PHOTOCHEMICAL INTERNALISATION FOR ENHANCING VACCINE IMMUNE RESPONSE - PRECLINICAL RESULTS AND PHASE I CLINICAL STUDY

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PCI BIOTECH

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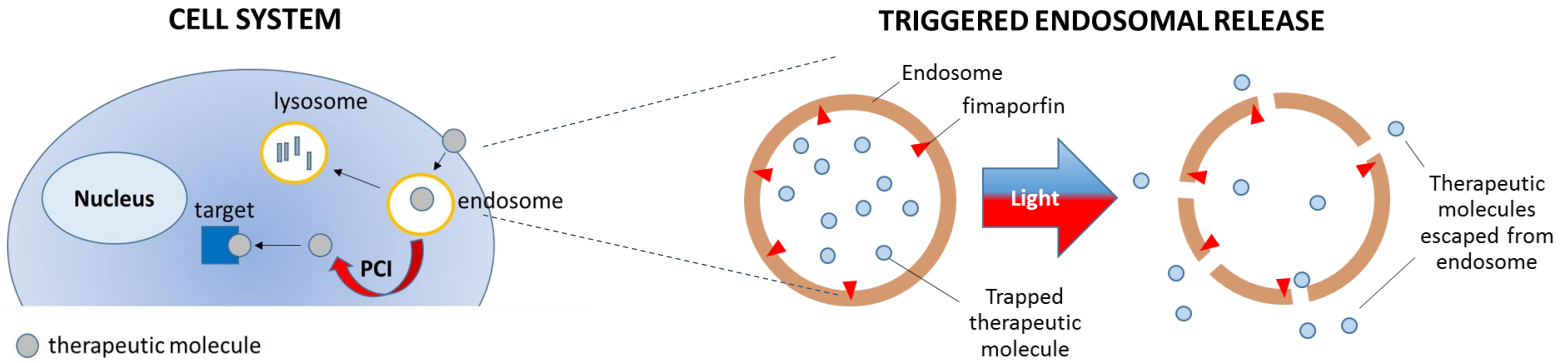
PCI BIOTECH AT A GLANCE

- Enabling drugs to reach intracellular therapeutic targets

- A listed (PCIB:NO) cancer-focused biotech company
- Photochemical internalisation ("PCI") technology, originating from the Oslo University Hospital
- **Fima**porfin ($TPCS_{2a}$) proprietary photosensitiser

