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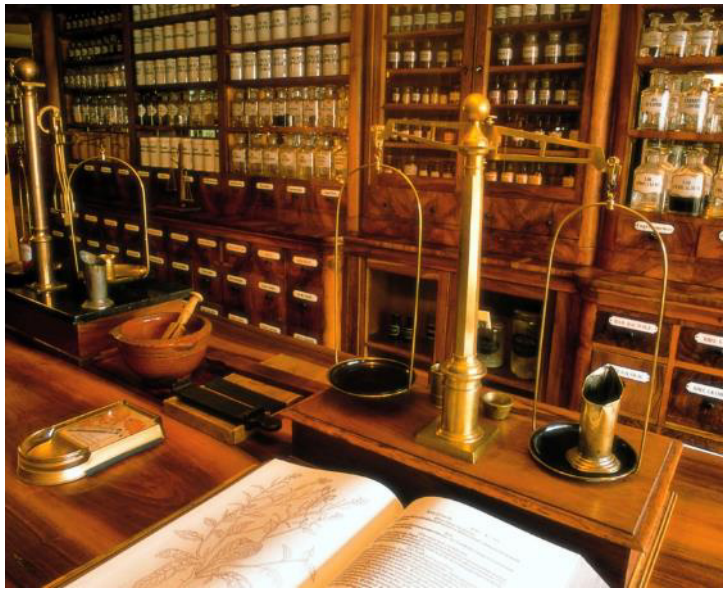
Personalized Medicine – Chances and Challenges

Frankfurt am Main, 24.11.2022

Personalized medicine is not a new thing

For centuries it has been the default option in medicine



It’s coming back – to the point of care!

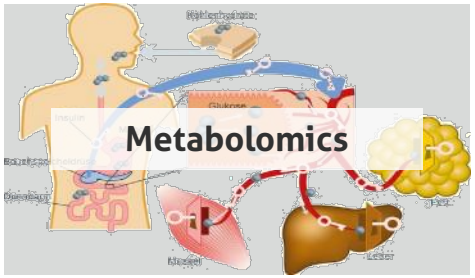
High expectations have been attached to personalized medicine

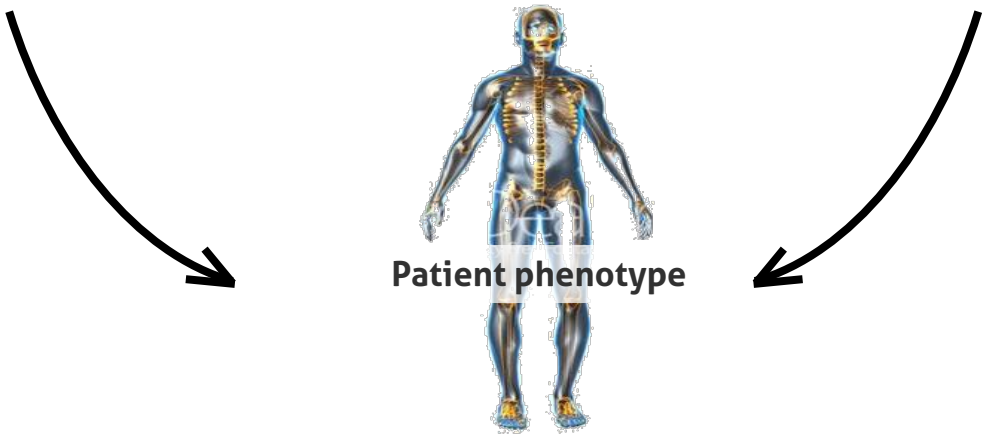
„The day will come when treatment decisions are based on a patient's genetic profile rather than on trial and error, when treatments are tailored to the actual causes of disease rather than symptoms.
That's our vision of **personalized medicine**."

Dr. Severin Schwan, CEO Roche in 2008

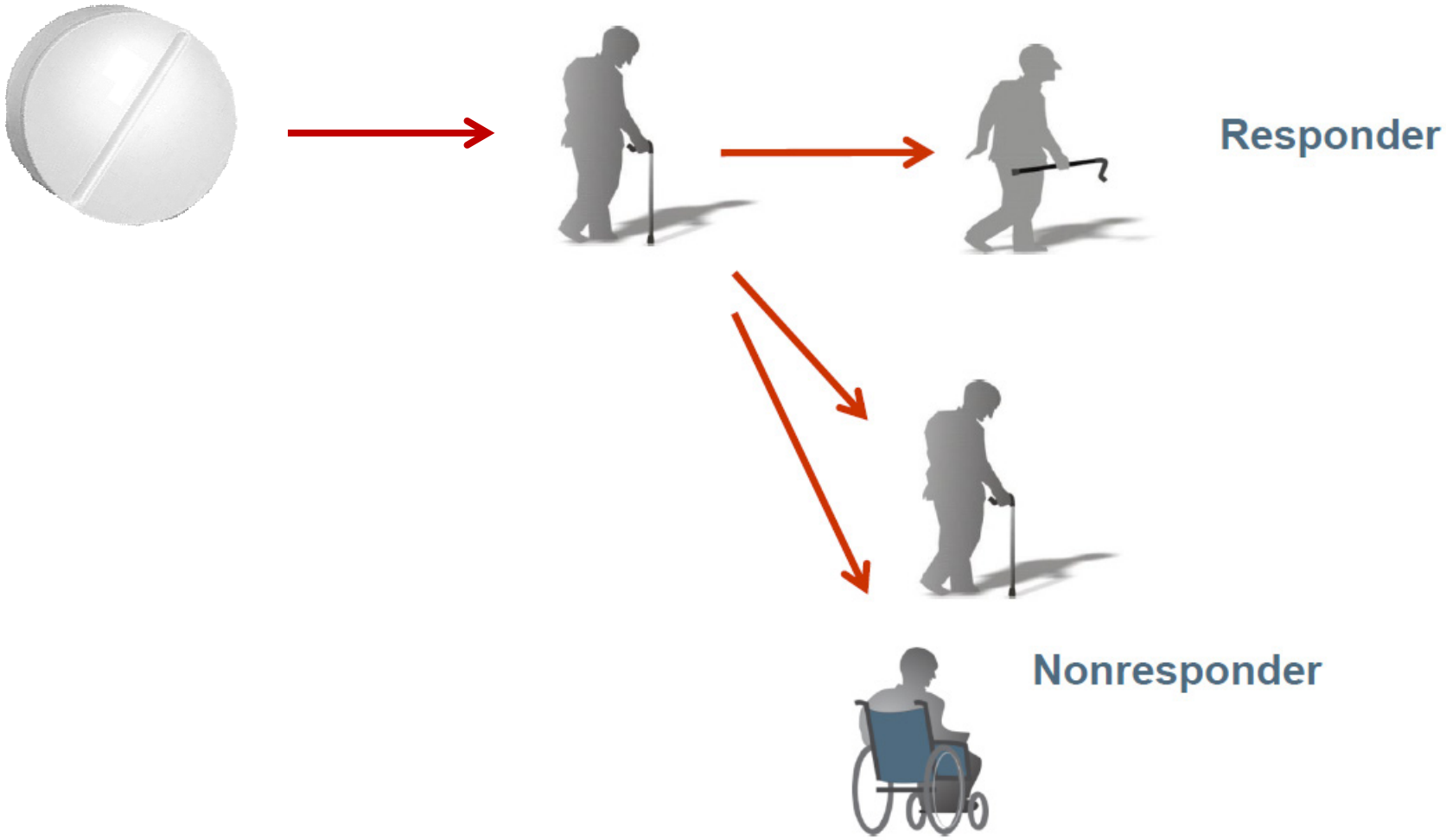
What did Dr. Schwan mean by personalized medicine?

