

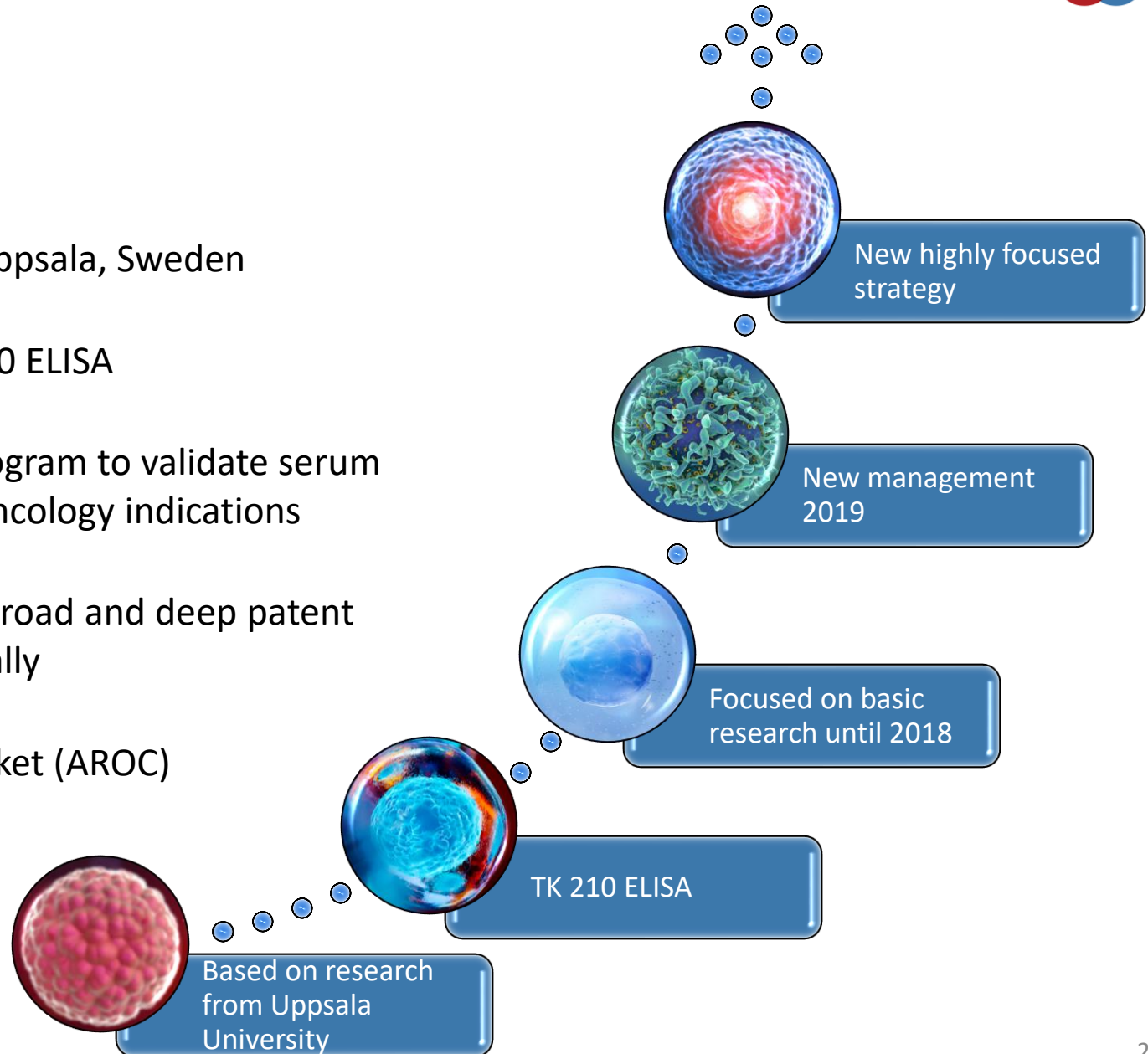
TK210 ELISA

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Not for use in diagnostic procedures.



