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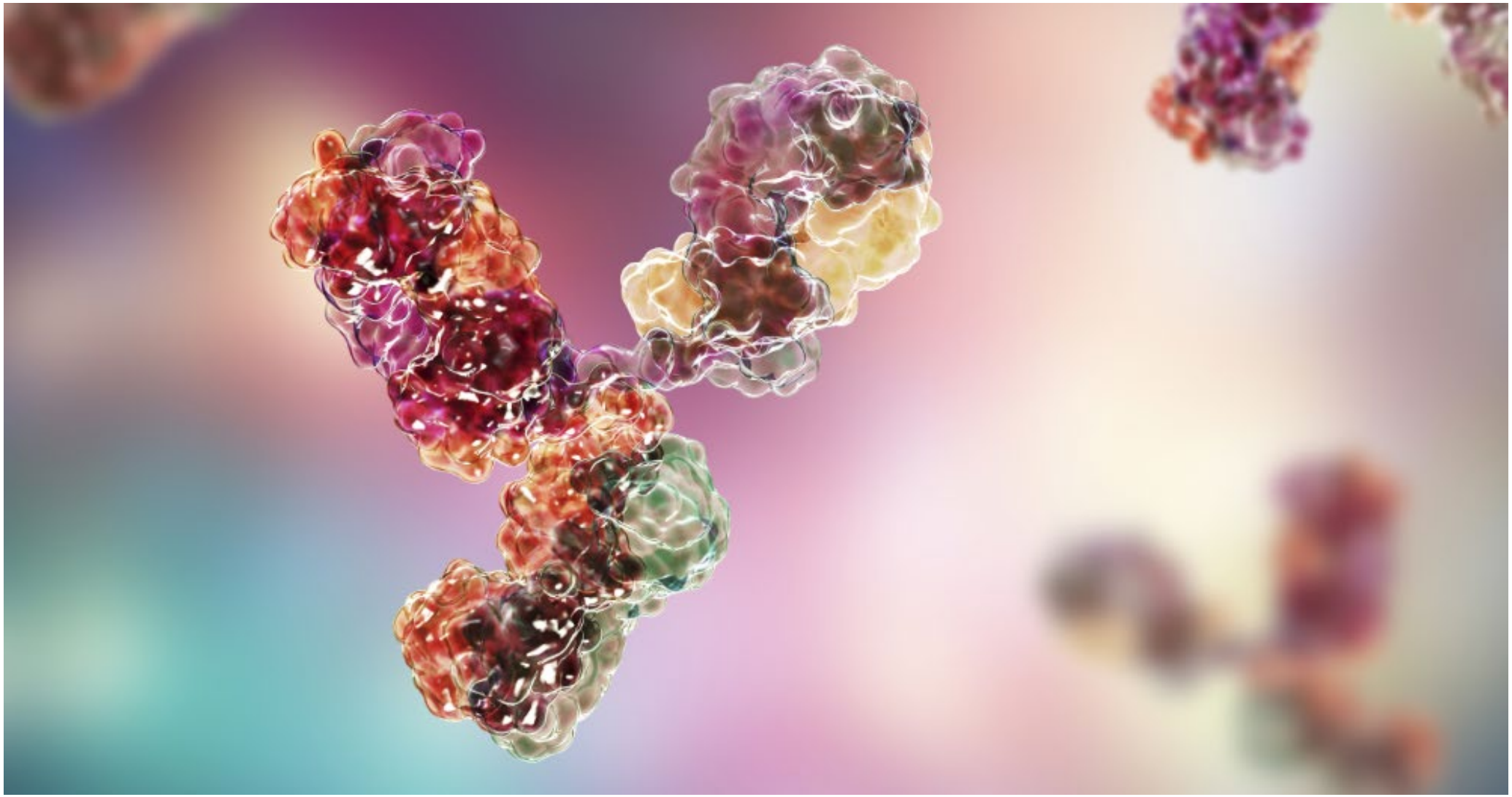


Biomarkers in cancer treatment

Michael Brobjer, CEO of Arocell, explains the importance of the biomarker in cancer treatment, and how they can be used to improve treatment, monitoring and survival for cancer patients. We also get a taste of what's going on and what challenges Arocell is facing right now.

