
Roche– Delivering on the Promise of Personalized Healthcare

Tod Bedilion Ph.D./ Global Biomarker Group/DBB
June 2011



Making 'Personalised Healthcare' a reality

Key steps to bringing new value to the practice of medicine



- 1 Understand heterogeneity of diseases
- 2 Discover and develop relevant biomarkers
- 3 Stratify patients with diagnostic tests
- 4 Build evidence for better benefit-risk ratio



Need for highly differentiated medicines that positively impact public health

Roche Diagnostics driving PHC

Creating medical value through new diagnostics tests

*Medical
Value*



- Screening
- Diagnosis
- Prognosis
- Prediction
- Monitoring

Diagnostics



Companion Diagnostics

- Treatment selection
- Response prediction
- Treatment monitoring

The Roche Group

Two Divisions focused on high-value healthcare



Roche Pharma	Genentech	Chugai
	 <i>A Member of the Roche Group</i>	 CHUGAI Roche Group

Roche Molecular Diagnostics	Roche Professional Diagnostics	Roche Tissue Diagnostics	Roche Applied Science	Roche Diabetes Care
		 VENTANA® <i>A Member of the Roche Group</i>		

Roche Diagnostics driving PHC

Creating medical value through new diagnostics tests

*Medical
Value*



- Screening
- Diagnosis
- Prognosis
- Prediction
- Monitoring

Diagnostics



Companion Diagnostics

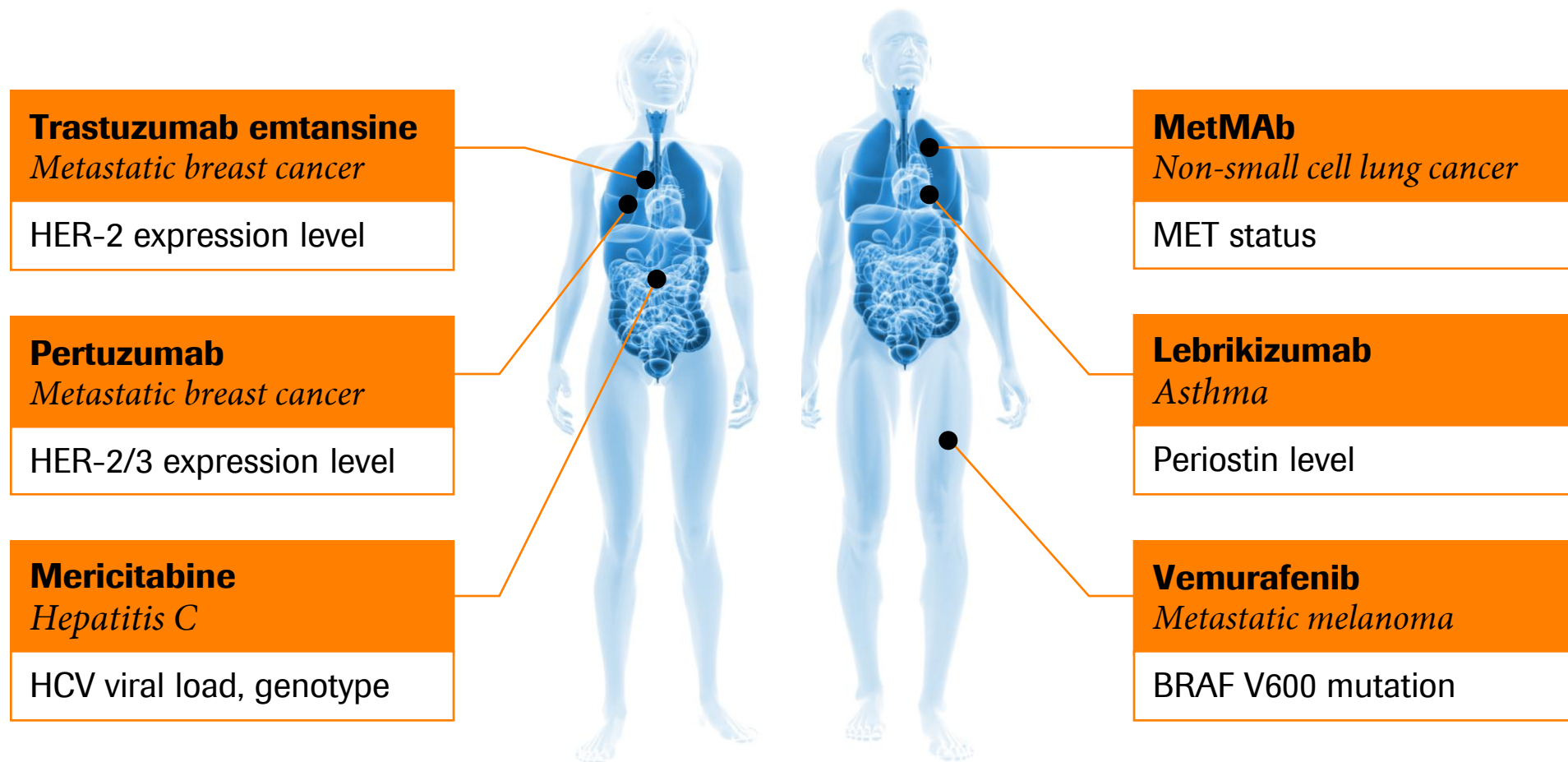
- Treatment selection
- Response prediction
- Treatment monitoring