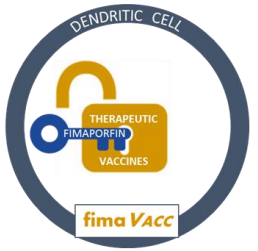
Mode of action



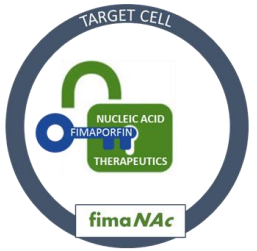
Broad application

PCI – the solution to a key challenge for several modalities

Enabling approved drugs to fulfil unmet local treatment need



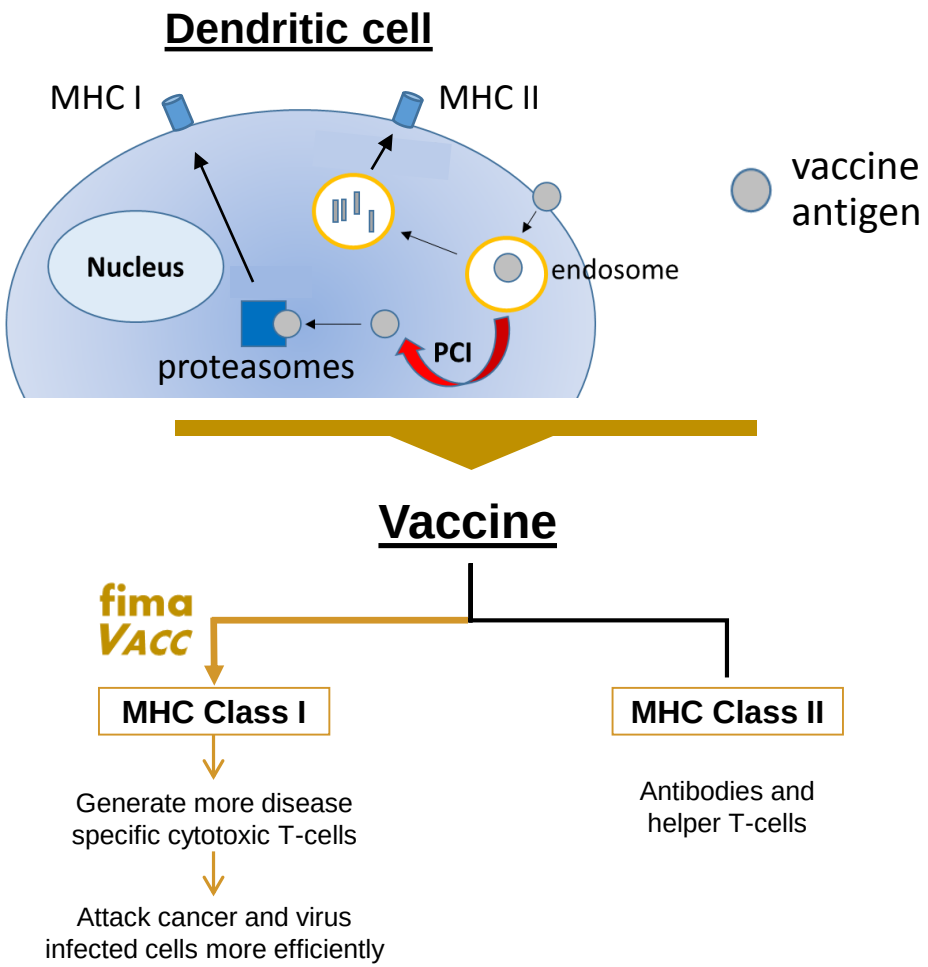
Enhancing cellular immune responses important for therapeutic effect