It is the development and selection of a drug according to **patient-specific efficacy** and patient **tolerability**.



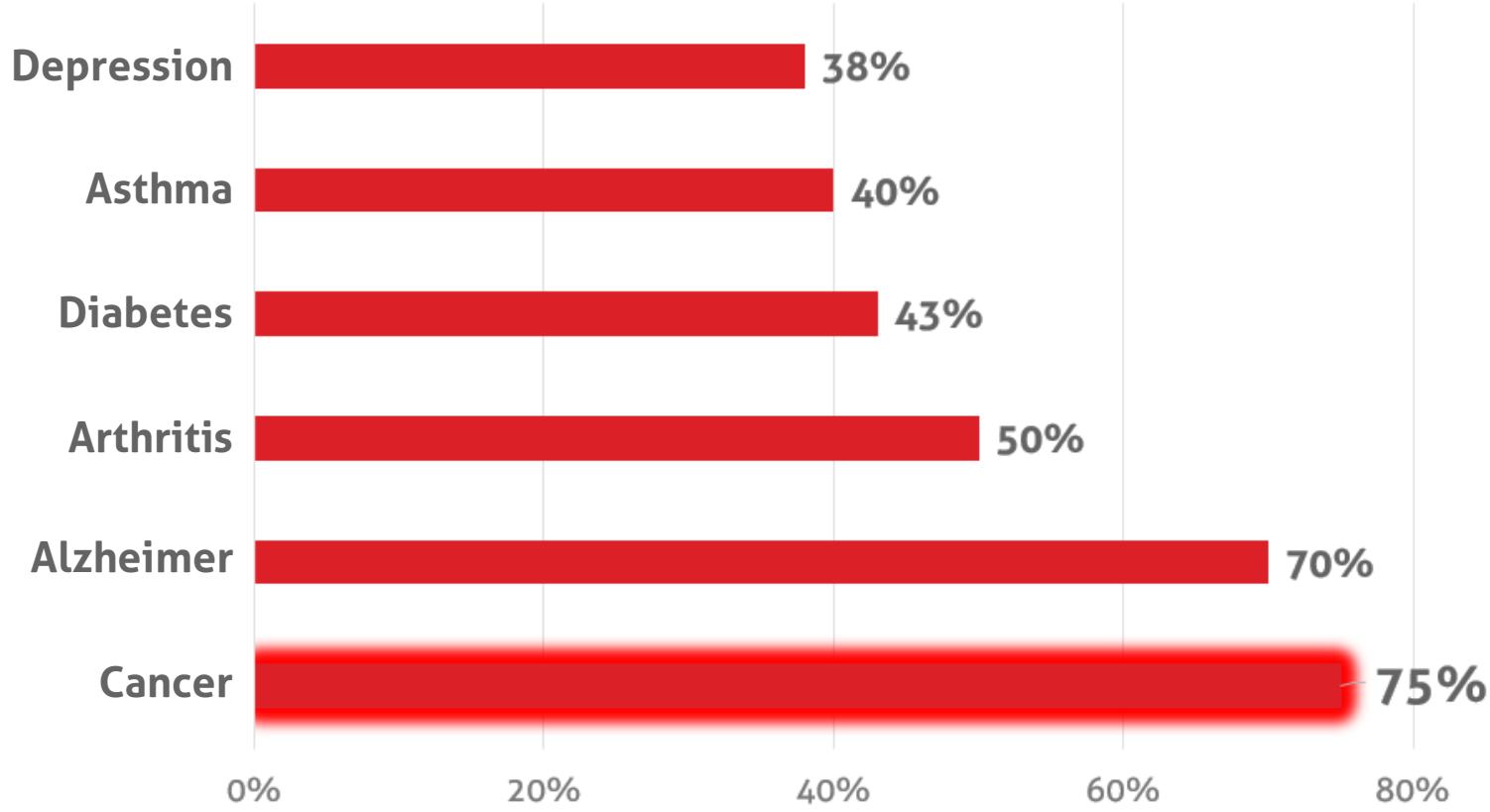


Why do we need personalized medicine?



Why do we need personalized medicine?