'New Medical Entities' in Roche's product pipeline

Progressing Personalised Healthcare

Late stage development projects

Six out of 12 NMEs require patient stratification



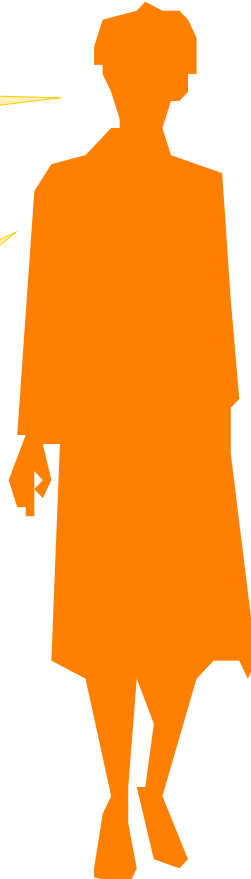
BRAF Test & vemurafenib

Pipeline ● ● ● ● ●

PHC in metastatic melanoma: *Targeted treatment for patients with BRAF mutations*

Oncogenic BRAF inhibitor vemurafenib

Unmet medical need



What is my prognosis?

How much time do I still have?

Does my cancer carry a mutated BRAF gene?

Metastatic melanoma

About 160,000 new cases diagnosed worldwide each year

Incidence expected to double within next 10 years

Average survival time of patients who have already developed metastases: 8-10 months