Providing a delivery solution for nucleic acid therapeutics

PCI TECHNOLOGY

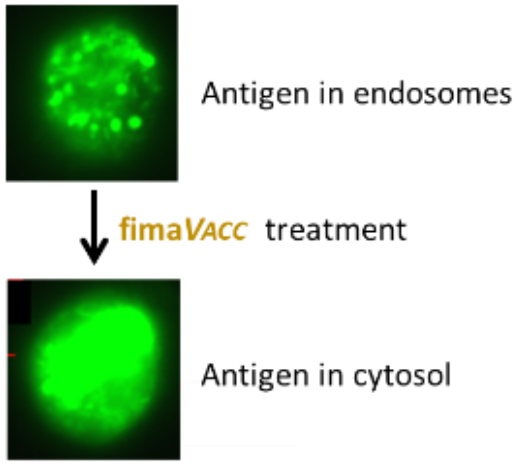
► fima VACC – mode of action

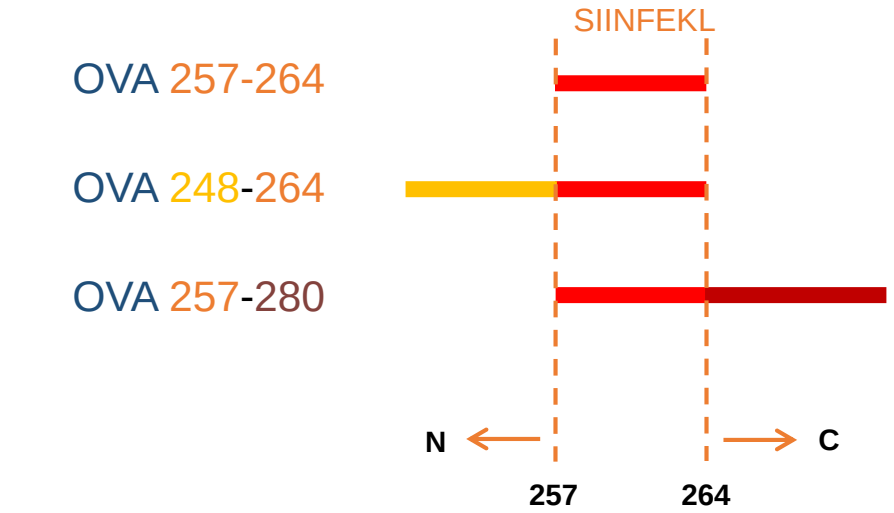


MECHANISM OF ACTION

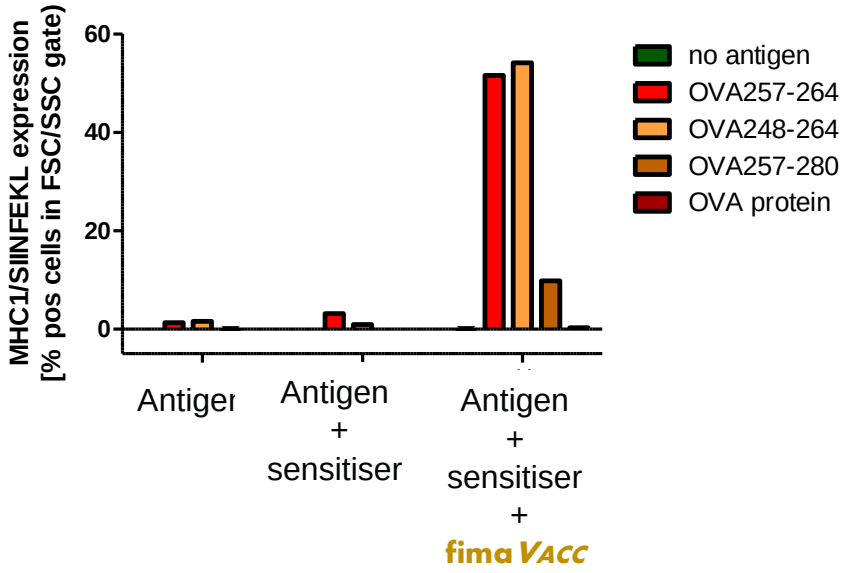
- **fima VACC** increases MHC I presentation of SIINFEKL (OVA) peptides

- Macrophage cell line
- Stained with antibody specific for SIINFEKL/MHC I complex





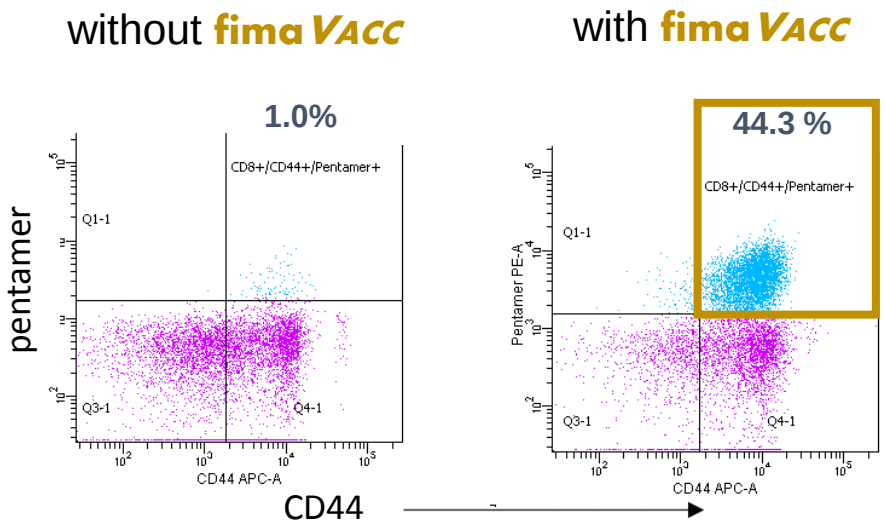
MHC1/SIINFEKL expression in B6 macrophage cell line, OVA peptides and proteins, concentrations of all antigens corresponds to 3 µg/ml of SIINFEKL

