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defeating cancer

Introducing S-TIR™

The revolutionary Technology Platform for Active Checkpoint Control Immunotherapy (ACCI) in multiple Oncology Targets

S-TIR™ = Specific Total Immune Remodulation

At a Glance

OncoQR ML's S-TIR™ Platform for Active Checkpoint Control Immunotherapies (ACCIs) in multiple Oncology Targets

Field of Research
Immunooncology / Therapeutic Vaccines / Active Immune Checkpoint Control (ACCI)

Type of Business Opportunity
patented S-TIR™ Immunotherapy Platform (100% owned by OncoQR ML GmbH)

Indication
Target specific Cancer Immunotherapy, suitable for different oncology indications

Development Stage
Late stage preclinical

Partnership Model
Available for Out-Licensing (world-wide)

- S-TIR™ platform as a whole or
- S-TIR™ platform on a target by target basis

- Lead candidate products
  - OQR200 (target: HER2/neu, breast cancer)
  - TYG100 (target: little gastrin G17)

Preclinical packages available under CDA

Unique Advantages of S-TIR™
ACCIs are more effective, specific, immunogenic and safer (than passive cancer immunotherapies, eg. like checkpoint inhibitors or monoclonals)

	1st gen. Monoclonals	**2nd gen.** Checkpoint inhibitors	**The NEW Era Active Checkpoint Control Immunotherapy (ACCI)**	
Efficacy	+ mimicking B Cell response	++ activating all T Cells	+++ B Cells and *specific* T Cells!	Unmasks tumors, combines efficacy of 1st (B Cell) and 2nd generation (T Cell) without activation of irrelevant immune cells. ACCIs mobilize the full potential of the immune system's defense mechanisms.
Safety profile	+	+/-	+++	Reversible immune response, without side effects because of specific T Cell activation
Therapeutic window	+ 1 monoclonal = 1 cancer target	+ 1 monoclonal = multiple cancer targets	+++	Sole unspecific checkpoint inhibition leads to an uncontrolled overshooting immune response (with the danger of autoimmunity and/or cytokine storms), resulting in only a narrow therapeutic window! The Solution is a SPECIFIC and TARGETED Checkpoint CONTROL for a larger therapeutic window without side effects.*
Tumor specificity	++	-	+++	
Natural immune response	-	-	+++	ACTIVE Immunotherapy: rapid and appropriate natural immune response generated

*) no side effects in over 60 treated subjects (non-human primates)

Further Advantages of S-TIR™
- **IP/Patents:** OncoQR ML's S-TIR™ Technology is protected by a robust international patent portfolio (technology and product patents). For more information please contact us directly.
- **Economical Aspects:** cost effective due to low cost of goods, low treatment dose and personalized low treatment frequency
- **Treatment Regimen:** personalized and patient-friendly treatment schedule (maintenance treatment every 2 to 4 months)
- **Rapid Product Development** of new vaccines typically between 6 and 9 months (from design to proof of concept in non-human primates) Info package available under CDA
- **Also suitable for Combination Therapies**

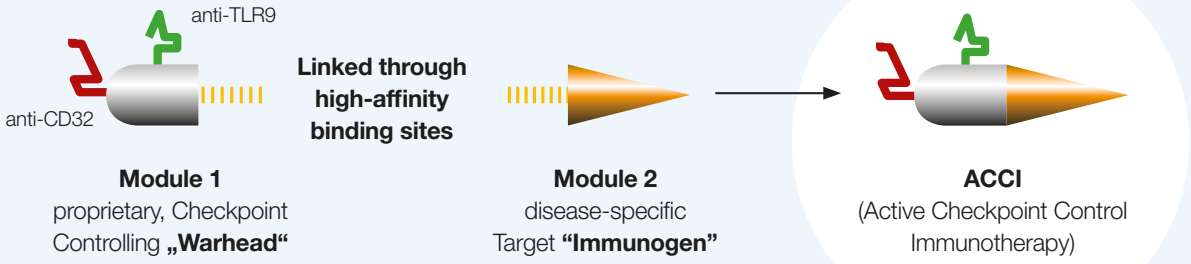
S-TIR™ Technology Platform

Overview

The S-TIR™ Technology is an **Active Checkpoint Control Immunotherapy (ACCI)** platform for therapeutic vaccines against multiple cancer targets.