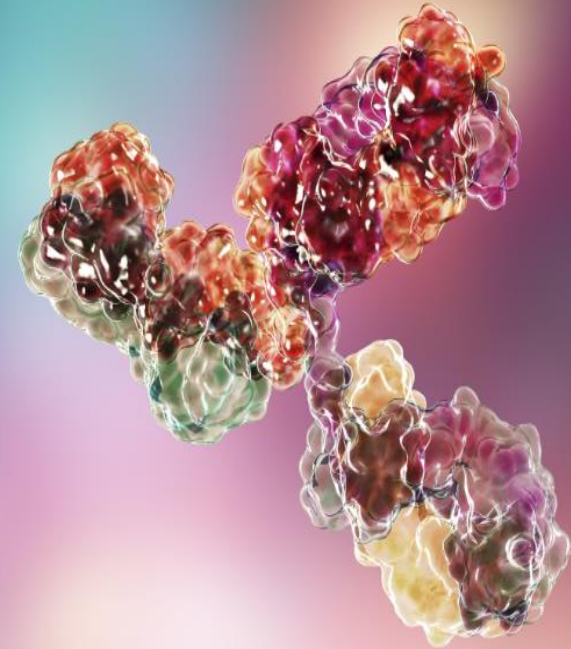
AroCell in a snapshot

- Oncology biomarker company based in Uppsala, Sweden
- Manufacturer of the unique AroCell TK210 ELISA
- Running an extensive clinical research program to validate serum TK1 as a clinical research biomarker for oncology indications
- Proprietary technologies protected by a broad and deep patent portfolio covering all major markets globally
- Listed on Nasdaq First North Growth Market (AROC)



Thymidine Kinase 1 (TK1)

- TK1 is a key enzyme in DNA synthesis, which is up-regulated during DNA synthesis (S- phase of the cell cycle)
- Intracellular TK1 is a well-known proliferation biomarker
- In malignant tumor cells TK1 levels are high and TK1 leaks out into the blood as a consequence of cell disruption, spontaneously or triggered by cancer therapy



Serum TK1 is a valuable biomarker for oncology research applications

TK1 - One protein with different potential clinical research roles to discover

A

Analytical/screening research?

Does this marker indicate staging of cancer?
Is this subject a good fit for our clinical study?

E

Early efficacy research?

Can this marker be used to investigate if this therapy is effective on this cancer type?

R

Recurrence research?

Does this marker indicate when a cancer comes back?

Analysis of TK1 in the blood as a measure of increased leakage of intracellular TK1 into the blood due to;

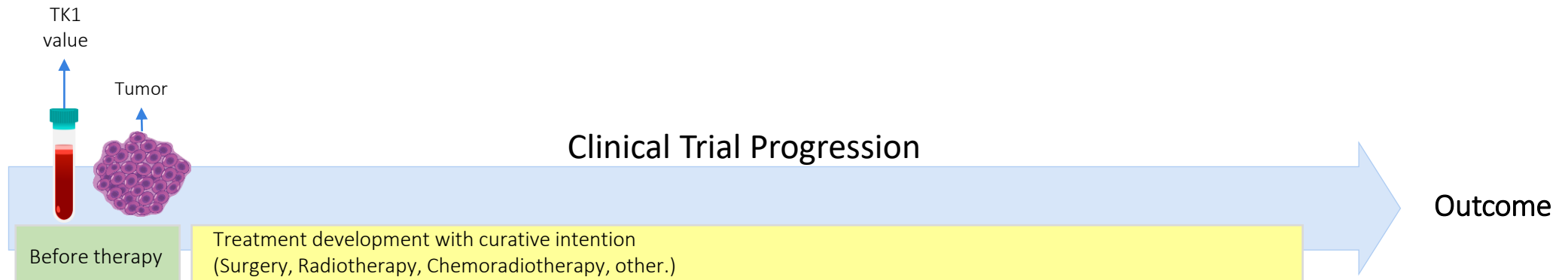
- Uncontrolled cell division (tumor)
- Cell disruption caused by e.g. chemotherapy or decreased leakage of intracellular TK1 into the blood caused by cell-cycle arrest