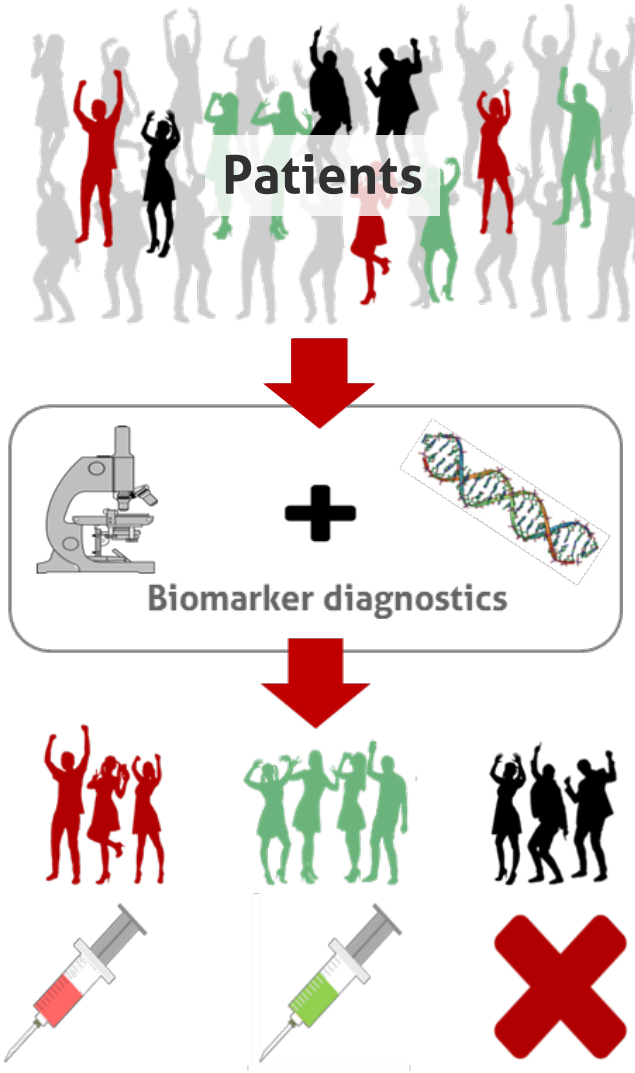
Percentage of the patient population for which a particular drug is ineffective, on average



Source: The personalized medicine report, Personalized Medicine Coalition 2020

Why do we need personalized medicine?

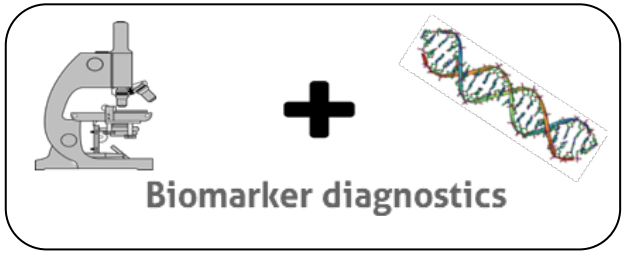
We needed a new treatment paradigm!



Why do we have personalized medicine today?

Huge innovation

- Better understanding the **biological and genetical characteristics** that drive diseases and influence a patient's response to treatment
- Capability to identify many of **related biomarkers**
  - Genetic, genomic and epigenetic biomarkers
  - Proteomic and metabolomic biomarkers



- Advances in **gene and cell therapies**
- Proof of concept of **mRNA therapies**
- Ability to develop the medicine together with the right **companion diagnostic**

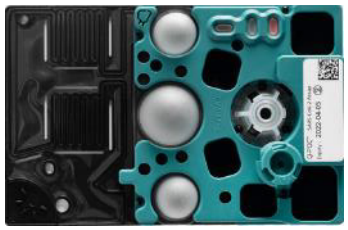
Why do we have personalized medicine today?

Innovations in In vitro diagnostics

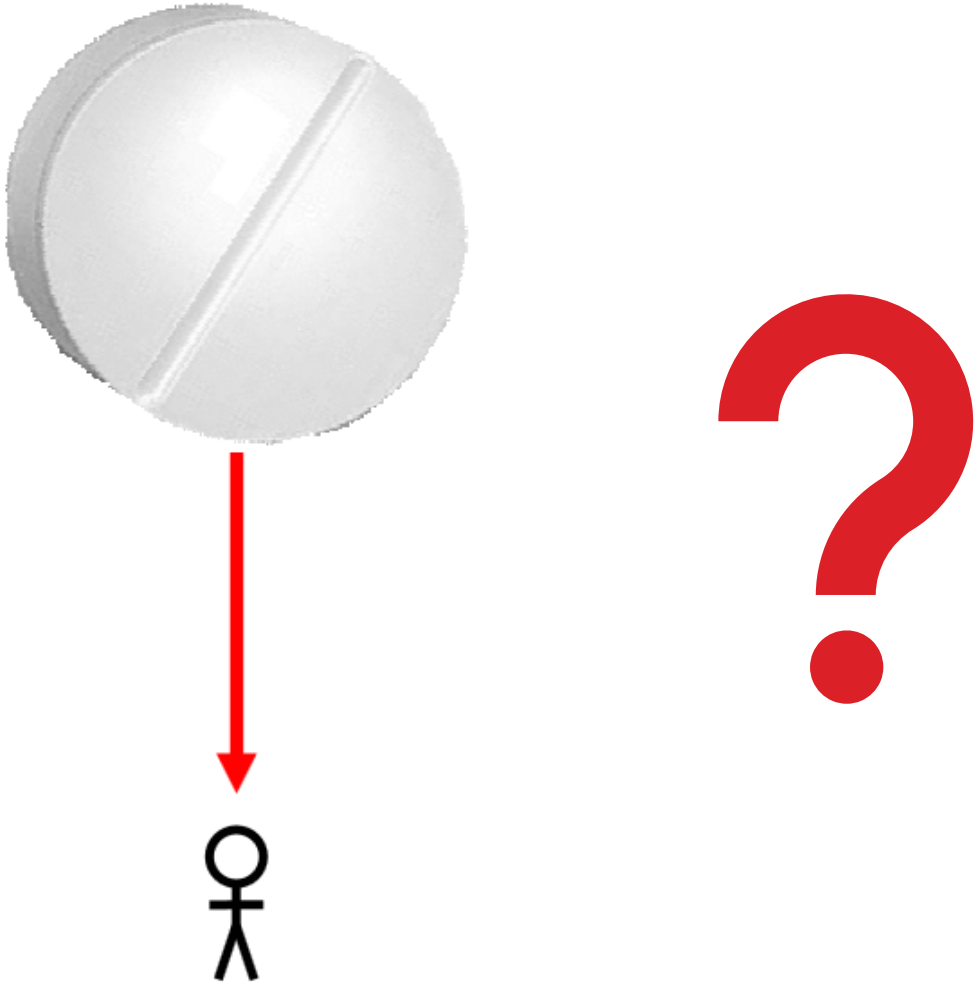
By the way:
Most IVD devices are being assembled in a bioburden-controlled environment!

