Activating the immune system to fight cancer

RedEye pre-ASCO seminar

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From a sequential treatment strategy directly targeting the cancer...

1. Surgery
   When possible, surgical resection to remove the tumor

2. Radiotherapy
   Tumor irradiation to shrink tumor volume

3. Chemotherapy
   Chemotherapy – the cornerstone treatment in most cancer forms
…to an integrated combination approach

HARNESSING THE POWER OF THE PATIENT’S OWN IMMUNE SYSTEM

- Immune modulators
  - Checkpoint inhibitors
- Immune activators
  - Vaccines, oncolytic viruses, cytokines
- Immune boosters
  - CAR-Ts, TCRs
- Targeted therapy
  - PARP inhibitors, gene therapy, TKIs, etc.

Targovax focus
TARGOVAX’ CORE FOCUS IS IMMUNE ACTIVATORS

<table>
<thead>
<tr>
<th>Immune activators</th>
<th>Description</th>
<th>Examples</th>
<th>Car analogy</th>
</tr>
</thead>
</table>
| Oncolytic viruses, vaccines | o Make the immune system aware of the cancer  
o Activate T-cells | IMLYGIC™ (talimogene laherparepvec) | Ignite the engine  
Switch on GPS |

<table>
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<th>Immune modulators</th>
<th>Description</th>
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<tbody>
<tr>
<td>Checkpoint inhibitors</td>
<td>o Block stop signals that down-regulate T-cell cytotoxicity</td>
<td>KEYTRUDA</td>
<td>Release the hand-brake</td>
</tr>
</tbody>
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<th>Immune boosters</th>
<th>Description</th>
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<td>CAR-Ts</td>
<td>o Boost the immune system attack on the cancer</td>
<td>KYMRIAH (tisagenlecleucel)</td>
<td>Engage the turbo-charger</td>
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<tr>
<th>Targeted therapy</th>
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<td>PARP Inhibitors, TKIs etc.</td>
<td>o Target particular genetic or molecular defects of the cancer</td>
<td>Lynparza olaparib</td>
<td>Replace broken spare parts</td>
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Mode of action

IMMUNE ACTIVATORS TURN COLD TUMORS HOT

Example from Targovax Phase I trial

Before injection of oncolytic virus
“Cold tumor”
No T-cell infiltration

After injection of oncolytic virus
“Hot tumor”
Full T-cell infiltration

CD8+ T-cell
Recognizes and destroys the cancer cells
Targovax has two complementary programs in clinical development, both PROVEN TO ACTIVATE THE IMMUNE SYSTEM

**ONCOS**
Oncolytic virus
- Genetically armed adenovirus
- Makes cancer antigens visible to immune system
- Induces T-cells specific to patients’ tumor

**TG**
RAS neoantigen vaccine
- Shared neoantigen, therapeutic cancer vaccine
- Targets oncogenic RAS driver mutations
- Induces mutant RAS-specific T-cells

Activate and direct the immune system
Specific to the patient’s cancer
No need for individualization
ONCOS
CLINICAL DEVELOPMENT STRATEGY

1. Mesothelioma
   - Orphan disease
   - Launch indication
     - Orphan drug status
     - Aim to become SoC
     - Ongoing phase I/II
     - 15,000 patients per year

2. CPI synergy
   - Intra-tumoral
   - Indications with no / limited effect of CPIs
     - Ongoing melanoma phase I, combo w/PD-1
     - >100,000 patients per year

3. CPI synergy
   - Intra-peritoneal
   - Peritoneal malignancies
     - Ongoing phase I, combo w/PD-L1
     - >100,000 patients per year

4. Next generation
   - ONCOS viruses
   - Double transgene adenoviruses
     - Novel targets
     - Ongoing in vivo testing
     - Broad spectrum of solid tumors
**ONCOS-102 target launch indication**

**MALIGNANT PLEURAL MESOTHELIOMA**

- **Orphan disease**, estimated 15,000 new cases per year (EU, USA, Australia)
- **Incidence is increasing** worldwide and is predicted to peak in 5-10 years
- Often **caused by asbestos** exposure, with a latency period of up to 40 years before diagnosis
- Aggressive cancer form with **median survival of 12 months**
- No significant treatment advance in the last decade
# Malignant pleural mesothelioma

