

Personalized Medicine
– diversity of approaches, promise,
realization and challenges

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m4 Local Heroes and Global Challenges, Munich, Nov. 29th 2011

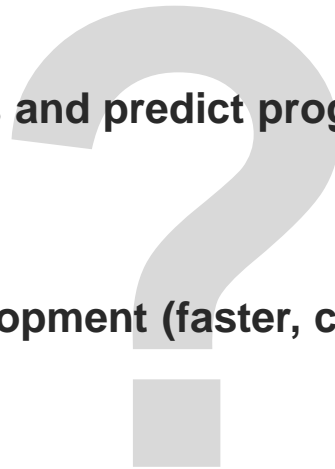
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A. The promise of Personalized Medicine

Does the promise of Personalized Medicine hold true?

- **Optimized therapeutic benefit risk ratio**
- **Identify disease variants and predict prognosis**
- **Improve drug development (faster, cheaper, higher success rates)**
- **Understand diseases on a molecular basis**

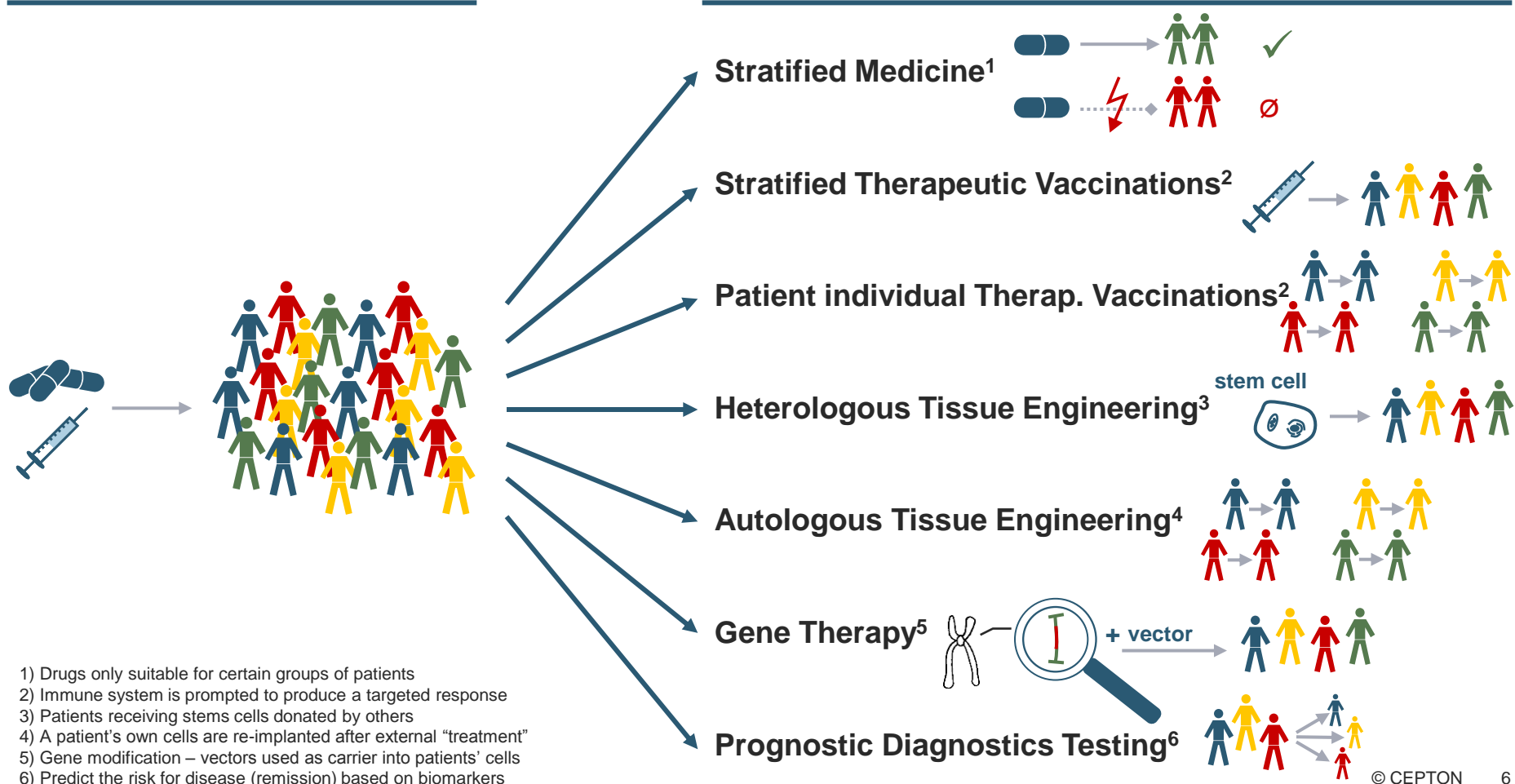


B. Diversified approaches of Personalized Medicine

The field of Personalized Medicine covers Stratified Medicine, Tissue Engineering, Onco Vaccinations, Gene Therapy and prognostic testing

Scope of Personalized Medicine

“One fits all”



1) Drugs only suitable for certain groups of patients
 2) Immune system is prompted to produce a targeted response
 3) Patients receiving stems cells donated by others
 4) A patient's own cells are re-implanted after external "treatment"
 5) Gene modification – vectors used as carrier into patients' cells
 6) Predict the risk for disease (remission) based on biomarkers






Especially the rise of targeted therapies has increased the relevance of personalized approaches

“One fits all”	Stratified Medicine	Individualized Medicine
<ul style="list-style-type: none"> • NSAIDs • Statins • PPIs • OAD • Anti-depressives • ... 	<p>Targeted therapies (esp. mAbs & kinase inhibitors in oncology)</p> <p>→ Identify responders</p>	<p>Patient individualized therapies</p> <p>→ Tailor therapy to patient</p>
	<p>Heterologous Tissue Engineering</p> <p>→ Secure histocompatibility</p>	<p>Autologous Tissue Engineering</p> <p>→ Patient derived cells</p>
<p>“Classical drugs” with “unspecific” MoA</p> <p>→ Identify patients at risk for severe side events</p>		
<p>Gene Therapy</p>		

B.1 Therapeutic Vaccination







Oncological “vaccines” stimulating the immune system for individual response have become promising

Therapeutic vaccines – stratified oncological examples

Drug	Company	Indication	Status	MoA / Technology
Astuprotimut-r		NSCLC, melanoma	Phase III	• MAGE-A3 antigen-specific immunotherapeutic
Trovax^{®1} (SAR-109659)		Renal cancer, metastatic Colorectal cancer, Mesothelioma	Phase III Phase II Discovery	• Delivery of 5T4 tumor antigen on attenuated modified vaccinia virus Ankara (MVA)
Stimuvax^{®2} (L-BLP 25)		NSCLC, (MammaCa)	Phase III	• MUC-1 peptide-based liposomal vaccine
RO-5217790		Cervical cancer	Phase II	• Human papillomavirus antigen (HPV)-targeted immunotherapeutic agent • Therapeutic vaccine not comparable to Gardasil [®] /Cervarix [®] -like HPV prevention
PT-107		NSCLC	Phase II	• First-in-class therapeutic vaccine for the treatment of non-small cell lung cancer

Oncological vaccination may provide a paradigm shift for healing – struggling with current clinical trial standards