- Biologics: biomarkers / reagents
- Electronics: sensors and software, lab-on-a-chip
- Photonics: optical systems for analytics
- Digitalization: connectivity and data analysis

- **All innovations are being reflected in the growing complexity of IVD devices**

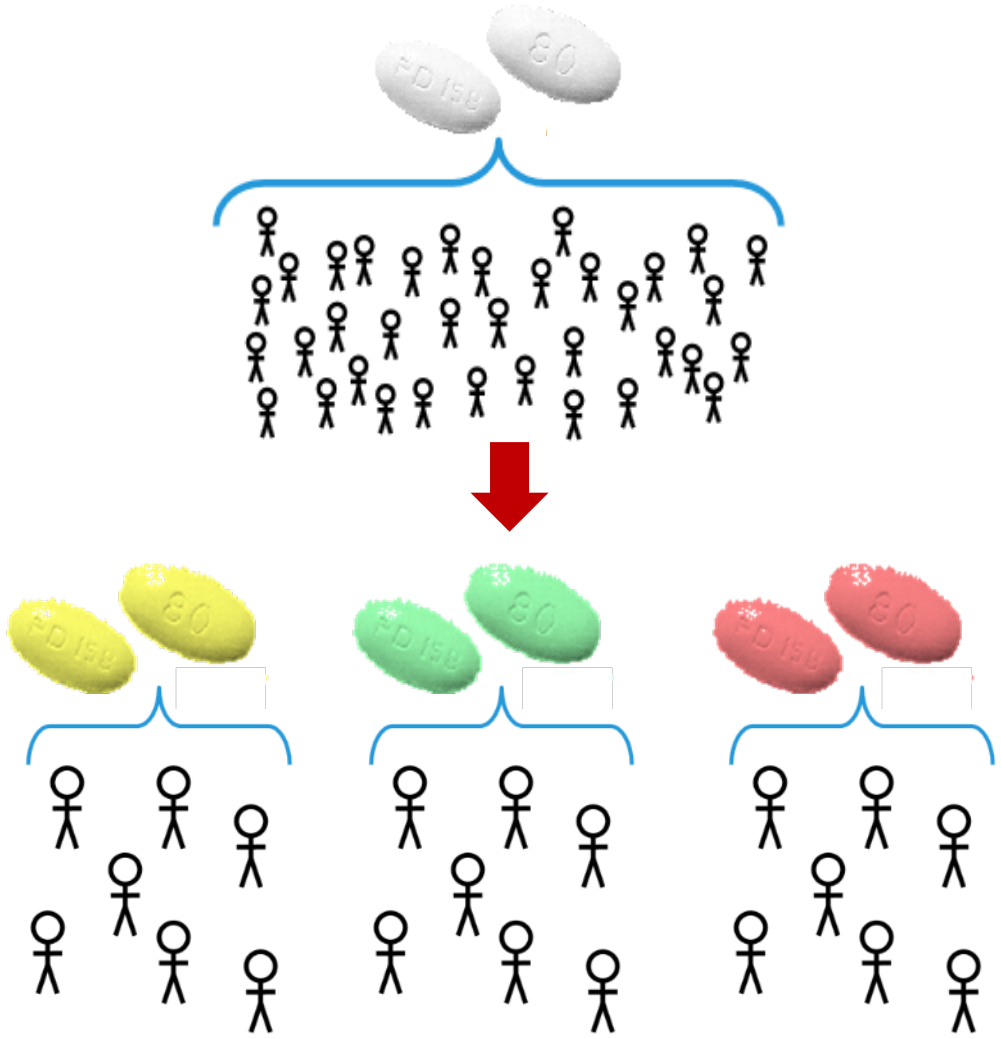


But do we really have personalized medicine today?



