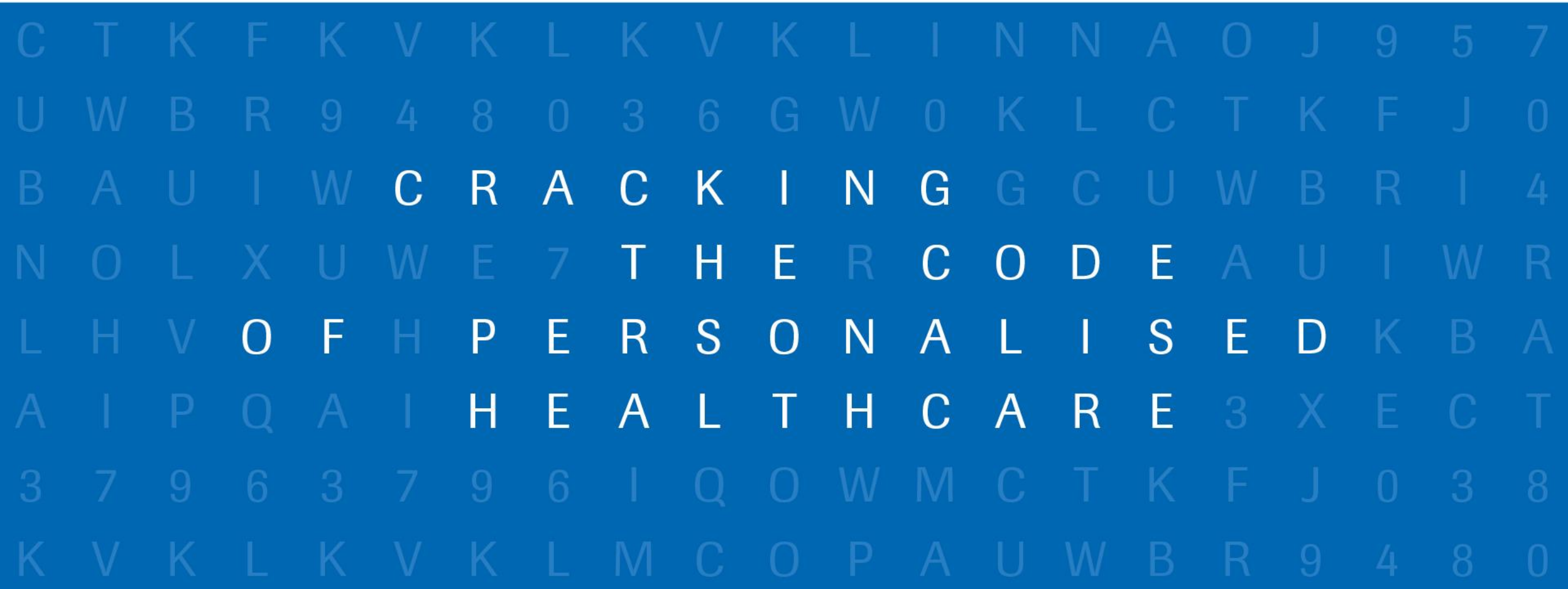
The integration of personalized healthcare in practice:

the interesting case discussion



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Agenda

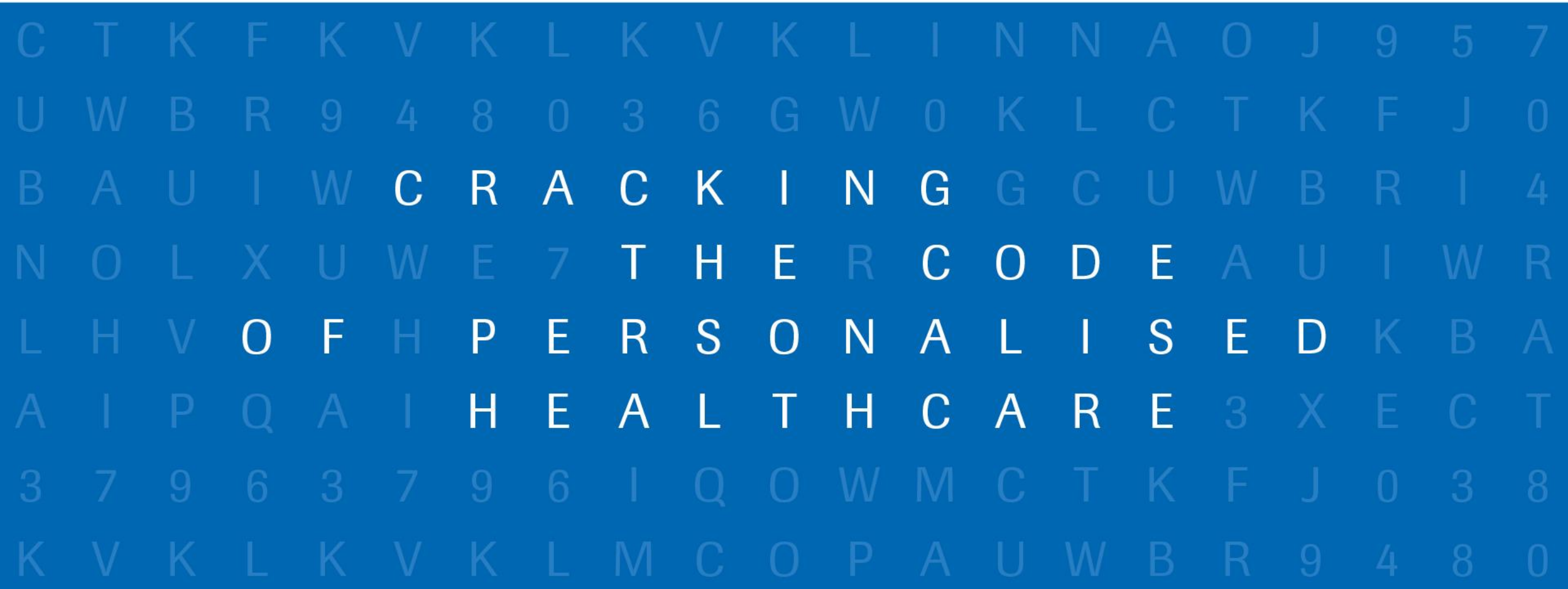
Time	Topics	Speaker
12.30-12.35	Welcome and opening	Dr.Surachat
12.35-12.55	The integration of personalized healthcare in practice	Dr.Virote
12.55-13.05	Interesting case sharing #1	Dr.Suebpong
13.05-13.15	Interesting case sharing #2	Dr.Potjana
13.15-13.25	Discussion	All
13.25-13.30	Closing	Dr.Surachat

