CANCER VACCINES – THE NEXT WAVE IN IMMUNO-ONCOLOGY

Cutting Edge Oslo
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Peter Skorpil
VP Business Development
peter.skorpil@targovax.com

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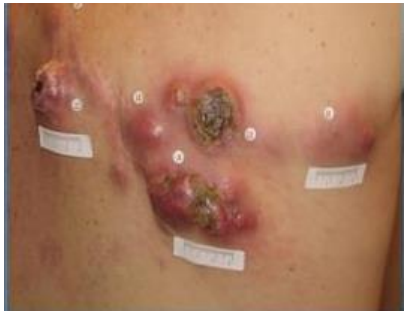
What is immuno-oncology?

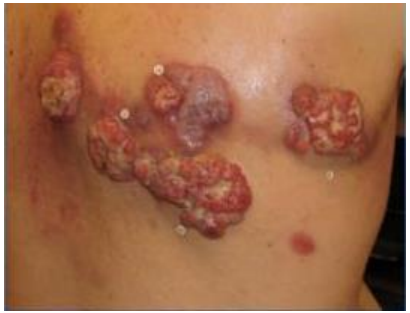
- The role of the immune system is to defend the body against threats, e.g. bacterial and viral infections, and also cancer
- Constant “power struggle” between the immune system and cancer
- If the immune system “looses” we get ill
- Immuno-oncology is about helping the immune system to beat cancer

Targovax has two technology platforms in development aiming to help the immune system to beat cancer

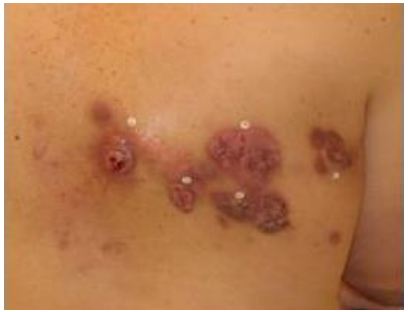
Immuno-oncology at work



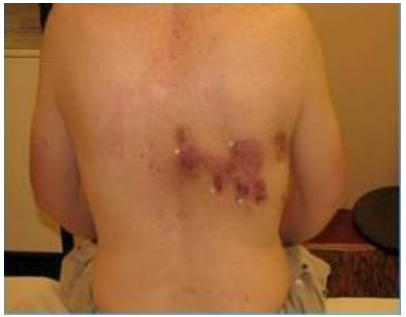
Prior to treatment



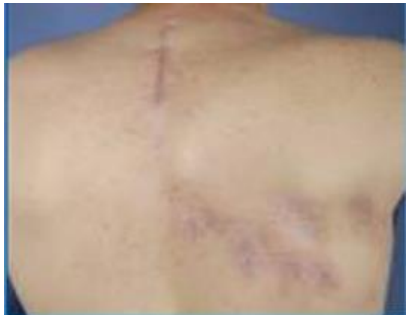
4 weeks



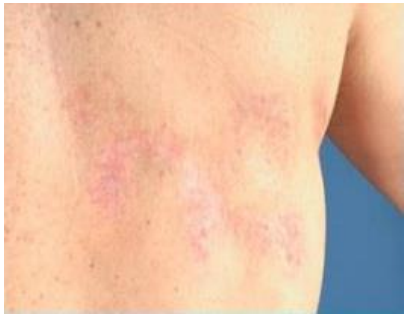
8 weeks



20 weeks



8 months



1 year

All pictures are an example of a melanoma patient who was treated with the immune checkpoint inhibitor Yervoy® (BMS)

Cancer immunotherapies are combined to maximize efficacy

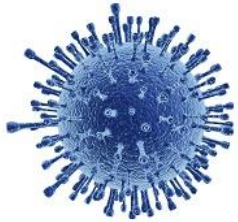
Immuno-oncology mechanisms	Wake up the immune system	Teach the T-cells at the lymph nodes	Attack the cancer with T-cells systemically	Disarm cancer's defense
 *Car analogy*	*Ignite engine*	*Switch on GPS–targeting*	*Press the gas pedal*	*Release brakes*
targovax TG - Peptide vaccines	3rd wave: cancer vaccines		✓	
targovax Oncos - Viral vaccines			✓	
Kite Pharma / BAVARIAN NORDIC Peptide-loaded viral vaccine T-Cell therapy	✓	✓	2nd wave: CAR-T	
MERCK, AstraZeneca, Genentech, Bristol-Myers Squibb, EMD Serono, Pfizer Immune checkpoint inhibitors (ICIs)				1st wave: ICIs