Therapeutic vaccines – patient-individual oncological examples

Drug	Company	Indication	Status	MoA / Technology
Provenge® (Sipuleucel-T)		Hormone refractory prostate cancer	Approved by FDA in 03/2010 (EU approval planned in 2012)	<ul style="list-style-type: none"> Cellular based “vaccination” Patient derived dendritic cells¹ loaded with prostatic acid phosphatase
Oncophage® (Vitespen)		Renal cancer	<ul style="list-style-type: none"> Approval in Russia 2008 Phase III in EU 	<ul style="list-style-type: none"> Extracted heat shock proteins isolated from patients tumor
BiovaxID®		NHL	Phase III	<ul style="list-style-type: none"> Purified patient-specific idiotype antibodies conjugated to an immune stimulant
MaxCyte GT		CLL	Phase II	<ul style="list-style-type: none"> IL-2- and CD40L-expressing cell-based autologous vaccine
AFTVac		Glioblastoma multiforme	Phase II	<ul style="list-style-type: none"> Autologous, formalin-fixed tumor vaccine (AFTVac) encapsulating GM-CSF and IL-2
PMP0025-01		NHL	Phase I	<ul style="list-style-type: none"> Tobacco plant-derived (magniCON technology) anti-idiotype vaccine

Dendreon's Provenge[®] against prostate cancer very recently received FDA approval as the first oncological "vaccine" to market










Patient individualized therapies – Provenge[®]

- **Cellular immunotherapy** that comprises **autologous antigen presenting cells** (APCs) co-cultured with a **recombinant fusion protein** containing prostatic acid phosphatase (PAP) for **IV treatment of prostate cancer** – one infusion / month for three months
- IMPACT study showed **prolonged patient life by 4.5 months** and **risk reduction of death by 22.5%**
- Previous attempt for approval in 2007 failed – **FDA approval** granted in April 2010
- 93,000 USD for full course of treatment – blockbuster status is anticipated for 2016¹
- Dendreon's further **active cellular immunotherapy pipeline** includes
 - Lapuleucel-T for breast, ovarian and colon cancer
 - CEA for breast, lung and colon cancer
 - CA-9 for kidney, colon and cervical cancer

B.2 Tissue engineering

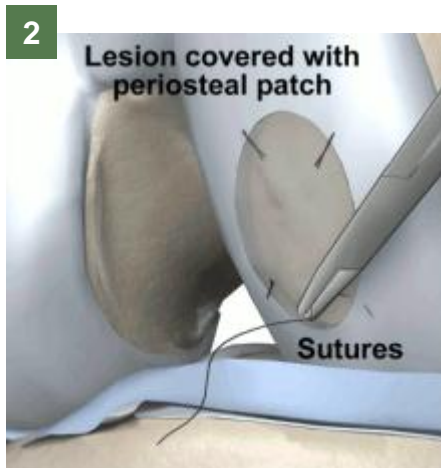
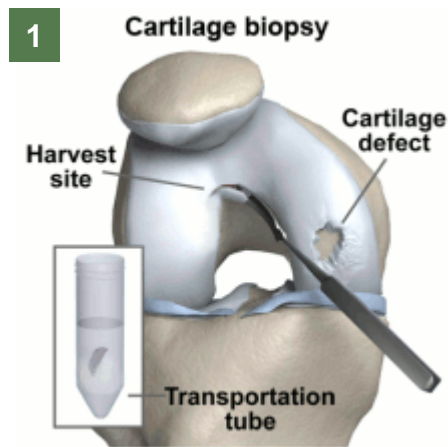
Autologous tissue engineering means entering a service business – processing patient’s tissue rather than selling products

Tissue Engineering – autologous & heterologous examples

	Drug	Company	Indication	Status	Description
Autologous	Carticel®		Articular cartilage damage	Launched in US	<ul style="list-style-type: none"> • Autologous chondrocyte implant • Chondrocytes grown ex vivo & re injected at site of damage
	Maci®		Articular cartilage damage	Launched in EU, Asia, Australia	<ul style="list-style-type: none"> • Matrix-induced autologous chondrocyte implant • Chondrocytes grown ex vivo in collagen matrix & reimplanted at site of damage
	CartiGro®		Articular cartilage damage	Launched	<ul style="list-style-type: none"> • Autologous chondrocyte implant • Chondrocytes grown ex vivo & re injected at site of damage
	Epicel®		Severe burns	Launched	<ul style="list-style-type: none"> • Cultured epidermal autograft • Keratinocytes grown ex vivo in the presence of proliferation-arrested, murine (mouse) fibroblasts
	Chondro Select®		Articular cartilage damage (knee)	Launched in EU	<ul style="list-style-type: none"> • Autologous chondrocyte implant • Chondrocytes grown ex vivo & re injected at site of damage
	NeoCart®		Articular cartilage damage (knee) ³	Phase III	<ul style="list-style-type: none"> • Autologous engineered neocartilage • Chondrocytes grown ex vivo in collagen matrix and reimplanted at site of damage
Heterologous	Prochymal®	 	<ul style="list-style-type: none"> • GvHD¹ • Crohn's disease • Acute radiation syndrome • T1D • Acute myocardial infarction • Pulmonary Disease 	<ul style="list-style-type: none"> • Phase III • Phase III • Discovery • Phase II • Phase II • Phase II 	<ul style="list-style-type: none"> • Heterologous mesenchymal stem cells • No histocompatibility issues
	Chondrogen®		Osteoarthritis (knee)	Phase II	<ul style="list-style-type: none"> • Heterologous mesenchymal stem cells • No histocompatibility issues

In autologous chondrocyte implantation, a patient's healthy cells are removed and reimplanted at the site of damage after external cultivation

Tissue Engineering – Autologous Chondrocyte Implant (ACI)





- Hyalin articular cartilage has a **limited regenerative capacity** for intrinsic repair
- Cartilage cells (chondrocytes) are removed from healthy tissue and **cultured externally for re-implantation**
- In a second intervention, the **cultured cells are injected into the damaged area** inducing formation of functional hyaline-like tissue

B.3 Gene Therapy







Gene Therapy aims to express specific genes utilizing vectors – Glybera® highlighting remaining high hurdles to the market

Gene Therapy categories and examples

Category	Product	Indication	Company	Vector	MoA & transfected genes
Persistent cDNA transfection	ProSavin® (Ph II)	PD ²		LentiVector® (retroviral)	Dopamin synthesis: dopadecarboxylase, GPT cyclohydrase & tyrosine hydroxylase
	RetinoStat® (Ph II)	AMD ³		LentiVector® (retroviral)	Anti-angiogenesis: Angiostatin and endostatin

Initial attempts in Gene Therapy in 1990's

2nd wave attempts in Gene Therapy since 2000







Transient cDNA transfection	Glybera® (Suspended) 	LPLD ⁴		Adeno-assoc. virus	Enzyme replacement: Ser447X variant of the human LPL gene
	Gendicine® (launched China)	HNSCC ⁵		Adeno-assoc. virus	Anti-proliferation: human p53 tumor suppressor gene
	CERE-120 (Ph II)	PD ²		Adeno-assoc. virus	Neurotrophic growth factor: neurturin (NTN)
	AV-201 (Ph I)	PD ²		Adeno-assoc. virus	Dopamin synthesis: L-amino acid decarboxylase & tyrosine hydrolase
	CERE-110 (Ph II)	AD ⁶		Adeno-assoc. virus	Neurotrophic growth factor: nerve growth factor (NGF)

RNA therapy	Angiozyme (Ph III)	mCRC ⁷ , cancer		pure RNA	Anti-angiogenesis: Ribozyme cleavage of VEGF-R1
	Eteplirsen (Ph II)	DMD ⁸		pure RNA	Exon skipping: skip dystrophin exon 51 (where often mutations are located)

B.4 Prognostic diagnostic testing

Prognostic tests aim to define the risk for a certain disease / remission and corresponding therapeutic options