TK1 as a biomarker in a variety of tumor type research

A

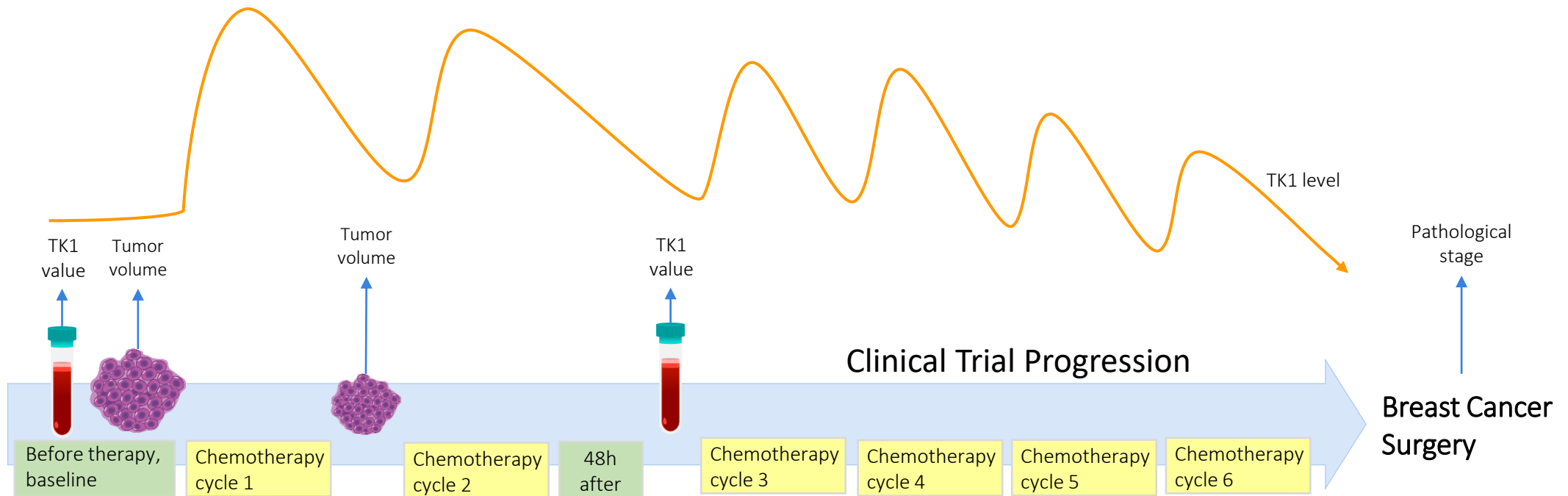
Analytical/Screening marker

Prognostic data: Does this marker show staging of this cancer?
Screening: Does this subject fit our clinical trial?