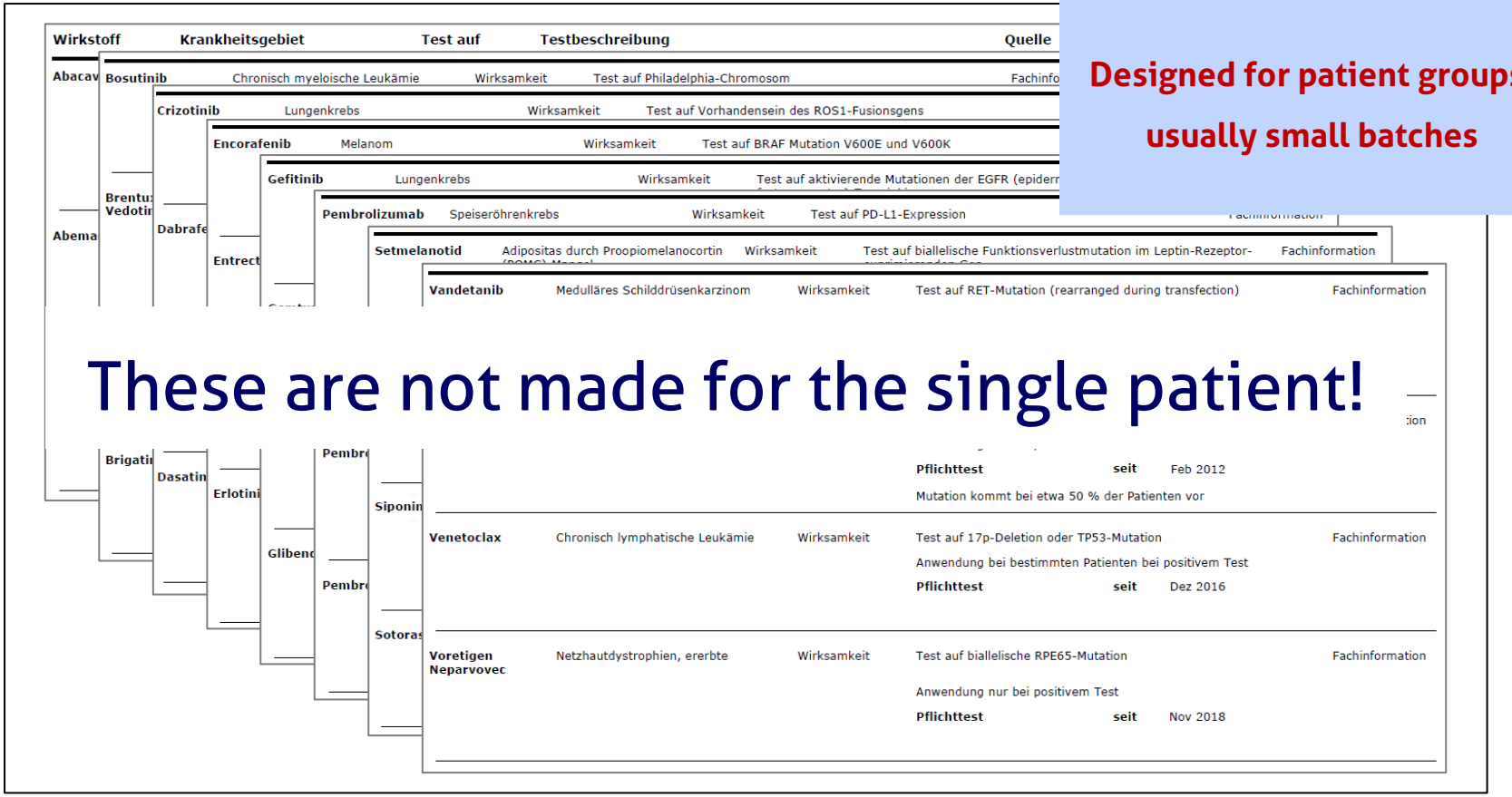
We have less impersonal medicine!

Just for clarification, not to blame



"Personalized medicine" is usually designed for patient groups

According to vfa there are 120 personalized drugs (APIs) approved in Germany for which a genetic test is mandatory or recommended before use



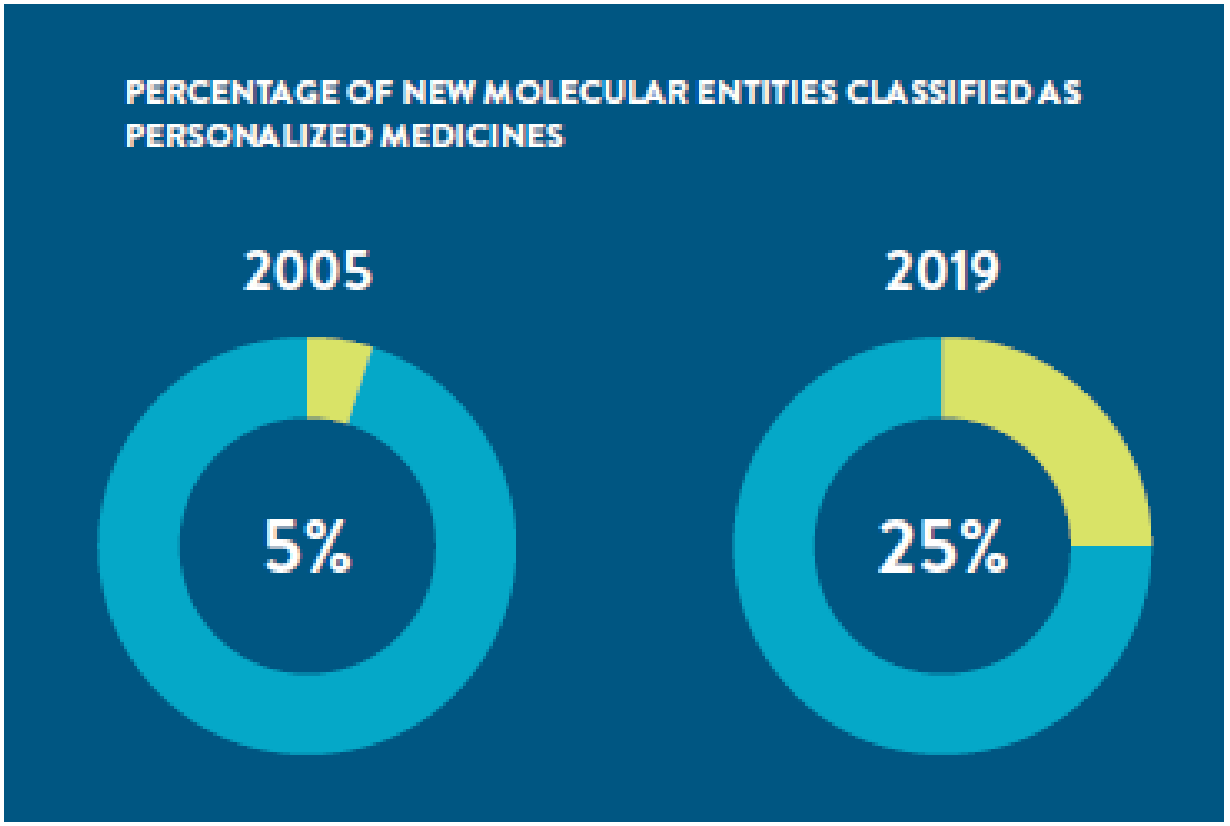
Designed for patient groups: usually small batches