Pre-Questionnaire

Please answer the questionnaire

The integration of personalized healthcare in practice

Virote Sriuranpong, M.D.
Medical Oncologist, King Chulalongkorn Memorial Hospital



Outline

Current treatment from “one-size fits-all” to personalized oncology

Changing paradigms in molecular testing of tumors: Choosing the right start for the best outcomes

Taking diagnostics to the next level: Liquid biopsy

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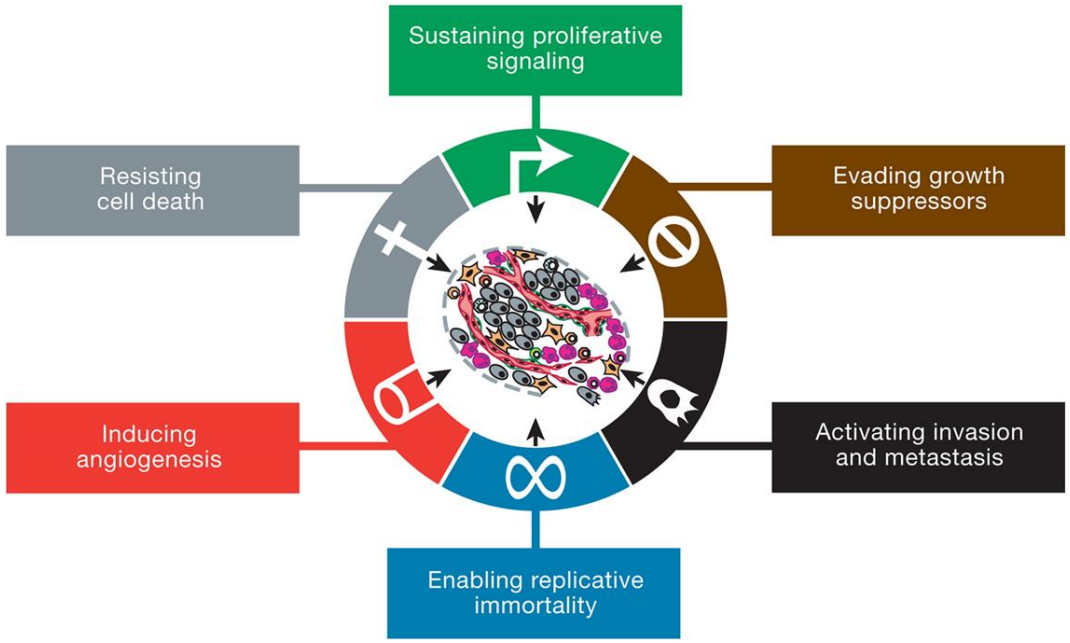
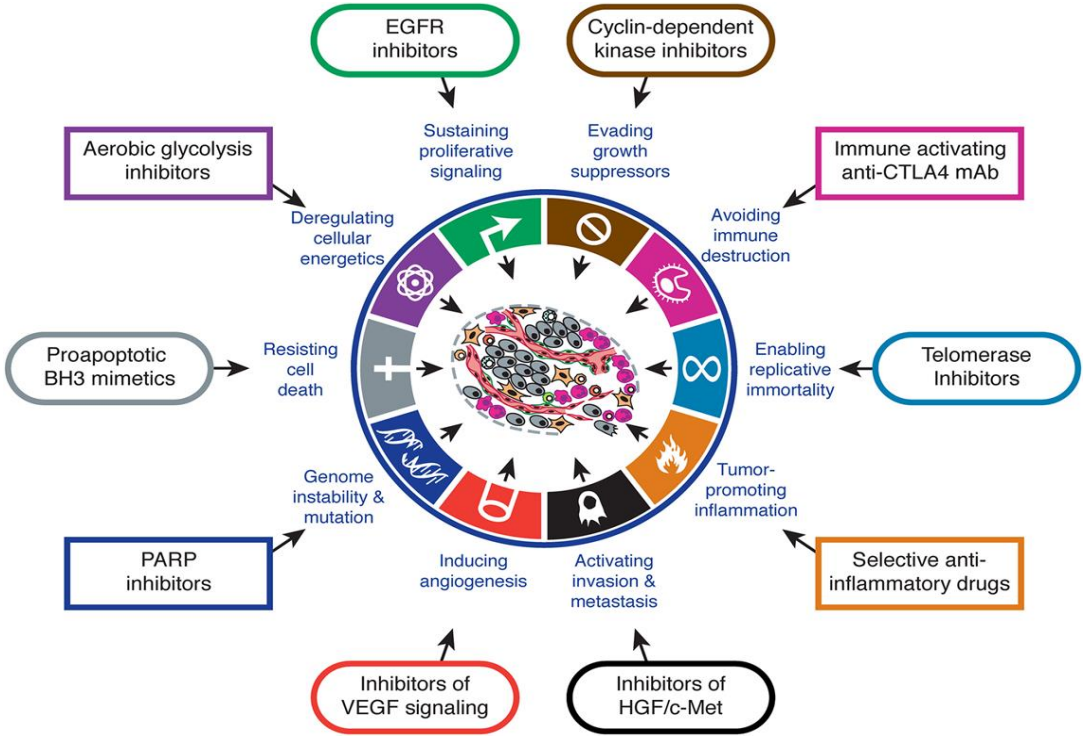
Hallmark of Cancer