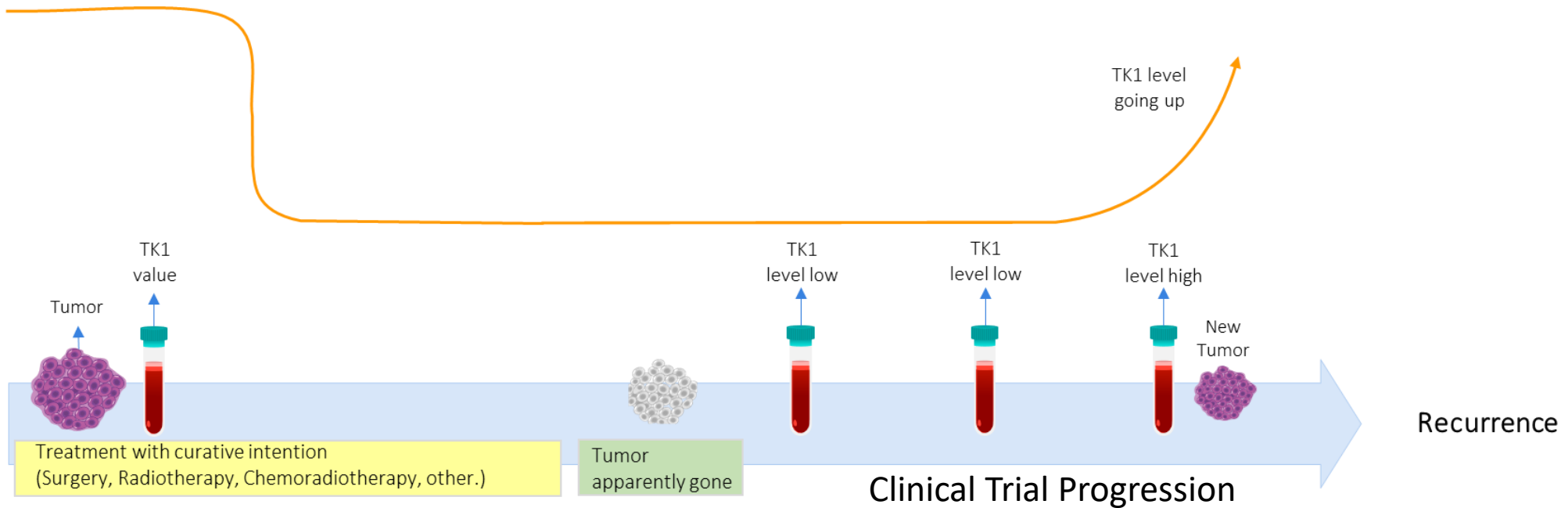
TK1 as an early efficacy in a variety of tumor type research

E Early efficacy marker
 Investigate response in treatment development.
 Can TK1 be used to indicate that this treatment works?



TK1 as a recurrence marker in a variety of tumor type research

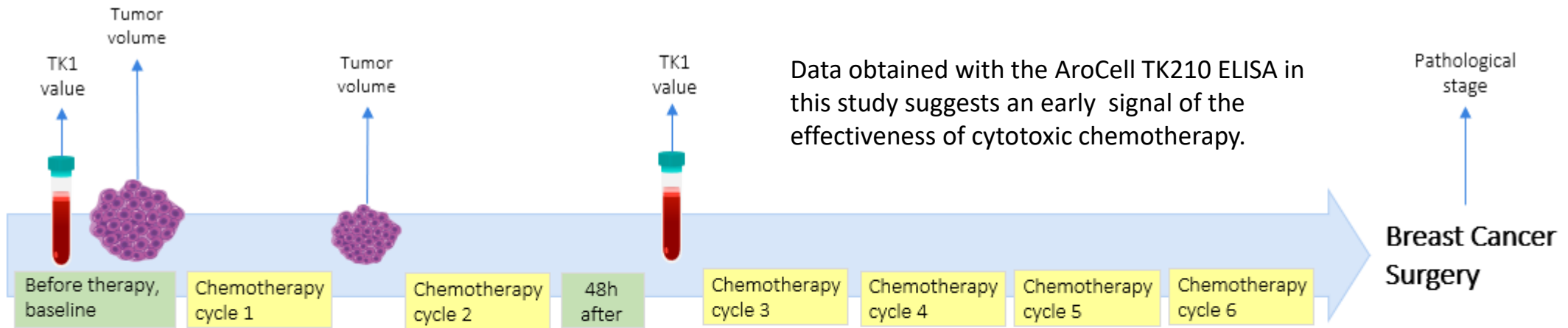
R **Recurrence marker**
 Investigate early detection of potential relapse in cancer.
 Does this marker indicate when the cancer comes back?