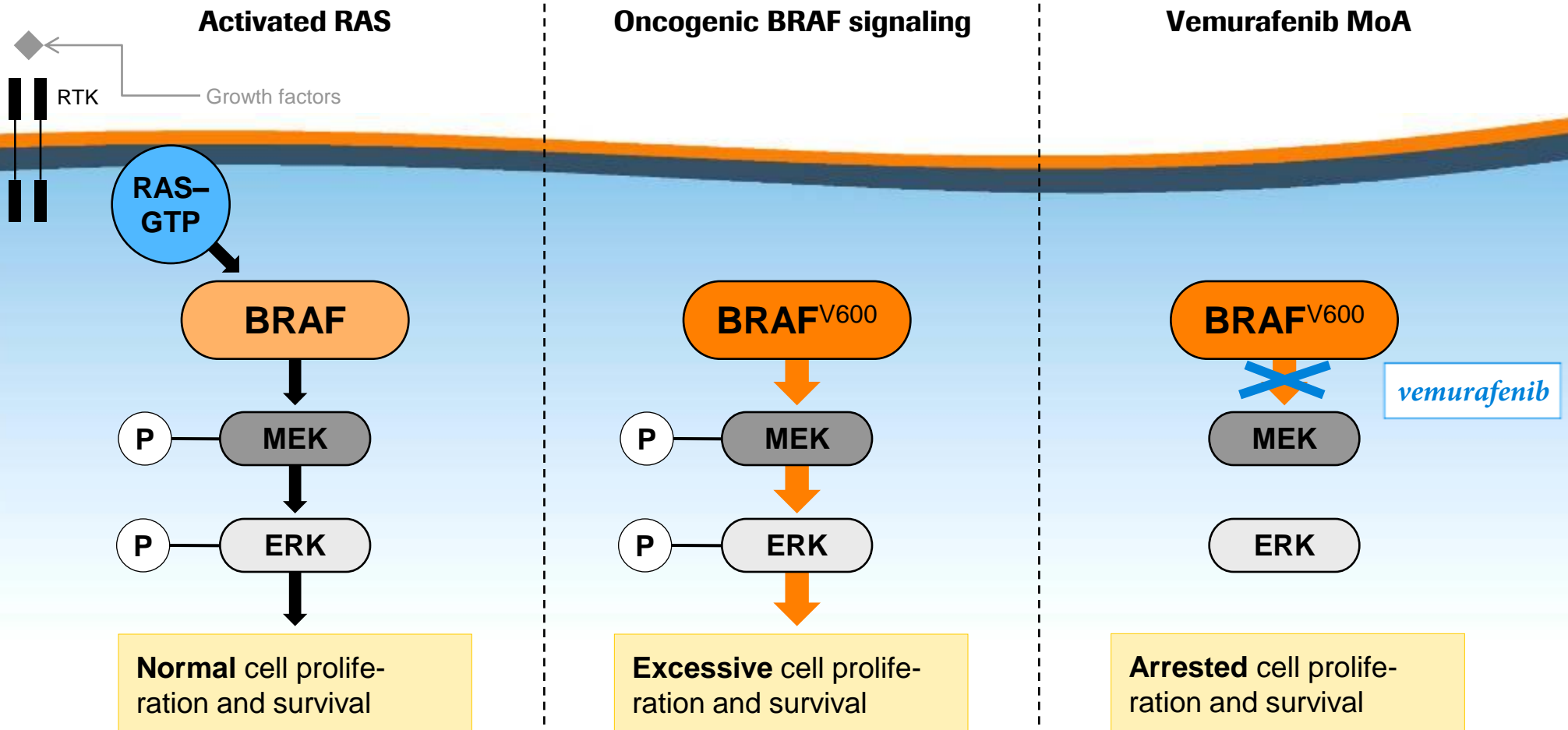
No significant therapeutic advances in this field for 30 years