Our knowledge is growing rapidly

2000



2011



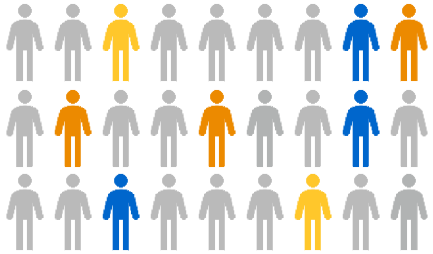
Hanahan et al., Cell, 2000; Hanahan et al., Cell, 2011

The future is tailored therapies for each cancer patient

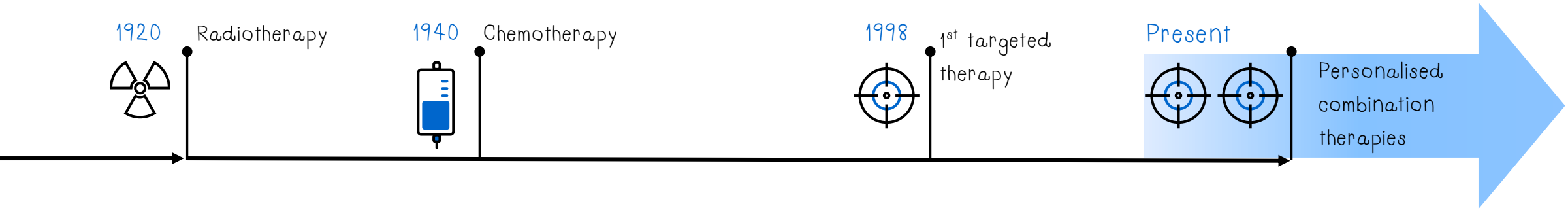
'One-drug-fits-all' treatment approach based on histology[1]

Tailoring treatment to the unique molecular profile of patient's cancer[1]

Personalised treatment based on comprehensive knowledge of patient's individual cancer[2]



The evolution of cancer care[2,3]



1. Agyeman, A.A. and Ofori-Asenso, R. (2015) *J Pharm Bioallied Sci* 7:239–44;
2. Schwaederle, M. and Kurzrock, R. (2015) *Oncoscience* 2:779–80; 3. Falzone, L., et al., (2018) *Front. Pharmacol* 9:1300.

Genomic alteration in lung cancer

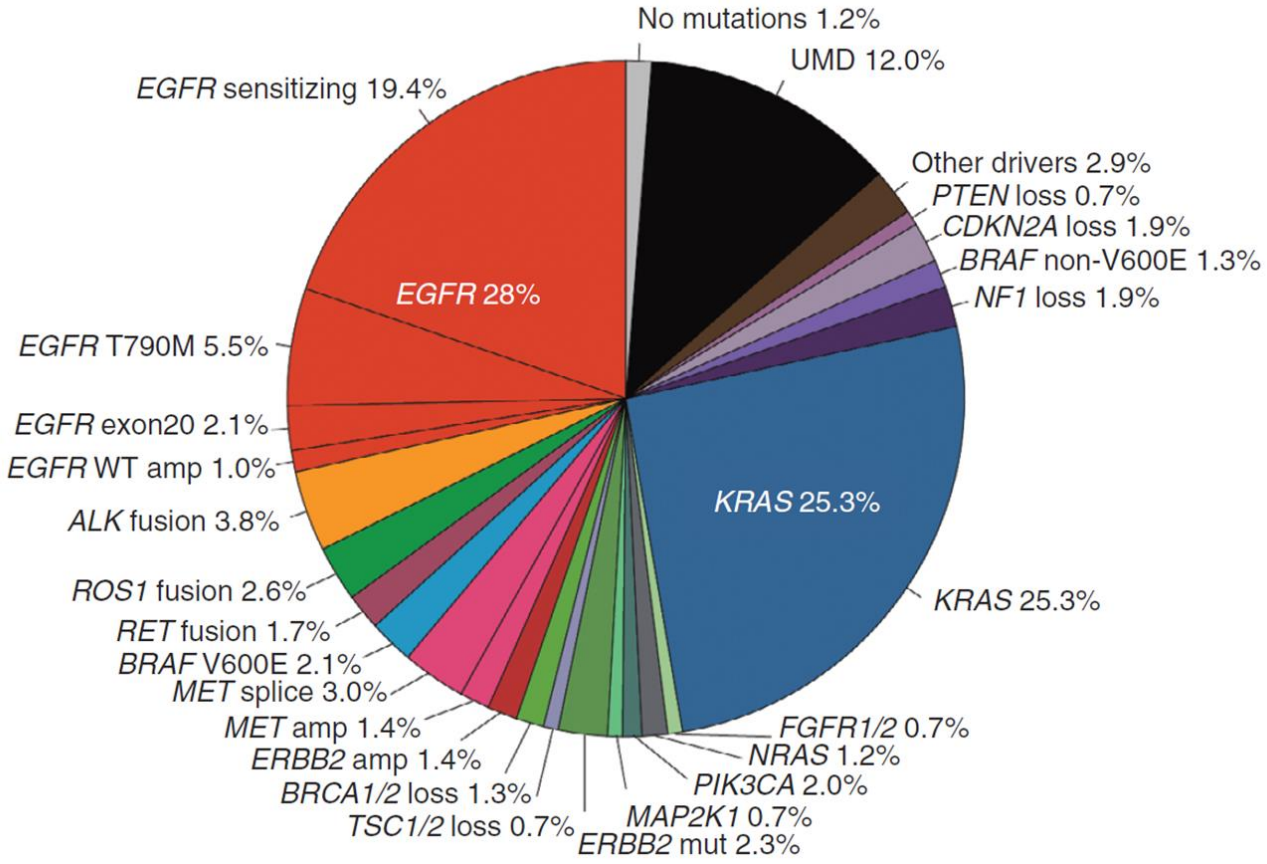
The number grew exponentially in the past decade