These are not made for the single patient!

vfa: Verband Forschender Arzneimittelhersteller (German Association of Research-Based Pharmaceutical Manufacturers)

Research for personalized medicine is growing

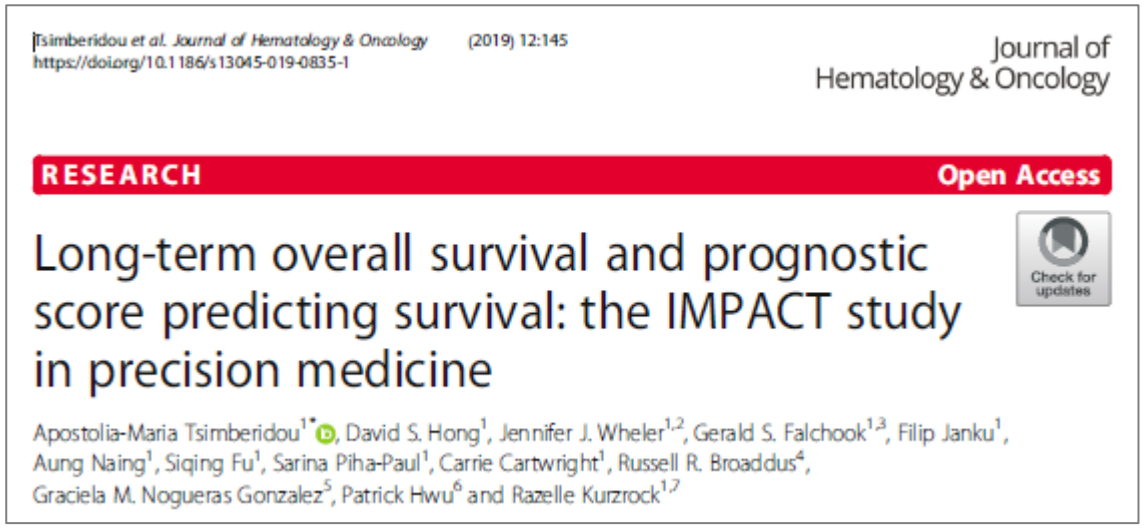
Increased approval by the US Food & Drug Administration



Source: The personalized medicine report, Personalized Medicine Coalition 2020

How well do these personalized medicines work?

Example: cancer treatment



Tsimberidou et al. Journal of Hematology & Oncology (2019) 12:145
https://doi.org/10.1186/s13045-019-0835-1

Journal of Hematology & Oncology

RESEARCH Open Access

Long-term overall survival and prognostic score predicting survival: the IMPACT study in precision medicine

Apostolia-Maria Tsimberidou[1*], David S. Hong[1], Jennifer J. Wheler[1,2], Gerald S. Falchook[1,3], Filip Janku[1], Aung Naing[1], Siqing Fu[1], Sarina Piha-Paul[1], Carrie Cartwright[1], Russell R. Broaddus[4], Graciela M. Nogueras Gonzalez[5], Patrick Hwu[6] and Razelle Kurzrock[1,7]

Over 10 years IMPACT assessed the correlation of factors, including genomically matched therapy, with overall survival for patients participating in early-phase clinical trials

- Median progressive free survival was **4 months compared to unmatched 2.8 months**
- Overall survival rates after 3 years: **15% vs. 7%**

Would you do it, even considering the side effects from therapy?

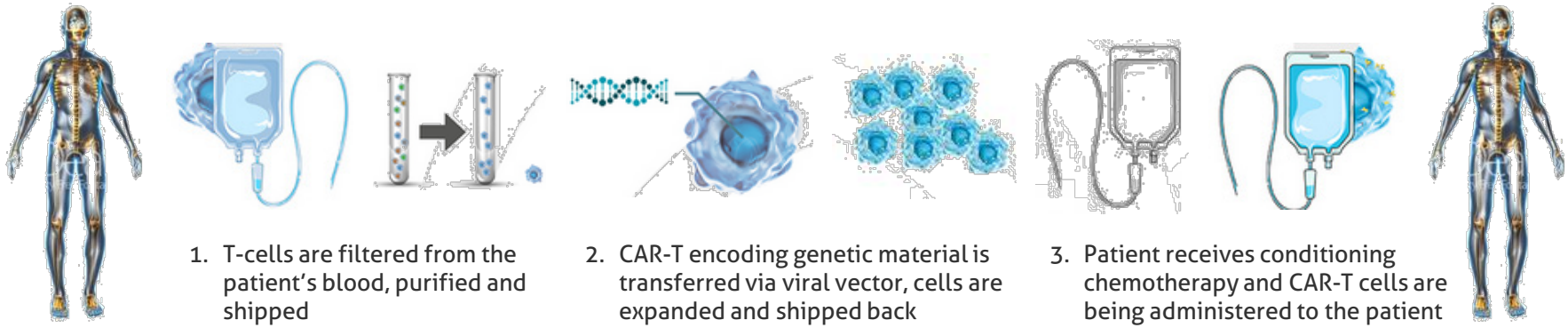
And how about "real" personalized medicine?

CAR-T cancer therapies

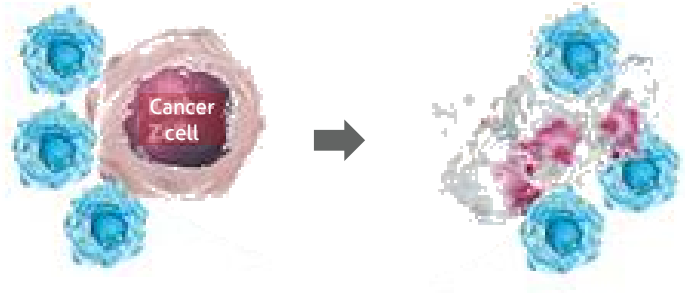
CAR = artificially generated Chimeric Antigen Receptors

By the way:
CAR-T cells are manufactured in clean rooms/isolators!