AroCell – Precision monitoring

In cancer, time is everything

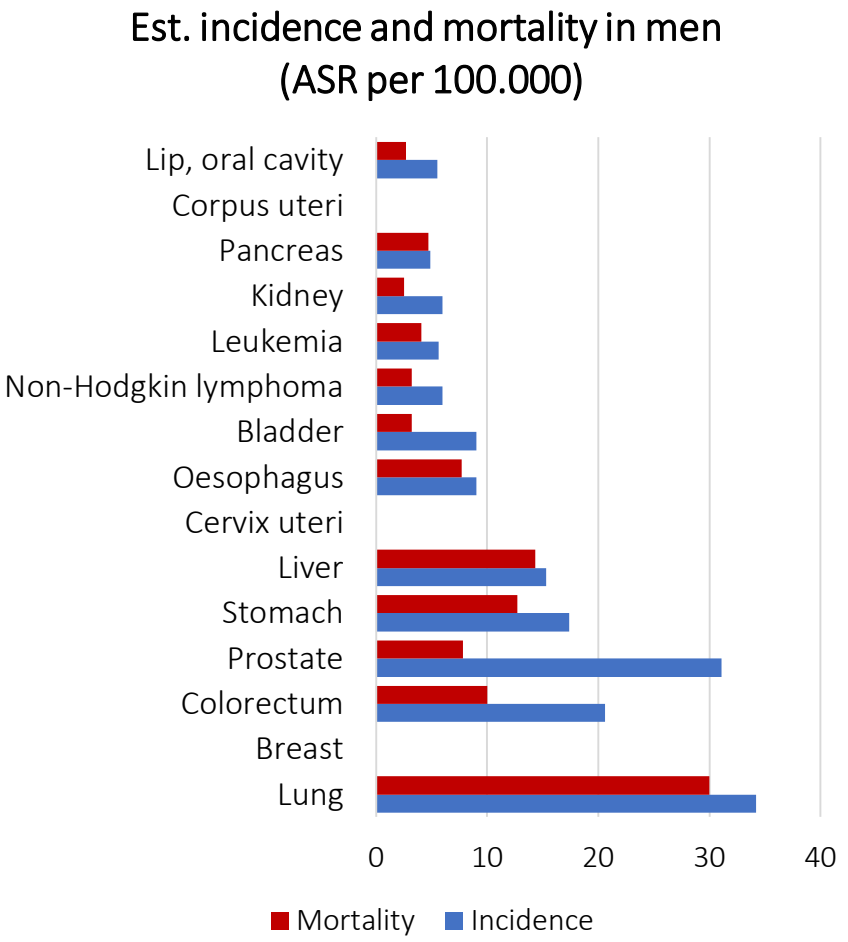
Oncology pharma

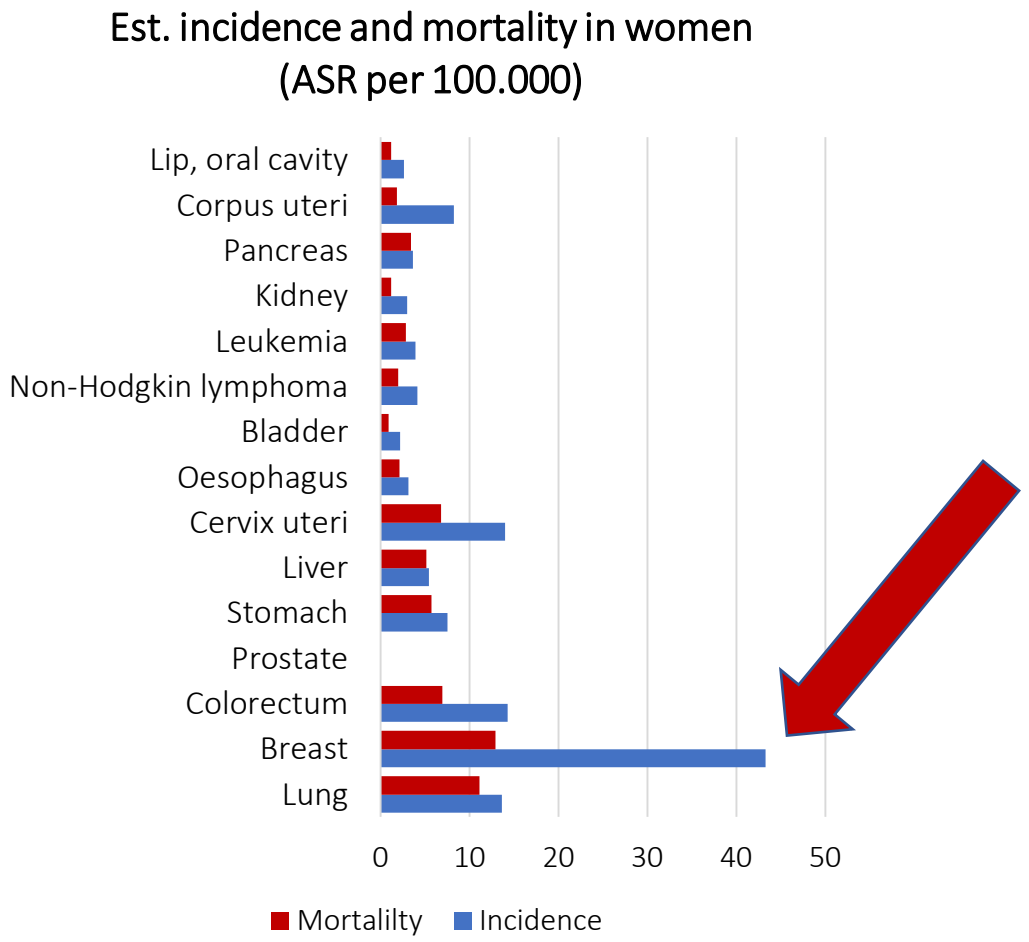
In vitro diagnostics

Efficient treatment for cancer patients

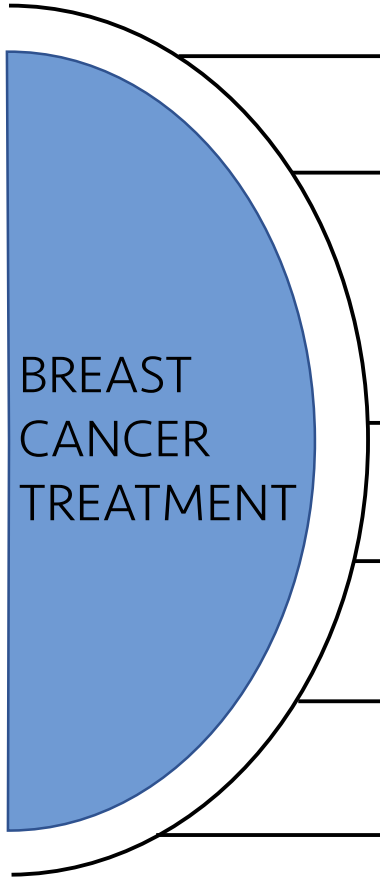
15 largest cancer diseases

In total >200 cancer types – several are rare diseases





Source: WHO, World Cancer Report, International Agency for Research on Cancer, 2014.
ASR = Average Survival Rate.



Local Treatment

Surgery: remove the whole breast, a mastectomy, or to remove just the tumor and tissues around it, a lumpectomy.

Radiation therapy: uses high-energy waves to kill cancer cells.

Systemic Treatment

Chemotherapy: uses drugs to kill cancer cells. As these powerful medicines fight the disease, they also can cause side effects.

