

**„Next generation sequencing“ v onkologii**

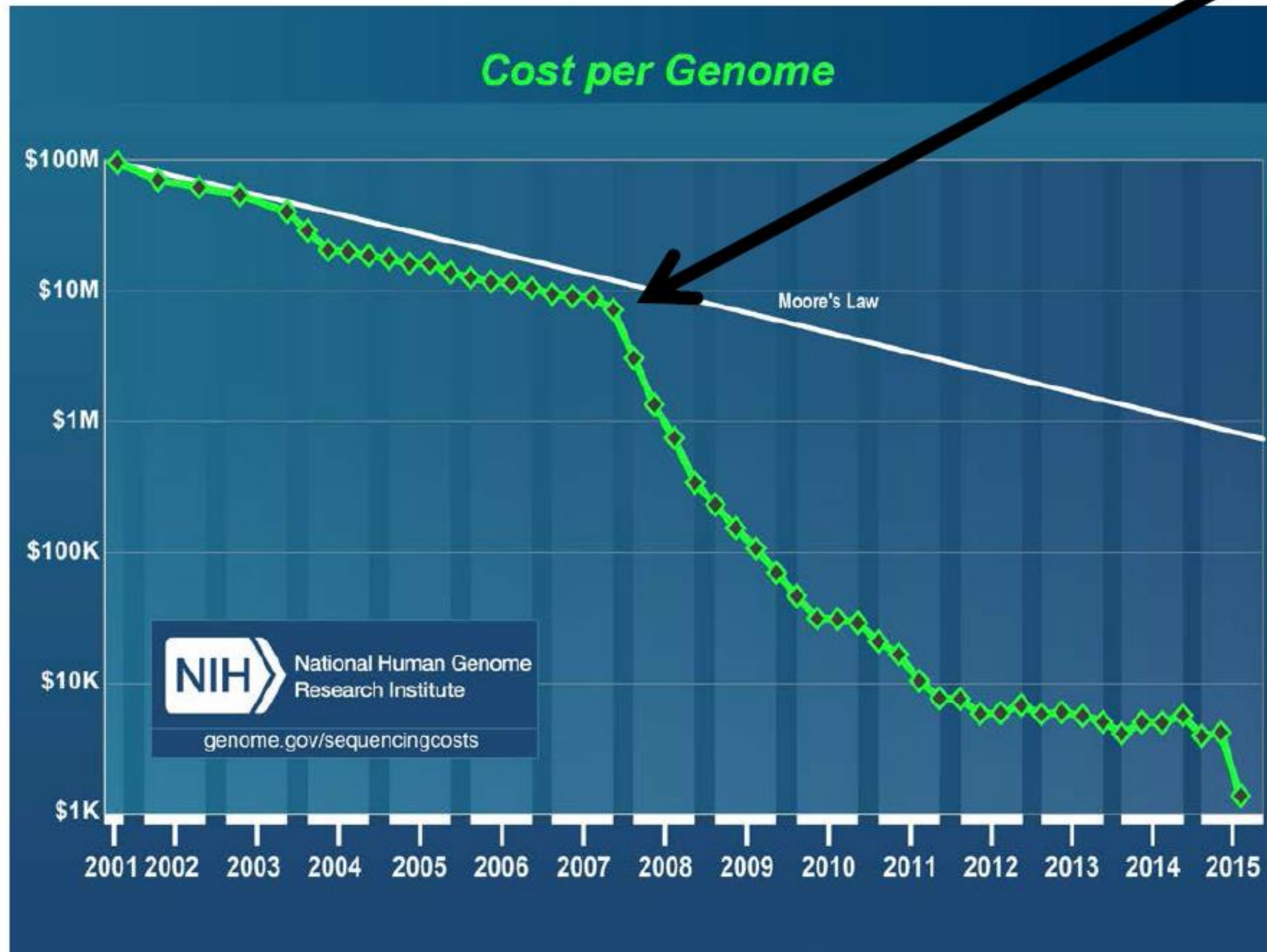
**„Next generation sequencing“ in oncology**