2003

Lung cancer was thought of as one single disease

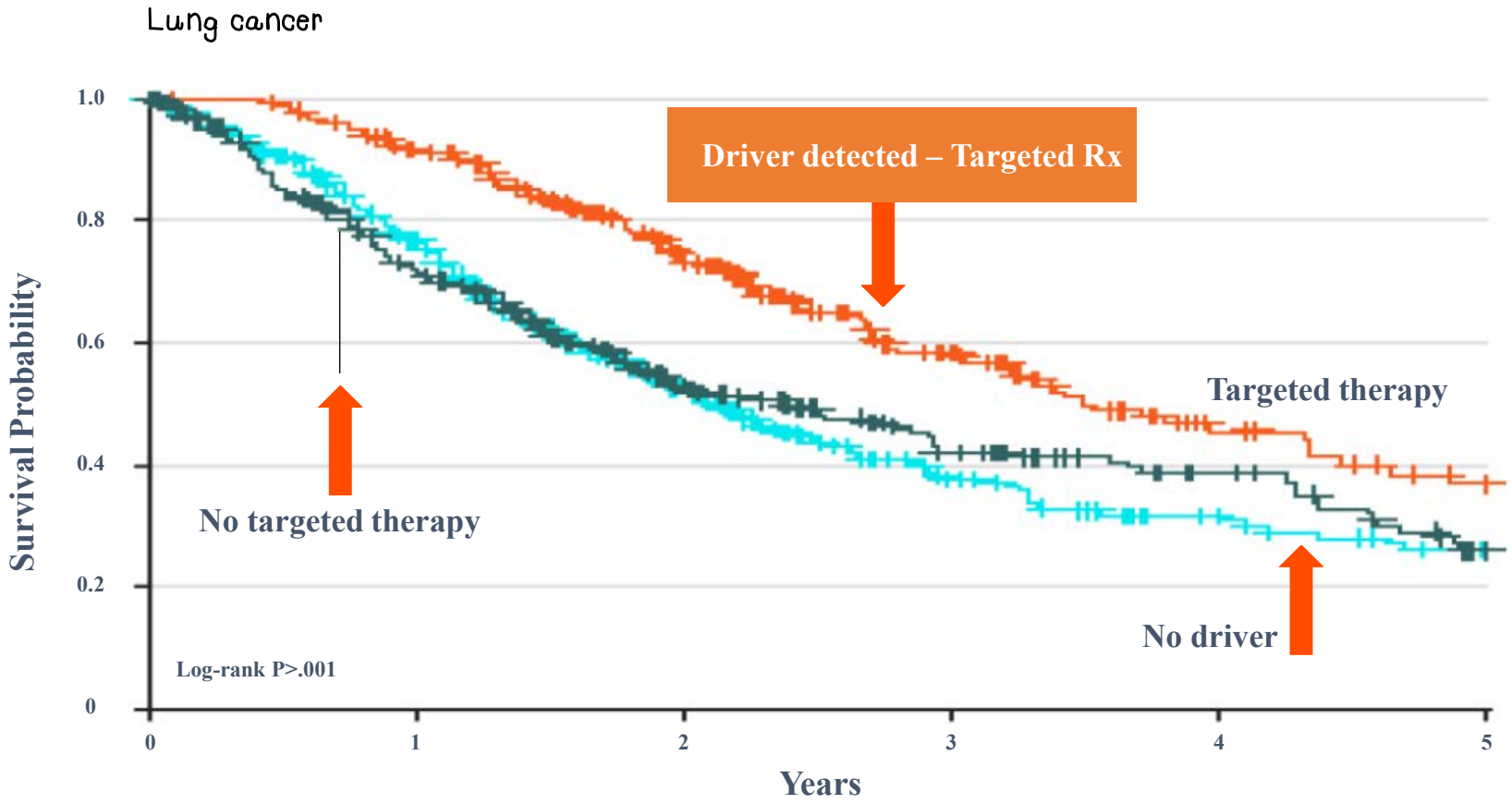
Lung cancer

2018



Modified from: Jordan et al, Cancer Discovery 2016

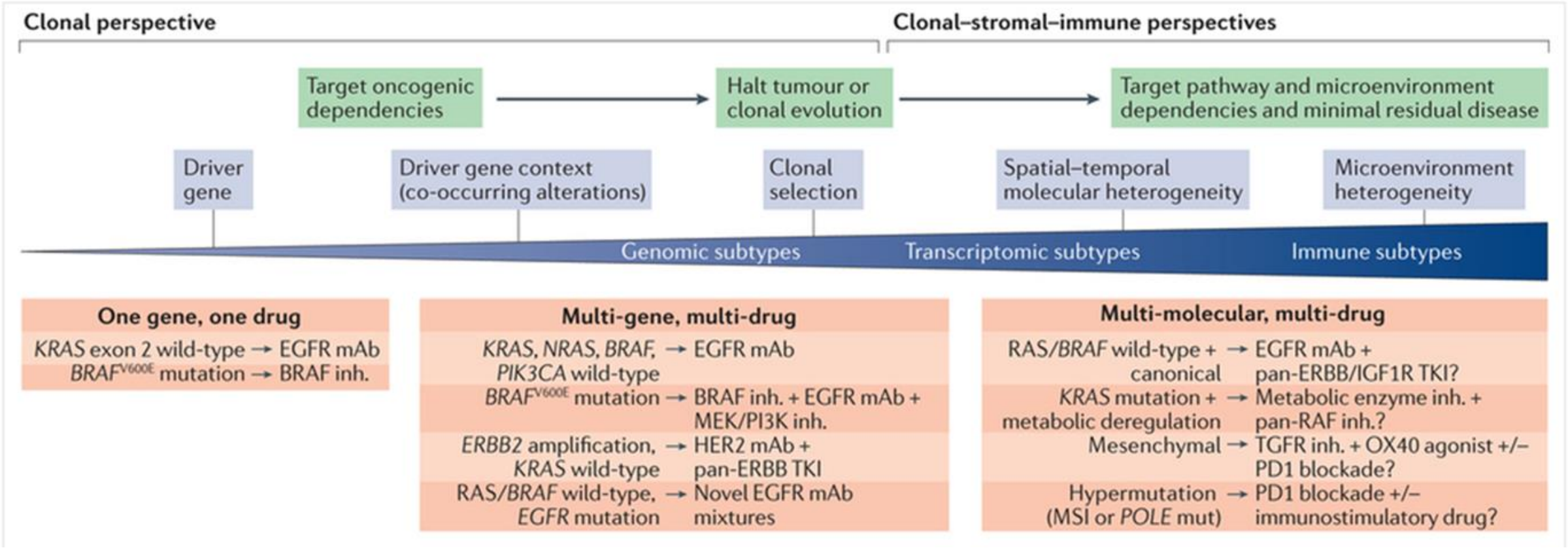
Testing for actionable genomic alteration and targeted treatment improves survival



Kris MG et al. *JAMA* 2014; 311, 1998-2006

Colorectal cancer: Beyond RAS and RAF?

Treatment options extend from single targeted therapy to immunotherapy combinations

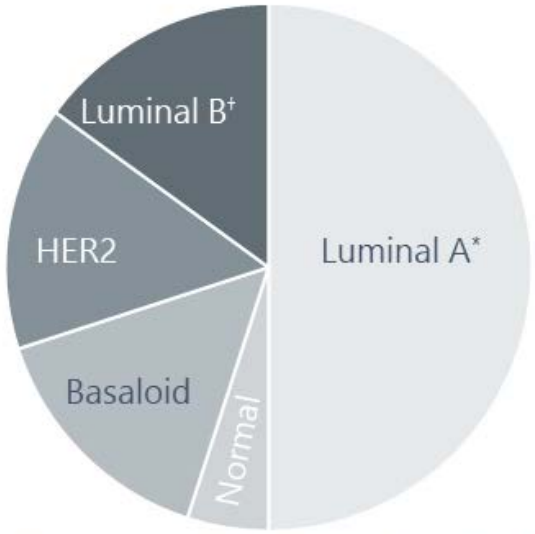


Dienstmann et al., Nat. Rev. Can., 2017

The evolving approach of clinical decisions in breast cancer treatment

