

Incorporating recent advances in cutting edge personalised medicine research into the real clinical practice



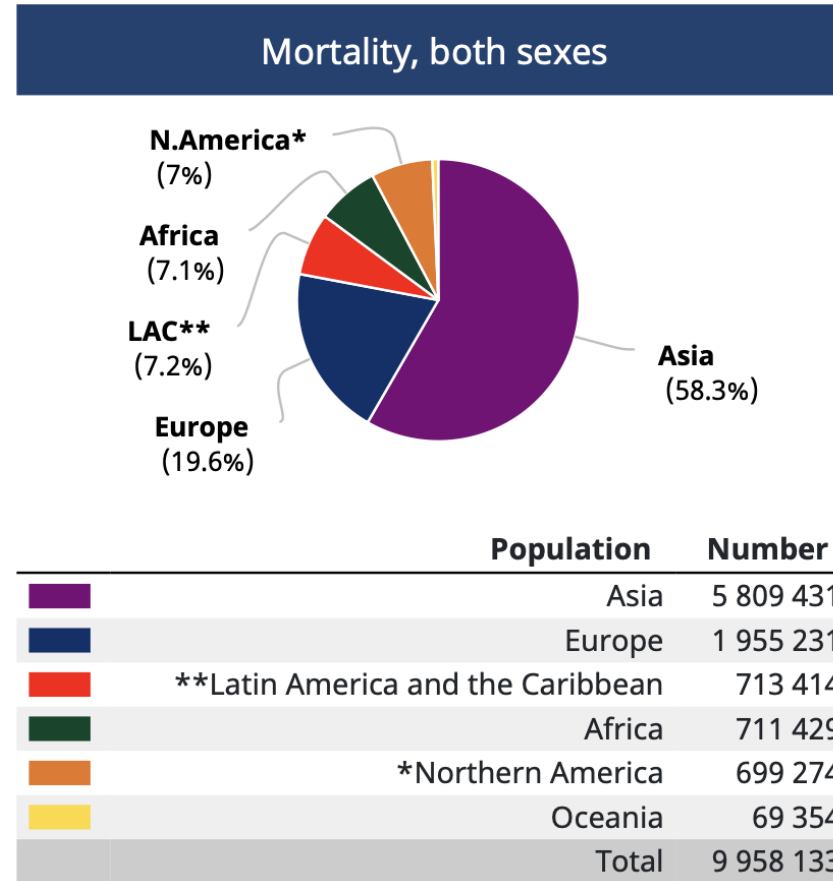
Benedikt Westphalen, CCC Munich LMU



- has received honoraria from AstraZeneca, Amgen, Bayer, BMS, Chugai, Celgene, Falk, GSK, Lilly, MSD, Merck, Janssen, Ipsen, QuiP GmbH, Roche, Servier, SIRTex, Taiho;
- served on advisory boards for AstraZeneca, Bayer, BMS, Celgene, Janssen, MSD, Servier, Shire/Baxalta, Rafael Pharmaceuticals, RedHill, Roche,
- has received travel support by AstraZeneca, Bayer, Celgene, Janssen, MSD, RedHill, Roche, Servier, Taiho and research grants (institutional) by Roche.
- serves as faculty for European Society of Medical Oncology (ESMO), Deutsche Krebshilfe (DKH) and Arbeitsgemeinschaft internistische Onkologie (AIO)
- is a member of the EU Commission expert group: Mission Board for cancer
- is a member of the BMBF expert group: Forum Zukunftsstrategie
- is a member of the BMBF steering committee: Strategiekreis Dekade gegen Krebs

Scaling Precision Medicine in Oncology *In OR Out of Reach?*

What are we facing today?



> 10 million people die of cancer each year!

<https://gco.iarc.fr/today/fact-sheets-cancers>

Precision Medicine versus Precision Oncology

Personalized Medicine:

Integrates patient-specific data to inform therapeutic management.

Aims:

- Optimised, holistic and patient-specific therapies.

Precision Medicine:

Applies Molecular Diagnostics (+/-NGS)

Aims:

- Biomarker-driven Therapies (SOC)
- Experimental Therapies (clinical trials)

Precision Oncology

Applies Molecular Diagnostics in Advanced Cancers

Aims:

- MTB discussion
- Experimental Therapies (off label / clinical trials)