***Doc. MUDr. Mgr. Marek Mraz, PhD***

***Associate Professor of Oncology  
IHOK FN Brno and CEITEC MU***

# Next Generation Sequencing (NGS)

Impact of NGS

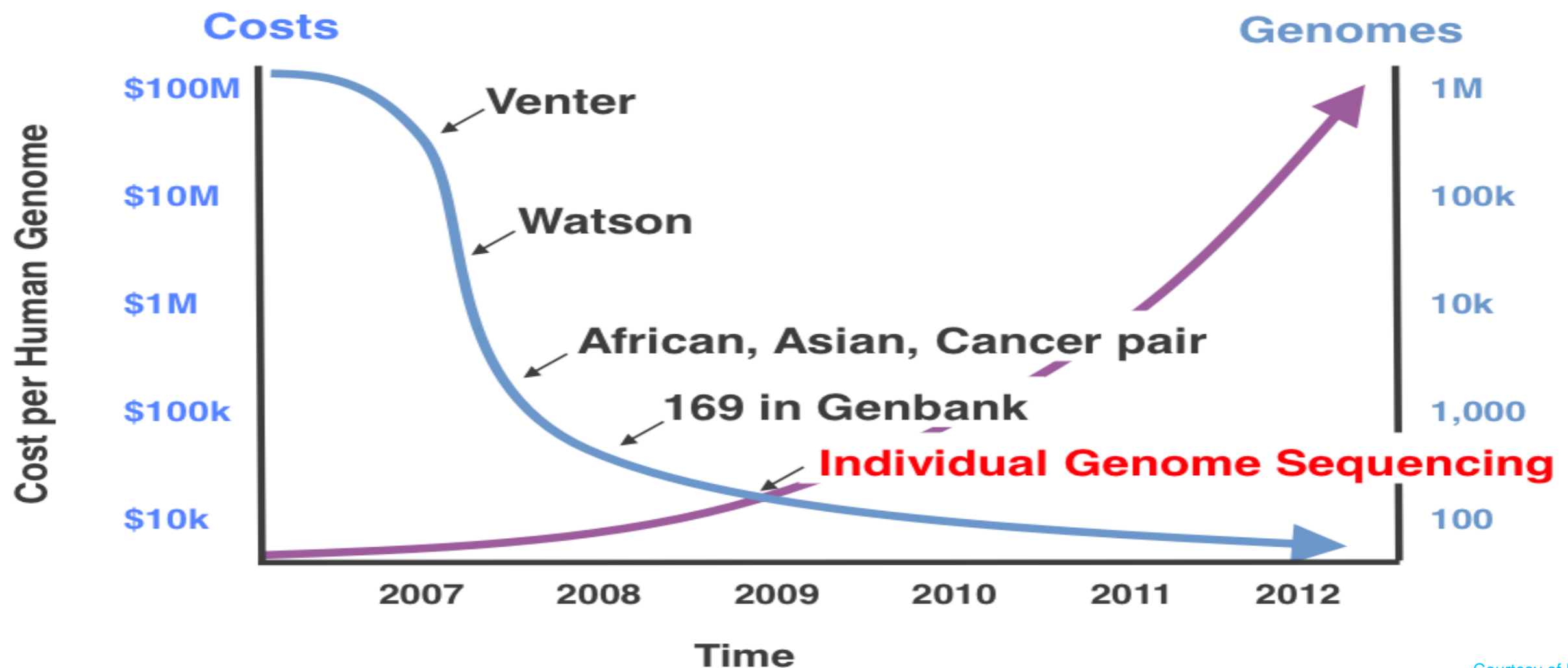


# Genomic Technology

## Breathtaking Progress Unparalleled in Human History

QUICKER, SMALLER, CHEAPER

Genome sequenced (publication year)	HGP (2003)	Venter (2007)	Watson (2008)	Current (2015)
Time taken (start to finish)	13 years	4 years	4.5 months	~1 days
Number of scientists listed as authors	> 2,800	31	27	
Cost of sequencing (start to finish)	\$2.7 billion	\$100 million	< \$1.5 million	~\$1000
Coverage	8-10 ×	7.5 ×	7.4 ×	30-50X
Number of institutes involved	16	5	2	
Number of countries involved	6	3	1	



