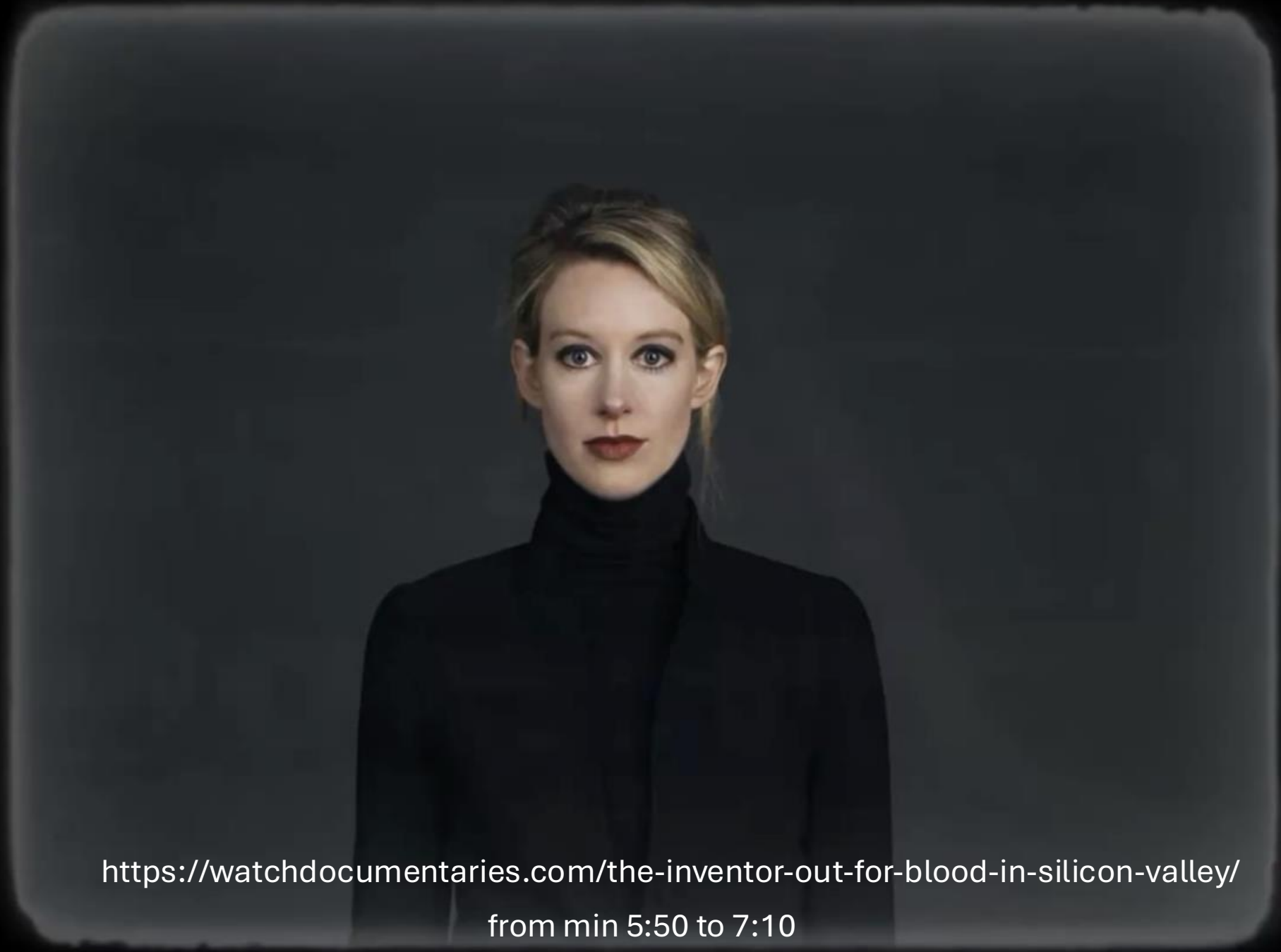


https://watchdocumentaries.com/the-inventor-out-for-blood-in-silicon-valley/

from min 5:50 to 7:10

nature medicine

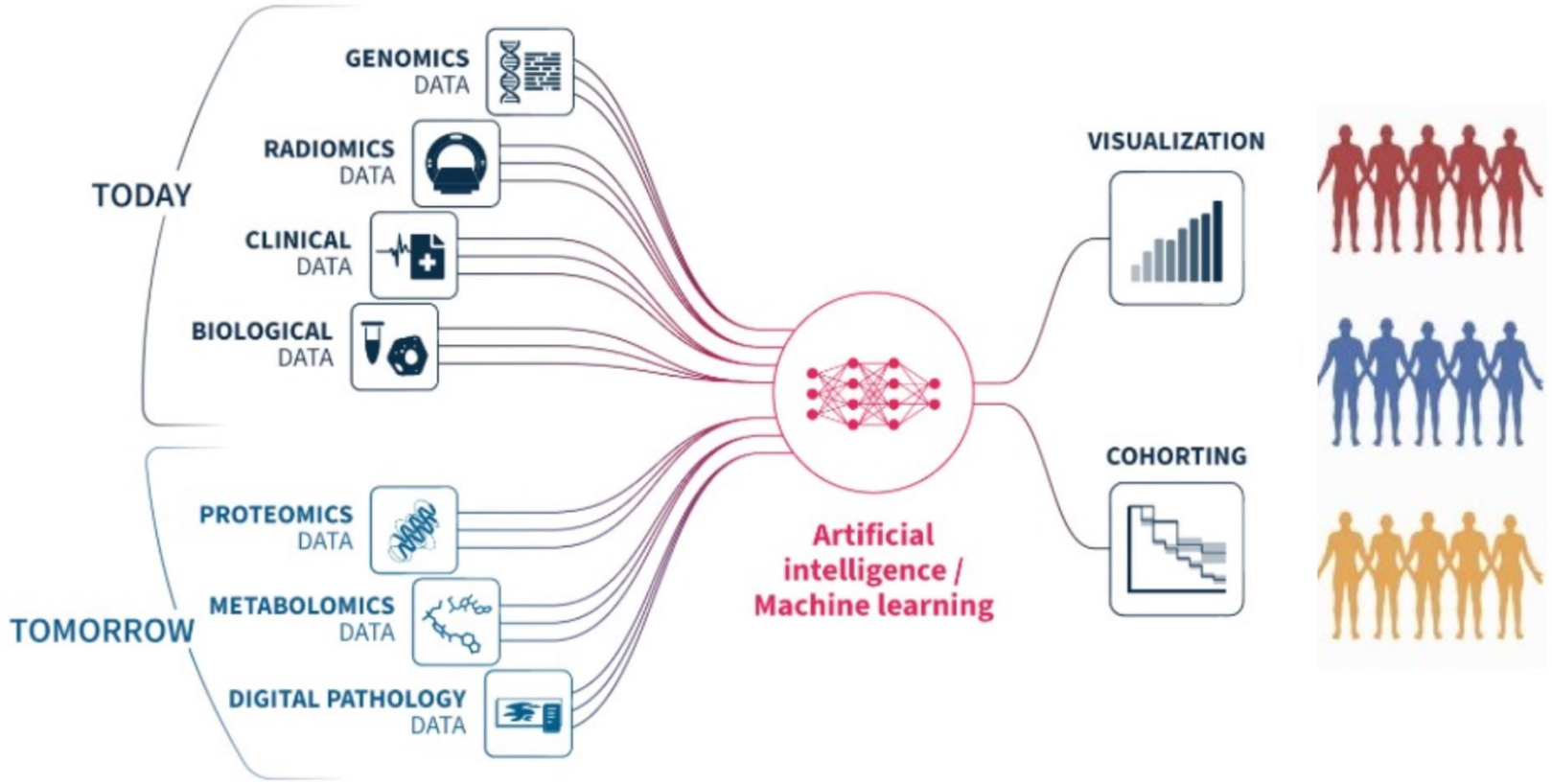
The Future of Medicine

“

What will medicine look like in 2055?
Perhaps healthcare will have transitioned from a reactive model to one that is proactive, **personalized** and preventive.
Advances in **multi-omics** - integrating genomics, transcriptomics, proteomics and metabolomics - may enable **precise prediction of individual disease risks**.

The Future of Medicine. *Nat Med* **31**, 1 (2025)

The future of medicine?