The PROMIX-study

Serum TK1 – Is it a biomarker of early treatment response?

Clinical research data, with serum TK1 as biomarker and for early treatment response, demonstrated potential utility in neoadjuvant stage II and III breast cancer (Tribukait BMC Cancer (2020) 20:440)

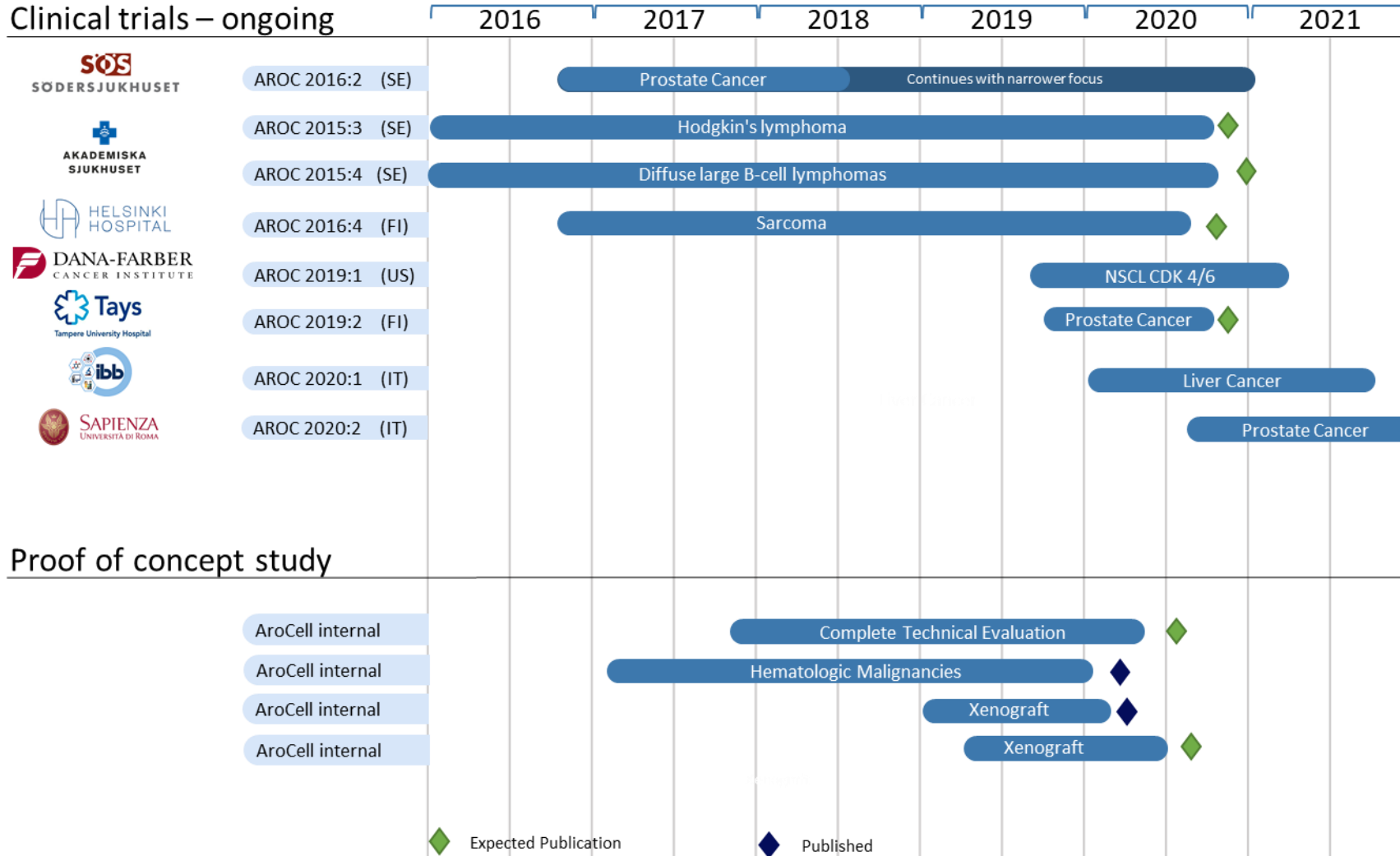


Relative increase in TK1 =
$$\frac{\text{TK1 value after cycle 2} - \text{TK1 value at baseline}}{\text{TK1 value at baseline}}$$