Vemurafenib – targeting the Ras-Raf pathway

A highly selective BRAF inhibitor

Oncogenic BRAF inhibitor vemurafenib

Mode of action

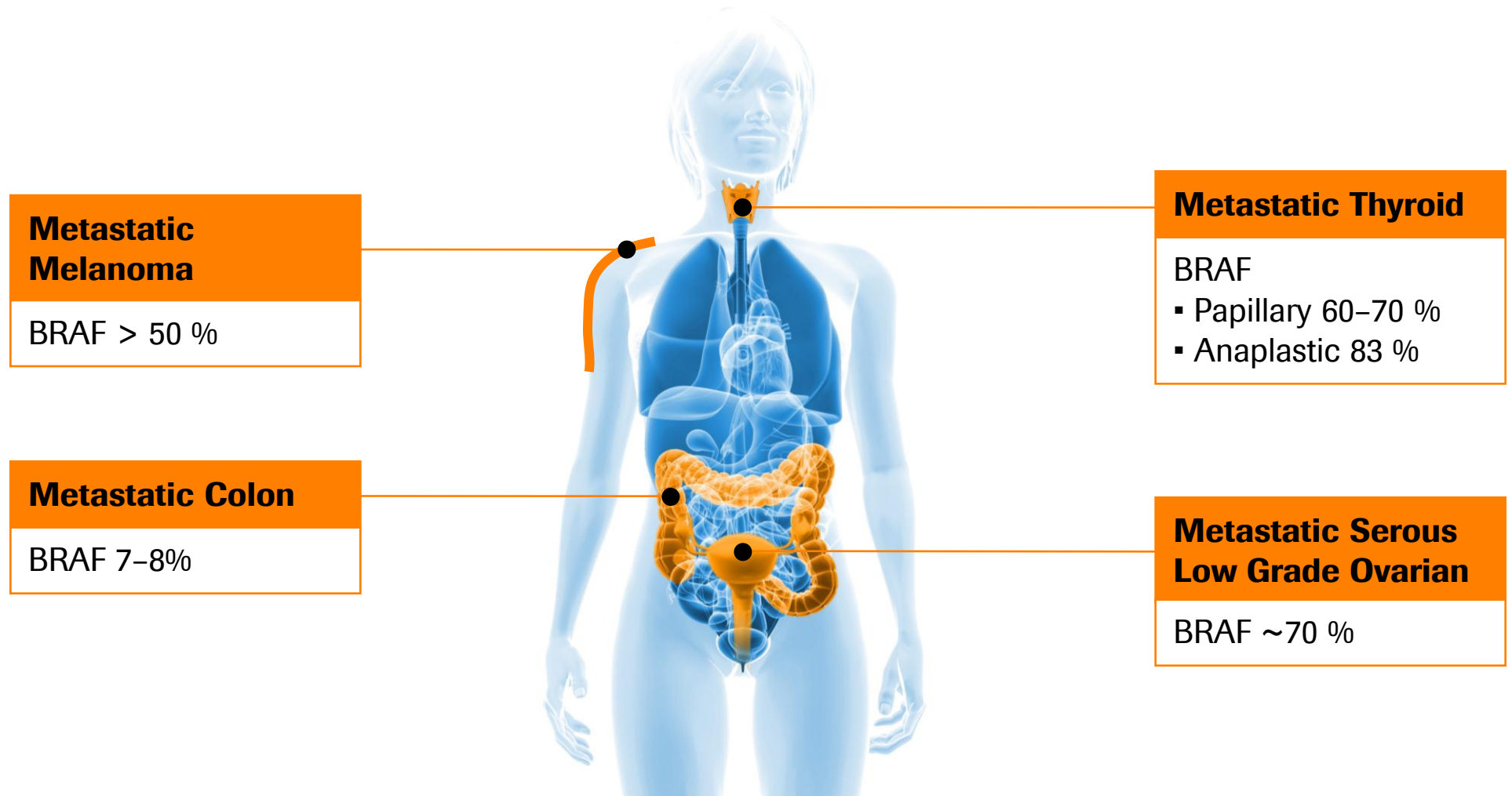


BRAF kinase – attractive drug target

Cancer with mutant BRAF gene has poor prognosis

Oncogenic BRAF inhibitor vemurafenib

Disease overview

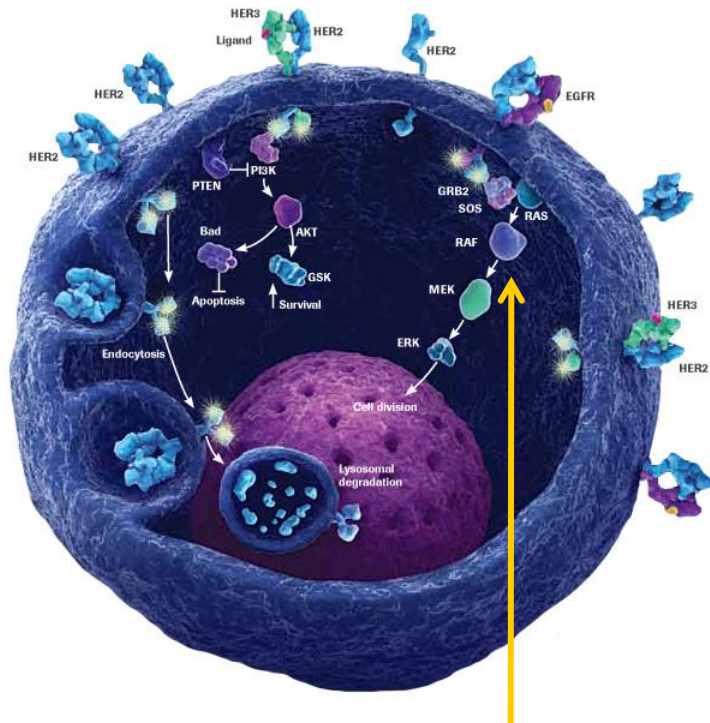


Mutation in BRAF kinase

Co-development of test and drug in oncology

Oncogenic BRAF inhibitor vemurafenib

Combined test & drug development



Single mutation in BRAF gene (BRAF^{V600}) causes activation in absence of normal growth factor stimulation

cobas[®] 4800 BRAF V600 mutation test*

Real-time PCR assay identifies patients whose tumor DNA carries BRAF V600 mutation

Result from FFPE tumor in <8hrs