CAR-T cell-therapy procedure



1. T-cells are filtered from the patient's blood, purified and shipped
2. CAR-T encoding genetic material is transferred via viral vector, cells are expanded and shipped back
3. Patient receives conditioning chemotherapy and CAR-T cells are being administered to the patient



4. CAR-T cells bind to and fight cancer cells

One patient, one batch
(except for the viral vectors)

How many CAR-T cell-therapies do exist?

Only 6 CAR-T cell products are approved in the EU for oncological diseases

Product	Indication	Estimated # of annual patients in DE (IQWiG)	Estimated therapy costs per patient in DE (IQWiG)
Tisagenlecleucel (Kymriah®)	B cell acute lymphoblastic leukaemia, diffuse large B-cell lymphoma and follicular lymphoma	647 – 686	271 k€
Axicabtagen Ciloleucel (Yescarta®)	Relapsed or refractory diffuse and primary mediastinal large B-cell lymphoma and follicular lymphoma	614 – 1813	283 k€
Brexucabtagen autoleucel (Tecartus®)	Mantle cell lymphoma	105 - 149	361 k€
Idecabtagen vicleucel (Abecma®)	Multiple myeloma	1029 – 1059	351 k€
Lisocabtagen maraleucel (Breyanzi®)	B cell acute lymphoblastic leukaemia, diffuse large B-cell lymphoma and follicular lymphoma grade 3B	Not yet evaluated	
Ciltacabtagen autotemcel (Carvykti®), cond. authoriz.	Multiple myeloma	Not yet evaluated	

- In 2019 and 2020, only about **300 patients** were treated with new CAR-T cell therapies in Germany
- At a **cost of about 100 million euros**

IQWiG: Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)

How well do CAR-T cell-therapies work?

There are good news

NOVARTIS

Novartis five-year Kymriah® data show durable remission and long-term survival maintained in children and young adults with advanced B-cell ALL

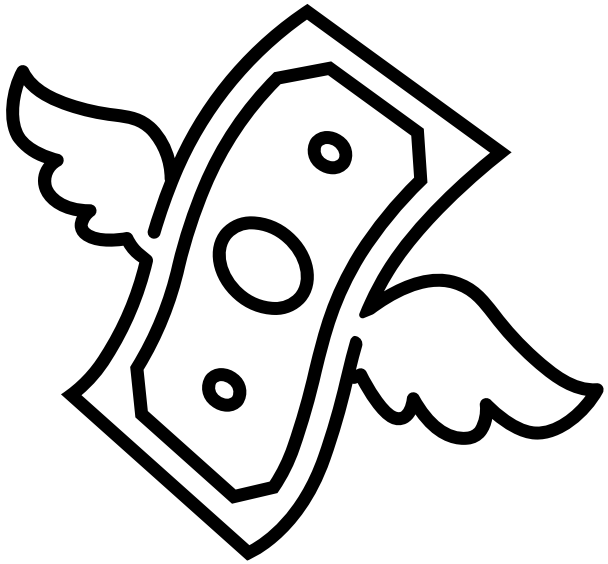
Jun 12, 2022

- *In final ELIANA analysis, 55% of patients with relapsed or refractory (r/r) B-cell acute lymphoblastic leukemia (ALL) who were treated with CAR-T cell therapy Kymriah were still alive after more than five years*[1]
- *44% of patients who experienced remission within three months of infusion were still in remission at the five-year mark, demonstrating the long-term benefit and curative potential of one-time Kymriah infusion*[1]

› A >5 times better chance to stay alive for 5 years and with a good chance in good conditions

› I would go for it – if my insurance does as well!

But there are also some bad news



- Around 520,000 people are currently diagnosed with cancer each year in Germany
- If in the future a quarter of all patients will have access to personalized therapies, this will lead to **annual expenditures of €43 billion** at today's costs

- **This is roughly equivalent to the amount spent by all public health insurers on all drugs in 2020!**

- We need a **new approach of financing** and a **broader approach on research!**

And the future?

Might not look too bright for CAR-T cell therapies...

- The number of clinical trials for CAR-T therapies is constantly growing
- However only 2% of all new clinical trials are related to such therapies
- It will take a **long time** until this type of personalized medicine might reach a **significant volume**

Clinical Trials Started per Year

Year	# Studies Phases 1, 2 & 3		
	Total	CAR-T	CAR-T share
2022	8.881	183	2,1%
2021	9.429	169	1,8%
2020	8.739	158	1,8%
2019	8.073	143	1,8%
2018	7.799	95	1,2%
2017	7.451	99	1,3%
2016	7.444	61	0,8%
2015	7.513	33	0,4%
2014	7.260	18	0,2%
2013	6.870	9	0,1%
Total 2013-2022	**79.459**	**968**	**1,2%**

Source: Clinical Trials.Gov

And the future?

… might in general still be better than expected!

By the way:
mRNA drugs are manufactured in clean rooms/isolators!

- Pfizer-BioNTech's and Moderna's Covid-19 vaccines have saved millions of lives
- The real strength of the technology is that mRNA can be individually customized
- The mRNA cancer therapy can tailor each vaccine to the characteristics of the specific tumor of a particular patient
- Tumor cells are taken from the patient and analyzed using gene sequencing

- Once the cells have been decoded, a patient-specific vaccine is produced that will enable the immune system to recognize and fight the tumor

„In 15 years, one in three newly approved drugs will be based on mRNA technology "

Dr. Ugur Sahin, CEO BionTech

Summary so far

- Personalized medicines work due to scientific progress in many areas
- The focus lies on drugs for patient groups rather than for individuals
- For real personalized medicine (i. e. CAR-T therapies) progress is slow
- Cost is the critical factor
- mRNA based therapies might become the game changer again, as proven in the pandemic

What else to say?