Prognostic Diagnostic Testing

Diagnostic test	Company	Indication	Biomarker	Prognosis for ...
MammaPrint®	 agendia <small>decoding cancer.</small>	Breast cancer	70-gene expression profile	... risk of distant metastasis
Oncotype DX® 16	 genomic health	Breast cancer	16-gene signature	... risk of remission for informed treatment decision (chemotherapy selection)
CompanDx® 31	 CompanDx	Breast cancer	31-gene signature	... time to metastasis
BRCA1/2	 MYRIAD®	Breast, ovarian cancer	BRCA1/2	... susceptibility for breast and ovarian cancer
AlloMap®	 XDx EXPRESSION DIAGNOSTICS	Heart transplantation	Gene expression profile of mononuclear cells	... of immune response to guide immunosuppressive therapy
Familion® 5	 TRANSGENOMIC® <small>the power of discovery</small>	Cardiovascular	5 gene profile	... preventive measures and optimal treatment selection for patients with inherited cardiac channelopathies

B.6 Stratified Medicine

Stratified Medicine aims to maximize the benefit-risk-ratio of drugs by predicting a better response for a sub-population of patients

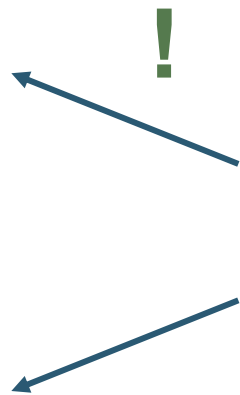
Principle of Stratified Medicine



+ Benefit
∅ Toxicity



+ Benefit
– Toxicity



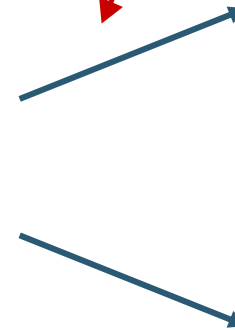
Patients sharing
one “diagnosis”



∅ Benefit
– Toxicity



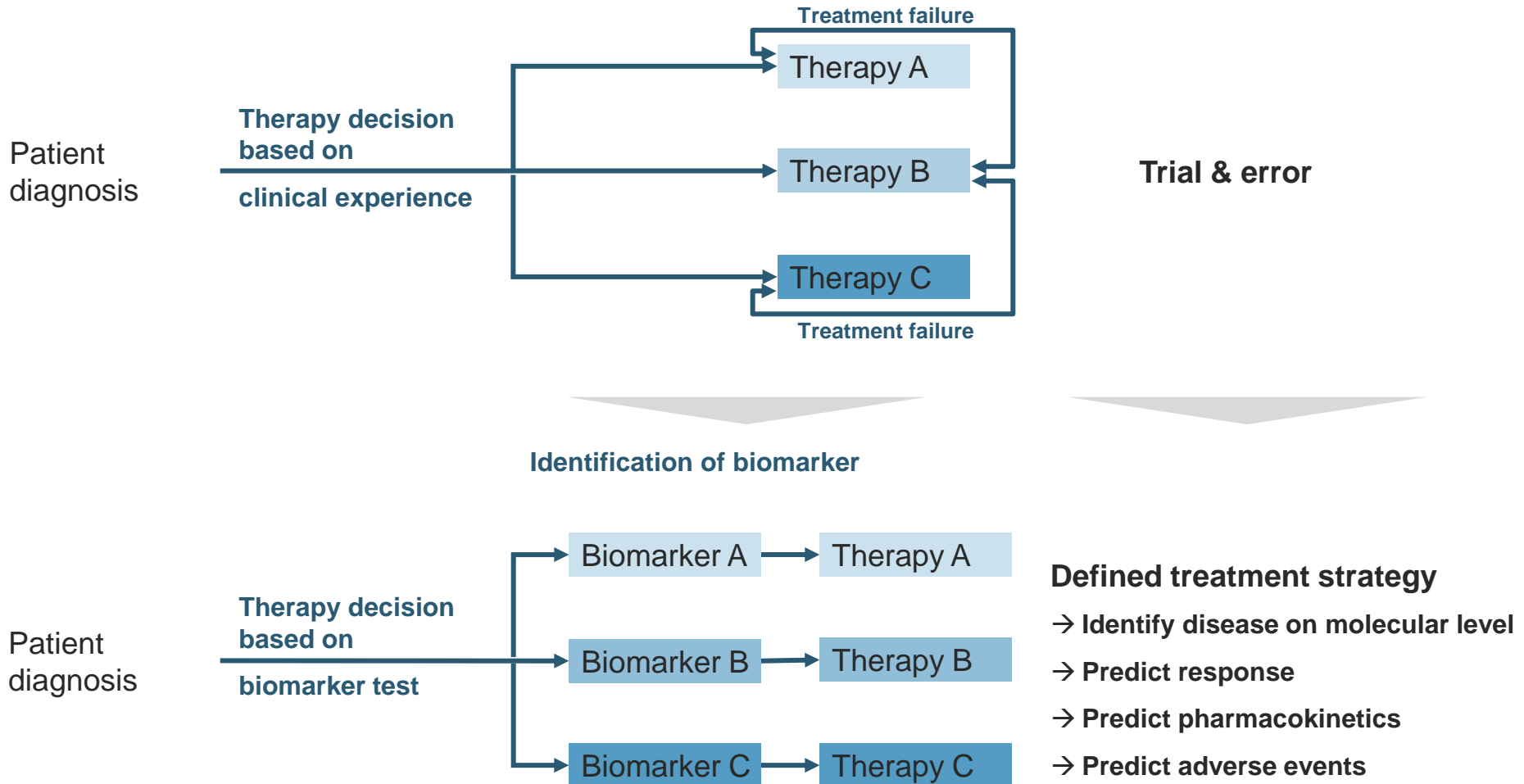
∅ Benefit
∅ Toxicity



▶ Maximize benefit-risk-ratio of drug












Stratified Medicine replaces trial and error with guided selection based on response and fit

Traditional diagnosis vs. Stratified Medicine



Many current blockbusters are stratified therapies – not necessarily targeted in daily routine, today

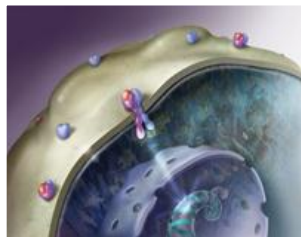
Stratified therapies – success stories

Drug	Company	Stratify for biomarker	Peak sales ² [\$m]
Plavix[®] (Clopidogrel)	 	CYP2C19 variant	9.492 ⁶
Herceptin[®] (MammaCa)		HER2 over-expression (25%) ¹	6.319 ⁴
Gleevec[®] (ALL+CML)		Philadelphia chr. (30%-95%) ² ¹	4.378 ⁴
Sprycel[®] (ALL+CML)		Philadelphia chr. (30%-95%) ² ¹	2.430
Erbix[®] (mCRC)		Wild-type KRAS (60%) ¹	2.372
Tasigna[®] (CML)		Philadelphia chr. (95%) ² ¹	1.974
Tarceva[®] (NSCLS)		HER1 over-expression (30%) ¹	1.664 ⁵
Tyverb[®] (MammaCa)		HER2 over-expression (25%) ¹	1.208
Tamoxifen (MammaCa)		Estrogen receptor (70%) ¹	1.024 ³
Vectibix[®] (mCRC)		Wild-type KRAS (60%) ¹	725

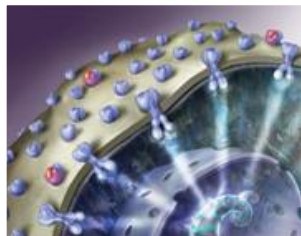
1) Percentage of eligible population 2) Global peak sales estimate according to consensus analyst forecasts (up to 2016) 3) Peak in 2001, generics from 2002 4) Peak in 2013
5) Peak in 2014 6) peak in 2009

The success stories are still limited to very few drugs (e.g. Herceptin®) for which there was upfront strong certainty on biomarker relevance

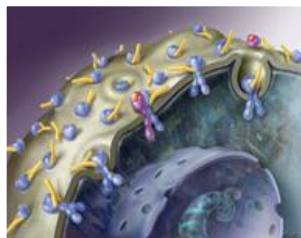
Stratified therapies – Herceptin® (trastuzumab) case