Increases feasibility of drug clinical development and probability of success

IVD timelines aligned with vemurafenib accelerated development plan

→ joint launch/approvals anticipated

PHC in metastatic melanoma – survival benefit shown

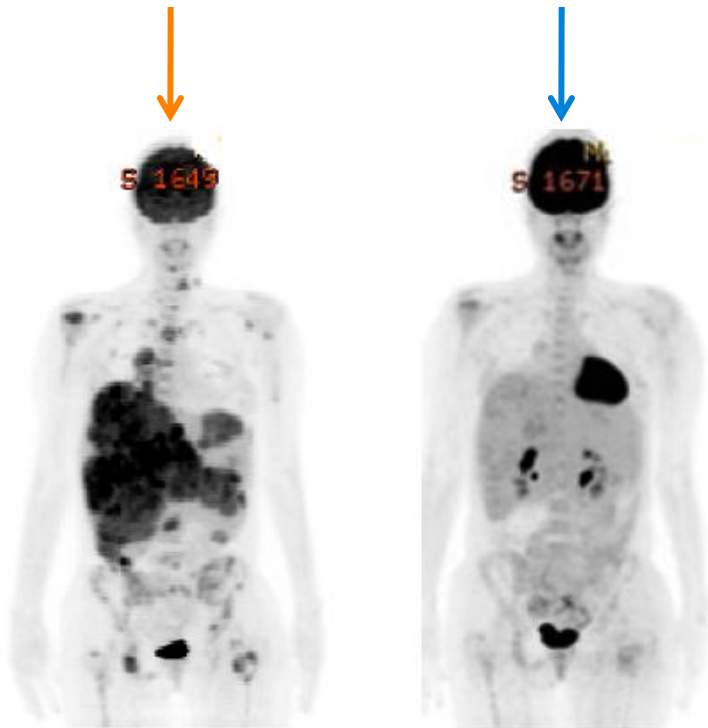
Clinical studies demonstrate encouraging results

Oncogenic BRAF inhibitor vemurafenib

Study results

Before treatment

After 15 days



Results from vemurafenib clinical studies in BRAF-positive metastatic melanoma patients

Tumors shrank by 30% or more for at least two consecutive scans in 52% of the patients (BRIM 2)*

On average, patients lived at least six months without their disease growing or spreading (median progression-free survival (PFS, BRIM 2)

Vemurafenib associated with 63% decrease in hazard of death ($p < .0001$) / BRIM 3**