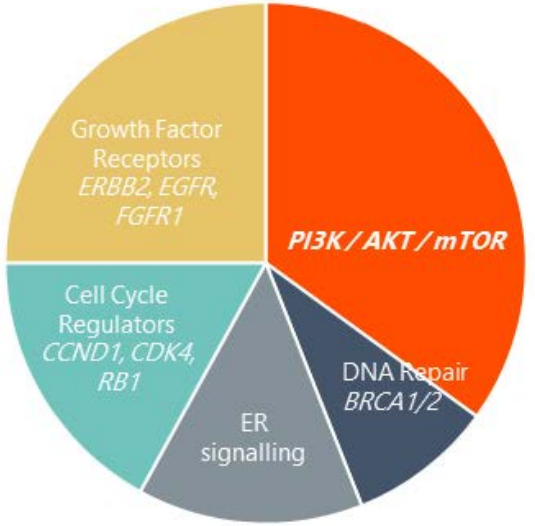
New avenues for molecularly targeted therapy improve patient stratification and can support the management of this complex disease

2000: Breast cancer subtypes[1]



Clinical decisions based on **affected tissue, histology** and **disease stage**

2016: Breast cancer genomic drivers[1]



Clinical decisions based on the **results of genomic profiling**

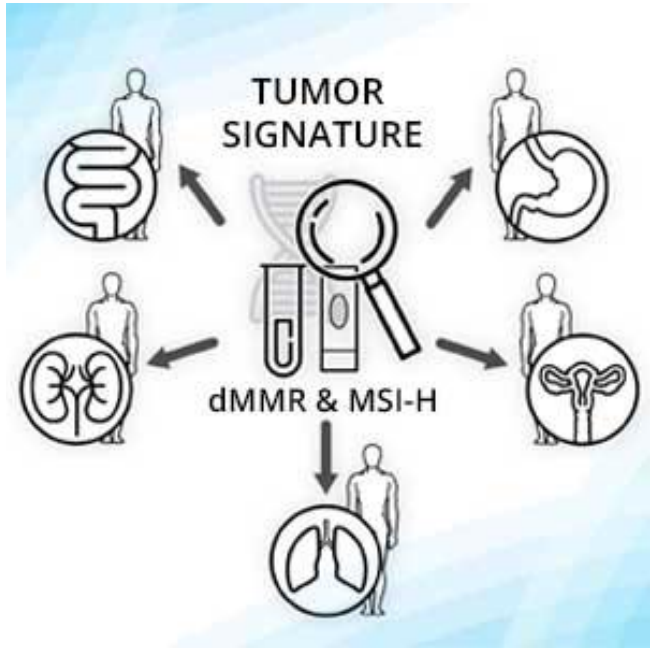
- Luminal A typically defined as ER+ or PR+ / HER2- with Ki67 ≤ 14%; † Luminal B typically defined as ER+ or PR+ / HER2- with Ki67 > 14%[3].