Diagnostics

Treatment

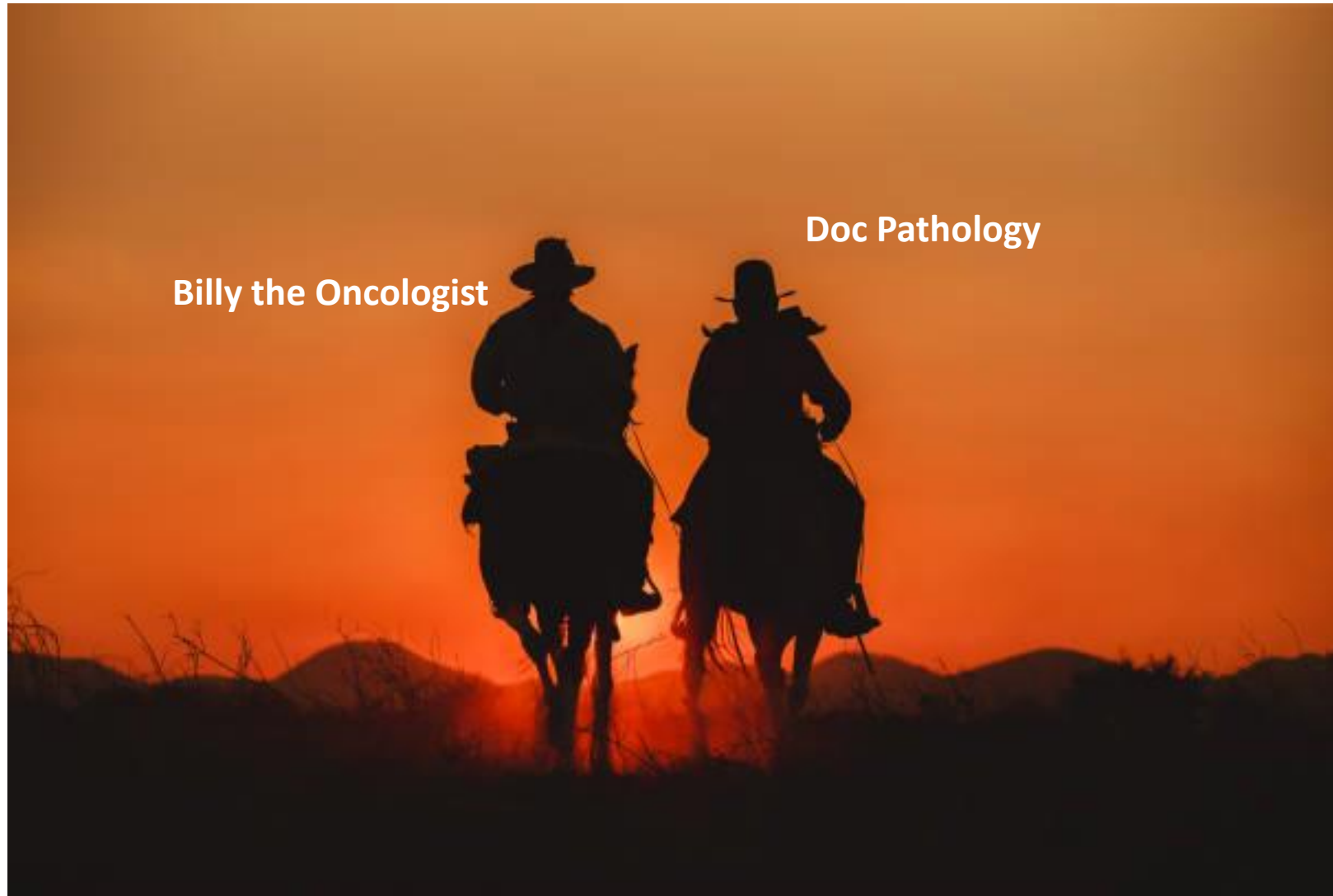
Re-thinking Cancer Care

**Do I have access to quality
ensured testing?**

**Do I have the expertise to act on
the results?**

**Do my patients have access to
treatment?**

A crucial relationship of TRUST and OWNERSHIP

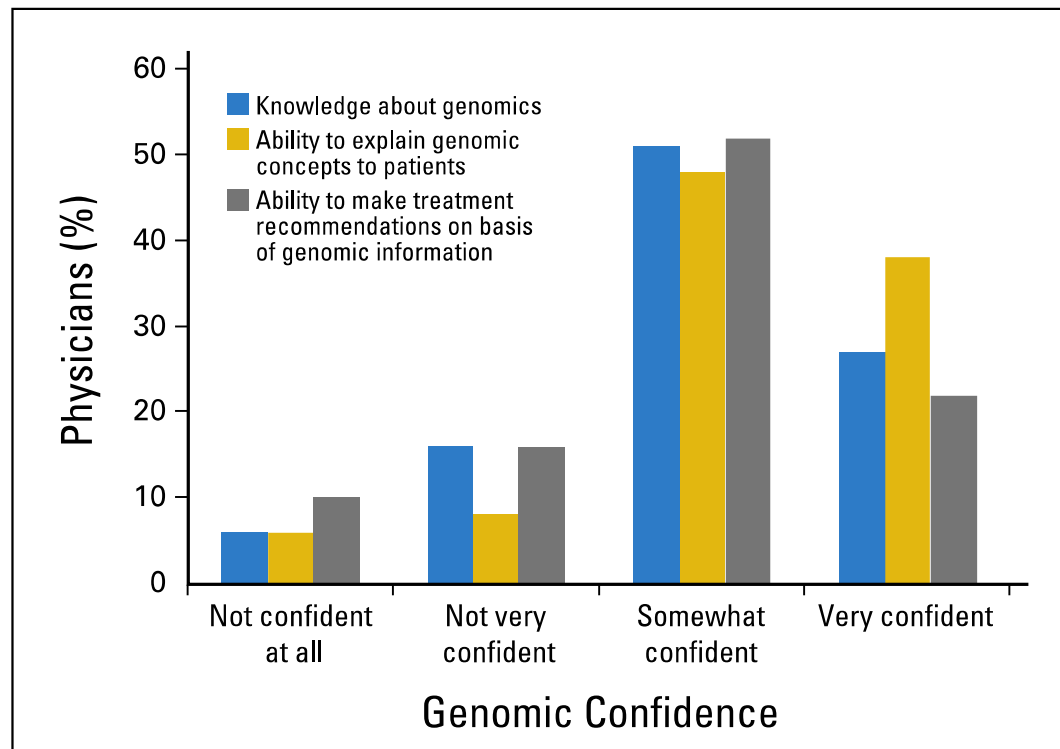




Do I have the expertise to act on the results...

Physicians' Attitudes About Multiplex Tumor Genomic Testing

Stacy W. Gray, Katherine Hicks-Courant, Angel Cronin, Barrett J. Rollins, and Jane C. Weeks



Editorial

<https://doi.org/10.1038/s41591-023-02522-1>

We need a genomics-savvy healthcare workforce

