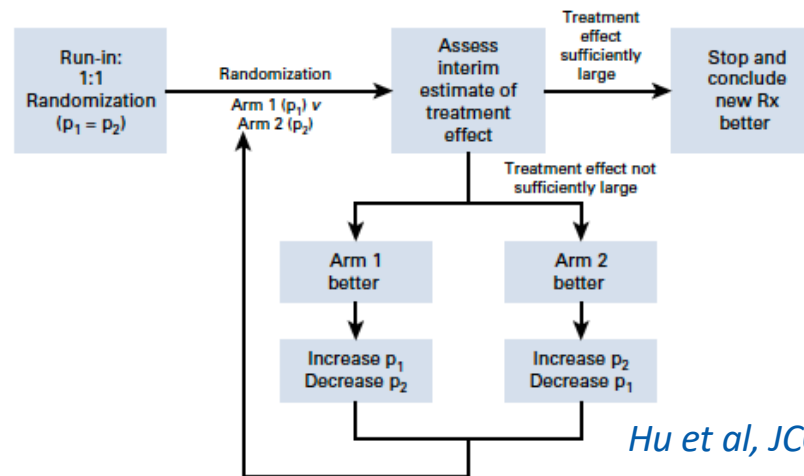
Umbrella trial



Seamless phase II/III design



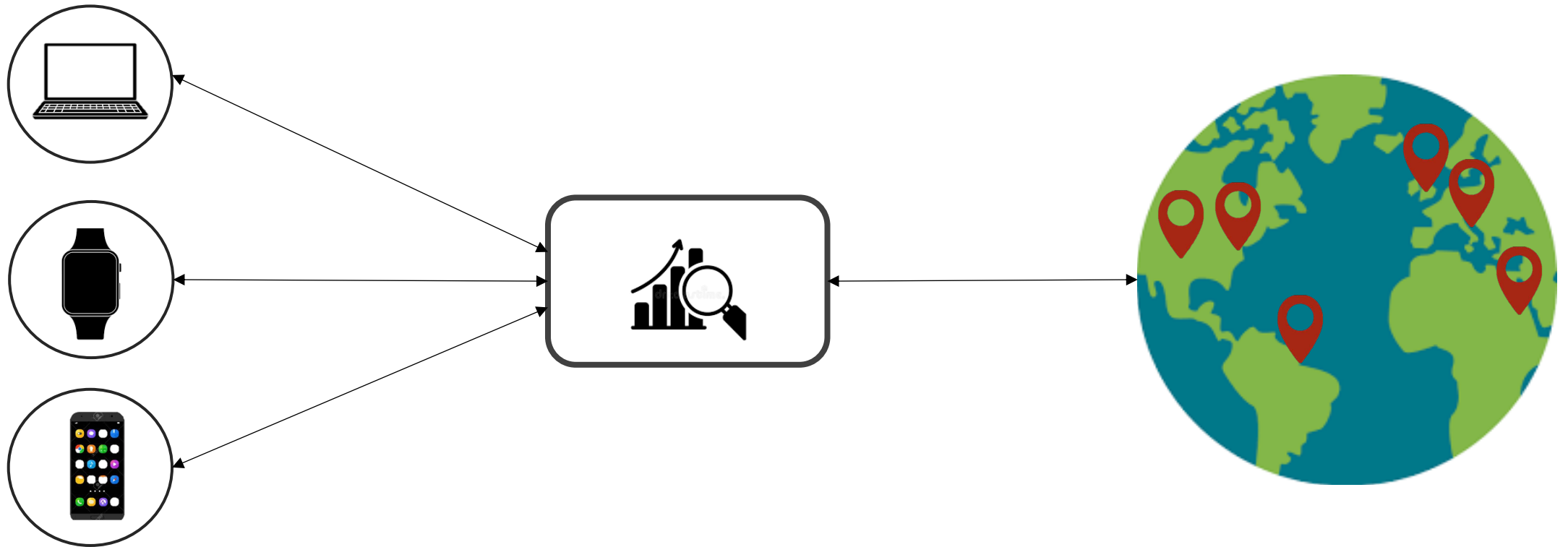
Outcome adaptive randomization



Hu et al, JCO Precision Oncology 2019

«DECENTRALIZED» CLINICAL TRIALS

Real time, world wide



Digital Technologies