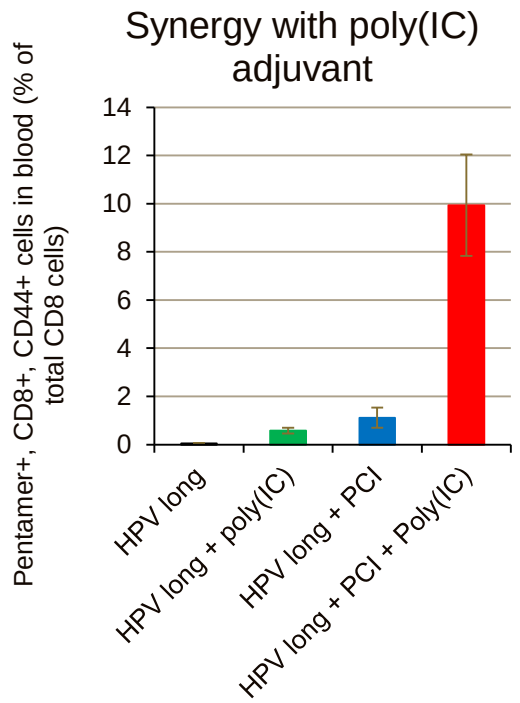


fima VACC STRONGLY ENHANCES VACCINATION EFFECTS WITH HPV PEPTIDE + POLY(IC) ADJUVANT

- Impressive effects with clinically relevant HPV therapeutic vaccine in mice

Amount of activated antigen-specific CD8 T-cells in blood





Cytotoxic (CD8) T-cells

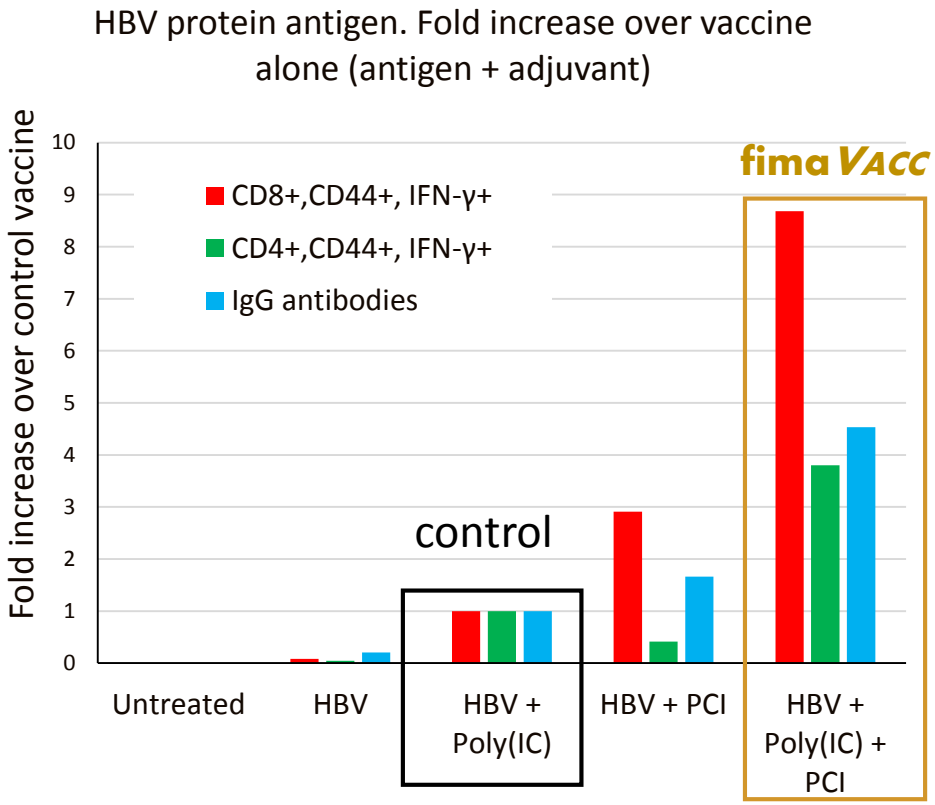
- Most important immune cells to fight tumours
- Difficult to induce with vaccination
- fima VACC strongly enhances the ability of vaccines to induce CD8 T-cells:

  >40 times enhancement seen in blood cell analysis

fima VACC acts synergistically with poly(IC) adjuvant (TLR3 agonist commonly used in peptide vaccination)

PCI CAN ENHANCE ALL BRANCHES OF THE IMMUNE RESPONSE TO AN INFECTIOUS AGENT PROTEIN ANTIGEN (HBV SURFACE ANTIGEN)

- **fima VACC** enhances both CD8, CD4, and antibody responses to infection antigen



- **fima VACC** enhances all branches of the immune response to a protein infection antigen
- Indicates that **fima VACC** has a large potential also in therapeutic and prophylactic vaccination against infectious diseases.