The presented therapies are not the only path to precision medicine

- Evaluation of patient data for medication
- Standard drugs, already approved
- Future mass market
- Application: Oral Solids
- Drivers:
  - Polypharmacy in old age
  - Wellness culture
  - Digital health, wearables
  - Diagnostic data

Solid dose personalized medicine

Several technologies are available yet

Technology	Criteria							
	> 5 APIs per pill	Individual dosing capability	Different release per API	Process-safety	Feasibility	Patient-friendliness	Suitable for existing generics	Suitable for new NCEs
3D-Print and Extrusion (FDM)	✓	✓	✓	✓	Still to be verified	✓	✓	✓
2D-Inkjetprint on ODF	Not > 100mg	10 - 40 mg per API	✓	✓	Still to be verified	✓	✓	✓
Microtablets in capsules	✓	✓	✓	✓	State of the art	✓	✓	Limited molecule sizes?

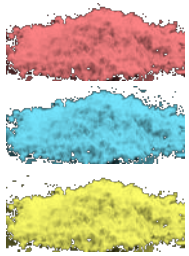
Solid dose personalized medicine: a new value chain?

Today

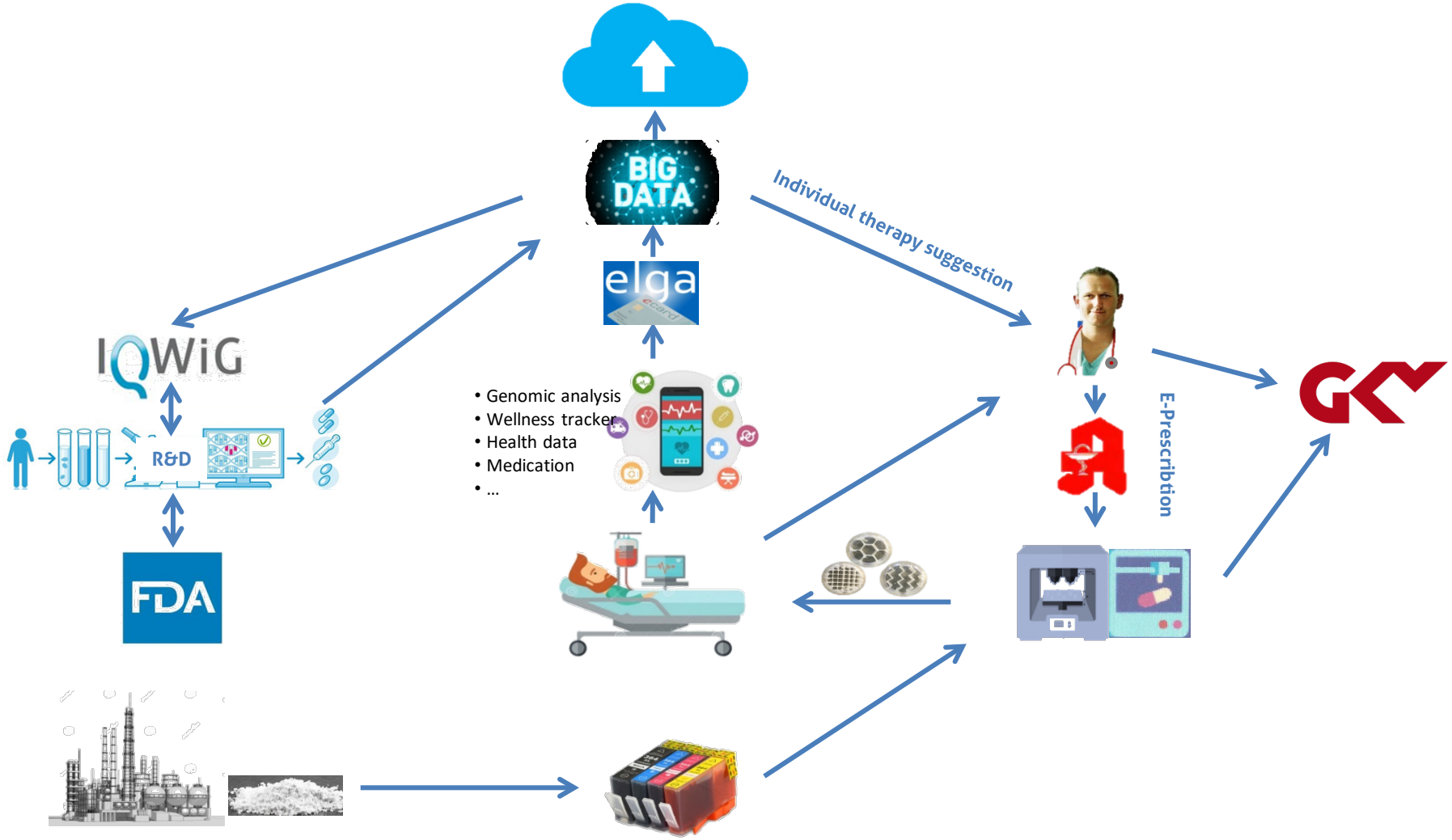




Tomorrow?



Even a new business model: Precision Medicine + Digital Health?



Benefits

- Tailor-made pharmacotherapies with respect to individual health situation
- Considering the physiologic constitution as well as the genetic, metabolic and gender-specific characteristics of the patient
- Individualized dosing
- Individualized release
- Reduced side-effects
- Increased patient compliance
- Integration of several drugs into one combination product
- Improved patient monitoring with data-based therapy decisions
- Learning curve for pharmaceutical researchers and regulatory bodies

And the future of manufacturing?

Mass production will still be the overwhelming model …

But …

- Batches will be smaller
- Production will be more decentralized
- And more automatic (glove-less isolators)
- And for real personalized medicine (batch size 1) one may expect production at point of care


The more precise the medicine, the more containment is required!

What do I hope for?

„I'll live to see this: personalized medicine can cure the major cancers!“

"Those who have knowledge, don't predict. Those who predict, don't have knowledge."

-- Lao Tzu, 6th Century BC Chinese Poet

Thank you very much for your participation!

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