Cell-loss metric =
$$\frac{\text{TK1 value after cycle 2}}{\text{Tumor volume before cycle 2}} - \frac{\text{TK1 value at baseline}}{\text{Tumor volume at baseline}}$$

Increased serum TK1 levels after cycle two associated with positive treatment outcome
 No increased serum TK1 levels after cycle two associated with progressive disease

AroCell's ongoing clinical studies program

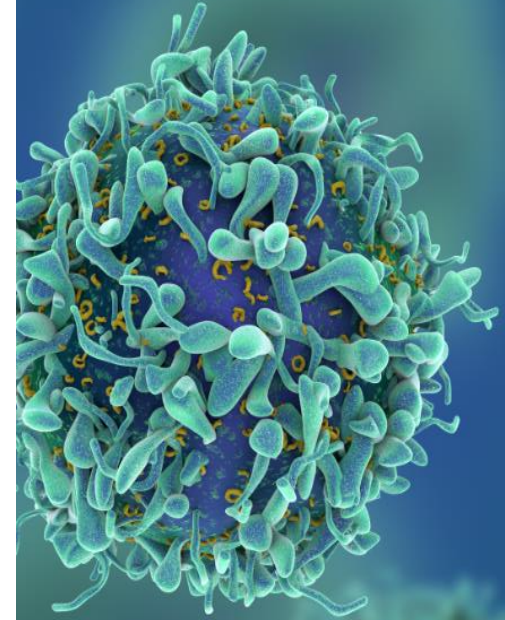


TK1 has the potential to provide early data to study several solid tumors as well as haematological malignancies.

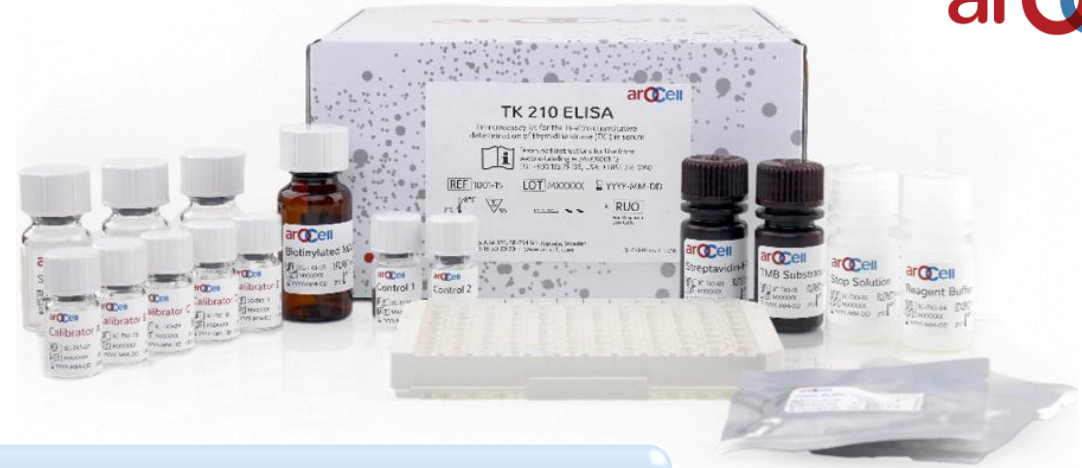
Challenges when measuring serum TK1

- Serum TK1 exists in blood as aggregates with differing molecular weights and enzyme activities
- Much of the TK1 in serum from subjects with solid tumors is enzymatically inactive. However, all TK1 forms express the TK 210 epitope
- TK1 levels are in the nanograms per mL serum