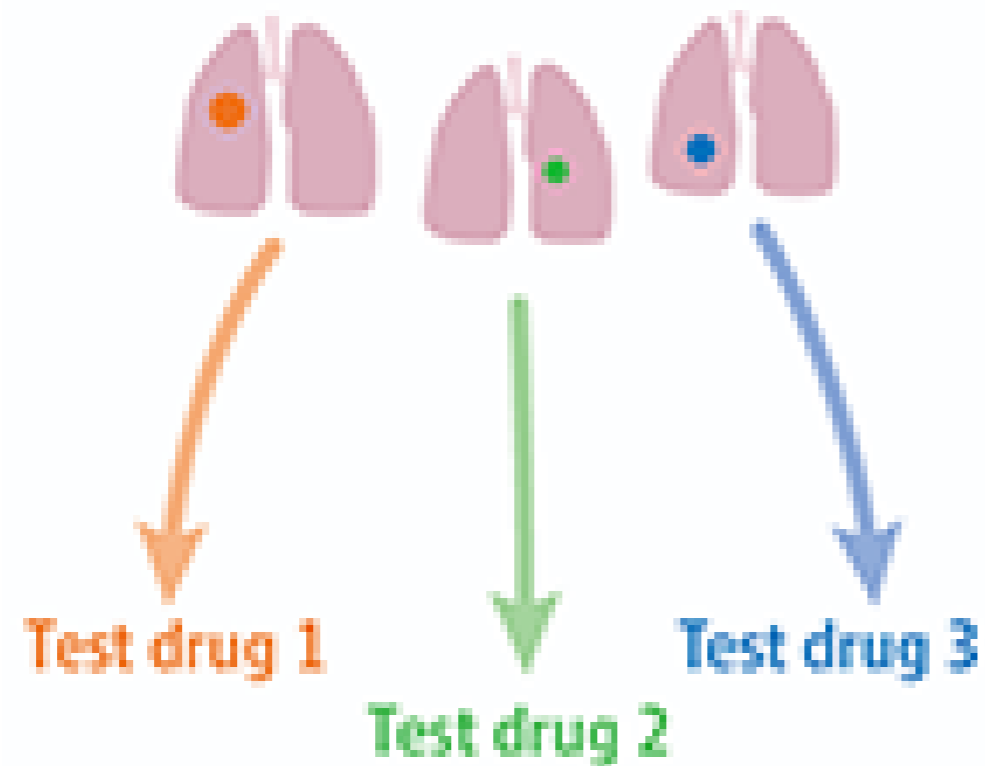
# REMEMBER THIS!

## Novel precision medicine trial designs

### Umbrella trial

1 type of cancer

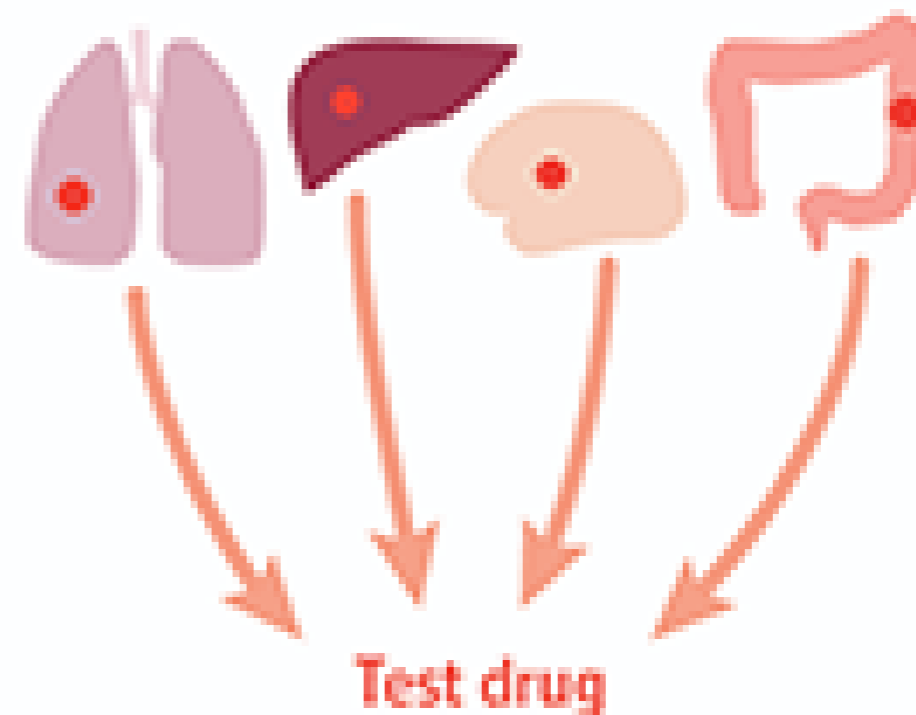
Different genetic mutations (●●●)