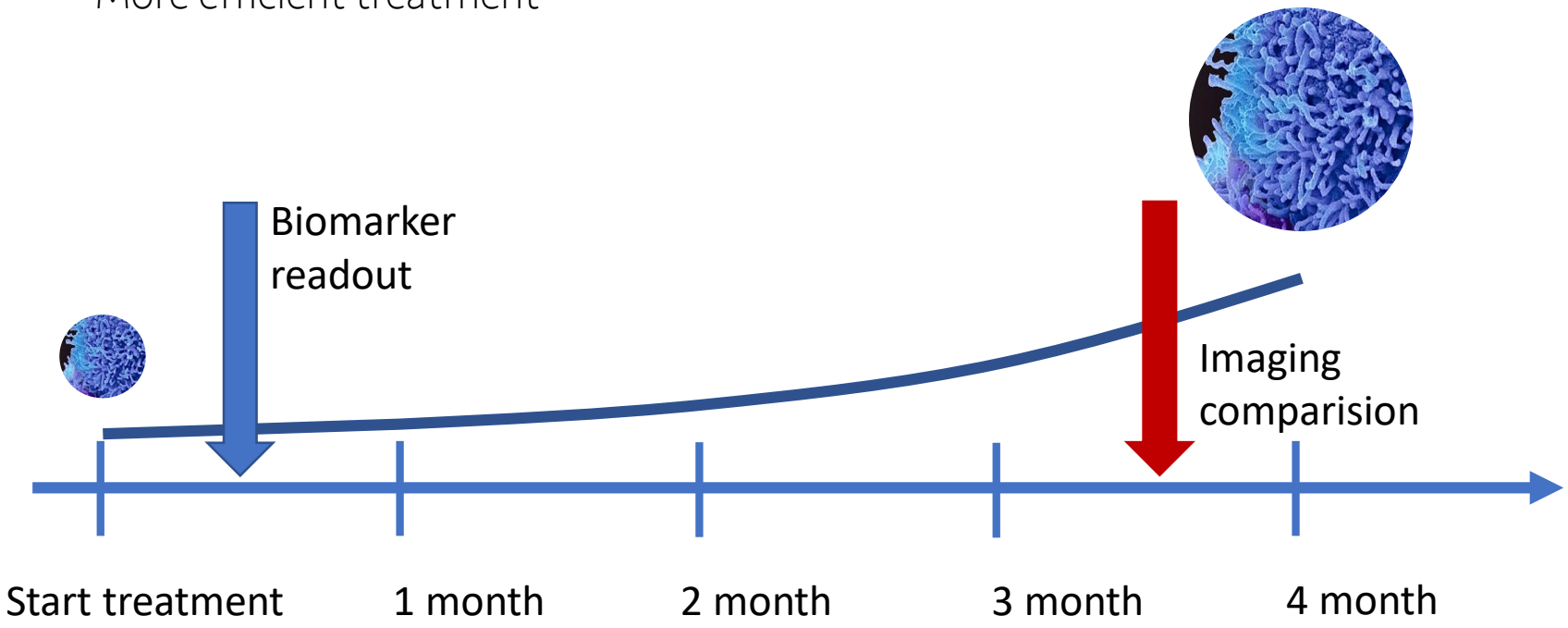
Hormone therapy: uses drugs to prevent hormones, especially estrogen, from fueling the growth of breast cancer cells.

Targeted therapy: drugs that target different changes in cells that cause them to grow out of control. CDK inhibitors, targeting HER2-pos.

Immunotherapy: use of medicines to stimulate a person's own immune system to recognize and destroy cancer cells more effectively.

Existing diagnosis are insufficient

- 70-80 % non responders in cytotoxic treatment of Breast cancer
- AroCell's assay enable early confirmation of treatment response
- More efficient treatment



Biomarkers in the cancer patient journey

Primary care/ Health center

Routine screening

Local hospital or cancer institute to undergo tests

Cancer not diagnosed

Diagnosis of cancer

Treatment

Palliative care

End of treatment

Continuous treatment

Long-term monitoring and follow-up

Relaps

Terminal care

Cure

Long term survival

Source: Fitch, 2003. From: Healthcare Quarterly, 8(3) May 2005.doi:10.12927/hcq.2005.17194

Different blood based biomarkers for breast cancer

Table 1. Main type of circulating biomarkers in breast cancer, together with their main uses/potential uses, advantages, and disadvantages.

Type of biomarker	Example	Key uses/potential uses	Advantages	Disadvantages
Protein	CA 15-3, CEA, TPA, TPS, sHER2	Surveillance, therapy monitoring, and prognosis	Easy and cheap to measure, automated assays available	Lack sensitivity and specificity
ctDNA	*ESR1*, *PIK3CA*, *TP53*	Identification of therapy resistance mechanism, and monitoring therapy	High specificity for malignancy, only non-invasive way to identify mechanism of therapy resistance	Expensive, assays not widely available, and labor intensive
CTC		Prognosis and monitoring therapy	Allow measurement of biomarkers at DNA, mRNA, and protein levels	Expensive, not widely available, and labor intensive

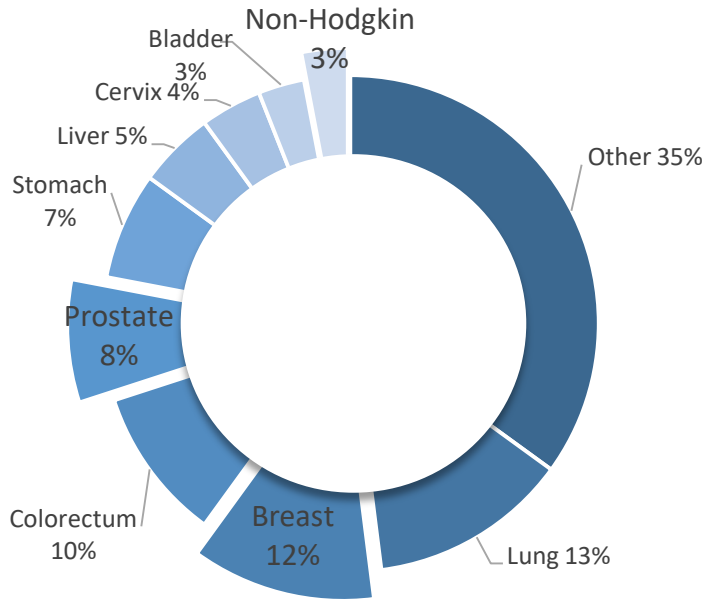
TPA: tissue polypeptide antigen; TPS: tissue polypeptide–specific antigen; sHER2: soluble HER2; ctDNA: circulating tumor DNA; CTC: circulating tumor cells.