*Twenty years after completion of the Human Genome Project, genetics is rapidly being integrated into everyday clinical practice. **But in this era of genomic revolution, genetically trained teams of healthcare workers are needed to optimize delivery of patient care.***

- National/regional virtual Molecular Tumor Boards (IMPACT India, Nordics, New England, Germany)
- Building of education programs around the globe (UK, Europe, USA, Germany)

Delivering precision oncology to patients with cancer

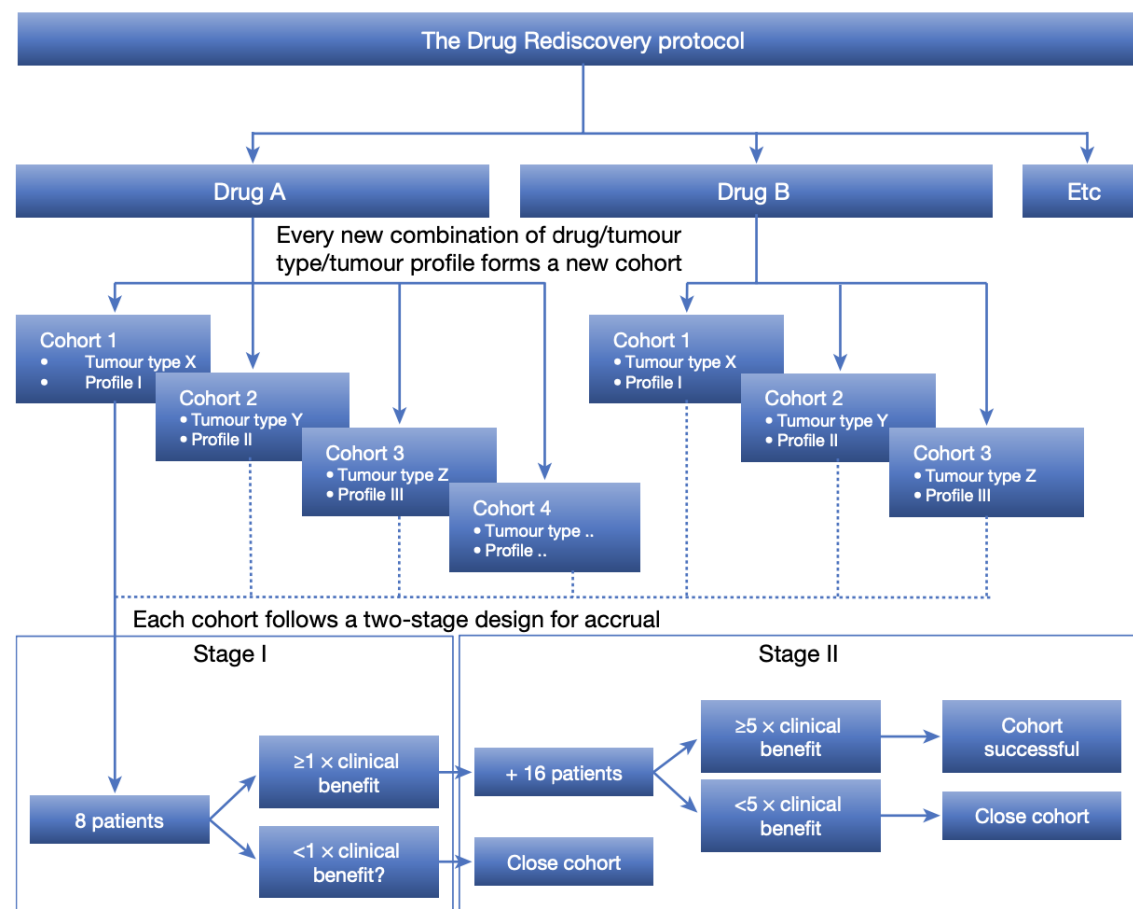
Joaquin Mateo^{1,18}, Lotte Steuten^{2,3,18}, Philippe Aftimos⁴, Fabrice André⁵, Mark Davies⁶, Elena Garralda¹, Jan Geissler⁷, Don Husereau⁸, Iciar Martinez-Lopez⁹, Nicola Normanno¹⁰, Jorge S. Reis-Filho¹¹, Stephen Stefani¹², David M. Thomas¹³, C. Benedikt Westphalen^{14,15,19} and Emile Voest^{16,17,19} ✉