Source: Company websites, press releases and filings, FactSet

Targovax has two immunotherapy platforms targeting neoantigens, both with promising Phase 1 data

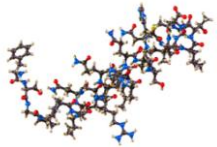
1 ONCOS-102

- ✓ Oncolytic adenovirus
- ✓ 1) inject ONCOS-102 into the tumor
  2) cancer cells break up
  3) release of cancer antigens
  4) tumor specific immune attack
- ✓ Phase 1 study showed immune activation in tumor and 40% of patients had stable disease



2 TG vaccine

- ✓ Target RAS (controls cell division/growth) mutations: 20-30% of all cancers
- ✓ 1) inject TG into the skin, mimics cancer antigens
  2) tumor specific immune attack
- ✓ Promising 1 year interim survival data in resected pancreas cancer Phase 1/2

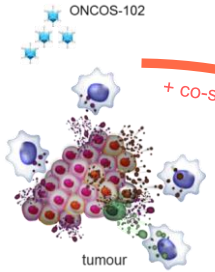


Targovax has two unique and complementary technologies

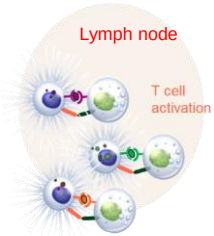
ONCOS

Injection:
The virus is injected, starts to replicate and lyse the tumor cells

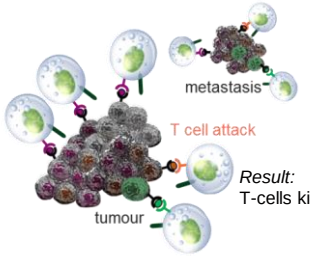
→ unique tumor antigens are released



+ co-stimulation



Response:
The immune system learns to recognize the unique cancer cells of each patient



Result:
T-cells kill the cancer

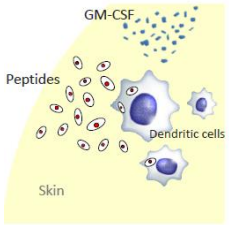
1 Activating the immune system

2 Teaching the system to recognize cancer as a threat

3 Mobilizing T-cells to attack cancer cells

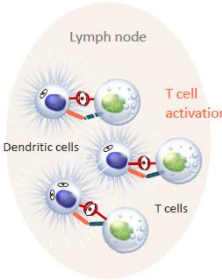
TG

Injection:
The peptides are injected into the skin together with an adjuvant (GM-CSF)