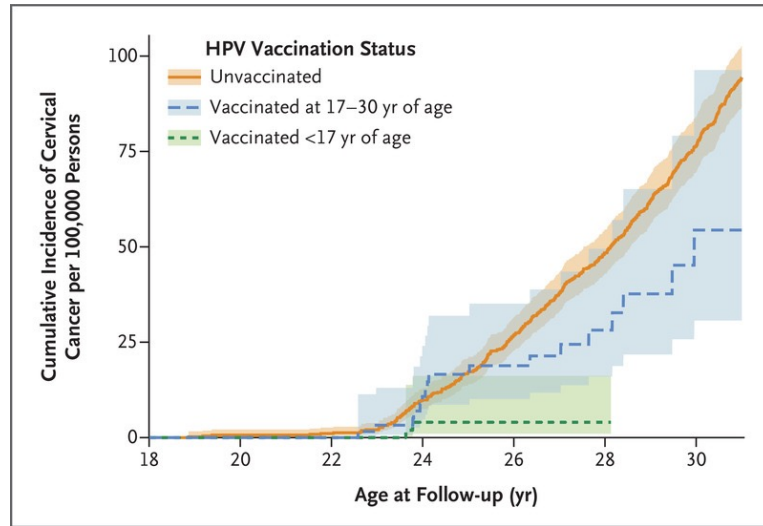
Data analytics

Global

WHY SHOULD WE PURSUE THIS STRATEGY?

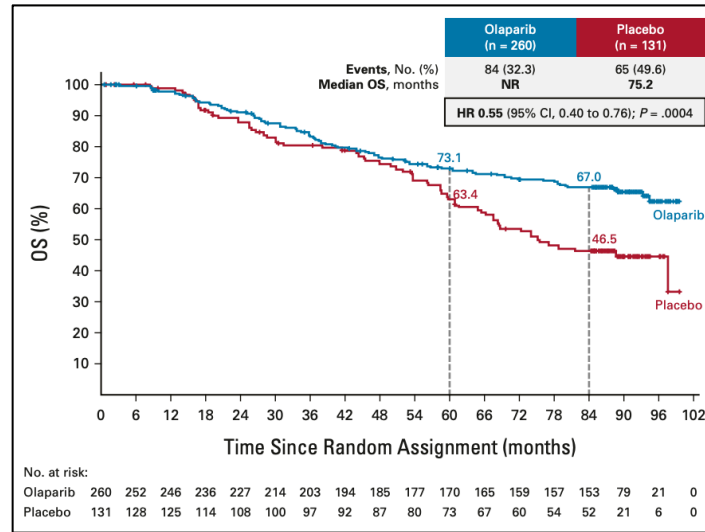
BECAUSE IT WORKS!!!

Closer to cure cancer



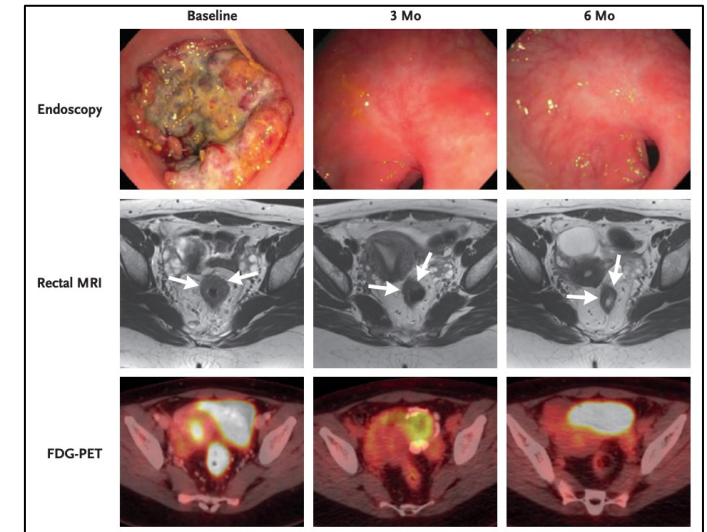
- Cervical cancer
- High risk HPV
- Vaccine