### Basket trial

Multiple types of cancer

1 common genetic mutation (●)



JAMA Oncology: doi:10.1001/jamaoncol.2016.5299

# Meta Analysis of 32,149 Patients in Phase II Clinical Trials

- **Non-personalized targeted arms led to poorer outcomes than cytotoxics arms**

(All  $P < 0.0001$ , except  $P = 0.048$  for OS meta-analysis).

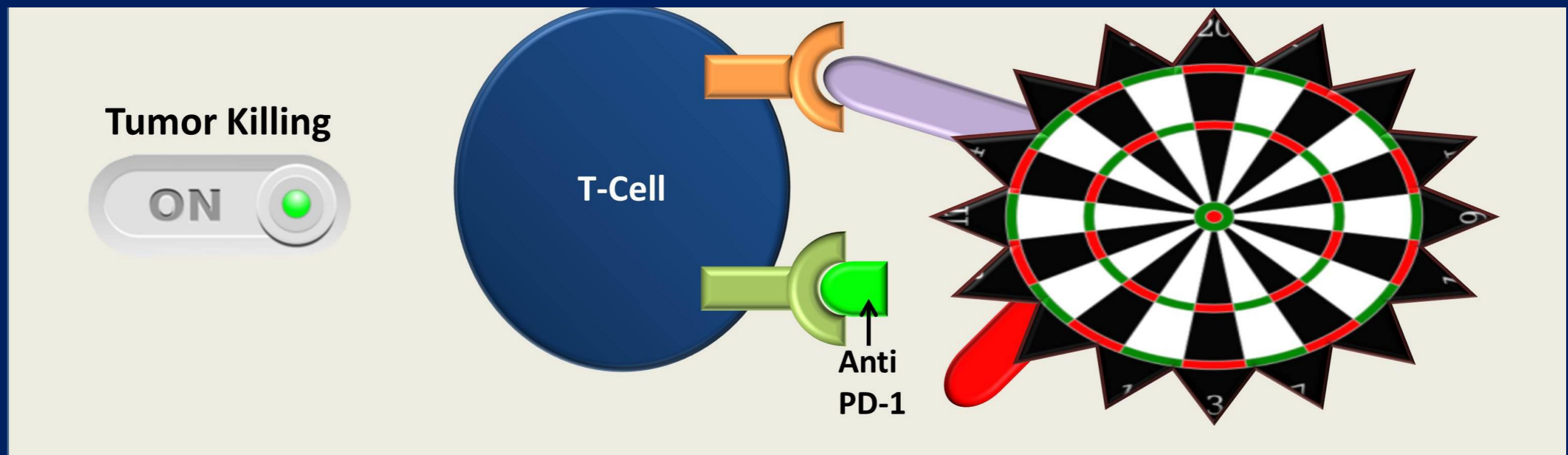
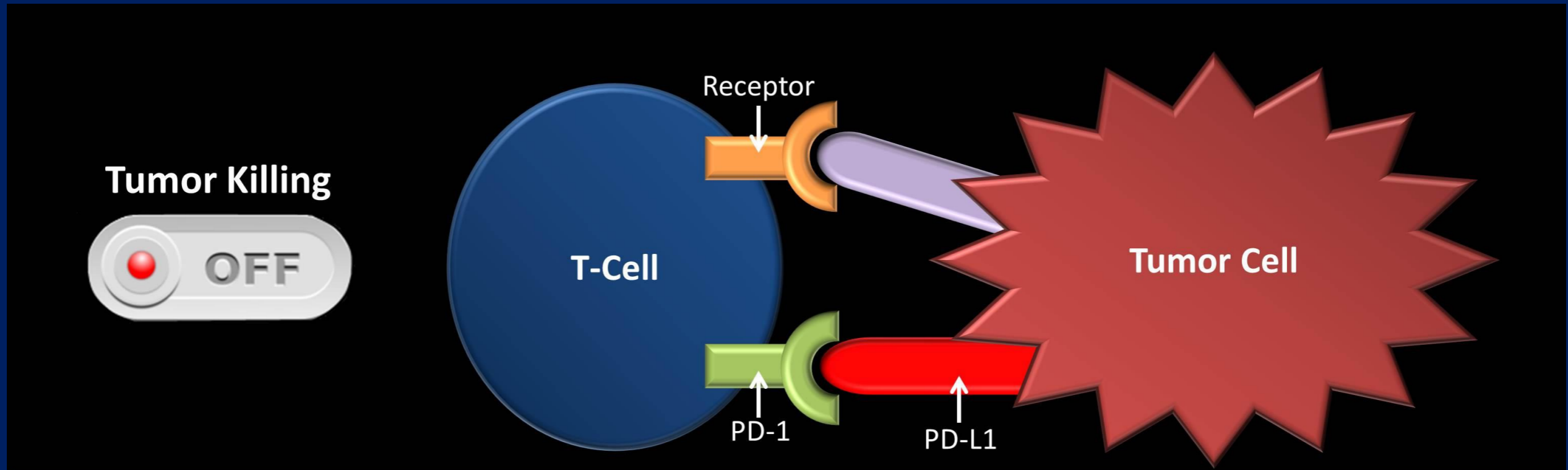
**Worst outcome**