“the delivery of its full potential and impact on clinical practice depends greatly on ensuring wide and equal patient access to diagnostic technologies and therapeutics, beyond a few academic centers in privileged countries”

Do my patients have access to treatment?

The Drug Rediscovery protocol facilitates the expanded use of existing anticancer drugs

D. L. van der Velden^{1,2,21}, L. R. Hoes^{1,2,3,21}, H. van der Wijngaart^{2,3,4,21}, J. M. van Berge Henegouwen^{2,3,5,21}, E. van Werkhoven⁶, P. Roepman⁷, R. L. Schilsky⁸, W. W. J. de Leng⁹, A. D. R. Huitema^{10,11}, B. Nuijten¹¹, P. M. Nederlof¹², C. M. L. van Herpen¹³, D. J. A. de Groot¹⁴, L. A. Devriese¹⁵, A. Hoebe¹⁶, M. J. A. de Jonge¹⁷, M. Chalabi^{1,18}, E. F. Smit^{2,19}, A. J. de Langen¹⁹, N. Mehra¹³, M. Labots⁴, E. Kapiteijn⁵, S. Sleijfer^{2,17}, E. Cuppen^{3,7,20}, H. M. W. Verheul^{4,13}, H. Gelderblom⁵ & E. E. Voest^{1,2,3*}



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What information can I get from the testing?

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What information can I get from the testing?

**Do I test according to standard
of care?**

**Does testing inform my
management?**

Do I screen for clinical trials?

SPECIAL ARTICLE

Recommendations for the use of next-generation sequencing (NGS) for patients with advanced cancer in 2024: a report from the ESMO Precision Medicine Working Group

M. F. Mosele^{1,2}, C. B. Westphalen³, A. Stenzinger⁴, F. Barlesi^{1,2,5}, A. Bayle^{5,6,7,8}, I. Bièche⁹, J. Bonastre^{7,8}, E. Castro¹⁰, R. Dienstmann^{11,12,13}, A. Krämer^{14,15}, A. M. Czarnecka^{16,17}, F. Meric-Bernstam¹⁸, S. Michiels^{7,8}, R. Miller^{19,20}, N. Normanno²¹, J. Reis-Filho^{22†}, J. Remon², M. Robson²³, E. Rouleau²⁴, A. Scarpa²⁵, C. Serrano¹¹, J. Mateo¹¹ & F. André^{1,2,5*}

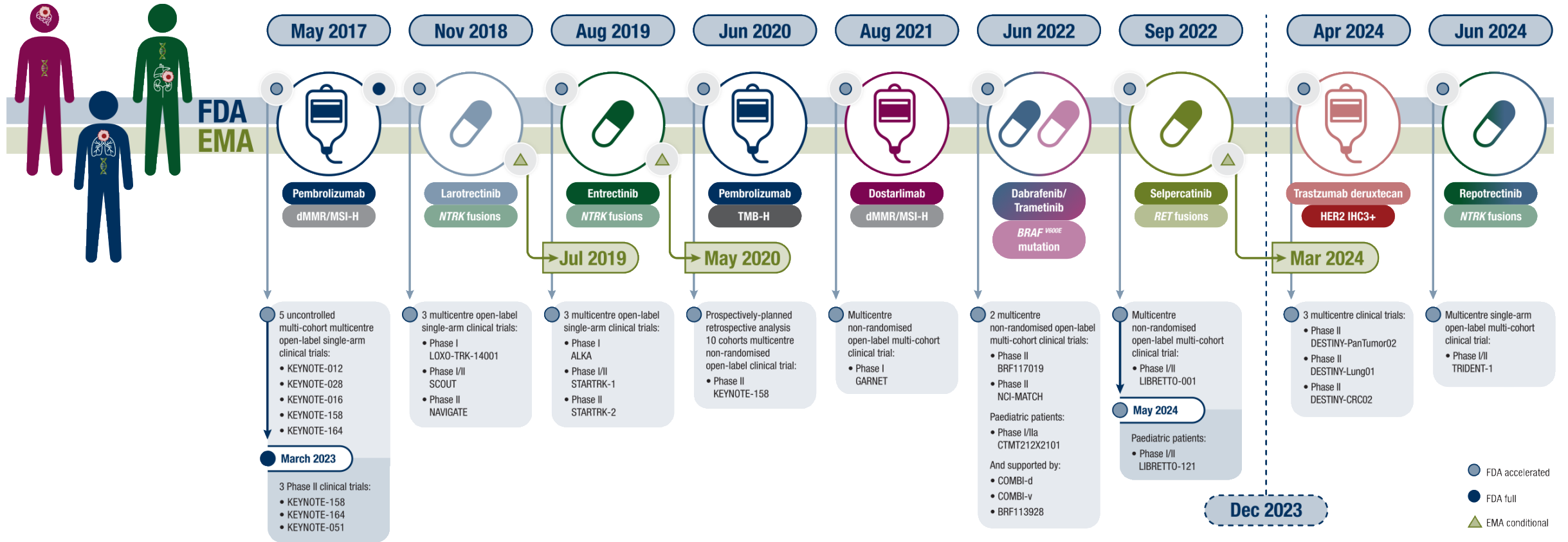
As for 2020 recommendations, ESMO recommends running tumour NGS in advanced **non-squamous non-small cell lung cancer (NSCLC)**, **prostate cancer**, **colorectal cancer**, **cholangiocarcinoma**, and **ovarian cancer**.