(Duffy et al., 2018)

Diagnostics Biomarker market

Breast cancer, prostate cancer and colorectal cancer are considered the most prevalent cancer types, globally.

Indications	Incidences ('000)	3-y Preval. ('000)	5-y Preval. ('000)	Market size (MUSD)	Biomarker Market size (Vol)	Est. CAGR % (2017-2025)
Lung Cancer	1 824	1 450	1 893	1 651	728 300	13%
Breast Cancer	**1 670**	**4 020**	**6 232**	**2 020**	**653 000**	**12%**
Colorectal cancer	1 360	2 409	3 543	1 345	536 500	12%
Prostate cancer	**1 094**	**2 581**	**3 857**	**1 000**	**525 800**	**11%**
Hematological Cancers	**844**	**1 203**	**1 751**	**1 601**	**190 500**	**12%**
Cervical cancer	524	1 041	1 547	706	478 200	11%
Sarcoma	**260**	**N/A**	**630**	**259**	**113 900**	**11%**



Global Cancer Incidence; number of new cases per year (2012)
Source: Global Cancer Biomarkers Market 2018-2015

Most commanly used serum protein biomarkers

- CA 15-3 (Cancer antigen 15-3)
- CA 27.29 (Cancer antigen 27.29)
- CEA (Carcinoembryonic antigen)
- sHER2 (Soluble HER2)

Clinical utility of CA 15-3 and CA 27.29

Screening/ Diagnosis	CA 15-3 and CA 27.29 are NOT recommended for screening/diagnosis of breast cancer
Therapy Monitoring	CA 15-3 and CA 27.29 are used to monitor patients with metastatic breast cancer during chemotherapy in conjunction with diagnostic imaging, history and physical examination.
Surveillance	CA 15-3 is recommended to monitor the patients with recurrence after primary breast cancer therapy

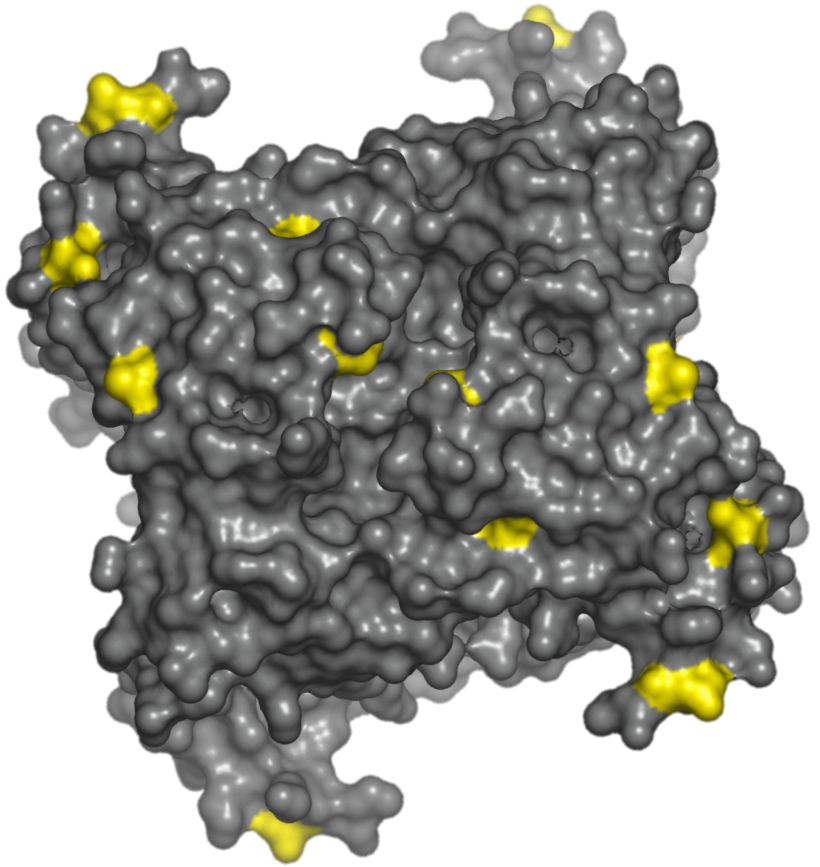
Thymidine kinase 1 (TK1)…

…a proliferation biomarker that has been used for prognosis and monitoring therapy response of different tumor types