HER2¹ normally expressing cell

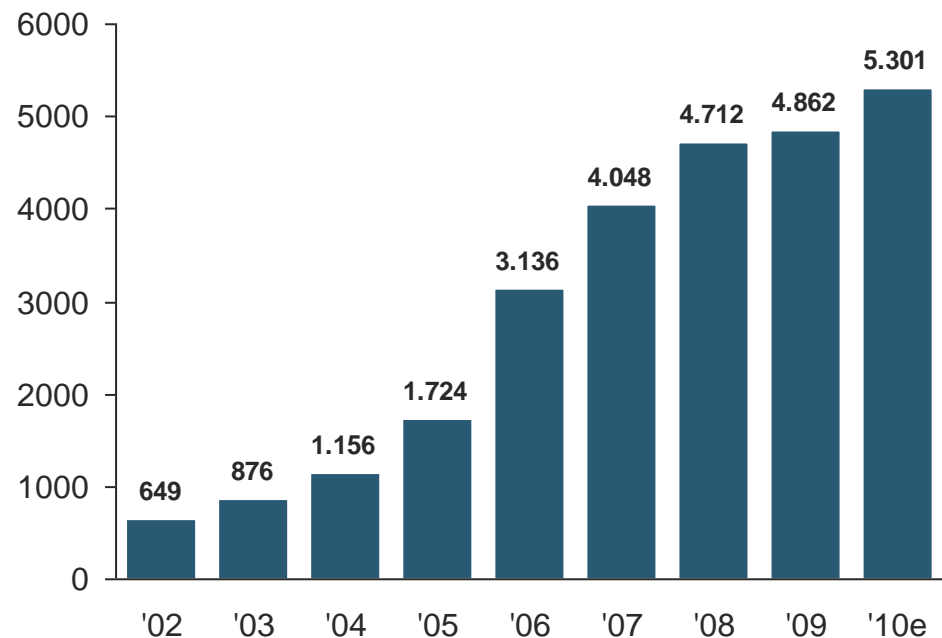


HER2 over-expression causing increased cell proliferation



HER2 antibodies binding to receptors thereby inhibiting tumor growth

Herceptin® global sales [US\$m]



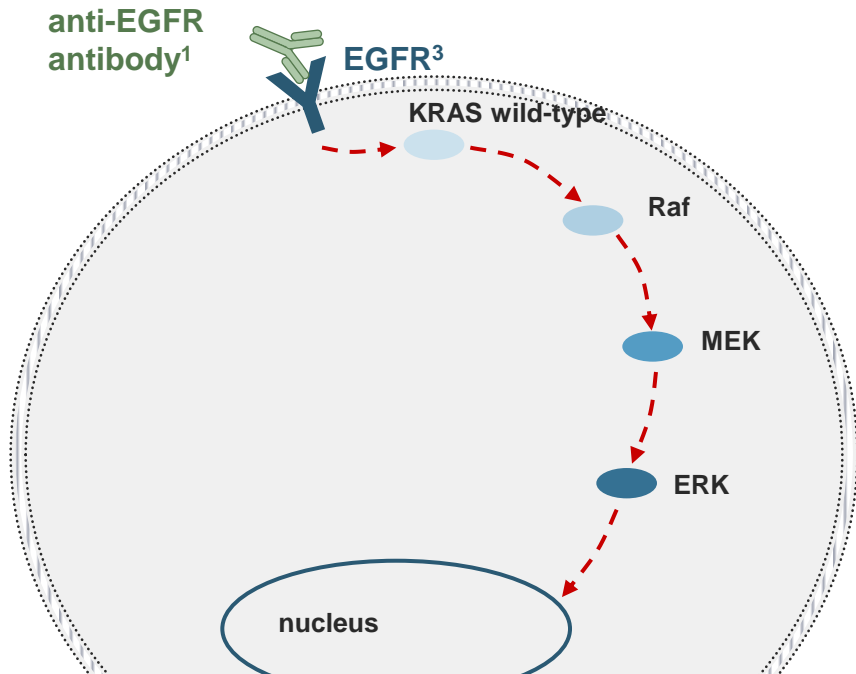
✓ HER2+ is predictive of Herceptin® response

✓ Testing for HER2 over-expression is mandatory

Mutant KRAS predicts a lack of response to anti-EGFR therapy in ~40% of all mCRC patients – inhibition overruled by constitutive signaling

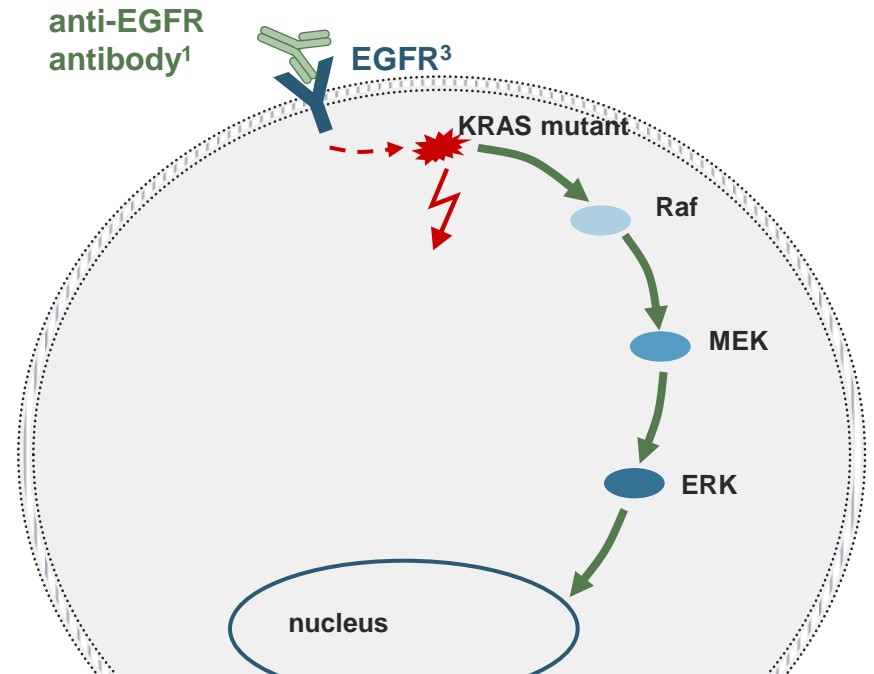
Targeted therapies – anti-EGFR therapy¹ and KRAS⁴

KRAS⁴ wild-type (60% in mCRC²)



---> Signal down-regulated due to receptor inhibition by anti-EGFR antibody

KRAS⁴ mutant (40% in mCRC²)
















—> Signal up-regulated due to constitutive KRAS activation

1) e.g. Cetuximab or Panitumumab 2) mCRC = metastatic colorectal carcinoma; wildtype KRAS in NSCLC (non-small-cell lung cancer) 80-90% and in head-and-neck cancer 95%
3) EGFR = epidermal growth factor receptor 4) KRAS = Kirsten rat sarcoma 2 viral oncogene homologue, a signaling protein activating among other the MAP-kinase signaling pathway
Source: CEPTON







Several stratified products have been launched in recent years – label varies significantly between FDA and EMA