The sensitivity and specificity of the AroCell TK 210 ELISA overcomes these challenges and provides new opportunities for studying serum TK1



AroCell TK 210 ELISA



Standardized method
ELISA sandwich assay

The first quantitative immunoassay kit for the determination of TK1 in serum

Specific for human TK1

Proprietary human monoclonal antibodies towards the TK 210 epitope. Does not cross-react with TK2 or non-human TK1

Sensitive –
Measures all TK1 complex forms

Unique pre-treatment buffer reduces the size of serum TK1 complexes and exposes the TK 210 antigen sites

Robust –
unaffected by TK1 enzyme inhibitors

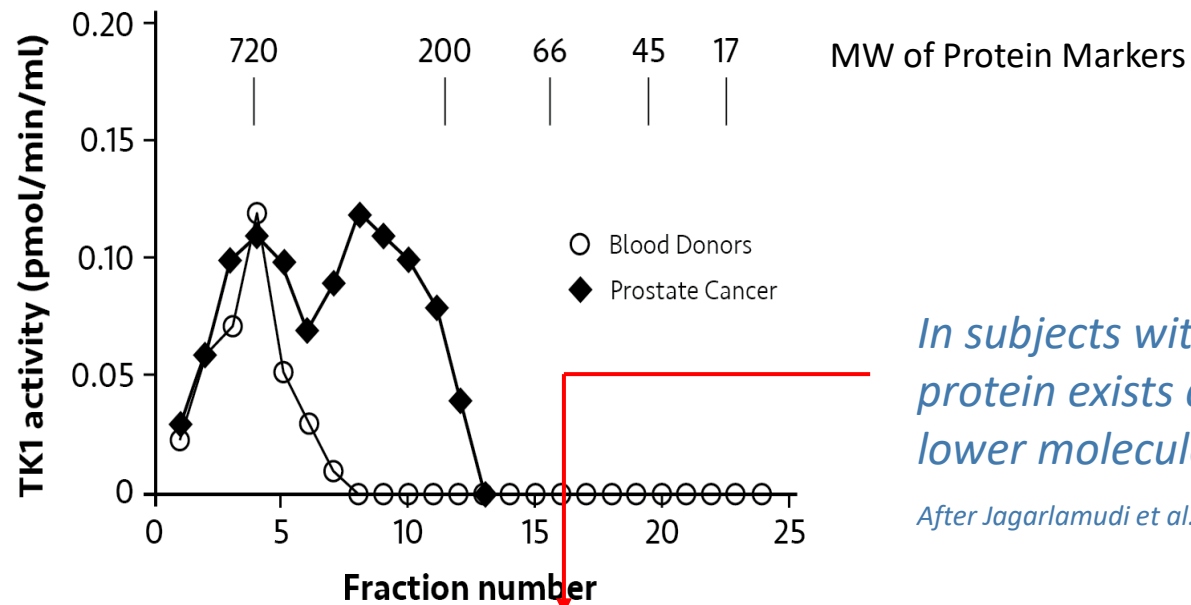
Provides direct measurement of TK1 protein concentration, not enzyme activity

Reliable and easy-to-use

Easy to automate and scale-up

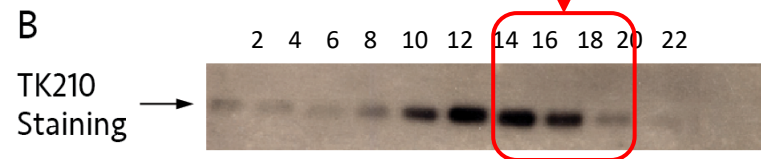
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TK1 activity and molecular weight




In subjects with solid tumors, much of TK1 protein exists as inactive TK1 complexes of lower molecular weight.