ER: oestrogen receptor; HER2: human epidermal growth factor receptor 2;
TNBC: triple-negative breast cancer. 1. Adapted from Ross, J. and Gay, L. (2016) *Pathology* 49:120-32; 2. Curtis, C., (2015) *Curr Opin Obstet Gynecol*. 27(1): 34–39.

From disease-specific treatment to tumor agnostic

In the past 2 years, three drugs have been approved for tumor agnostic indications that involve NTRK and MMR genes

Tumor Agnostic Approval Signals New Phase for Precision Medicine



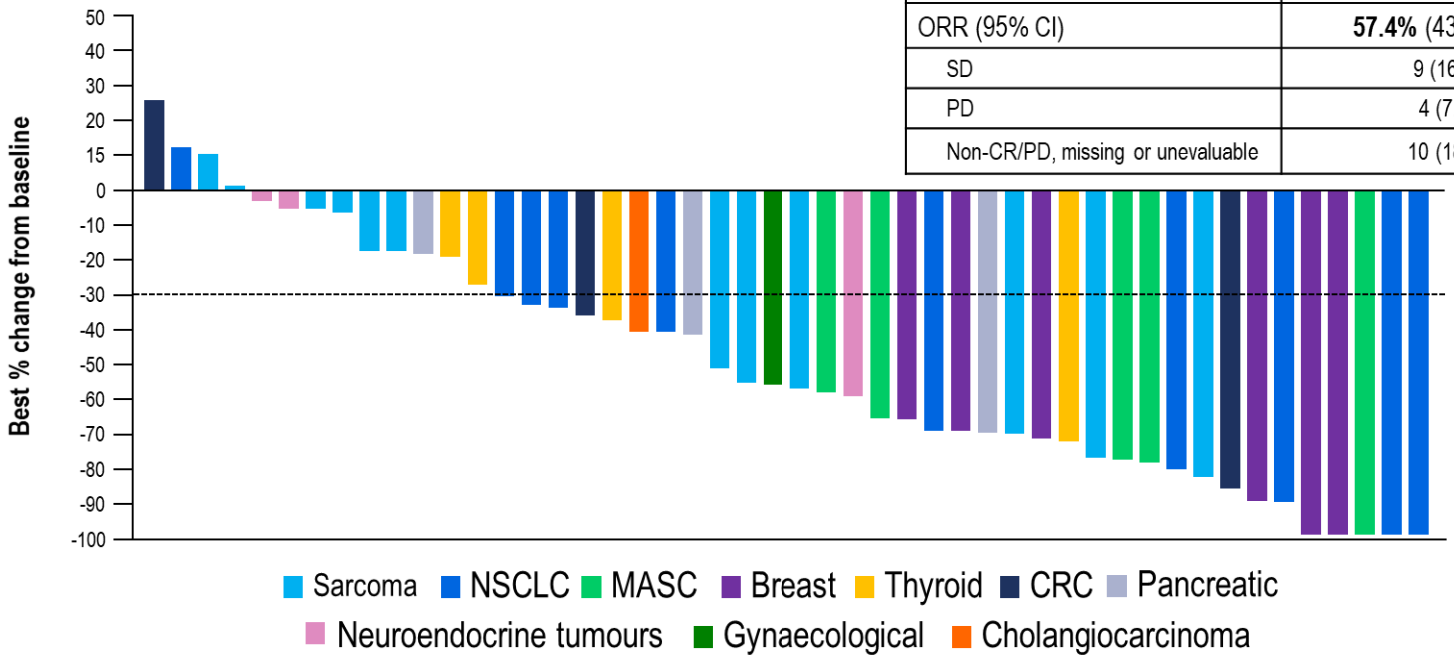
Source: Flagship Bioscience

Tumor agnostic is a type of therapy that uses drugs or other substances to treat cancer based on the cancer's genetic and molecular features without regard to the cancer type or where the cancer started in the body

- National Cancer Institute, USA -

Activity of NTRK inhibitor in *NTRK* fusion-positive solid tumours: individual patient responses by tumour type

	NTRK+ patients (n=54)
ORR (95% CI)	**57.4%** (43.2–70.8)
SD	9 (16.7)
PD	4 (7.4)
Non-CR/PD, missing or unevaluable	10 (18.5)