Examples for stratified medicines recently approved by FDA and EMA

Drug	Company	Biomarker	TA	Test for	FDA classification	EMA classification
Cetuximab (Erbix [®])		EGFR, KRAS negative (60%) ³	Oncology	Efficacy	required	required (2008)
Crizotinib (Xalkori [®])		ALK	Oncology	Efficacy	required	– ²
Dasatinib (Sprycel [®])		Ph Chrom. (FISH/PCR) (ALL 30% / CML 95%) ³	Oncology	Efficacy	required	required (2006)
Lapatinib (Tyverb [®])		Her2/neu (25%) ³	Oncology	Efficacy	required	required (2008)
Maraviroc (Celsentri [®])		CCR5	Antivirals	Efficacy	required	required (2007)
Panitumumab (Vectibix [®])		EGFR, KRAS (40%) ¹	Oncology	Efficacy	required	required (2007)
Rasburicase (Fasturtec [®])		G6PD	Oncology	Side-effects	required	required
Trastuzumab (Herceptin [®])		Her2/neu (25%) ³	Oncology	Efficacy	required	required (2000)
Vemurafenib (Zelboraf [®])		BRAF	Oncology	Efficacy	required	– ²
Abacavir (Ziagen [®])		HLA-B*5701 (95%) ³	Antivirals	Side-effects	recommended	required (2008)
Erlotinib (Tarceva [®])		EGFR (10-15%) ³	Oncology	Efficacy	for information only	required (2011)
Imatinib (Gleevec [®])		Ph Chrom. (FISH/PCR), (ALL 30% / CML 95%) ³ C-Kit, PDGFR, FIP1L1-PDGFRa	Oncology	Efficacy	for information only	required (2001)
Nilotinib (Tasigna [®])		Ph Chromosome (FISH/PCR), UGT1A1 (95%) ³	Oncology	Efficacy	for information only	required (2007)

Looking at onco-pipelines today reveals numerous future targeted therapies

Targeted onco therapies in pipeline with stratification potential

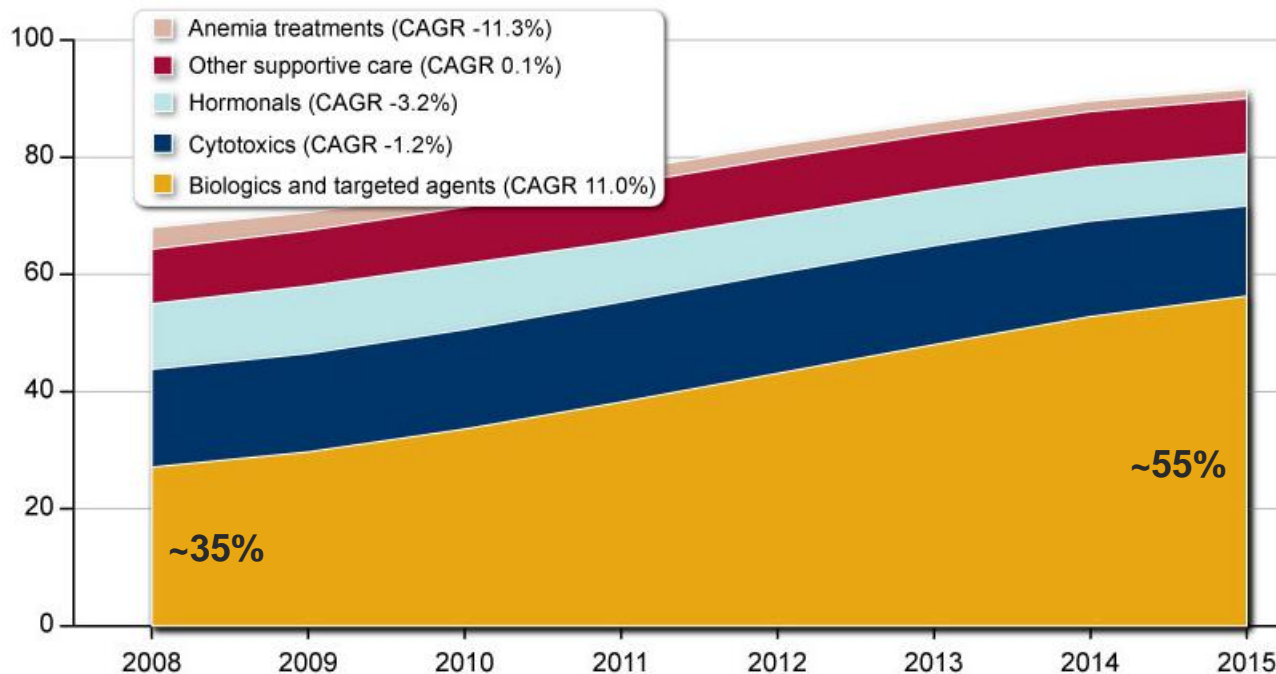
Compound	Company	Indic.	MoA	Rationale / Biomarker → Stratification pot.	
Midostaurin		AML ² (ph. III) / ASM ³ (ph. II)	Inhibition of FLT- 3RTK & c-KIT	<ul style="list-style-type: none"> • FLT3 mutated in approx. 1/3 of patients with AML² - associated with poor prognosis • c-KIT mutated in 80% of patients 	✓
Iniparib		Triple negative breast cancer (back from III)	Inhibition of PARP- 1 (single strand DNA repair)	<ul style="list-style-type: none"> • Stratify for efficacy • Biomarker: non-expression of estrogen, progesterone or HER2 receptors (triple-negative) 	✓
Olaparib		Ovary, CRC ⁴ , gastric; (phase II-III)	Inhibition of PARP- 1 (single strand DNA repair)	<ul style="list-style-type: none"> • Associated with BRCA (double strand DNA repair) mutation – required for effective inhibition 	✓
Cixutumumab ⁶		Multiple	Inhibition of IGF-1R	<ul style="list-style-type: none"> • IGF-1R overexpressing tumors 	✓
MetMab ⁷ (onartuzumab)		NSCLC ⁸ (phase II)	Inhibition of HGF binding to c-Met	<ul style="list-style-type: none"> • MET overexpression (in ~55% of patients) 	✓
Tigatuzumab		Multiple	Activation of DR 5	<ul style="list-style-type: none"> • Overexpression of DR 5 in many tumor types 	✓

1) Triple negative breast cancer 2) Acute myelogenous leukemia 3) Aggressive systemic mastocytosis 4) Colorectal cancer 5) additional various other cancer indications 6) in combination therapy with capecitabine and lapatinib 7) in combination therapy with erlotinib 8) Non small cell lung cancer 9) in phase II for various other cancer indications

C. Current success and future challenges

With the rise of targeted therapies – exemplified in oncology – the need for stratification significantly increases

Market evolution of oncological therapies, global sales [\$bn]



- Targeted therapies drive market value based on penetration of innovative high priced therapies
- Price decline due to generification in “classical” cytotoxics and anti-hormonals is partly compensated by overall volume increase in oncology due to increasing incidence and “chronification” of therapy

To control the cost burden by targeted therapies healthcare systems are increasingly implementing selected cost containment measures