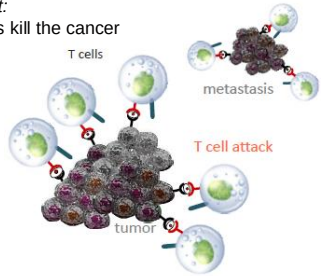


+ GM-CSF co-stimulation

Response:
The immune system learns to recognize the RAS mutations



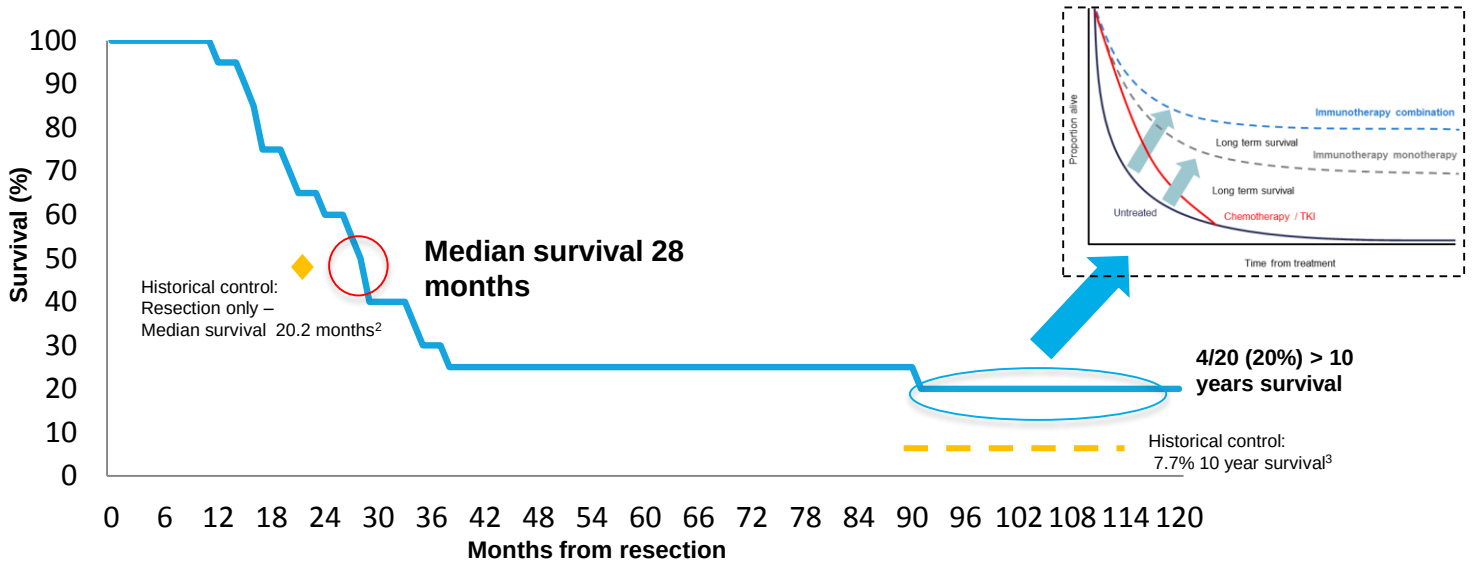
Result:
T-cells kill the cancer



Source: Ranki *et al.*, OncoImmunology 2014; Vassilev *et al.*, OncoImmunology 2015

Resected pancreatic cancer: Retrospective analysis showed encouraging long-term survival for patients treated with TG01 or single TG peptides

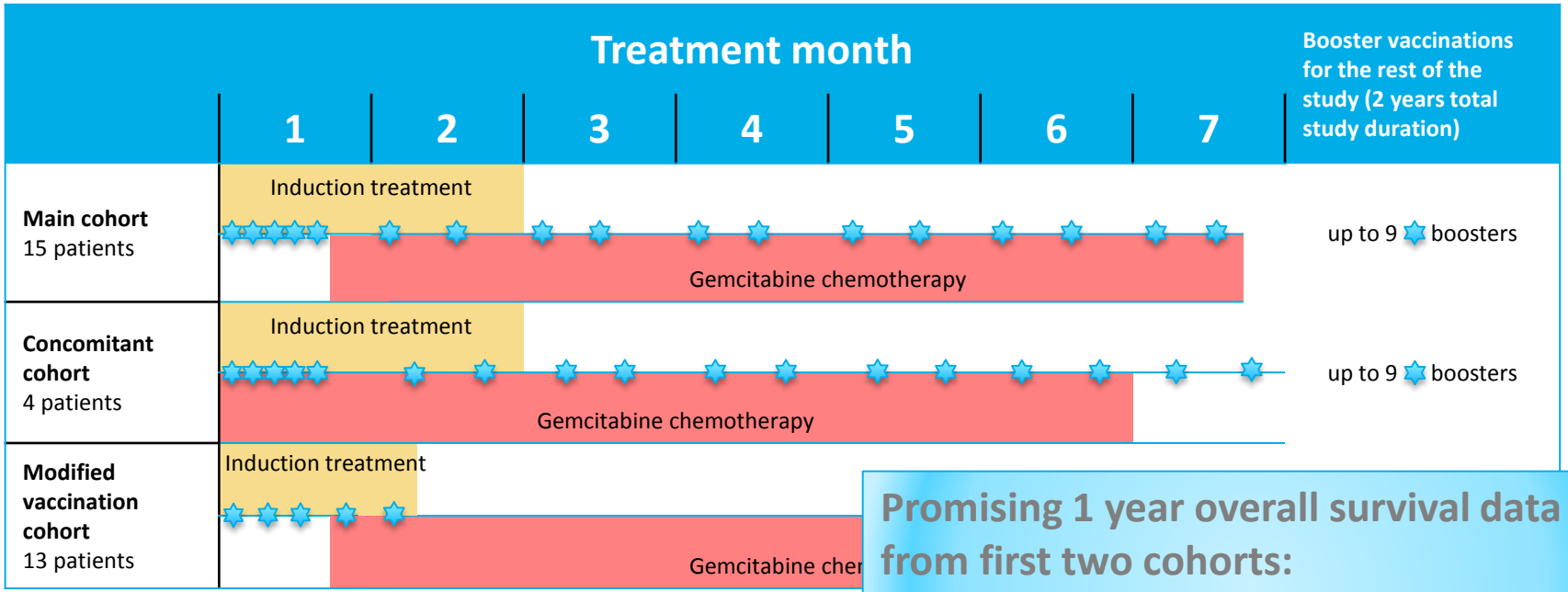
Combination of 2 trials with RAS peptide mono-therapy with 20 patients[1]
Survival curve typical for effective immunotherapy