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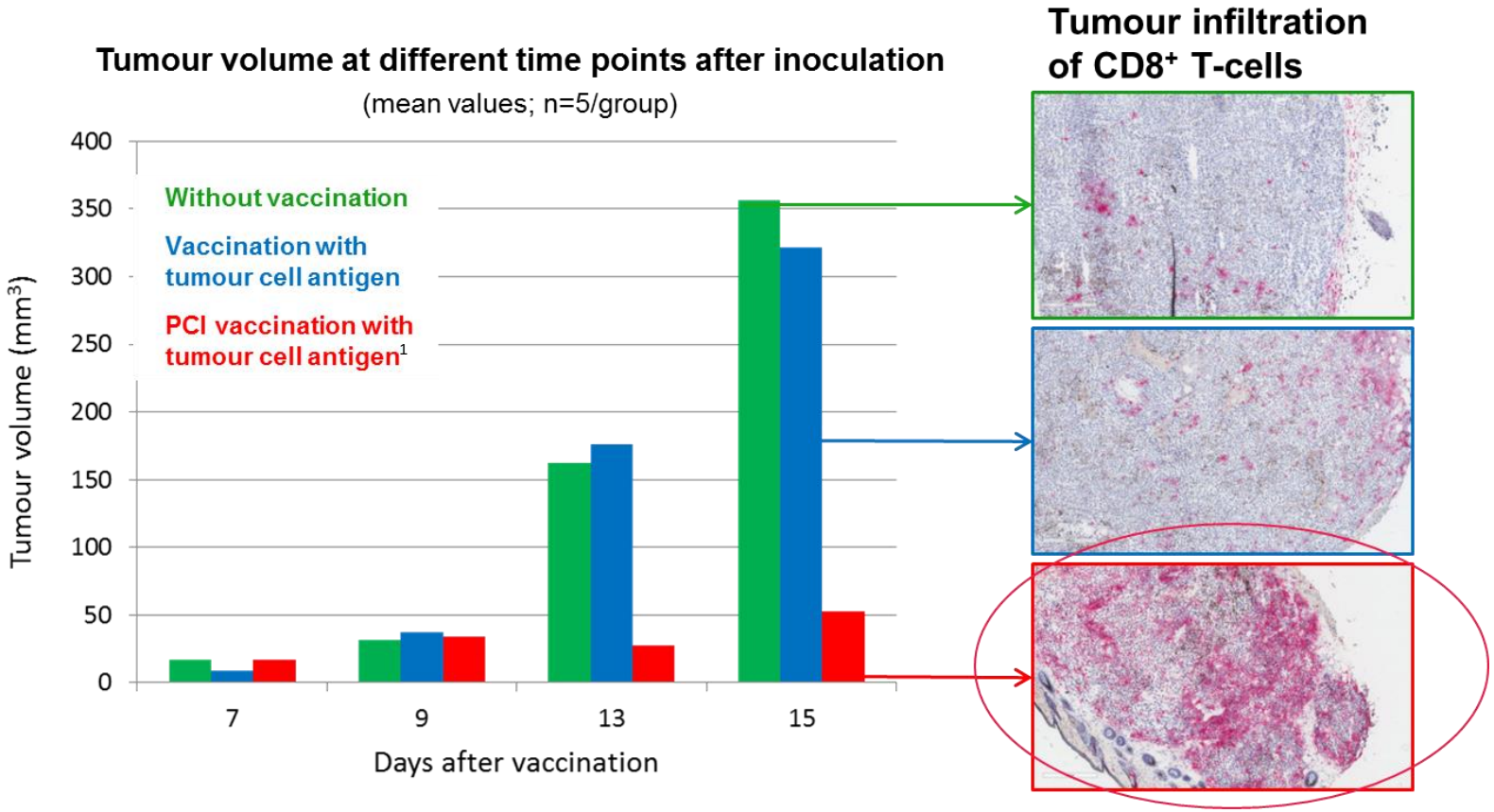
THERAPEUTIC VACCINATION IN TUMOUR MODEL