Moreover, it is recommended to perform tumour NGS in clinical research centers and under specific circumstances discussed with patients.

In this updated report, the consensus within the group has led to an expansion of the recommendations to encompass patients with **advanced breast cancer** and **rare tumours** such as **gastrointestinal stromal tumours (GISTs)**, **sarcoma**, **thyroid cancer**, **and carcinoma of unknown primary (CUP)**.

Finally, ESMO recommends performing tumour NGS to detect tumour-agnostic alterations in patients with metastatic cancers where access to matched therapies is available.

What is Standard of Care?



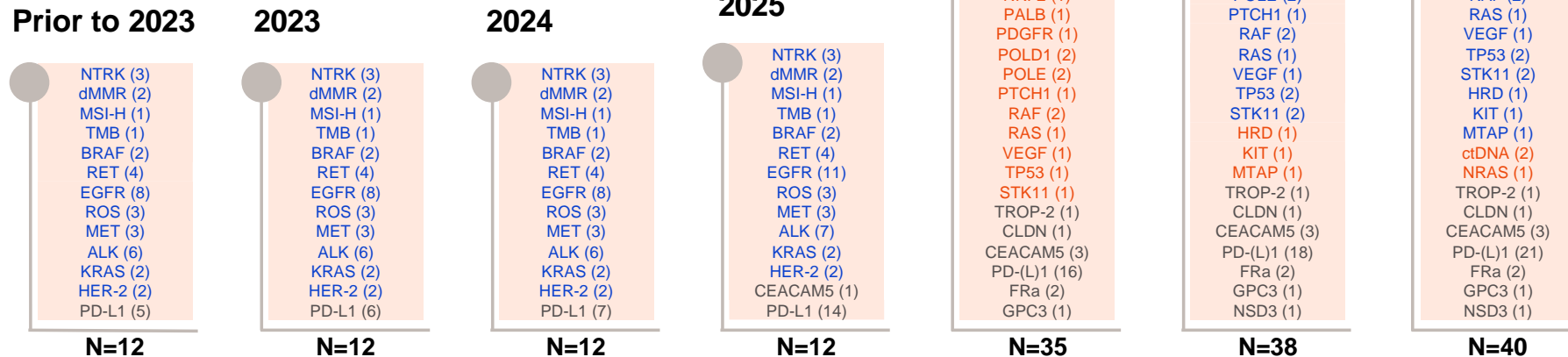
Westphalen et al. Annals of Oncology 2024

Biomarker-dependent drugs are becoming increasingly important in oncology

Biomarkers likely to have approved targeted therapies with tumour agnostic indications*

Analysis includes Phase 1/2, Phase 2 & Phase 3 trials initiated before April 1, 2023

- = Established biomarker suitable for CGP
- = New biomarker suitable for CGP
- = Biomarker without immediate relevance for CGP (other detection methods more appropriate!)