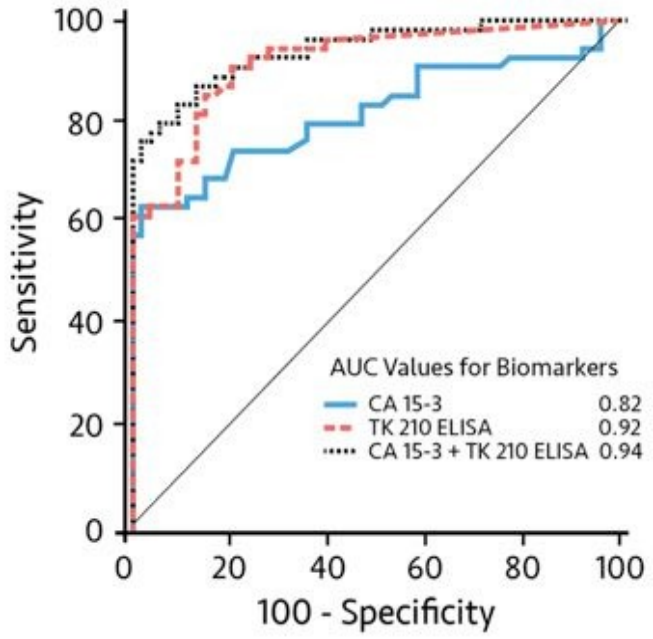
The logic behind TK1

A strong signaling enzyme

- TK1 is a key enzyme in DNA precursor synthesis, that upregulates intracellularly prior to cell division (phase –S) and down regulates at cell division
- Increased levels of TK1 in the blood can indicate an abnormal cell turnover. Decreased levels can indicate the opposite, a slowdown of abnormal cell turnover.
- TK1 is a **biomarker** for early detection of disruption of dividing cells
- TK1 can be measured in several cancer indications



Combining with other Tumor Biomarkers



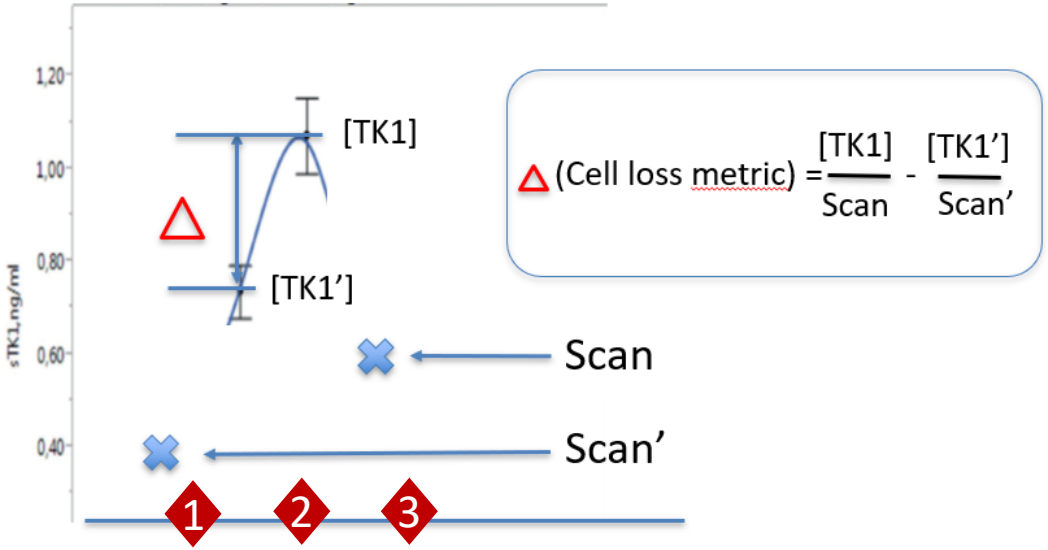
TK 210 ELISA and CA15-3 in Breast Cancer (T2) Patients