- **fima VACC** induces cytotoxic T-cells that infiltrate tumours

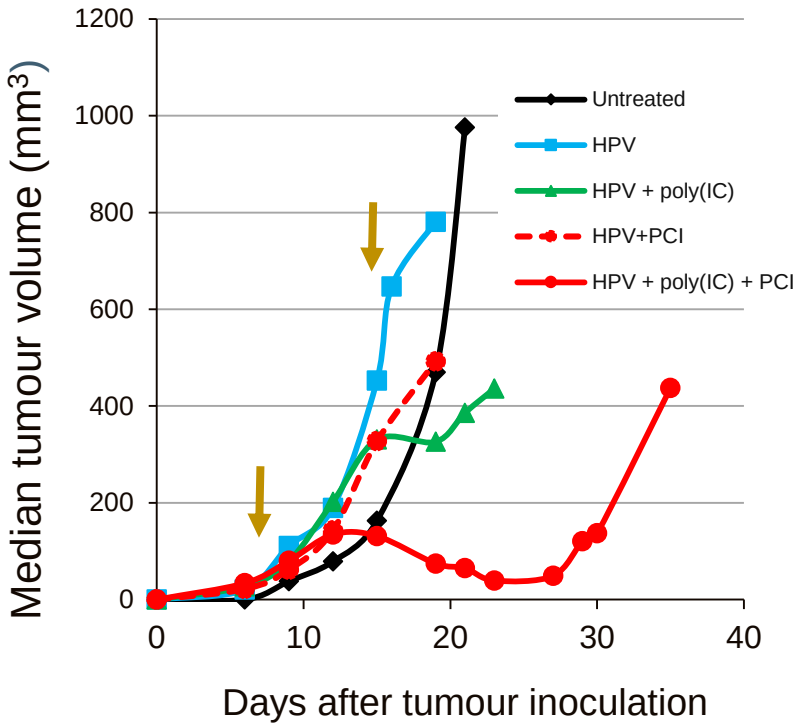
Therapeutic fima VACC vaccination with OVA in animal tumour model (B16-OVA melanoma/OT-1)



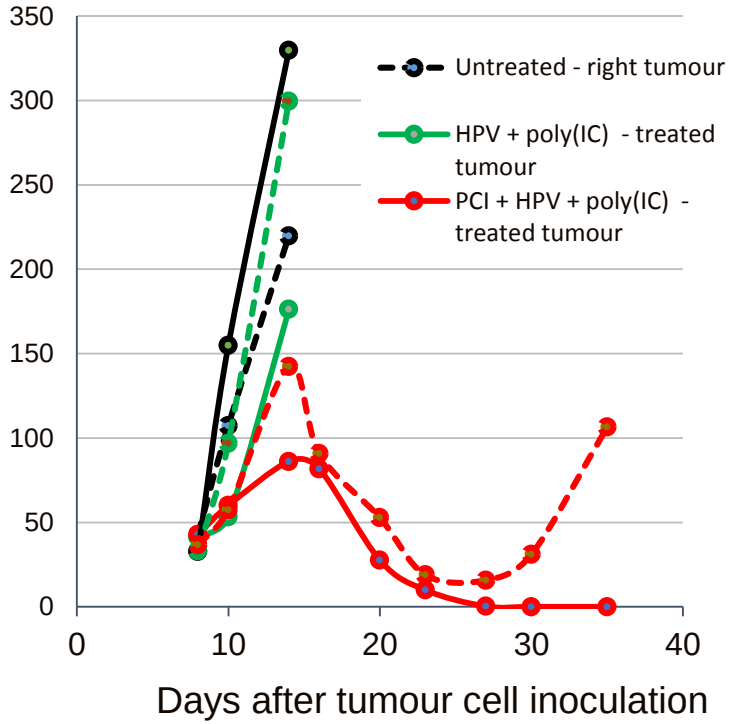
fima VACC IN TC-1 MOUSE MODEL FOR HPV-INDUCED CANCER

- Intradermal and intratumoural therapeutic vaccination with **fima VACC** induces strong anti-tumour response

Intradermal vaccination



Intratumoural vaccination in animals with two tumours.



- **fima VACC** with HPV long peptide and poly(I:C)
- Strong synergy between **fima VACC** and poly(IC)
- Intra-tumoural immunisation generates an immune response capable of destroying untreated tumours
- "Cured" mice immune to new challenge with tumour cells

PHASE I STUDY IN HEALTHY VOLUNTEERS

► Overview

► Main Objective:

- Determine the safety, tolerability and immune response of **fima VACC** when given as intradermal injections in combination with an adjuvant (Hiltonol) and antigens (KLH and HPV E7 peptides) in healthy subjects