[1]Two clinical trials with TG01 peptides conducted by **Norsk Hydro** at **Radiumhospitalet** in the period 1994-2000 were designed to only investigate safety and immune responses against the mutated RAS peptides, not to assess long term survival. Patients were treated with either a single TG01 peptide (9 patients) or TG01 (11 patients). The retrospective analysis was undertaken and published by the investigators (Wedén *et al*., 2011)

[1] Wedén *et al.*, 2011 and Clinical trial reports
[2] Oettle H *et al*., JAMA 2007, vol 297, no 3
[3] Oettle H *et al*., JAMA 2013, vol 310, no 14

TG01 Phase 1/2 in Pancreatic Cancer – Three treatment cohorts



In the modified vaccination cohort, the total number of vaccinations was reduced fr
gemcitabine chemotherapy was much reduced. Importantly, the modified vaccinati
leads to the same level of immune activation as observed in the first two cohorts.

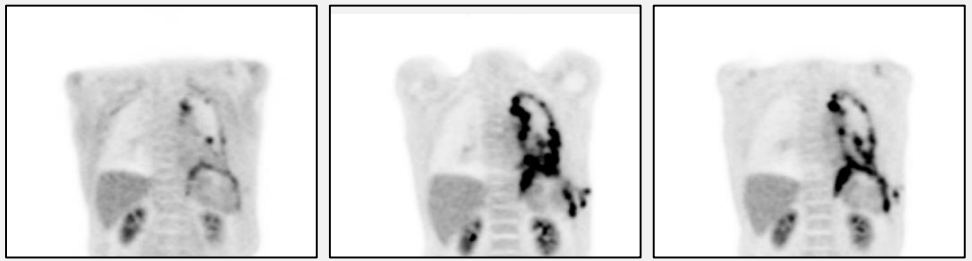
Promising 1 year overall survival data from first two cohorts:
14 out of 15 patients that could be followed were still alive after one year

= TG01 intra-dermal vaccination

Immunological findings were linked to clinical benefit

40% of evaluable patients in Phase 1 showed stabilization of disease ("SD") after 3 months

Patient	RECIST[1] (3 months)
FI1-01 Ovarian	Stable disease
FI1-02 Colon	Stable disease
FI1-04 Colon	Progressive disease
FI1-06 Liver	Progressive disease
FI1-08 Lung	Progressive disease
FI1-09 Mesothelioma	Progressive disease
FI1-13 Rectum	Progressive disease
FI1-14 Mesothelioma	**Stable disease**
FI1-17 STS	Progressive disease
FI1-19 Ovarian	**Stable disease**