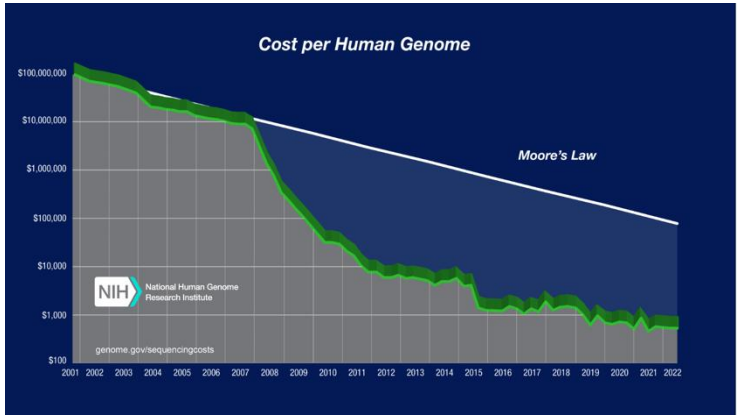


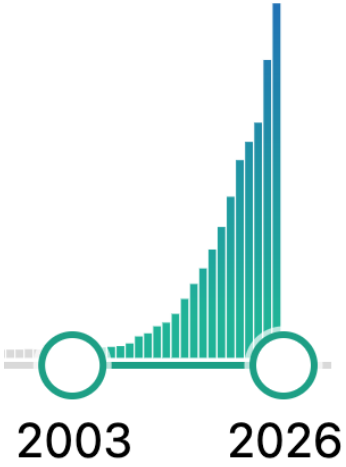
Adapted from Sophia Genetics Inc. 2024

Holy Grail

THE PRECISION MEDICINE INITIATIVE

“*What if matching a cancer cure to our genetic code was just as easy, just as standard?*





or bubble?

TIME

HEALTH • COMPANIES

Theranos Has Junked Two Years of Blood Test Results

AP

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LIVE Trump administration Election Day 2025 Dick Cheney dies at 84 Supermoon Jonathan Bailey

Elizabeth Holmes gets more than 11 years for Theranos scam

2 of 11 | Theranos founder and CEO Elizabeth Holmes, center, walks into federal court with her partner Billy Evans, right, and her parents in San Jose, Calif., Friday, Nov. 18, 2022. A federal judge will decide whether Holmes should serve a lengthy prison sentence for duping investors and endangering patients while peddling a bogus blood-testing technology. (AP Read More

SCIENCEINSIDER | BIOLOGY

Frustrated U.S. FDA Issues Warning to 23andMe

Direct-to-consumer genome service under fire after stalled approval process

25 NOV 2013 · BY KELLY SERVICK

The U.S. Food and Drug Administration (FDA) is cracking down on DNA testing company 23andMe for the marketing of its Personal Genome Service (PGS). In a 22 November

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Research News ›

FDA Authorizes 23andMe BRCA Genetic Test, but Test Only IDs Three Mutations

The FDA has authorized a direct-to-consumer test to identify BRCA mutations, but it's important to know that the test only looks for three mutations that are extremely rare in the general population.

Published on March 7, 2018

Genetic testing firm 23andMe files for bankruptcy

By Juliana Liu, CNN

2 min read · Updated 9:04 AM EDT, Mon March 24, 2025

or bubble?

JAMA

Viewpoint

Seven Questions for Personalized Medicine

Michael J. Joyner, MD[1]; Nigel Paneth, MD, MPH[2,3]

Personalized or precision medicine maintains that medical care and public health will be radically transformed by prevention and treatment programs more closely targeted to the individual patient. These interventions will be developed by sequencing more genomes, creating bigger biobanks, and linking biological information to health data in electronic medical records (EMRs) or obtained by monitoring technologies. Yet the assumptions underpinning personalized medicine have largely escaped questioning. In this Viewpoint, we seek to stimulate a more balanced debate by posing 7 questions for the advocates of personalized medicine.

Conclusions

Even though personalized medicine will be useful to better understand rare diseases and identify novel therapeutic targets for some conditions, the promise of improved risk prediction, behavior change, lower costs, and gains in public health for common diseases seem unrealistic. Proponents of personalized medicine should consider tempering their narrative of transformative change and instead communicate a more realistic set of expectations to the public.

Joyner *et al.*, *JAMA (2015)*

or bubble?

nature

Perspective: The precision-oncology illusion

Precision oncology has not been shown to work, and perhaps it never will, says Vinay Prasad.

Idea: link patients with a drug based of genetic testing, irrespective of the tissue of origin of the tumor

“

Few patients benefit from precision oncology, enthusiasm has been fuelled by reports of **super responders**

→ Considering the patients receiving targeted therapies and the response rate: **~1.5% of patients will benefit**

Vinay Prasad *is a haematologist–oncologist at the Knight Cancer Institute, Oregon Health and Science University, Portland, Oregon, USA.*

Prasad, *Nature* (2016)

Show me the data!