**Best outcome**

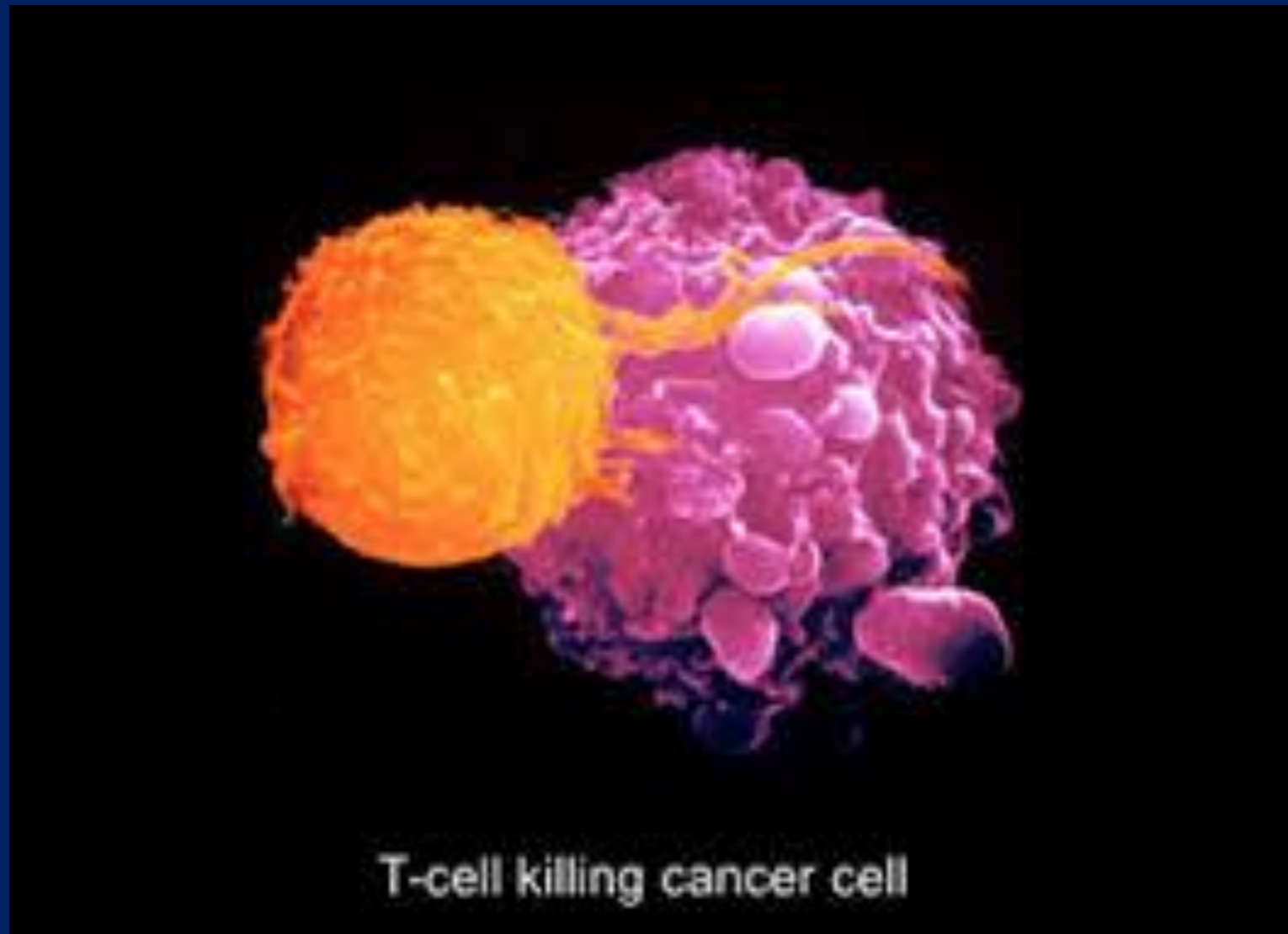
ARMS type	POOLED Analysis			Meta-analysis		
	R Rate (%)	PFS (Mos)	OS (Mos)	RR (%)	PFS (Mos)	OS (Mos)
Non-personalized targeted	4	2.6	8.7	7.5	2.5	8.3
Cytotoxic	12	3.3	9.4	16.1	3.3	9.3
Personalized targeted	30	6.9	15.9	31.3	6.1	13.7

# Checkpoint inhibitors



# Harnessing the Immune System

The immune system is the  
bringing the fight to the same level



# Bridging

## Genomics and Immunotherapy

### Mutanome-Directed Immunotherapy

The more mutated the tumor,  