Adapted from D. Thomas, ESMO 2023

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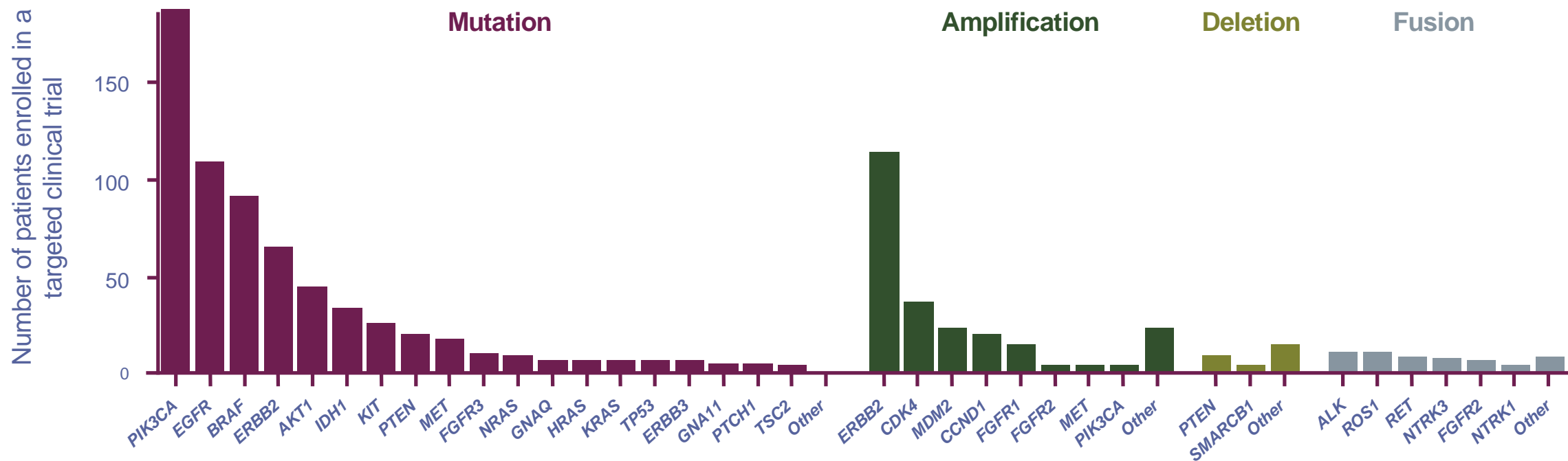
What information can I get from the testing?

Do I screen for clinical trials?

Do I Screen for Clinical Trials?

> 10,000 patients screened using CGP

11% enrolled in molecularly-guided clinical trials



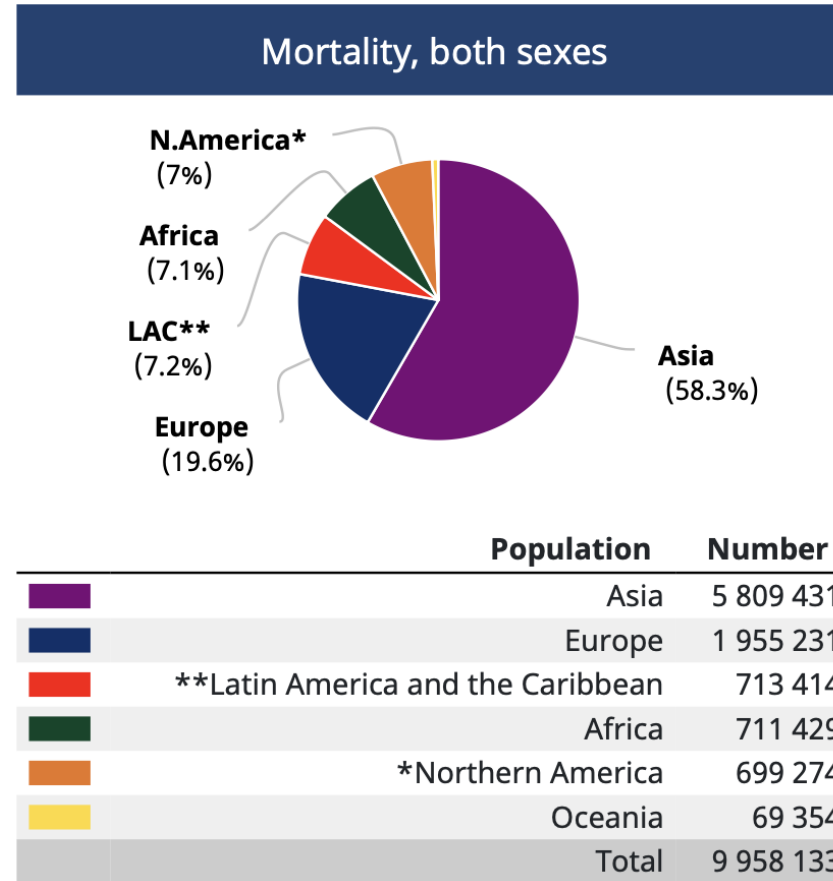
Adapted from: Zehir et al.; Nature Medicine 2017

- The landscape of molecular insights and molecularly guided therapeutics is rapidly evolving
- Current guidelines can only insufficiently capture this evolution in time
- Access to quality ensured testing, expertise and treatment are pivotal
- Comprehensive tumor profiling can
 - → Inform standard of care
 - → Support screening for clinical trials
 - → Provide caregivers with (additional) clinical information

At Crossroads...