Comparison of the restriction of innovative oncological therapies

Exemplary

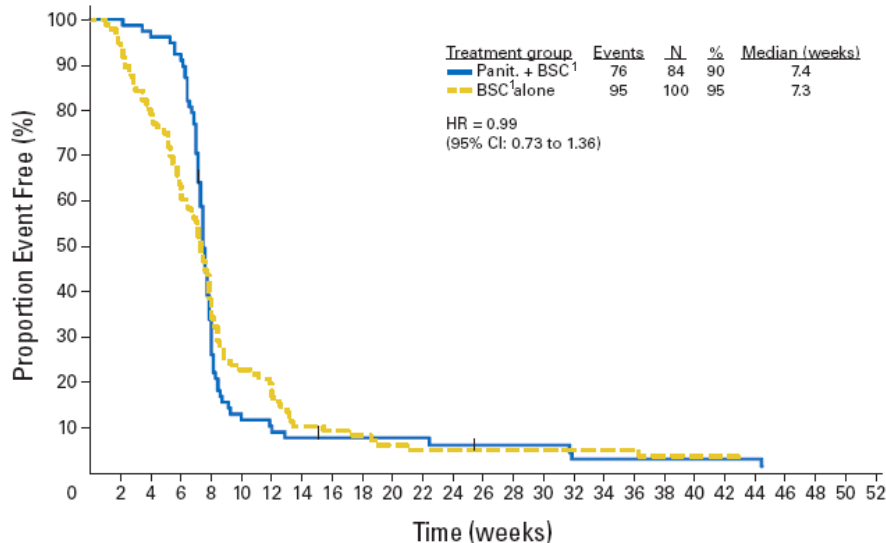
	UK	France	Germany	Spain	Italy
Gleevec®	Restrictions by NICE ¹	<ul style="list-style-type: none"> • Initiated in hospital • Rx by specs only • Renewals restricted 	<i>No restrictions</i>	• Initiated in hospital	• Hospital only
Herceptin®	Positive NICE ¹ appraisal took 2 years	<ul style="list-style-type: none"> • Rx from hospital • Rx by specs only • Renewals restricted 	<i>No restrictions</i>	• Hospital only	<ul style="list-style-type: none"> • Hospital only • Patient registry required at AIFA
Avastin®	Declined by NICE ¹ & SCM ² in mCRC ³ and renal cell carcinoma	<ul style="list-style-type: none"> • Price/Volume agreements • Hospital only ther. • Rx by specs only • Renewals restricted 	<i>No restrictions</i>	• Hospital only	<ul style="list-style-type: none"> • >6 months delay between approval & launch • Hospital only • Patient registry required at AIFA
Erbix®	Declined by NICE ¹ & SCM ² in mCRC ³	<ul style="list-style-type: none"> • Price/Volume agreements • Hospital only ther. • Rx by specs only • Renewals restricted 	<i>No restrictions</i>	• Hospital only	<ul style="list-style-type: none"> • Price/volume agreements • Obligatory observat. studies • Hospital only. • Patient registry

1) National Institute for Clinical Excellence 2) Scottish Medicines Consortium 3) metastasierendes kolorektales Karzinom
Source: CEPTON research

But proper selection of patients using predictive biomarkers may “rescue” a low efficacy drug by revealing its real efficacy

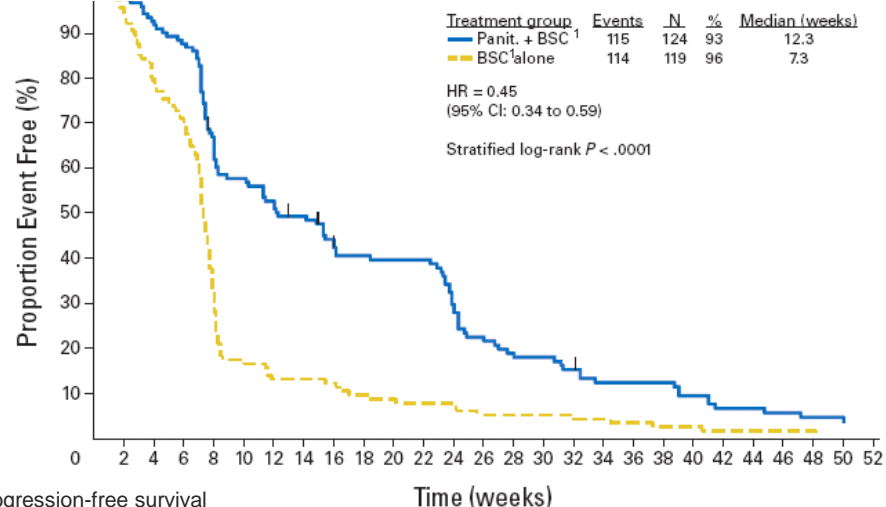
Example

Mutant
KRAS



- Patients with mutant KRAS do not benefit from targeted therapy

Wild-type
KRAS



- Survival without disease progression (PFS²) is significantly increased in wild-type KRAS group

- Side-effects in non-responders are avoided

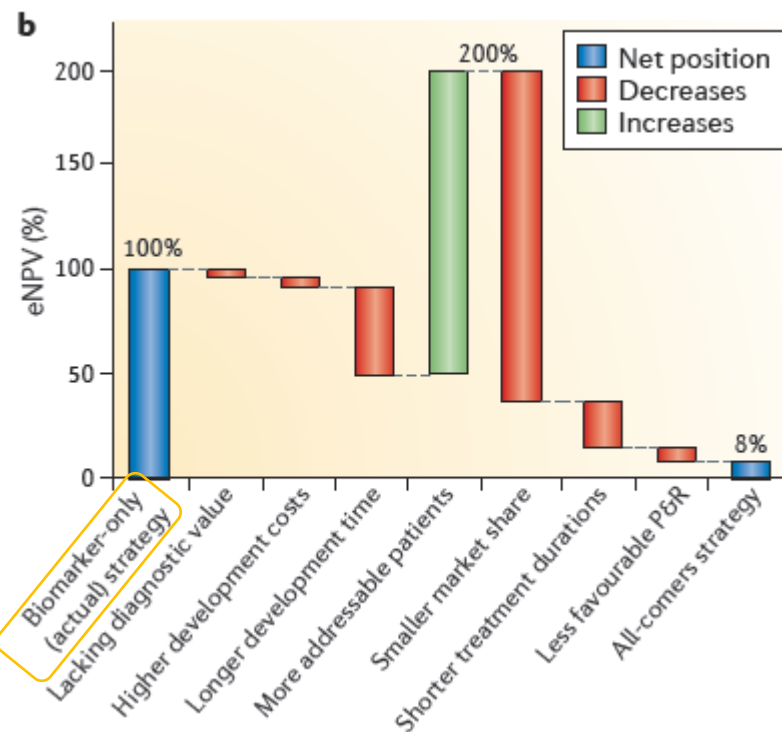
1) Best supportive care 2) Progression-free survival

D. Impact on R&D paradigm and commercial decision making

Depending on the underlying therapy the different paradigms result in significantly different commercial value

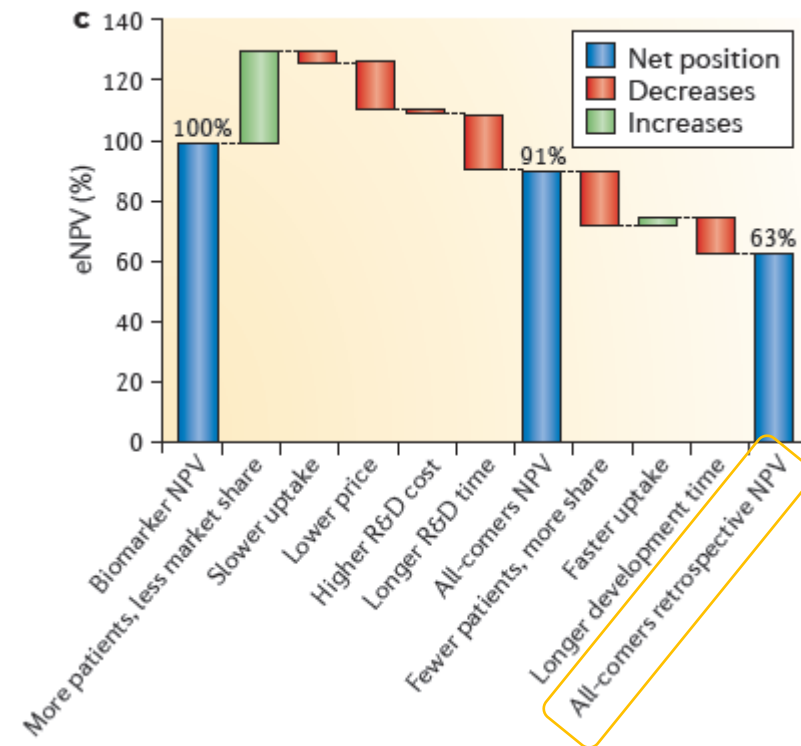
Comparison of trastuzumab and panitumumab cases under theoretical paradigms

Herceptin® (trastuzumab)



Upfront stratification provides clearly favorable value over one-fits-all strategy

Vectibix® (panitumumab)



Retrospective stratification decreases value over one-fits-all strategy and upfront stratification

Pharmaceutical companies need to comprehensively answer an array of questions to succeed in the emerging field of personalized medicine

Questions to answer by pharmaceutical companies

- Which **scientific rationale** do we follow for developing new therapeutic targets?
- How can we **protect IP** to gain a competitive advantage?
- Which **regulatory hurdles** do we have to anticipate facing FDA and EMEA discussions?
- Which **scientific platforms** exist and do we have to build them on our own?
- How do we adapt **pre-clinical** and **clinical research organizations** in order to generate validated biomarker data early enough?
- Which **commercial decisions** do we have to take and how do we **adapt** commercialization?
- Do we **make or buy** the development and commercialization of **diagnostic tests**?
- Who might be the **right partner in diagnostics** or for future **commercialization**?