the better the response to immunotherapy

- 4% response rate for low mutational burden
- 26% response rate for intermediate
- 45% response rate for high
- 67% response rate for very high mutational burden

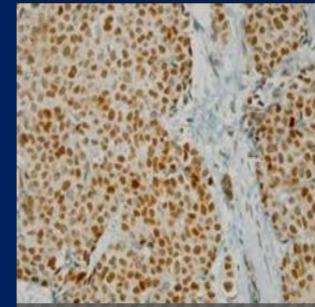
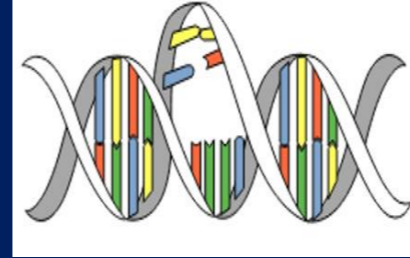
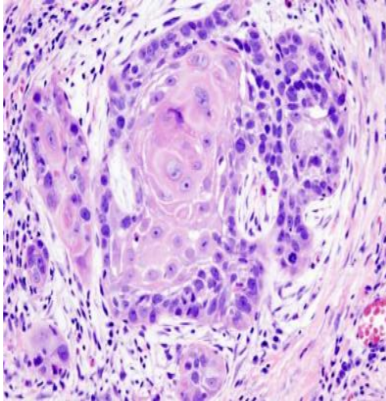


# Molecular Tumor Board

- Multidisciplinary discussion of patients
- Molecular profiling (clinical-grade) (N ~ 8000)
- Targeted, tailored treatment recommendations