FOUNDATIONONE®CDx is the central test for determining molecular eligibility

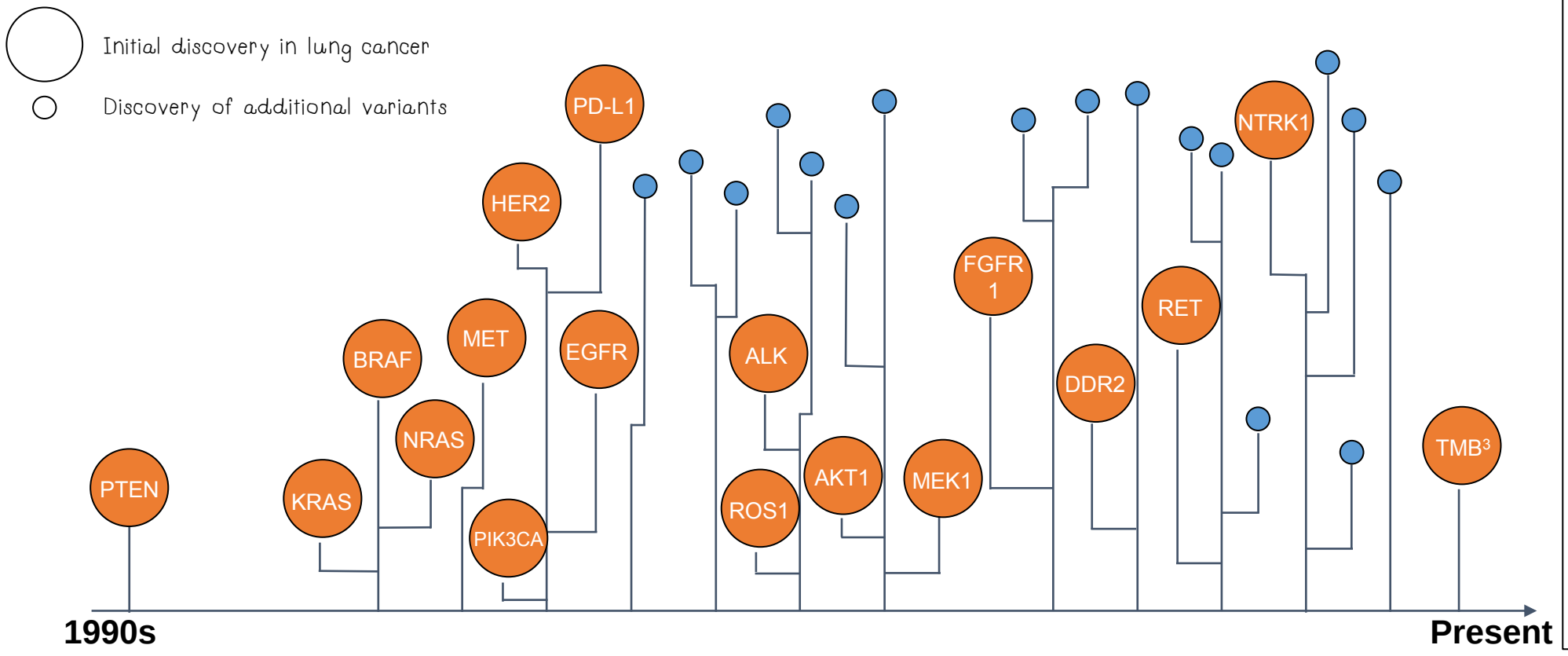
CI: confidence interval; CRC: colorectal cancer; MASC: mammary analogue secretory carcinoma; NSCLC: non-small cell lung cancer

Cut-off date: 31 May 2018

Note: Patients (n=6) without matched pre/post therapy scans were excluded from the plot

Demetri et al., ESMO., 2018

An increase in oncogenic drivers and related drug approvals in lung cancer



2003 / 2004
1st EGFR inhibitors
(gefitinib, erlotinib)[1]

2011
1st ALK inhibitor
(crizotinib)[2]

2016
1st ROS1 inhibitor
(crizotinib)[3]

2017
1st pan-tumour drug
(pembrolizumab▼)[4,5]

2018
1st NTRK inhibitor
(larotrectinib)[6]

Therapies marked with ▼ are subject to additional monitoring. Reporting suspected adverse reactions after authorisation of the medicinal product is important. Adverse events should be reported to your respective local office Merck Sharp & Dohme B.V: Pembrolizumab. 1. Drugs.com. Accessed August 2019. Available from https://www.drugs.com/history/; 2. Kazandjian D., et al. (2014) *Oncologist* 19: e5–e11; 3. FDA expands use of crizotinib. Accessed September 2019. Available from https://www.drugs.com/newdrugs/fda-expands-xalkori-crizotinib-ros-1-positive-non-small-cell-lung-cancer-4354.html; 4. Darvin P., et al. (2018) *Experimental & Molecular Medicine* 50:165. 5. FDA.gov. Accessed August 2019. Available from https://www.fda.gov/news-events/press-announcements/fda-approves-first-cancer-treatment-any-solid-tumor-specific-genetic-feature; 6. FDA.gov. Accessed September 2019. Available from https://www.fda.gov/news-events/press-announcements/fda-approves-oncology-drug-targets-key-genetic-driver-cancer-rather-specific-type-tumor. Graphic adapted from The Lung Cancer Project 2019. Accessed August 2019 at www.thelungcancerproject.org.