Roche's approach to combine diagnostics and therapeutics pipeline is an exception in the industry

Strategies to approach companion diagnostics

BackUp

Rx-Dx
colla-
boration



Collaboration with Genzyme genetics on BCR/ABL testing for CML drugs



Collaboration with Monogram Biosciences for HIV drugs
Monogram's Trofile Assay is used to test CCR5 for Maraviroc

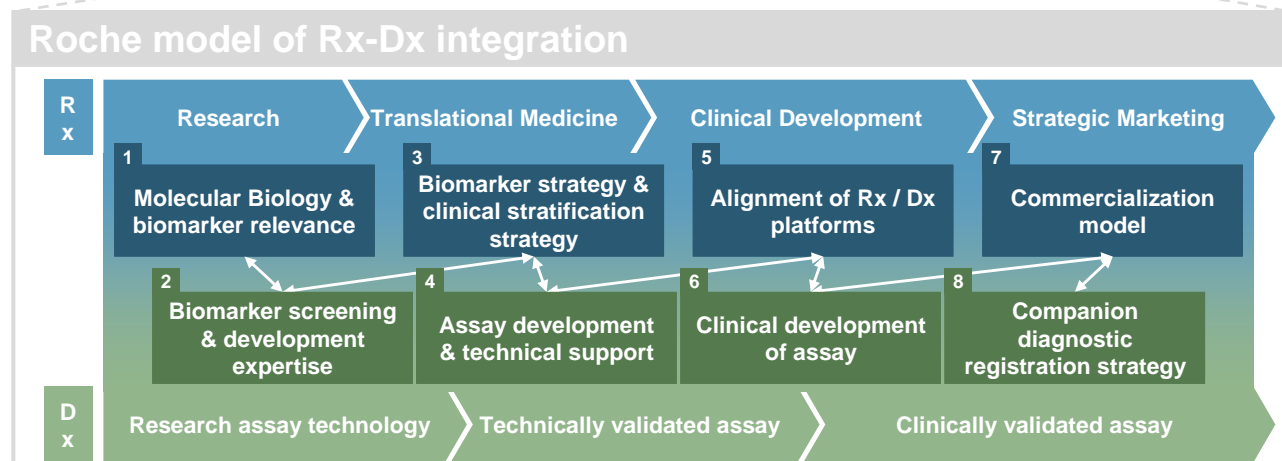


Collaborated with University of North Carolina for breast cancer studies on Gemzar



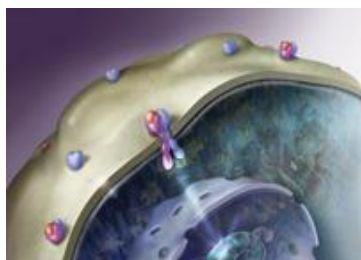
Most integrated Rx/Dx – close cooperation between Rx and Dx to validate novel Oncology markers for personalized medicine test

Integrated
Rx & Dx
divisions

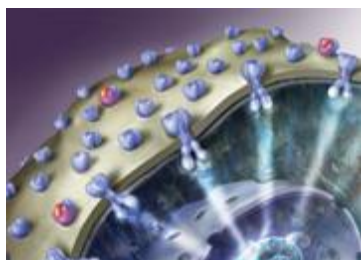


Collaborations are the prevalent approach to develop and commercialize companion diagnostic tests

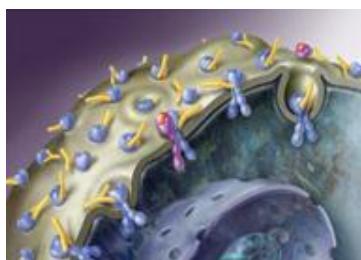
Targeted therapies – Herceptin® (trastuzumab) case