Precision oncology - SHIVA trial

Ultimate judge of a therapeutic strategy**: randomized controlled trial**

THE LANCET
Oncology

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

- Any kind of metastatic solid tumors

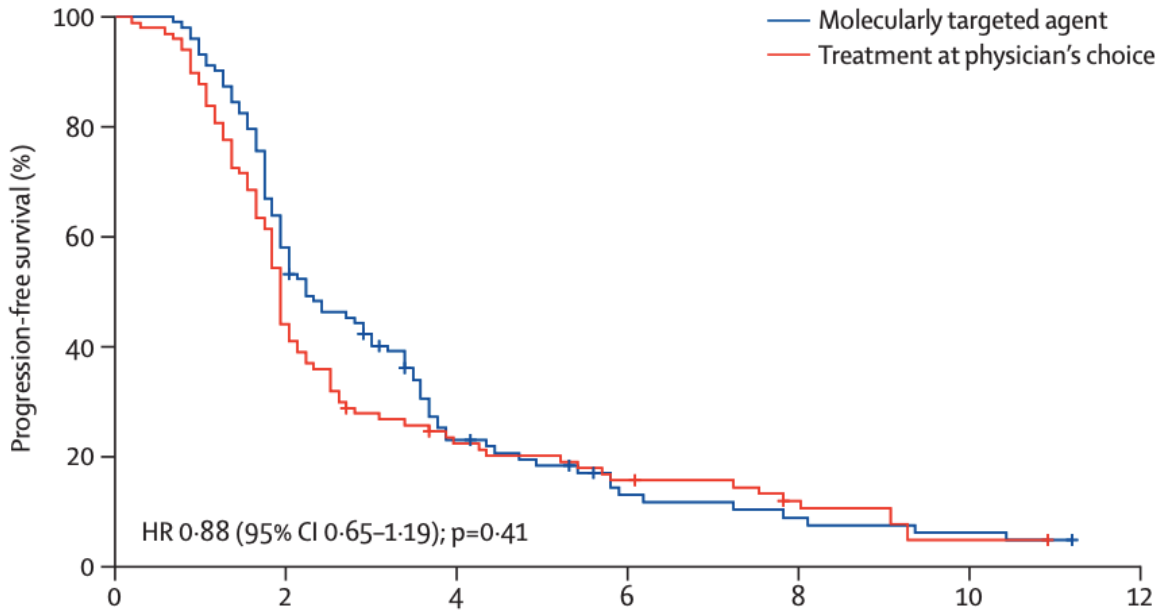
- Molecular alterations in three molecular pathways (hormone receptor, PI3K/AKT/mTOR, RAF/MEK) matched to one of 10 regimens (molecularly tageted agents) used off-label - molecular profiling by sequencing

→ Matched molecularly target agent vs physician's choice

Le Tourneau *et al.*, *The Lancet Oncology* (2015)

Precision oncology - SHIVA trial

Primary endpoint: Progression Free Survival (PFS)



PFS = 2.3 vs 2.0 months matched drug vs physician's choice

Interpretation

The use of molecularly targeted agents outside their indications does not improve progression-free survival compared with treatment at physician's choice in heavily pretreated patients with cancer.

Le Tourneau *et al.*, *The Lancet Oncology* (2015)

Precision oncology - tumor-agnostic approach

Targeting some specific **tumor-agnostic biomarkers** induces **considerable clinical benefits**

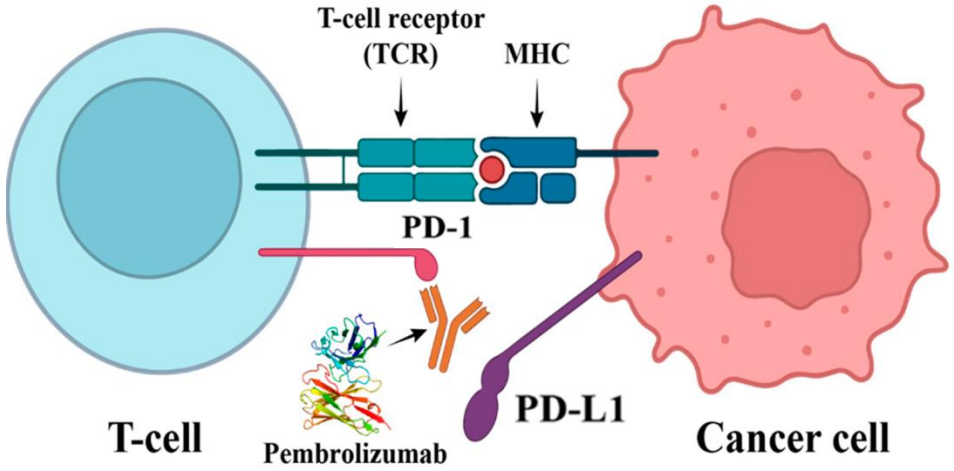
- **High-microsatellite instability - MSI-H**
- **High tumor mutational burden (hTMB)**
- **HER2-expressing solid tumors**
- **NTRK gene fusions tumors**
- **BRAF V600 mutation-positive tumors**
- **RET-fusion tumors**