After Jagarlamudi et al. BMC Cancer 2015



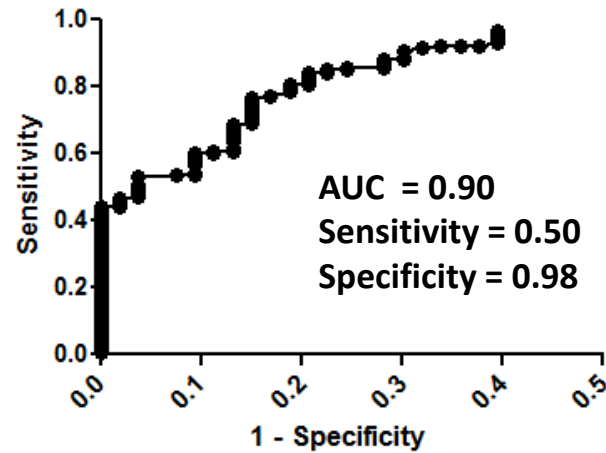
Competition – Activity assays for serum TK1

 AroCell TK210 ELISA	TK1 enzyme activity assays
Measure total TK1 protein in serum	Measure TK1 enzyme activity in serum
Not sensitive to TK1 enzyme inhibitors	Sensitive to TK1 enzyme inhibitors
No cross-reactivity with TK2	Cross react with TK2
No cross-reactivity with non-human TK1	Cross react with non-human TK1
Pre-incubation buffer enables measurement of inactive TK1 complexes	No data on inactive complexes
Reliable and easy-to-use ELISA assay Easy to automate and scale-up	Requires the specific platforms Complicated assay procedures

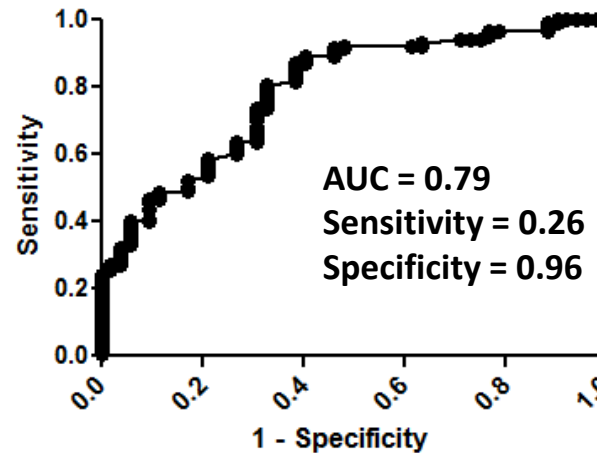
AroCell TK 210 ELISA - sensitivity

Comparison of serum TK1 protein concentration and enzyme activity in breast cancer subjects

TK1 Protein Concentration



TK1 Activity



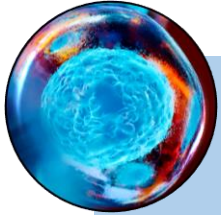
After Kumar et al. Tumor Biology 2016

AroCell TK 210 ELISA is twice as sensitive as enzyme activity assays for solid tumors

AroCell TK 210 ELISA markets 2021

Market	Pre-Clinical Research	Clinical Research
Regulatory label	RUO	RUO
Target customers/users	Pre-clinical researchers Pharma companies	Clinical researchers Pharma companies CRO companies Hospital labs
Target areas	Drug development Basic Research	Drug development Clinical research
Target Applications	In-vitro studies Xenograft studies	Early response in drug development PERM in biomarker studies Mechanistic studies
Opportunity for translational studies		

AroCell TK 210 ELISA Benefits



Quantitatively measures all forms of the human TK1 protein in serum - not enzyme activity



Transferrable from cell culture to xenograft models and further to clinical studies



Unique sensitivity for inactive TK1 aggregates found in subjects with solid tumors



Reliable and easy-to-use ELISA assay which is easy to automate and scale-up



Utility demonstrated in several clinical studies

arOCell

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