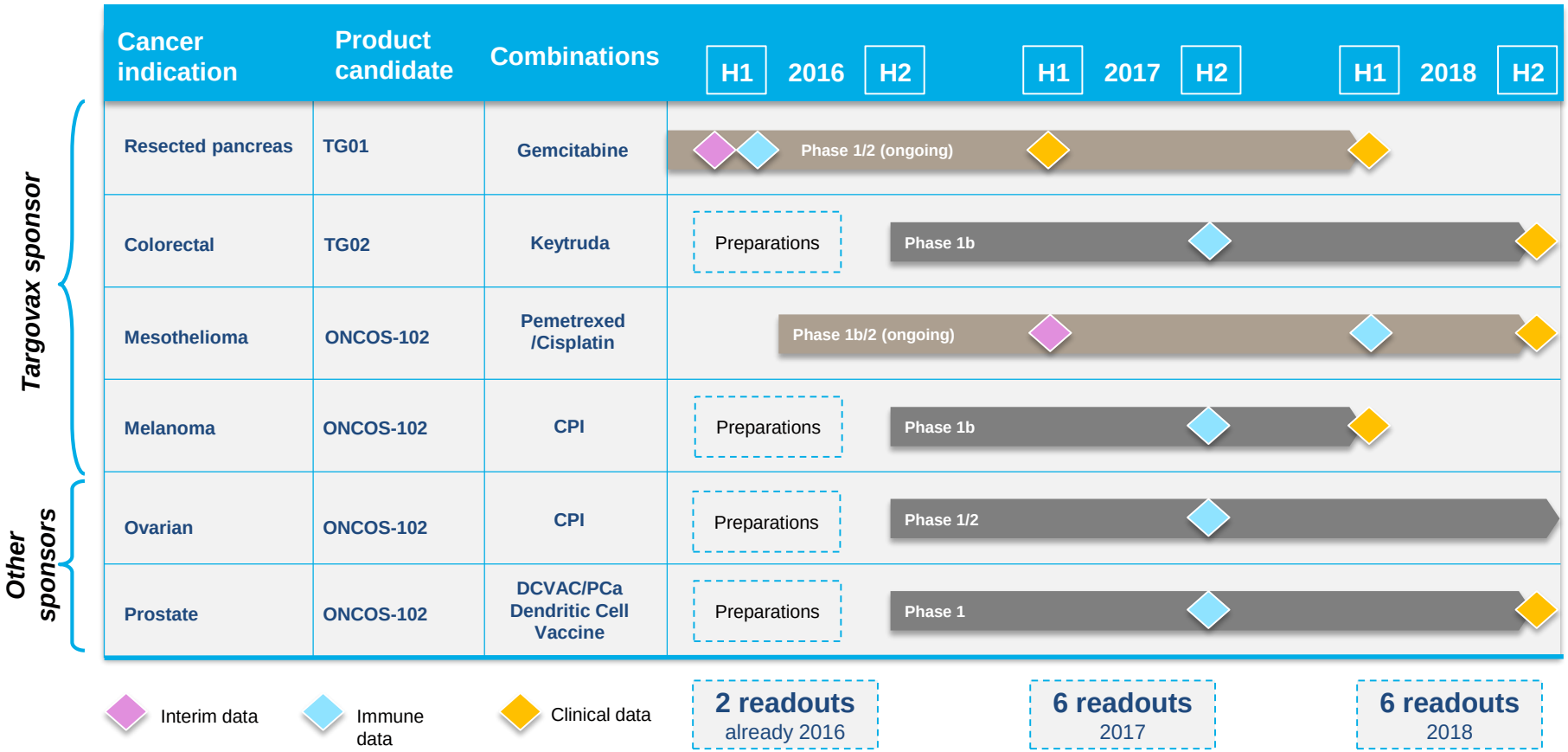
47% reduction in total tumor activity
Tumor specific T-cells in blood = systemic effect

- Previously therapy resistant patient is still alive with stable disease 31 months after treatment
- Tumor specific T-cells (NY-ESO-1) present in blood 17 months after last vaccination
- = Systemic effect that was maintained

[1] Response Evaluation Criteria In Solid Tumors (RECIST) is a set of internationally agreed rules that define when tumors in cancer patients improve/respond, stay the same/stabilize or worsen/progress during treatment. Complete response= all tumor disappeared, Partial response= >30% disappeared, Stabile disease= neither disappeared or progressed, Progressive disease= >20% increase

Source: Internal data on file

Clinical development program: six separate shots on goal




Thank
You
Merci
Gracias
Grazie
Biyan
Juspaxar
Shukria
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Arigato
Dankscheen
Mehrbani
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