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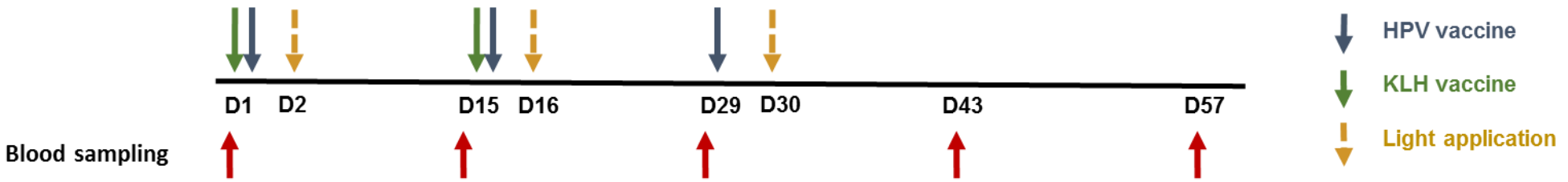
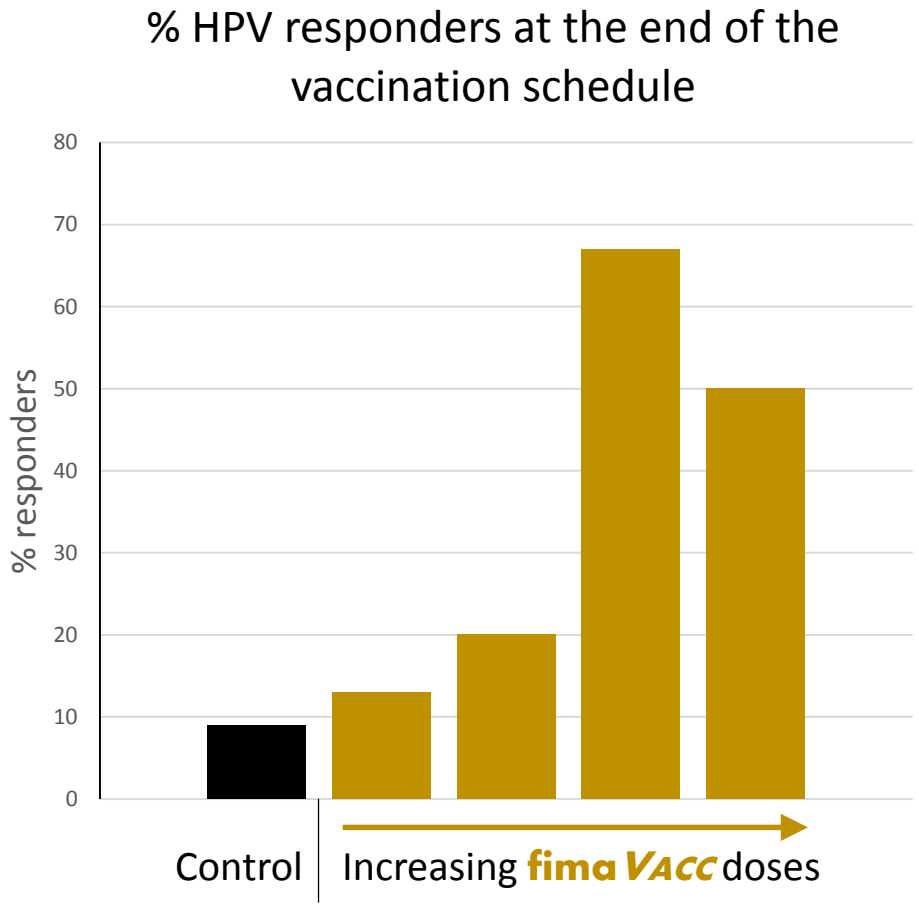
Study Treatments:

- 6-12 subjects in each cohort – different doses of fimaporfin photosensitiser
- Adjuvant: Hiltonol (poly-ICLC; adjuvant), 50µg
- Control group: Adjuvant + Antigens
- **fima VACC** groups: Adjuvant + Antigens + **fima VACC**
- Intradermal injections with 2 weeks intervals (rotating injection sites)
- Light application 200 sec, 20 (± 4) hours after ID dosing