What are we facing today?



> 10 million people die of cancer each year!

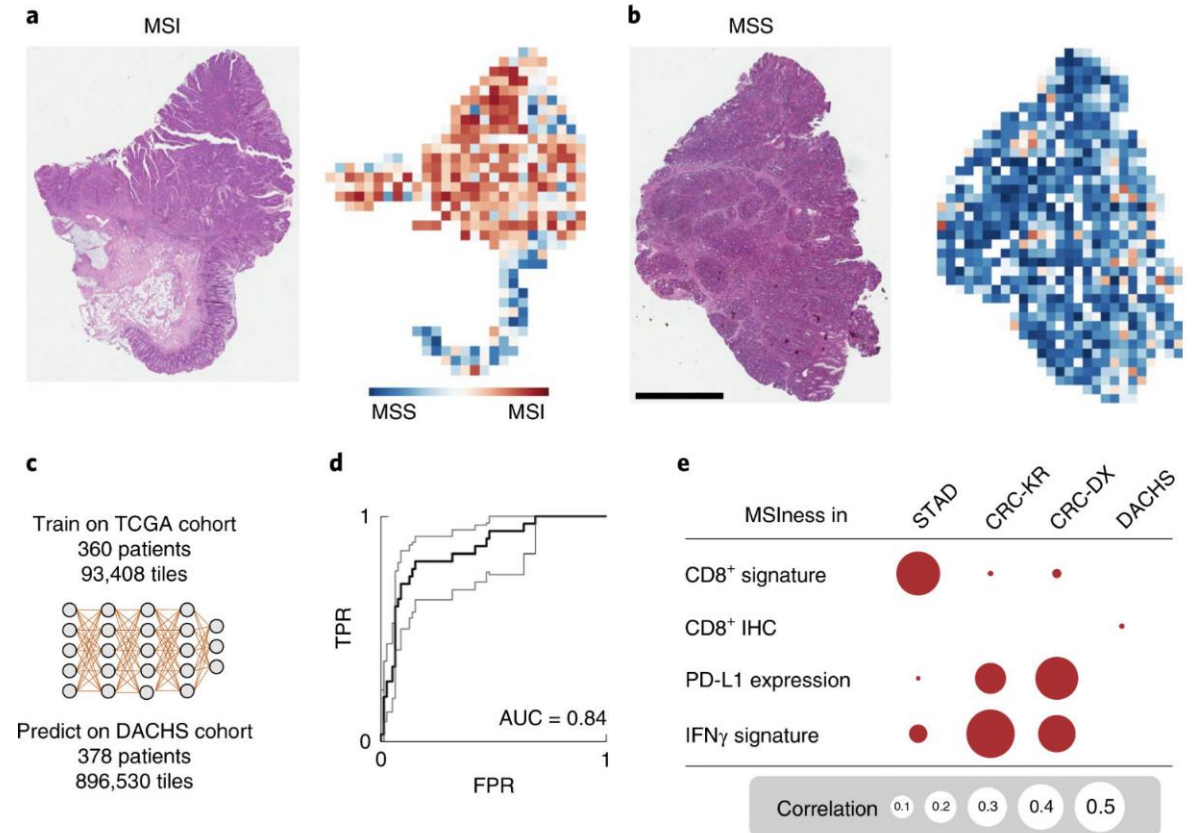
<https://gco.iarc.fr/today/fact-sheets-cancers>

How to scale?

— _ (ツ) _ / —

Deep learning can predict microsatellite instability directly from histology in gastrointestinal cancer

Jakob Nikolas Kather^{1,2,3,4,5,*}, Alexander T. Pearson⁴, Niels Halama^{2,5,6}, Dirk Jäger^{2,3,5}, Jeremias Krause¹, Sven H. Loosen¹, Alexander Marx⁷, Peter Boor⁸, Frank Tacke⁹, Ulf Peter Neumann¹⁰, Heike I. Grabsch^{11,12}, Takaki Yoshikawa^{13,14}, Hermann Brenner^{2,15,16}, Jenny Chang-Claude^{17,18}, Michael Hoffmeister¹⁵, Christian Trautwein¹, Tom Luedde^{1,*}



The NEW ENGLAND JOURNAL of MEDICINE

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Neoadjuvant Immunotherapy in Locally Advanced Mismatch Repair–Deficient Colon Cancer