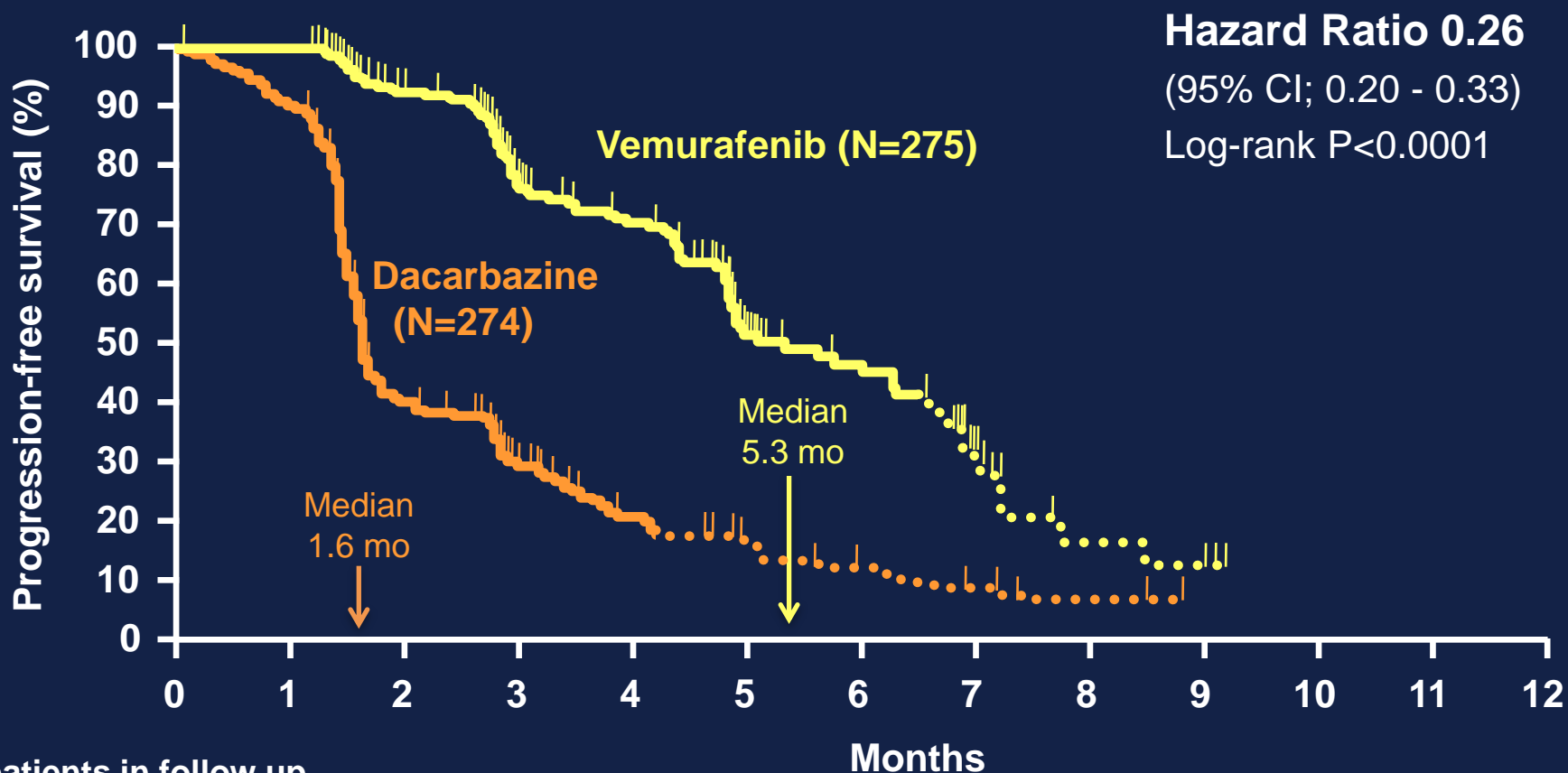
74% decrease in hazard of tumor progression ($p < .0001$) BRIM 3**

*First single drug for melanoma to improve response rate, progression-free survival, and overall survival compared to active chemotherapy***