OVERALL T-CELL RESPONSES – HPV E7 PEPTIDES – ELISPOT ANALYSIS

- Substantial increase in the percentage of subjects responding to vaccination

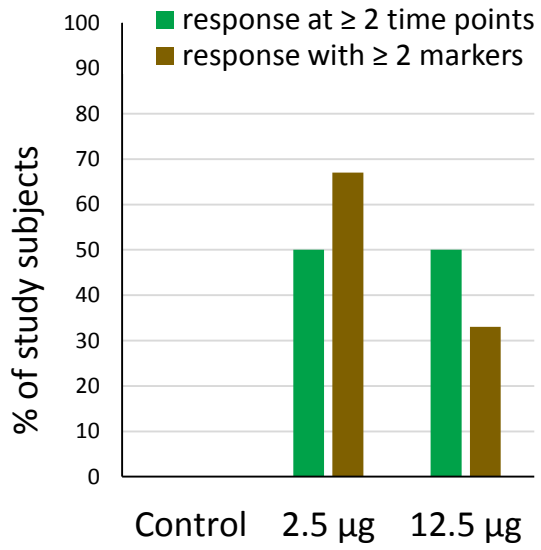


- Elispot analysis (IFN-γ) after completion of the HPV E7 peptide vaccination schedule (3 vaccinations)
- **fima VACC** induces about 8 times more T-cell responders than the control with a state of the art adjuvant technology (poly(IC) (Hiltonol))

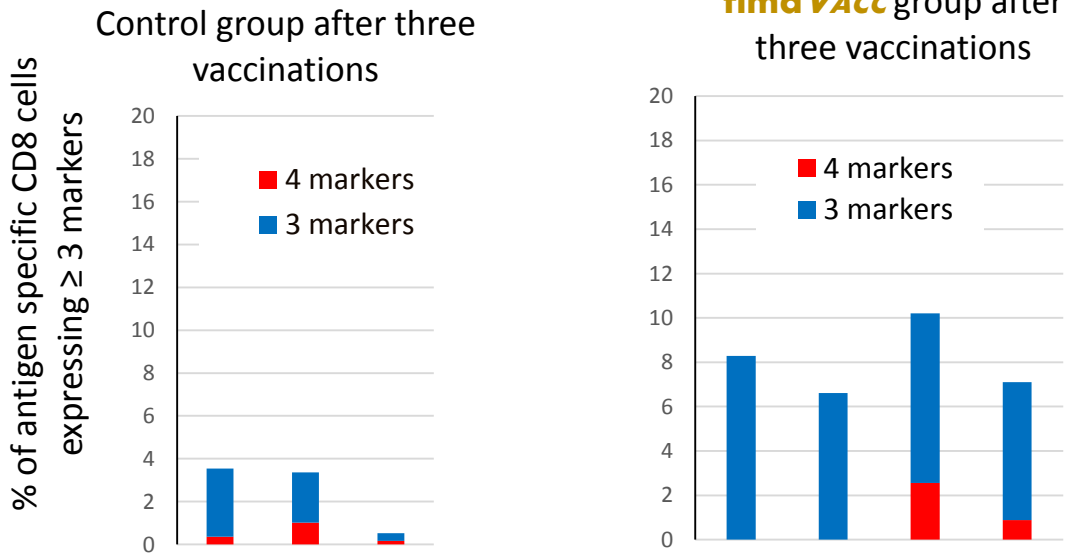
CD8 T-CELL RESPONSES – HPV E7 PEPTIDES

- ► fima VACC Induces robust C8 responses
- ► fima VACC substantially increases the frequency of polyfunctional CD8 T-cells

- Flow cytometry analyses by group of Sjoerd van der Burg (Leiden University)
- fima VACC induces more CD8 T-cell responders and more robust responses
- CD8 T-cell responses in control group were less frequent and generally borderline (1 time point, 1 marker, near LOD)



- As compared to the control group, fima VACC substantially increases the frequency of polyfunctional CD8 T-cells (expressing ≥ 3 functional markers)
- CD8 T-cell polyfunctionality is an important parameter indicating the ability of the T-cells to combat cancer cells and to give proper protection against viral infections



CLINICAL TRANSLATION OF fima VACC TECHNOLOGY

- Opportunity to play a key role in second generation cancer immunotherapy
- Unique mode of action
  - – CTL-induction by MHC class I antigen presentation in dendritic cells and macrophages
- Broad applicability
  - – Peptide and protein antigens -– Prophylactic & therapeutic vaccination
- Excellent stability of fimaporfin
  - – Stable at room temperature in solution and can be autoclaved
- More than 90 subjects enrolled in phase I clinical study:
  - Substantial increase in number of T-cell responders to HPV E7 peptides at tolerable fimaporfin dose
  - Clearly enhanced overall T-cell responses
  - More robust CD8 T-cell responses (notoriously difficult to induce with E7)
  - Increased functionality of the induced CD8 T-cells
- Follow up with study in cancer patients


Thank you