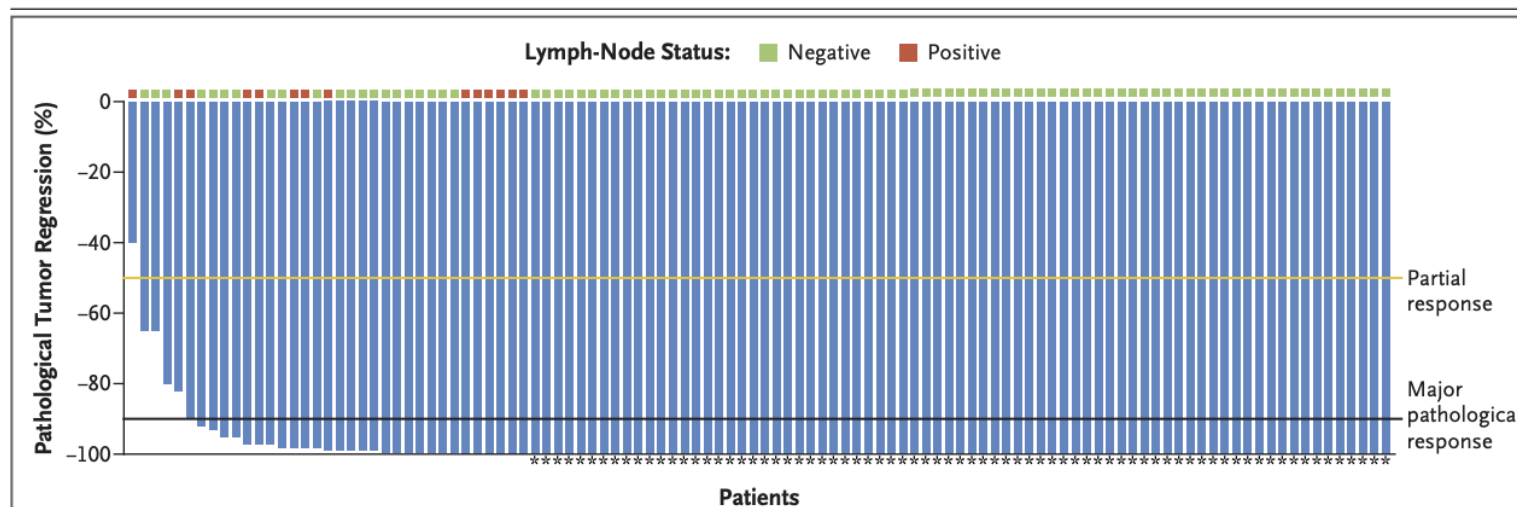


Figure 2. Pathological Responses among Patients in the Efficacy Analysis.

The waterfall plot shows the percentage of pathological tumor regression per tumor among the 110 tumors that could be evaluated for a pathological response. Boxes above each bar indicate the corresponding pathological lymph-node status. Patients with a pathological complete response in both the primary tumor and the lymph nodes are indicated by an asterisk. The black horizontal line indicates the threshold for a major pathological response, specified as at least 90% tumor regression. The yellow line indicates the threshold for a partial response, specified as at least a 50% regression.

And Why?



And What Will Happen?

NHS
Galleri Trial

GRAIL



KING'S COLLEGE LONDON
CANCER PREVENTION
TRIALS UNIT

[Taking part](#) [About the trial](#) [Contact](#)

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Detecting cancer early

Help the NHS with research into early
cancer detection



An Actionable Inflammatory Axis for Air Pollution Induced Non-Small Cell Lung Cancer

Charles Swanton Francis Crick Institute and UCL Hospitals

BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 30 1950

SMOKING AND CARCINOMA OF THE LUNG PRELIMINARY REPORT

BY

RICHARD DOLL, M.D., M.R.C.P.

Member of the Statistical Research Unit of the Medical Research Council

AND

A. BRADFORD HILL, Ph.D., D.Sc.

Professor of Medical Statistics, London School of Hygiene and Tropical Medicine; Honorary Director of the Statistical Research Unit of the Medical Research Council

Possible Causes of the Increase

Two main causes have from time to time been put forward: (1) a general atmospheric pollution from the exhaust fumes of cars, from the surface dust of tarred roads, and from gas-works, industrial plants, and coal fires; and (2) the smoking of tobacco. Some characteristics of the former have certainly become more prevalent in the last 50 years, and there is also no doubt that the smoking of cigarettes has greatly increased. Such associated changes in time can, however, be no more than suggestive, and until recently there has been singularly little more direct evidence. That evidence, based upon clinical experience and records, relates mainly to the use of tobacco. For instance,



@charlesswanton



So...



- **Precision Oncology as a concept has the potential to fundamentally change our approach and perception to public health**
 - **Personalized treatment**
 - **Personalized early detection**
 - **Personalized prevention**
- **This realization**
 - **Has socio-economic and ethical implications**
 - **Underscores the need for integrated health care solutions**
 - **Underscores the need for true (!) collaboration &**
 - **Underscores the need for multi-stakeholder & trans-sectoral approaches**

„Incorporating recent advances in cutting edge personalised medicine research into the real clinical practice“

- Define priorities!
- Seek clinically-relevant solutions
- Don't overcomplicate things – search for simple solutions that are fit for purpose
- Know what lies ahead:
 - Regulatory Surroundings

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What needs to happen?

You alone...



Working together...

You alone...

Working in teams



Need For a Leap...



Let's Discuss



 **@BenWestphalen**

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