After Kumar et al. Tumor Biology 2016

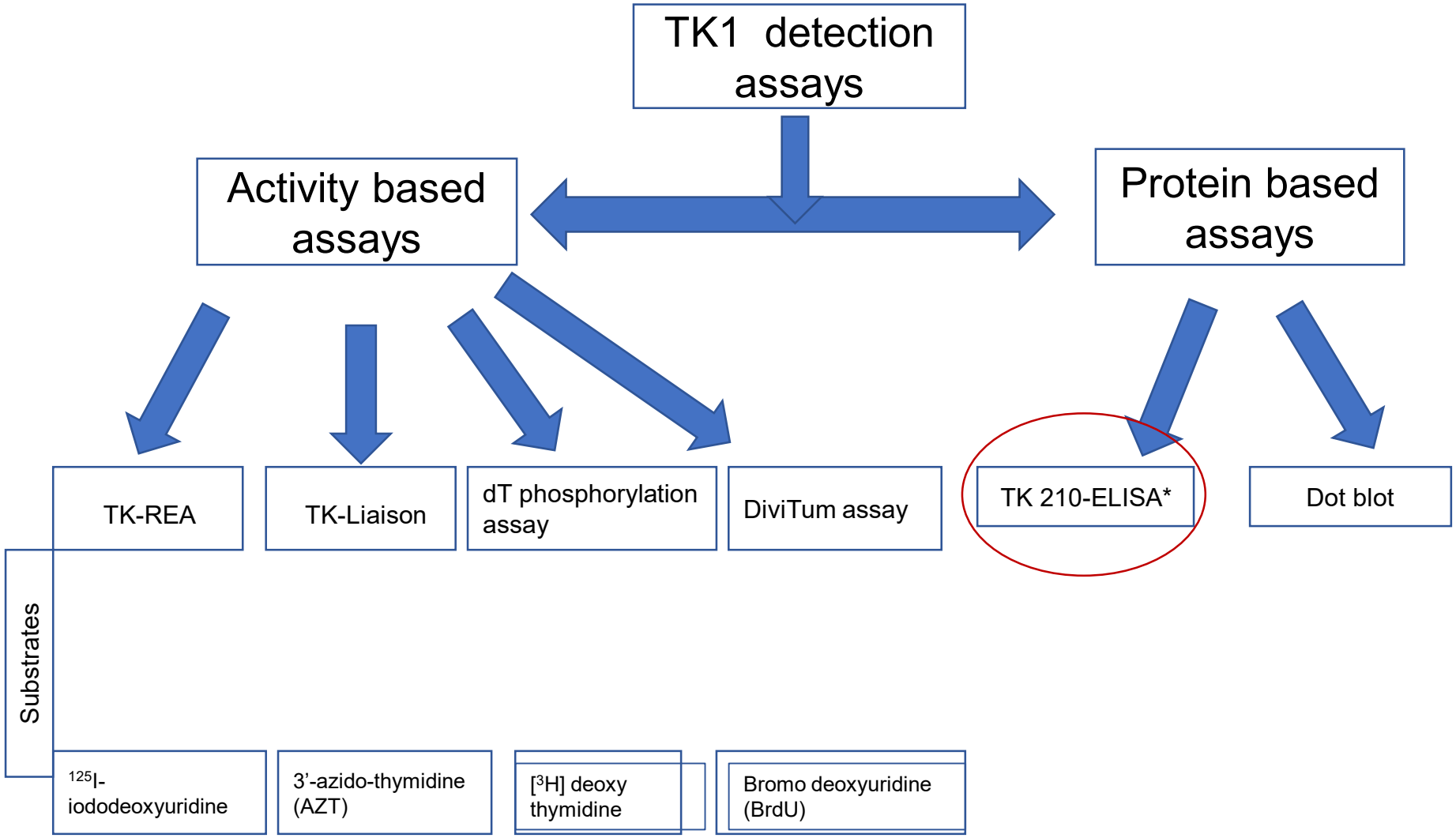
Early treatment response in Breast cancer

- Patients treated with cytotoxins (Epirubicin and Docetaxel) before surgery were followed by their thymidine kinase (TK1) levels in blood to directly observe treatment response.
- The results show that a TK1-based cell-loss metric after two cycles of therapy predicted the status at the operation after six cycles of chemotherapy.