Marchetti *et al.*, *Nat Med* (2025)

High-microsatellite instability - MSI-H

dMMR, thousands of somatic mutations, highly immunogenic

→ **Pembrolizunab:** anti-PD-1 monoclonal antibody, approved in 2014 for metastatic melanoma



Adapted from Wang *et al., Int. J. Mol. Sci. (2023)*

Journal of Clinical Oncology
An American Society of Clinical Oncology Journal

Efficacy of Pembrolizumab in Patients With Noncolorectal High Microsatellite Instability/Mismatch Repair–Deficient Cancer: Results From the Phase II KEYNOTE-158 Study

KEYNOTE-158: single-arm, not randomised

→ **Objective response rate 34.3%**

KEYTRUDA approved for MSI-H by FDA in 2023

First immunotherapy full approval based on tumor-agnostic biomarker

The NEW ENGLAND JOURNAL of MEDICINE

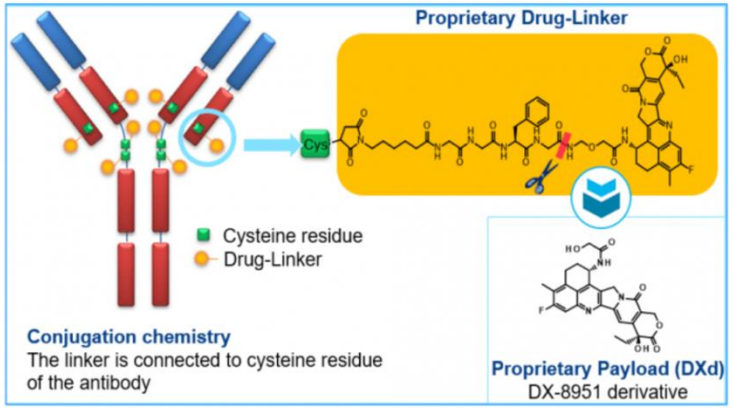
Pembrolizumab in Microsatellite-Instability–High Advanced Colorectal Cancer

KEYNOTE-177: two-arm, randomised, cancer specific trial

→ **Progression Free Survival 16.5** vs **8.2 months** anti-PD-1 vs chemo

Marabelle *et al.*, *J Clin Oncol* (2020) | André *et al.*, *N Engl J Med* (2020)

HER2-expressing solid tumors



Trastuzumab deruxtecan: antibody-drug conjugate
Approved in breast, gastric cancer and NSCLC

Journal of Clinical Oncology
An American Society of Clinical Oncology Journal

Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial

DESTINY-PanTumor02: single-arm, not randomised

→ **Objective response rate**: **61.3%** HER2 IHC 3+

Funda Meric-Bernstam *et al.*, *J Clin Oncol* (2024)

Ultimate judge - randomized evidence?

Randomized evidence supporting the clinical superiority of precision oncology approaches, guided by **tumor-agnostic biomarkers**, compared to standard of care remains **limited**

Marchetti *et al.*, *Nat Med* (2025)

Precision oncology - ROME trial

nature medicine

Genomically matched therapy in advanced solid tumors: the randomized phase 2 ROME trial

Published: 29 September 2025

11k Accesses | **1** Citations | **82** Altmetric | Metrics

- Advanced solid tumors after one or two lines of treatments

- Genomic profiling on tissue and blood samples
  → FoundationOne CDx and FoundationOne Liquid CDx + centralized NGS

- Tailored Treatment (TT) vs Standard of Care (SoC)

→ Tailored treatment discussed and approved in a **Molecular Tumor Board**

897 patients evaluated, 400 accepted and randomized in TT and SoC

Marchetti *et al.*, *Nat Med* (2025)