* 7th International Melanoma Research Congress of the Society for Melanoma Research, Sydney, Australia 2010

** BRIM 3; Chapman, et al.: ASCO 2011

Progression-free survival (12/30/10 cutoff)



No. of patients in follow up

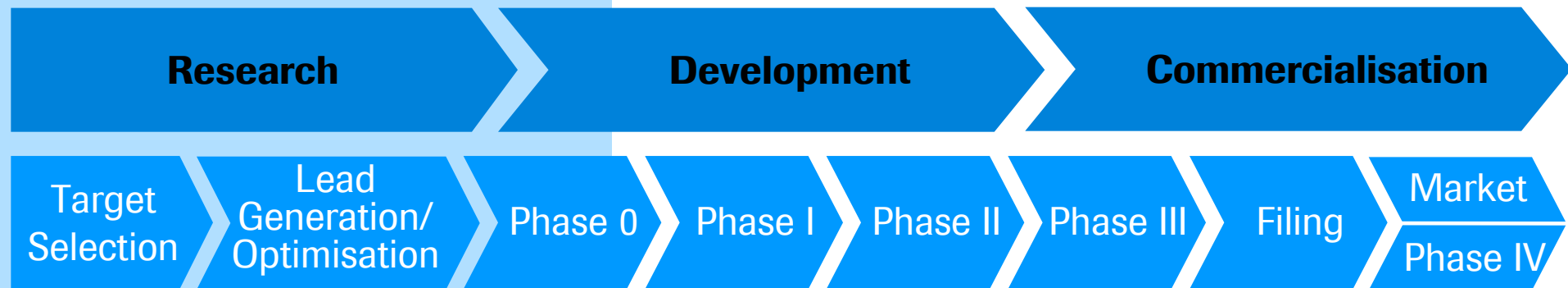
Dacarbazine	274	213	85	48	28	16	10	6	3	0
Vemurafenib	275	268	211	122	105	50	35	16	4	3



Personalised Healthcare at the center of our business

Diagnostics input – from discovery to market

Pharmaceuticals



2002

Oncogenic BRAF Discovered

Davies, et al., Nature, 2002

2006

IND filed

**Plexxicon/Roche Pharma
Roche Dx**

2011

Comp. of Pivotal PhIII: BRIM 3

Chapman, et al. ASCO 2011

Research assay

**Technically validated
IVD assay**

**Clinically validated
IVD assay**

Diagnostics

Roche Diagnostics driving PHC

Creating medical value through new diagnostics tests

*Medical
Value*



- Screening
- Diagnosis
- Prognosis
- Prediction
- Monitoring

Diagnostics



Companion Diagnostics

- Treatment selection
- Response prediction
- Treatment monitoring

Cervical cancer: cobas HPV test

Market ● ● ● ● ●

Cervical cancer

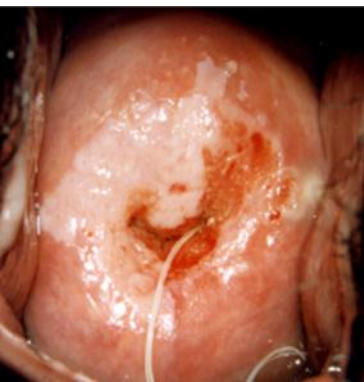
Screening for cancer causing human papilloma virus

cobas HPV test

Medical need

Cervical cancer

- Cervical cancer is 2nd most common cancer in women and 5th cause of cancer death
- 99% of cervical cancers caused by HPV
- 75% of women exposed, but most will clear
- There are >100 types of HPV, of which most are harmless; only about 30 types represent serious health risk; HPV genotypes 16 and 18 are the most relevant
- Despite screening, ~11,200 cases and ~4,000 deaths annually in US
- Despite current guidelines recommending HPV testing w/ PAP for women over 30/ compliance is currently low in screening pop