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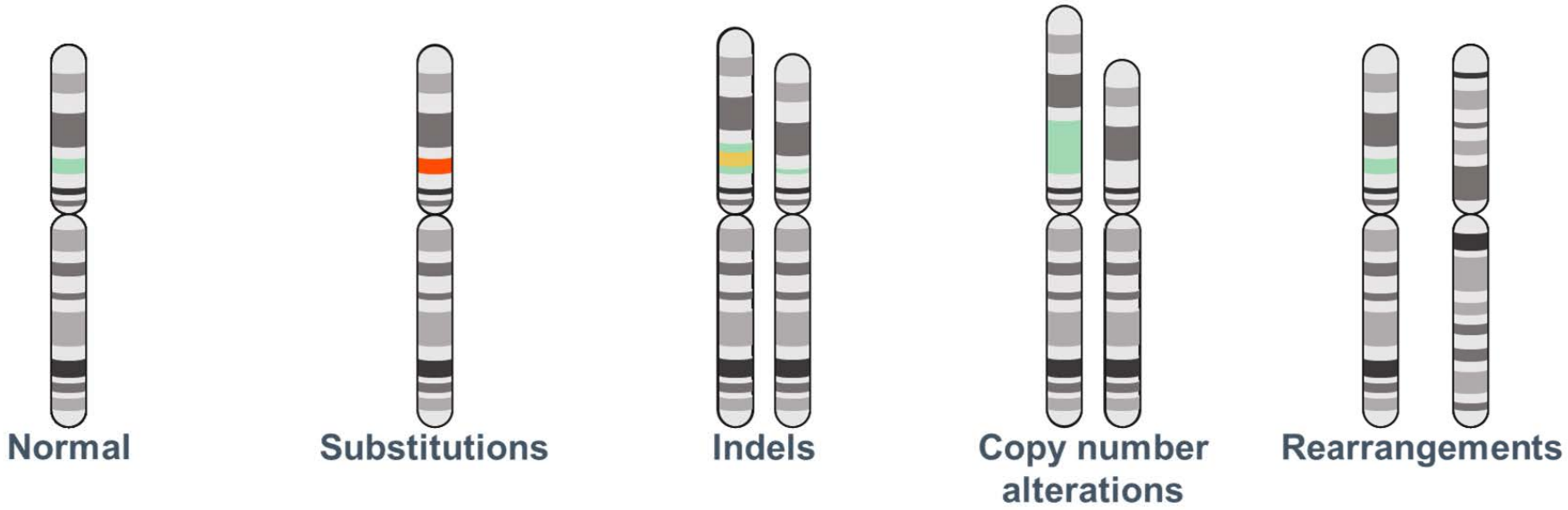
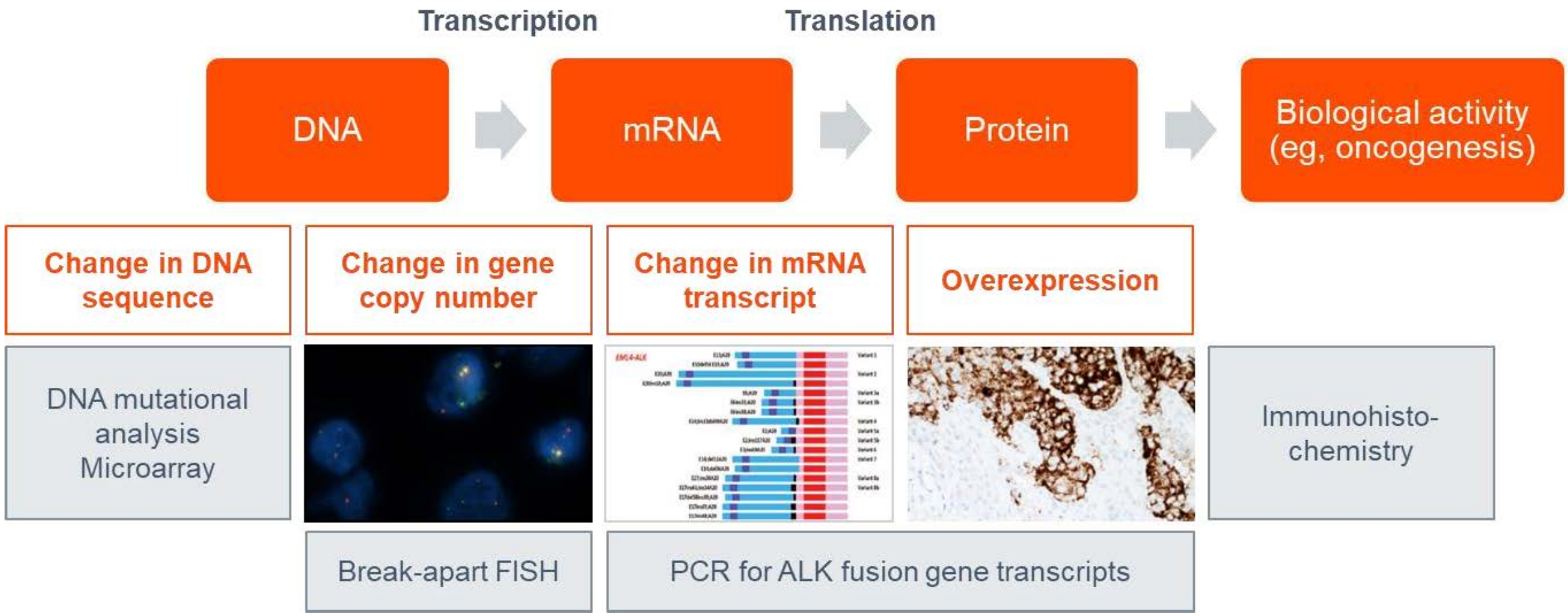
The four main types of genomic alterations in cancer

They require different molecular technique to detect



Molecular testing complexity



Single vs Multiple Biomarker Testing

Single biomarker testing

- Tests for only one biomarker at a time
- More commonly used
- Less expensive per test, but price may vary by testing centre
- **Serial single marker testing may exhaust tissue sample**
- **May miss aberrations not known ahead of time**

Multiple biomarker testing

- **Tests for multiple potential molecular drivers and markers at the same time**
- Includes gene sequencing as well as other modalities (e.g. microarray technology, multiplex PCR, microbead arrays)
- Potential to deliver superior diagnostic value vs single-biomarker testing

1. Petricoin EF, Liotta LA. A Revolutionary Approach to Biomarker Discovery. The Scientist 2006. Available at: https://www.the-scientist.com/?articles.view/articleNo/24452/title/A-Revolutionary-Approach-to-Biomarker-Discovery/. Accessed 12 Mar 2018.
2. Hsueh CT, et al. *Biomarker Res* 2013;1:1. 3. van Nagell Jr J, Hoff J. *Int J Women Health* 2013;2014:25—33