Precision oncology - ROME trial

Primary endpoint: Overall response rate (ORR)

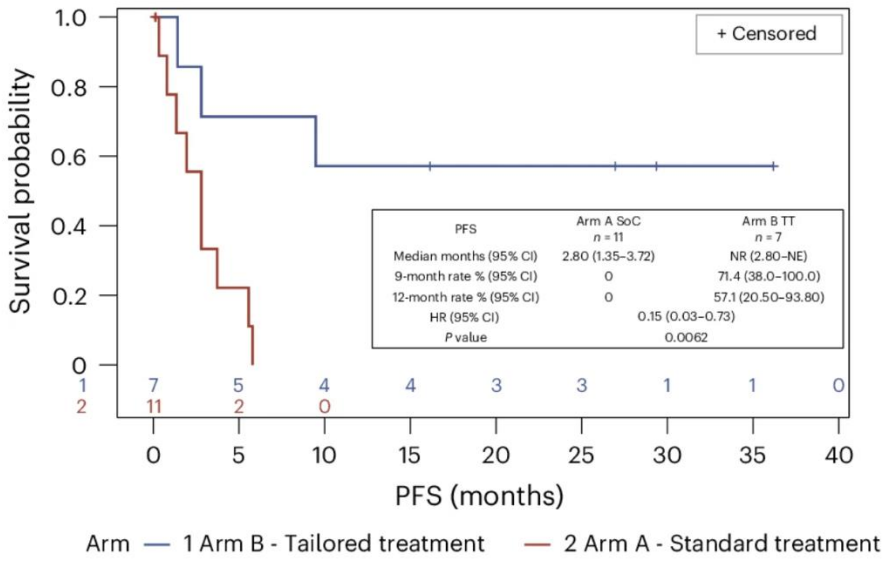
→ **ORR: 17.5%** vs **10%** TT vs SoC - **Statistically significant** (3% in TT vs no complete response in SoC)

Progression Free Survival improved: **3.5** vs **2.8** months

→ No significant difference in median overall survival, but 59% crossover rate at the end of the trial

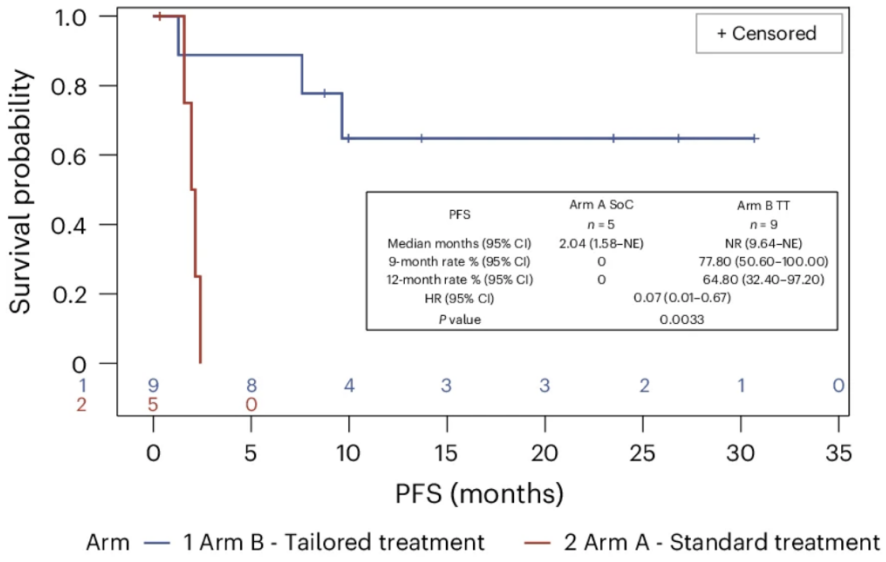
Subgroup analyses

MSI-H



PFS not reached vs 2.8 months

BRAF alteration



PFS not reached vs 2.0 months

Marchetti *et al.*, *Nat Med* (2025)

Conclusions

ROME trial: **relevant evidence** supporting a **tumor-agnostic** precision oncology strategy, guided by genomic profiling and molecular tumor boards

Important limitation: less than half of patients was actually enrolled, due to the lack of targetable alterations

→ **Overall showed precision oncology feasibilty even under a healthcare system point of view**

Marchetti *et al.*, *Nat Med* (2025)

Thank you for your attention!