High-grade Precursor



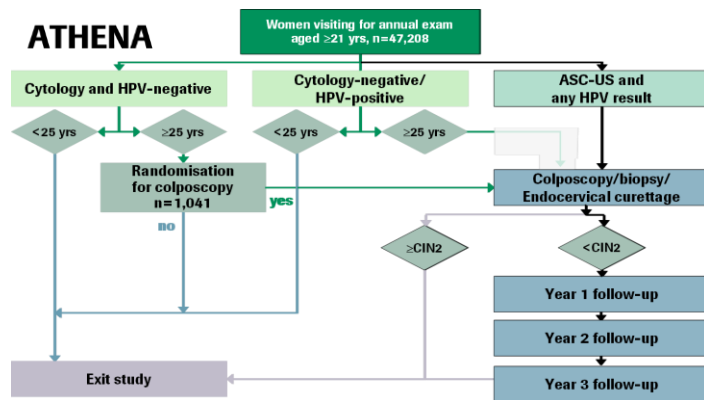
Invasive Cancer

HPV test covering high-risk HPV genotypes

New test allowing more effective patient management

cobas HPV test

Tests for screening



Pre/cancer detected



Cytology only



Cytology/HPV with 16/18 GT



HPV only

cobas HPV Test*

- Detects the 14 major high-risk HPV genotypes, including type 16 and type 18 which account for > 70% of cervical cancer cases**
- Based on **47,000+ pt ATHENA trial- largest unbiased prospective screening trial in cervical cancer**
- FDA approved in 2011(10.5 mo after filing) for triage of ASC-US and co-testing w/cytology
- **Individual HPV 16/18 genotyping: 1 in 10 women who had normal pap & tested positive for HPV-16 and/or 18 had high grade lesions on biopsy (≥CIN2)**
- Pending 3 year outcomes data may enable primary screening
- Fewer patients may require unnecessary testing and/or invasive procedures like colposcopy

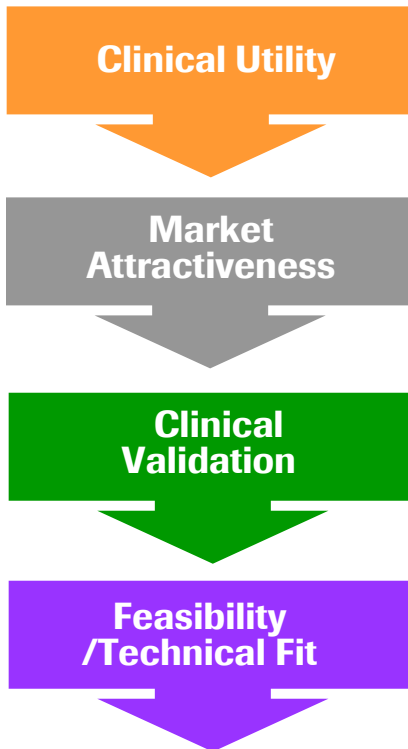
* Not available in the US

** Athena study: American Journal of Clinical Pathology 2011; 135: 468

Biomarker Assessment Criteria

Medical value prioritized in standardized comprehensive process

Considerations



Key Issues

Addresses significant unmet medical need

- Result enables novel and important physician action
- COINS/ Pathways

Market Attractiveness of Disease Area & Test

- Addressable population
- HECON support of healthcare value
- Competitive Environment
- Commercial access to clinical decision maker

Level of Clinical Evidence to support clinical utility claims

- Current level of clinical evidence
- State of physician acceptance or Inclusion in medical guidelines

Financial & Technical Feasibility

- Required R&D investment to bring test to market
- Sample type/ platform fit/ Development risk
- Access to license / IP environment

Decision

Rule
in/out

Rule
in/out

Prioritization

Prioritization

PHC benefits all stakeholders in healthcare

Patients

→ Best treatment



Physicians & Providers

→ Maximum benefit
→ Minimum toxicity



PHC

Payers & Reimursers

→ Efficient use of healthcare budgets



Regulators & Policy Makers

→ Increased efficacy & safety





We Innovate Healthcare