- The vaccine is composed of a generic module **("warhead")** and a disease-specific module **("immunogen")**, linked by high-affinity connectors.
- The warhead ensures specific delivery of the immunogen to those cells that determine and (re-) direct the outcome of an immune response (i.e. dendritic cells and B-cells). In addition, the warhead specifically activates these cells and thereby strongly boosts the therapeutic effect of the vaccine.
- The modular concept allows the combination of the warhead with different immunogens, resulting in multi-purpose cancer immunotherapies.

Specific Mode of Action



Module 1
proprietary, Checkpoint Controlling **„Warhead"**

Module 2
disease-specific Target **"Immunogen"**

ACCI
(Active Checkpoint Control Immunotherapy)

Module 1

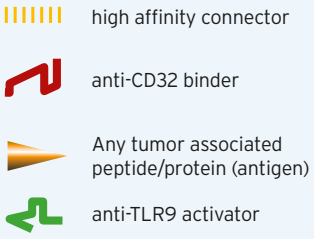
the "warhead" is designated to combine 4 major elements and functions:

1. Binding to plasmacytoid dendritic cells (pDCs) through specific interaction with FcgammaRIIa (CD32a), which facilitates enhanced and specific uptake of the vaccine by the relevant professional antigen presenting cells (APCs). pDCs are a rare subset of circulating dendritic cells which can be found in blood, skin and in peripheral lymphoid organs and which express both CD32 and TLR9.
2. Triggering of pDCs to produce large amounts of Th1-inducing cytokines through a specific interaction with the Toll Like Receptor 9 (TLR9), which therefore serves as intrinsic "adjuvant".
3. Activation of TLR9 primes pDCS to break tolerance against tumor associated antigens present in module 2.
4. Binding to "Module 2" specific B cells through a low affinity interaction with CD32b on the B cells together with a (most likely) low affinity interaction with the B cell receptor specific for "Module 2". High-affinity binding to the immunogen through a specifically designed dimerization motive that connects with its counterpart in module 2.

Module 2

the "immunogen" part of the drug, combines 2 basic elements:

1. Activation of tumor specific T and B cells
2. High affinity binding to the warhead through a specifically designed dimerization motive that connects with its counterpart in module 1.