HER2¹ normal expression



HER2 over-expression

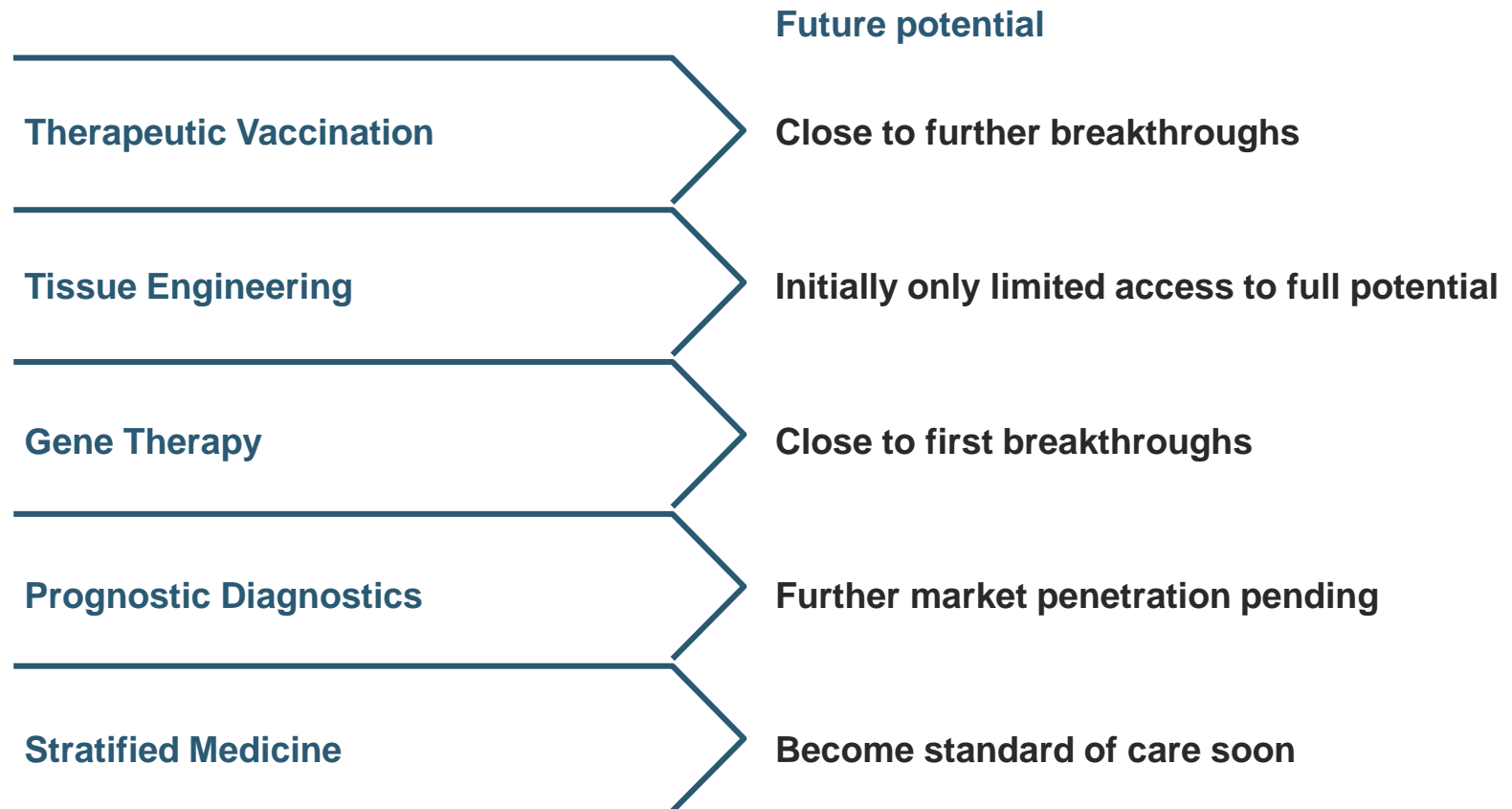


HER2 antibodies binding to receptors, inhibiting tumor growth

Drug Name	Company	CDx Name	Company	Indication	Reg. agency
Selzentry® Maraviroc	• Pfizer	• Trofile®	• Monogram Bioscience	• HIV	• FDA
Ziagen® Abacavir	• GSK	• HLA-B*5701	• Many LDTs ²	• Infectious disease	• EMEA
Erbitux® Cetuximab	• Merck • BMS	• EGFR pharmDx™	• Dako	• Colorectal cancer	• FDA • EMEA
		• TheraScreen® K-RAS	• Qiagen / Roche		
Vectibix® Panitumumab	• Amgen	• EGFR pharmDx™	• Dako	• Colorectal cancer	• EMEA
		• TheraScreen® K-RAS	• Qiagen / Roche		
Herceptin® Trastuzumab	• Roche	• HercepTest™	• Dako	• Breast cancer	• FDA • EMEA
		• Pathway®	• Roche		
Tykerb®/Tyverb® Lapatinib	• GSK	• HercepTest™	• Dako	• Breast cancer	• EMEA
		• Pathway®	• Roche		
Tarceva® Erlotinib	• Roche	• EGFR pharmDx™	• Dako	• NSCLC	• EMEA
Iressa® Gefitinib	• AZ • Teva	• EGFR pharmDx™	• Dako	• NSCLC	• EMEA
Epitol®/Tegretol® Carbamazepine	• Novartis	• HLA-B*1502	• Many LTDs ¹	• Neuropsychiatric disorders	• EMEA

E. The vision of Personalized Medicine

**The different segments of Personalized Medicine are in varying stages
– Stratified Medicine being the most mature segment**



Therapies will be increasingly personalized with an improved understanding of molecular foundation of patient specific disease

The vision of Personalized Medicine

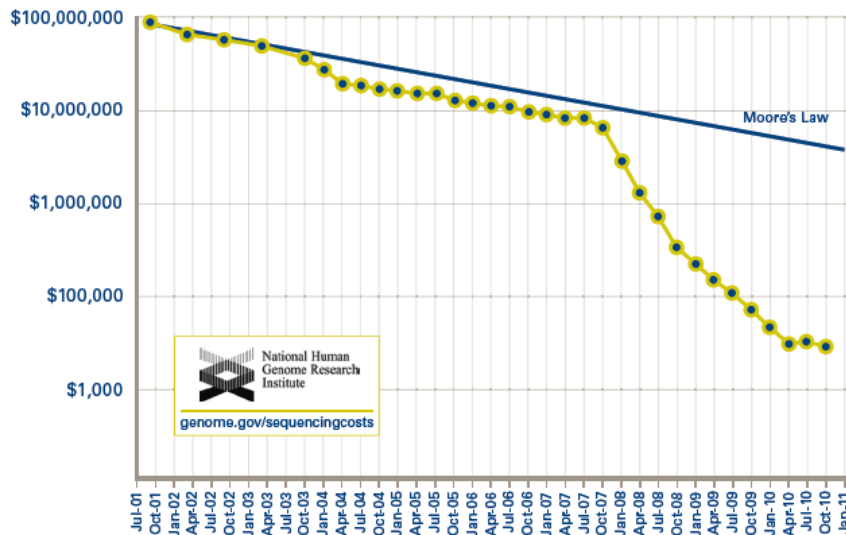
Approach	One-fits-all	One-fits-all	Stratified	Personalized
MoA	<p>Broad</p>	<p>Targeted</p>	<p>Targeted</p>	<p>Combination</p>
Weaknesses	<ul style="list-style-type: none"> Adverse events 	<ul style="list-style-type: none"> Lower efficacy due to non-responder 	<ul style="list-style-type: none"> Non-response due alternative or “blocked” pathways 	<ul style="list-style-type: none"> Pricing Complexity of therapy
Prerequisites	None	None	<ul style="list-style-type: none"> Companion diagnostics 	<ul style="list-style-type: none"> Patient profiling

Personalization

The future of fully profiling both individual patients and patient groups is nearing with low cost approaches on the horizon

Examples for large scale profiling initiatives

Full genome sequencing of one patient



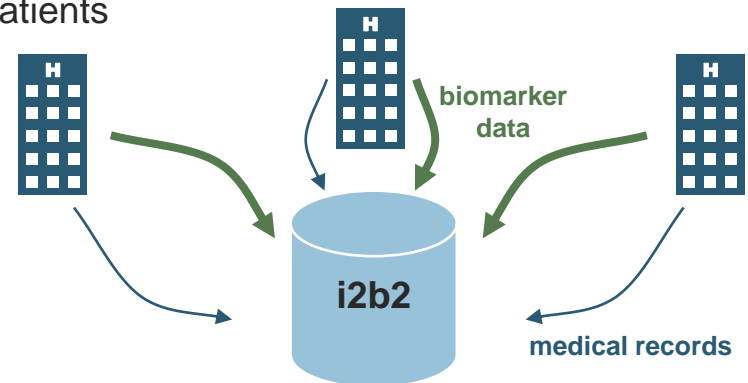
Low-cost large scale diagnostics (e.g. full genome sequencing) makes profiling feasible

Correlated medical record and biomarker data

i2b2

Informatics for Integrating Biology & the Bedside

i2b2 is a scalable informatics framework that enable clinical researchers to use existing clinical data combined with genomic data for discovery research on targeted therapies for individual patients



Low-cost large scale correlation of patient records and biomarker data

F. About CEPTON Strategies

CEPTON Strategies is currently operating from 5 locations

- Founded in 2006
- Strategy Consulting Firm
- 6 Partners in 5 international offices
- > 30 Consultants
- Focus on dedicated industries
 - Pharmaceuticals
 - Medical Devices
 - Biotechnology
 - Consumer Products
 - Process industries
 - Automotive



CEPTON
Strategies

CEPTON - high value advice with small teams, senior team members and Partners dedicated to project work

- **Small effective teams** of senior experts and dedicated Partners
- **No Junior Consultants**
- Partners have **many years** own **experience** in related industries as well as in Consulting
- Focus on international **industry know-how** and specifically adapted **methods**
- Integrating the client's organization and existing data
- Fostering implementation even as interim managers

“Cepton will be working **with rather than for** your organization”

Our offering covers a spectrum of solutions

CEPTON Offerings

Strategic Management

- Corporate Strategy
- Therapeutic Area Strategy
- Regional Strategy
- Portfolio-Management
- Access and Governmental Affairs Strategies

- Reorganization
 - BU-Organization
 - Governmental Affairs
 - Strategic Marketing
- PMI
- Turnaround Management

Transformation

Performance

- Launch Readiness (MAXXIMizing®)
- Marketing & Sales Force Effectiveness
- Cost optimization
- Brand management
- Restructuring

- Business Development support
- Due Diligence (commercial)
- Acquisition Screening & Valuation
- Carve Out Preparation

Transactions

We focus on selected industries in which we have gathered long term relations and know-how

Our Focus



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