# Comprehensive Profiling



## PREDICT/ IPREDICT Clinical Trial

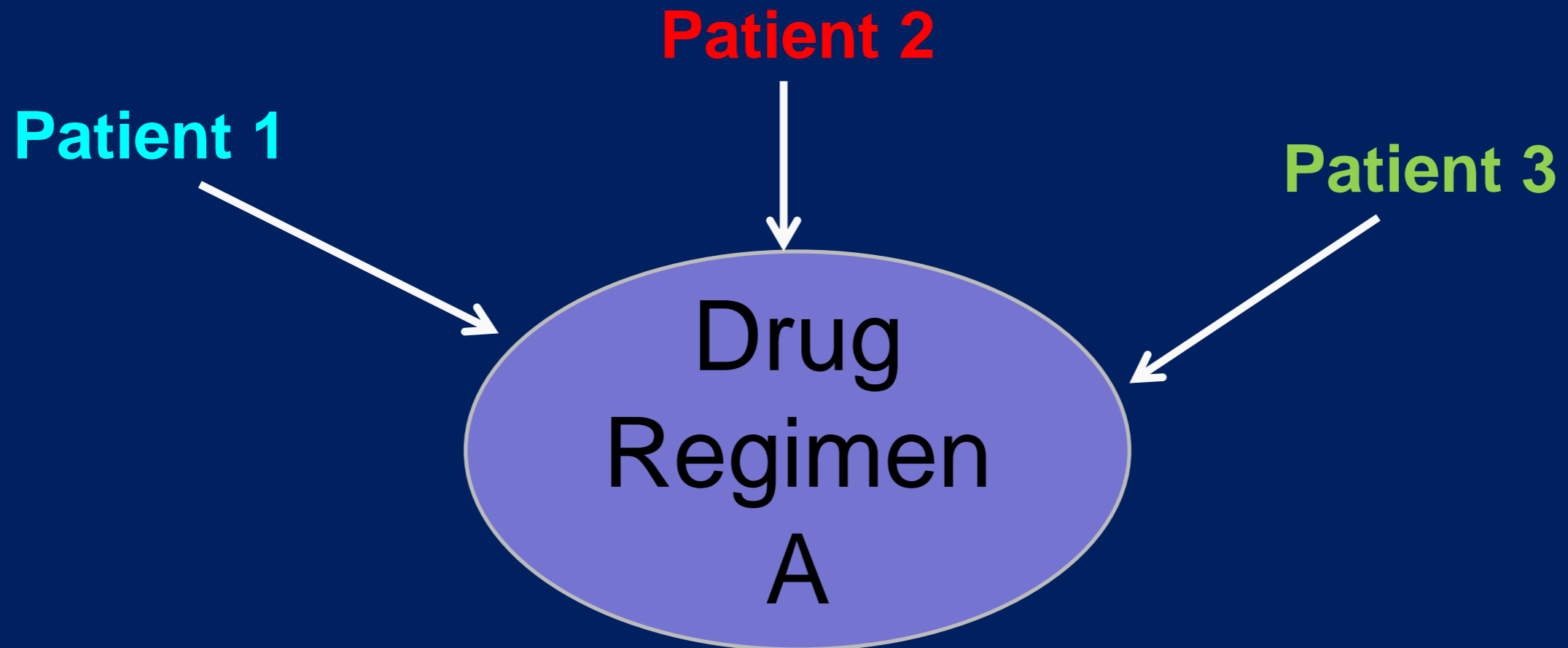
Tumor

### Comprehensive molecular profiling:

- Next-Generation DNA Sequencing
- Protein analysis
- Immune signature analysis
- Liquid biopsy (cancer DNA detection from blood )