## NEED FOR NEW TREATMENT APPROACHES

<table>
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<tr>
<th>Surgery</th>
<th>Radiotherapy</th>
<th>Immunotherapy</th>
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<tbody>
<tr>
<td>Only 10% of patients suitable for resection</td>
<td>Rarely effective due to tumor shape</td>
<td>Mixed signals from early IO trials</td>
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<tr>
<td>Technically challenging due to location</td>
<td>Shape of tumors make them hard to target</td>
<td>Slight median OS improvement in early CPI trials</td>
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<tr>
<td>Diagnosis often too late for surgery</td>
<td>Mainly palliative care</td>
<td>No/few other oncolytic viruses in development</td>
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### Surgery
- Technically challenging due to location
- Diagnosis often too late for surgery

### Radiotherapy
- Rarely effective due to tumor shape
- Shape of tumors make them hard to target
- Mainly palliative care

### Chemotherapy
- Standard of care (SoC) has limited efficacy
- Only approved SoC option is pemetrexed/cisplatin
- 6 month PFS and 12 month median OS in 1st line

### Immunotherapy
- Mixed signals from early IO trials
- Slight median OS improvement in early CPI trials
- No/few other oncolytic viruses in development
ONCOS-102 in malignant pleural mesothelioma

SIGNAL OF EFFICACY IN THE FIRST 6 PATIENTS

1. Safety

- ONCOS-102 well-tolerated in combination with chemotherapy

2. Innate immune activation

- Systemic increase of pro-inflammatory cytokines in 6/6 patients (IL-6, TNFα and IFNγ)

3. Adaptive immune activation

- Increase in tumor infiltration of CD4+ and CD8+ T cells in 3/4 patients

4. Clinical efficacy

- Clinical activity seen in 3/6 patients after 6 months
- 50% disease control rate
ONCOS-102 in malignant pleural mesothelioma
DEVELOPMENT STRATEGY AND INDICATIVE TIMELINES

2018

Ongoing
Phase I/II 30 pats, randomized

2019

Planned
Expansion of randomized Phase II, 90 pats

2020

2021

2022

Future
Phase III

- Randomized ORR and OS data 30 patients
- Decide on possible CPI combination arm
- EMA & FDA advisory meetings

- Randomized ORR and OS data 90 patients
- Potentially use as basis for a submission for conditional approval
- Go/No-go for phase III OS trial for full MAA
## Targovax overall

### CLINICAL PROGRAM TIMELINES

<table>
<thead>
<tr>
<th>Cancer Indication</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
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<tbody>
<tr>
<td></td>
<td>H1</td>
<td>H2</td>
<td>H1</td>
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<tr>
<td><strong>TG</strong></td>
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<tr>
<td>Resected Pancreas</td>
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<tr>
<td>Resected Pancreas (Planned reg)</td>
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<tr>
<td>Colorectal</td>
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<td></td>
<td>Phase I/II</td>
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<tr>
<td><strong>ONCOS-102</strong></td>
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<tr>
<td>Melanoma</td>
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<td></td>
<td>Phase I</td>
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<tr>
<td>Mesothelioma</td>
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<td></td>
<td>Phase I/II</td>
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<tr>
<td>Ovarian &amp; Colorectal</td>
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<td>(Collab. w/CRI, Ludwig &amp; MedImmune)</td>
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<td>Phase I/II</td>
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<td>Prostate</td>
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<td>(Collab. w/Sotio)</td>
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<td>Phase I</td>
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- **Interim data**
- **Clinical, immune and safety data**
ACTIVATING THE PATIENT'S IMMUNE SYSTEM
to fight cancer

Broad clinical program
Six shots on goal
Several upcoming data points

Defined path to market
Aim to become frontline treatment in high unmet need cancers
Orphan status in mesothelioma and pancreas

Innovative pipeline
Next gen double transgene viruses in testing
IV program under evaluation