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

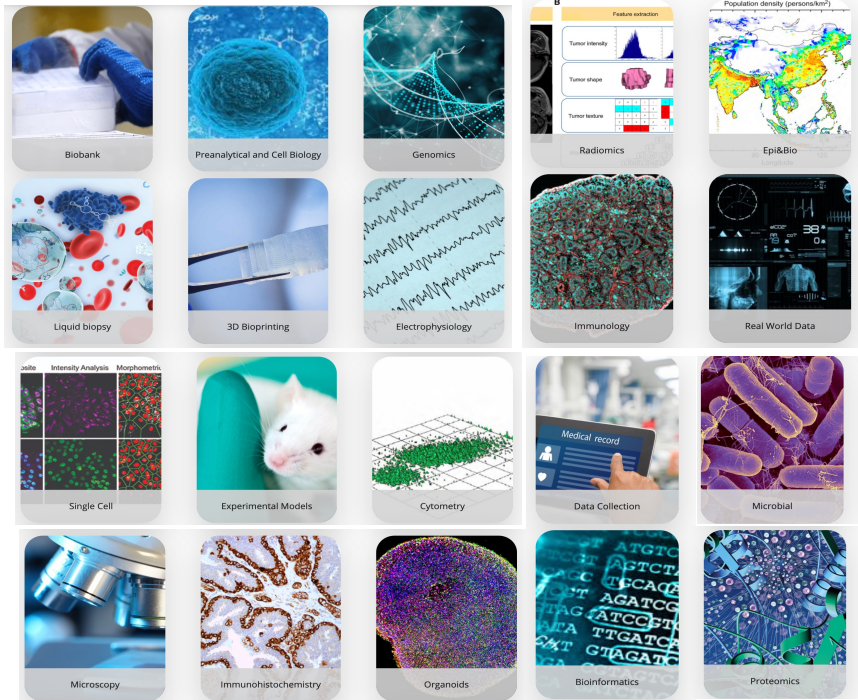
Cercek A et al, NEJM 2022

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



**FPG500
PROGRAMMA
DI PROFILAZIONE
GENOMICA
DEI TUMORI**

COS'È?

FPG500 è un programma dedicato ai **pazienti oncologici** che consente di effettuare una profilazione genomica a **500 geni** su tessuto tumorale e successiva valutazione in ambito multidisciplinare.

La metodica utilizzata è la tecnica di Next Generation Sequencing (NGS), che consente di sequenziare un alto numero di geni in tempi rapidi, in modo da ottenere informazioni circa la caratterizzazione molecolare della neoplasia.

FINALITÀ

L'obiettivo è quello di identificare ed interpretare eventuali **alterazioni genomiche** suscettibili di **terapie mirate** ad oggi disponibili. Il programma prevede l'utilizzo di un pannello a 500 geni che consente, oltre all'analisi dei geni già riconosciuti nei Livelli Essenziali di Assistenza (LEA), di ampliare le informazioni sul profilo mutazionale del tumore, estendendo la possibilità di accesso a nuovi farmaci.

A CHI È RIVOLTO?

La profilazione genomica è indicata in pazienti con neoplasie per le quali, ad oggi, vengono determinati marcatori riconosciuti nella pratica clinica o per cui sono disponibili terapie target nel contesto di studi clinici o programma di accesso precoce al farmaco.

La profilazione genomica è attualmente raccomandata in numerose neoplasie, tra cui:

- POLMONE
- OVAIO
- PROSTATA
- PANCREAS
- MELANOMA
- MAMMELLA
- GIST
- COLON
- TIROIDE

PERCORSO FPG500

- Verifica** dei Criteri di Inclusion da parte del Medico Referente e Firma del Consenso Informato
- Verifica** della disponibilità del campione tumorale
- Estrazione** del DNA e/o RNA e sequenziamento con pannello a 500 geni
- Elaborazione** del referto
- Valutazione** dei risultati ed **eventuale discussione** in sede del Molecular Tumor Board (MTB)
- Identificazione** della terapia target se disponibile