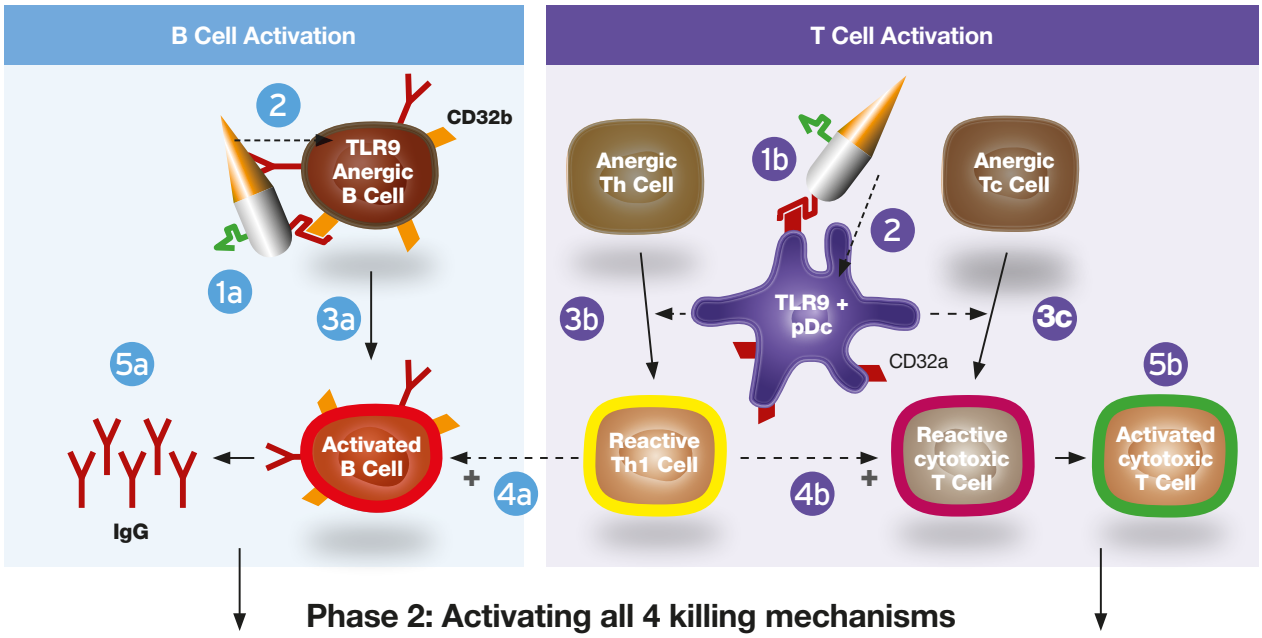


Scientific Evidence

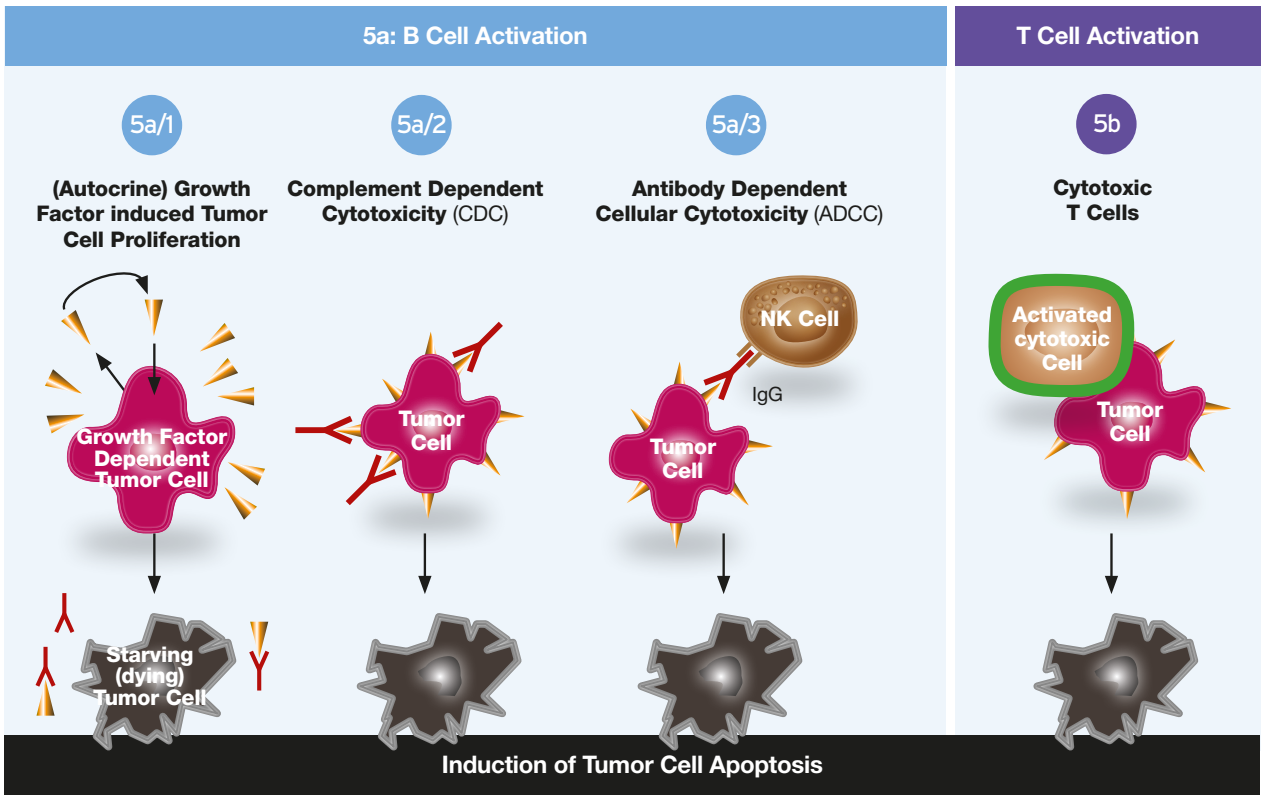
Within 6 studies so far a total of 64 subjects (non-human primates) were treated with S-TIR™ platform vaccines that resulted in > 99% responders and the non-GLP tox indicated no side-effects; a non-GMP manufacturing process is already available; next steps: the conclusion of a GMP process development and the GLP tox

Active Checkpoint Control Immunotherapies activate all naturally available Tumor killing Mechanisms