➢ The metric predicted **early** on whether or not the chemotherapy works.



sTK1(ng/ml) before and 48h after Treatment 2, and 48 hours later. Mean Values ± SE



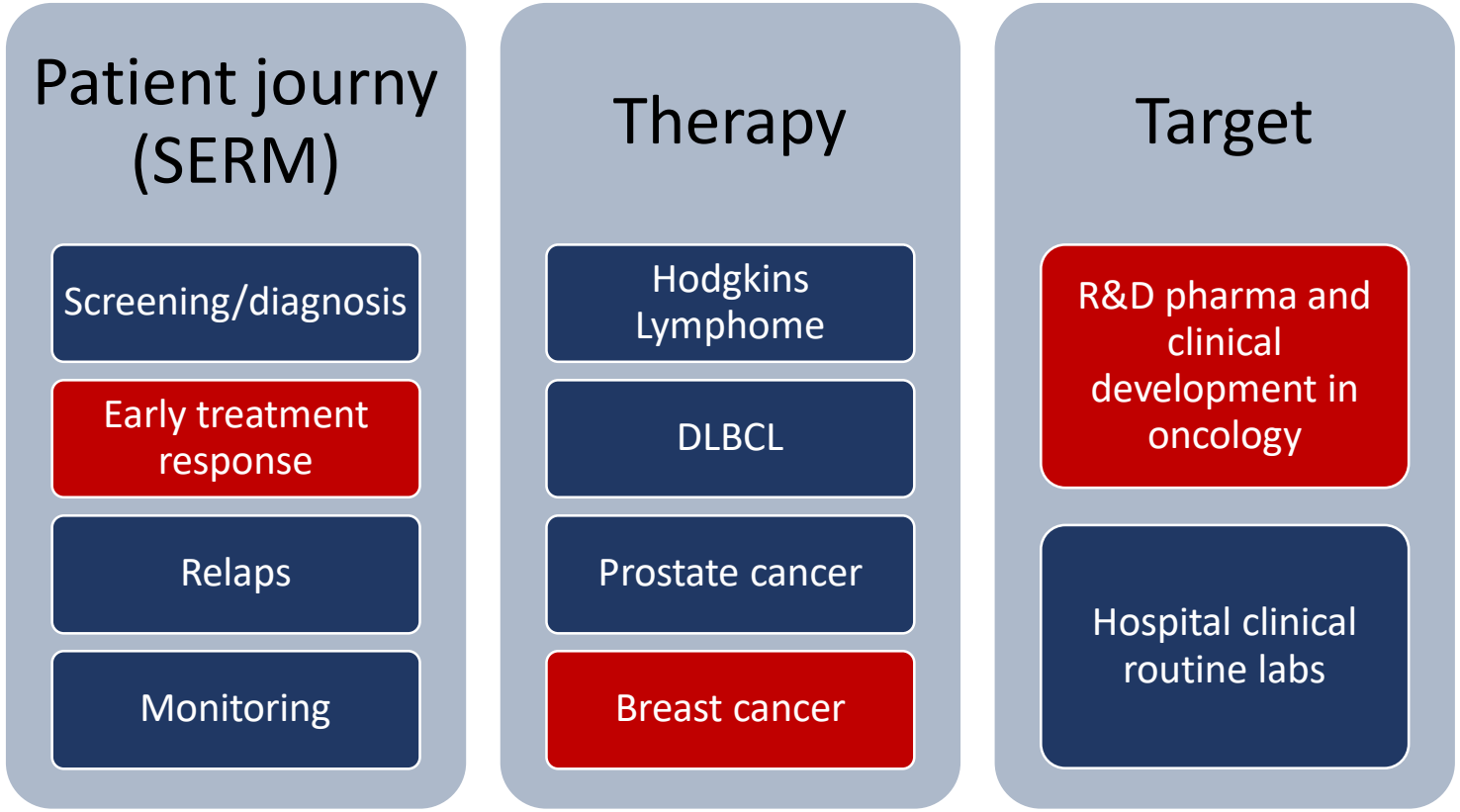
*Only CE marked ELISA for TK1

AroCell TK 210 ELISA

In cancer, time is everything

- AroCell TK210 ELISA measure concentration of Thymidine Kinase 1 in blood
- Superior to all other methods for measurement of TK1
- Unique pre-treatment buffer reduces the size of the TK1 serum complexes and exposes the TK210 antigen sites
- Standardized method – ELISA sandwich assay
- Protected by a broad and deep patent portfolio
- CE-marked in EU

AroCell 's strategic focus



AroCell

Overview

- Listed NASDAQ First North Stockholm (AROC)
- Market Cap MSEK 110
- Over 2500 shareholders
- Founder still in the company
- Based in Uppsala, Sweden

Highlights

- Several ongoing studies to support TK 210 ELISA
- Global out license agreement with Roche 2018
- TK 210 ELISA CE mark in EU
- Major markets covered by distributors
- Strong patent portfolio

Thank you!