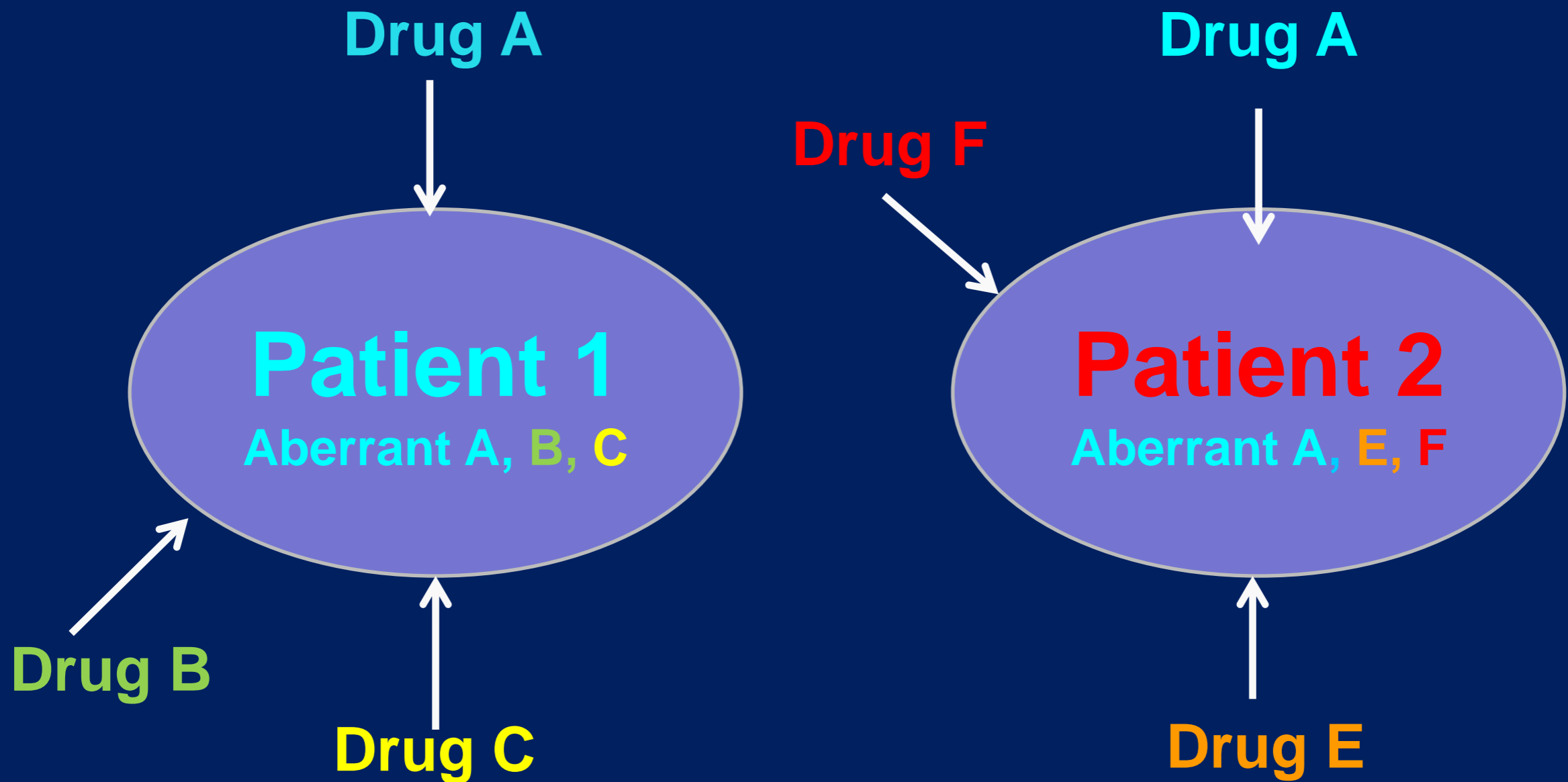
**“MATCH” the therapy based on the profiling.  
Personalized/Precision Medicine approach.**

# Drug-Centric Trial (Traditional)



**Strategy:** Find common feature between patients (e.g. type of cancer or type of molecular aberration) and place all on same drugs

# Patient-Centric Trial (N-of-One)



**Strategy:** Molecular matching for each patient with customized therapy combination

**THANK YOU**  
**for your attention**

**Marek Mraz**  
**CEITEC MU and FN Brno**  
**[Marek.mraz@email.cz](mailto:Marek.mraz@email.cz)**