Phase 1: Arming the Immune System



Phase 2: Activating all 4 killing mechanisms



- 1a ACCI is recognized by auto-antigen specific B cell and binds to CD32b (with low affinity) and auto-antigen specific B cell receptor (with low affinity) -> increased avidity -> stable binding of ACCI
- 1b ACCI binds stably to CD32 (high affinity) on pDCs
- 2 ACCI is actively internalized by B cells and pDCs
- 3a TLR9 is triggered and will change anergic B cells into reactive B cells, who will present auto-antigen Th cell epitopes on HLA class II molecules
- 3b TLR9 is triggered while pDCs present autoantigen T cell epitopes on HLA class I and II molecules to anergic Tc cells and Th cells respectively (cross presentation) -> induction o reactive Th and Tc cells
- 4a Reactive Th cells provide help for auto-reactive B cells -> IgG anti autoantigen production
- 4b Reactive Th cells provide help for auto-reactive Tc cells -> activated Tc cells induction
- 5a/1 IgG molecules bind to target (growth hormone) leading to tumor starvation
- 5a/2 IgG molecules bind to target and mediate CDC
- 5a/3 IgG molecules bind to target and mediate ADCC
- 5b Activated Tc cells recognize tumor cell and kill the target

The New Era

ACCIs activate all four naturally available tumor killing mechanisms of the body

		Monoclonals mimicking B Cell response	Checkpoint inhibitors activating all T Cells	Active Checkpoint Control Immunotherapy (ACCI) B Cells and specific T Cells
4 Killing Mechanisms	Growth factor inhibition	+	-	++
	CDC*	+/-	-	+
	ADCC*	+	-	++
	Cytotoxic T Cells	-	+	+***

S-TIR™ combines the Benefits of 1st and 2nd Generation Cancer Immunotherapies in terms of Efficacy and Immunogenicity, however without Side Effects.*** **Christof LANGER, MBA (CEO)**

With S-TIR™ we step into the New Era of Cancer Immunotherapies by simultaneously triggering tumor specific humoral and cellular Immune Responses. **Geert Mudde, PhD (CSO)**

Pipeline Products

TYG100

Lead candidate TYG100 (formerly OQR100, out-licensed to TYG Oncology Ltd.) is an ACCI for the treatment of gastroenterological cancers such as pancreatic, stomach, colon, and gastro-esophageal cancer. The immunogen of TYG100 contains a small part of G17 (little gastrin). In-vivo proof of concept in non-human primates has been validated for TYG100 -> target: pancreatic cancer for EGF neutralization -> Neutralization of the 17 AA gastrin peptide starves G17-dependent cancer cells to death, FDA orphan drug designation

OQR200

Lead candidate OQR200 is a new candidate against HER2/neu, the by far best characterized and clinically validated target to treat breast cancer indications. A reversible induction of HER2/neu specific antibodies has been demonstrated. In vitro, the immune response induced by OQR200 has been shown to have superior efficacy in a direct side by side comparison with successful clinical products (Herceptin / Perjeta). In-vivo proof of concept in non-human primates has been validated for OQR200 -> target breast cancer for CDC* and ADCC** -> reversible induction of erbB2 specific antibodies demonstrated)

Scientific Reference:

Confidential information available under mutually signed non-disclosure-agreement (NDA).

*) CDC: Complement Dependent Cytotoxicity **) ADCC: Antibody Dependent Cellular Cytotoxicity
***) Significantly lower – if at all – side effects through specific T cell activation

Let's join forces to win the fight against cancer!

About OncoQR ML

Privately held OncoQR ML, based in Vienna/Austria, is a pre-clinical biotech company that offers novel therapeutic cancer vaccines based on its unique, proprietary and broadly applicable S-TIR™ (Specific Total Immune Remodulation) technology platform.

Unlike any other currently available therapy, the platform is capable of boosting the patient's immune system to generate a strong, specific and controlled immune response against cancer. This "Active Checkpoint Control Immunotherapy" (ACCI) activates all naturally available tumor killing mechanisms of the immune system without triggering side effects.

The company's lead candidate TYG100 (formerly OQR100), co-developed with TYG Oncology Ltd. and Cancer Research UK, targets pancreatic cancer and induces neutralizing antibodies against little gastrin (G17), a major growth factor for pancreatic- and other forms of gastric cancer.

OQR200 is directed against HER2/neu over-expressing breast cancer and induces strong polyclonal humoral (IgG) and cellular (CD4 and CD8) immune responses, superior to trastuzumab, pertuzumab or passive checkpoint inhibitors.

The revolutionary S-TIR™ technology platform as well as both lead candidates, which have achieved in vivo Proof of Concept in non-human primates are now available for out-licensing.

OncoQR QR ML was founded by two experienced, senior pharma professionals with top-level research & development as well as management backgrounds: Christof Langer, MSc, MBA (CEO) and Geert C. Mudde, PhD (CSO).