

PCI-controlled intracellular delivery of cancer therapeutics: Pre-clinical and clinical status

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Conflict of Interest

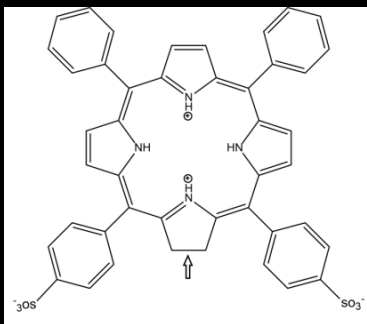
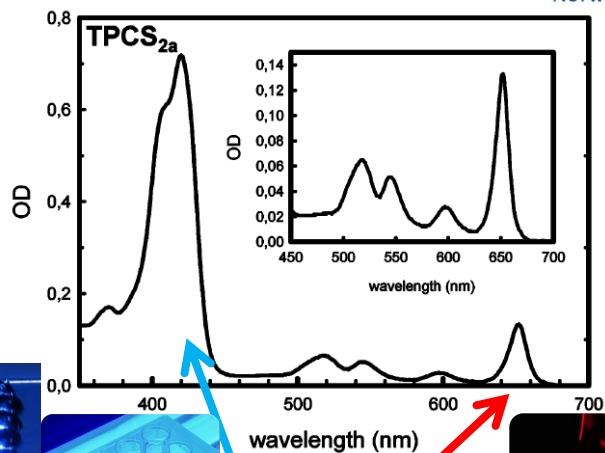
We are inventors on several patents and patent applications on the PCI technology.

AH is CSO and a shareholder in PCI Biotech.

Disulfonated tetraphenyl chlorin (TPCS_{2a}), a novel photosensitizer developed for clinical utilization of photochemical internalization

Kristian Berg,^{*a} Solveig Nordstrand,^b Pål Kristian Selbo,^a Diem Thuy Thi Tran,^a Even Angell-Petersen^a and Anders Høgset^c

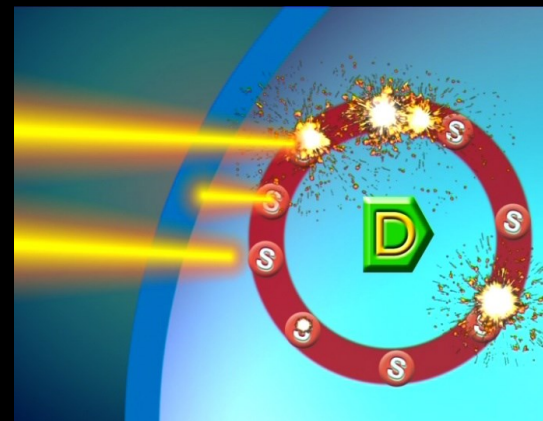
Received 26th April 2011, Accepted 15th June 2011
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TPCS_{2a} or fimaporfin

S = photosensitizer

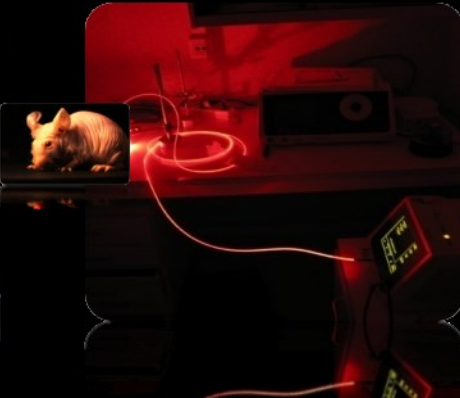
D = Drug



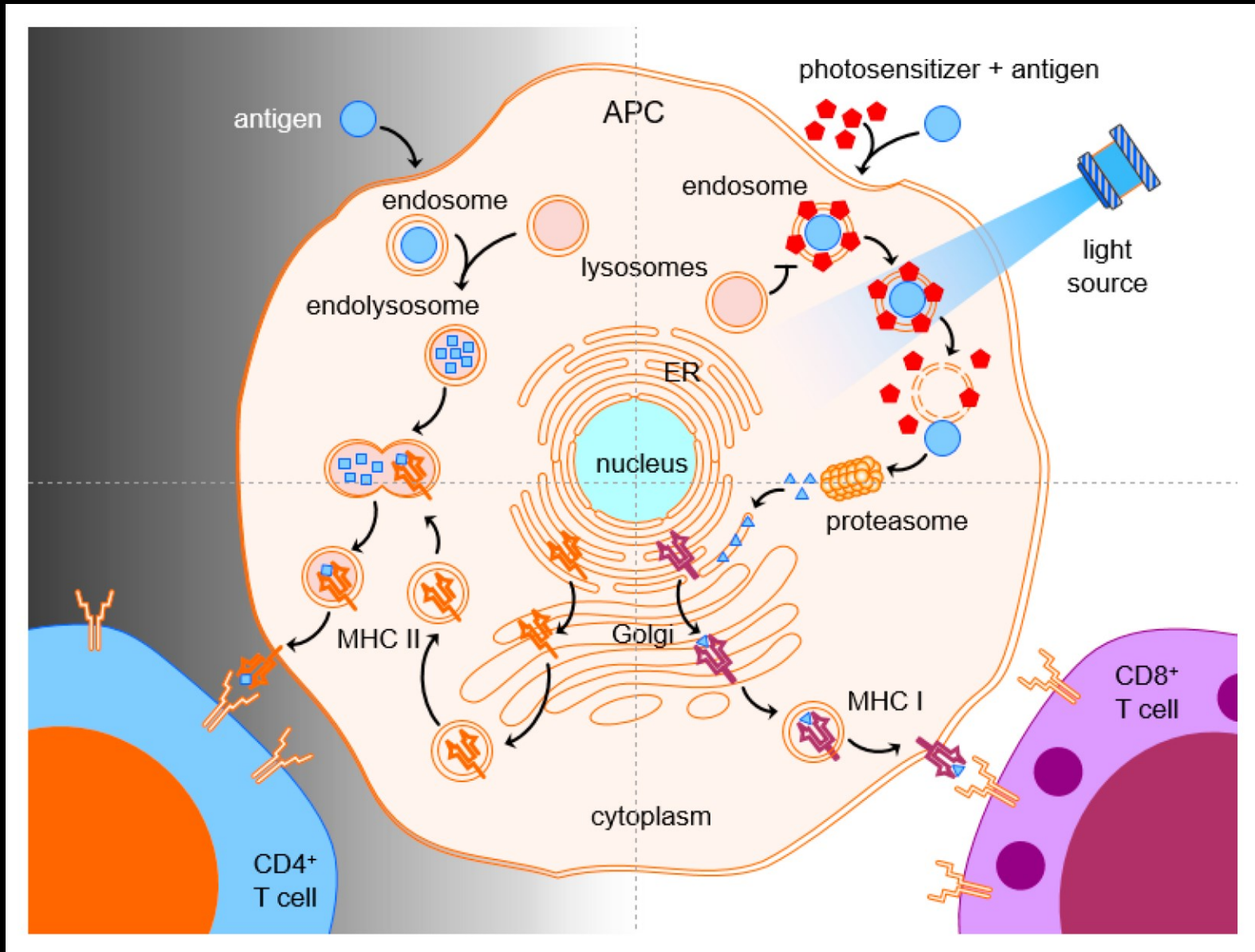
T = Target

PCI-enhanced peptide- or protein-based vaccination

Model vaccine antigens:
Ovalbumin (OVA, protein)
SIINFEKL (OVA peptide)

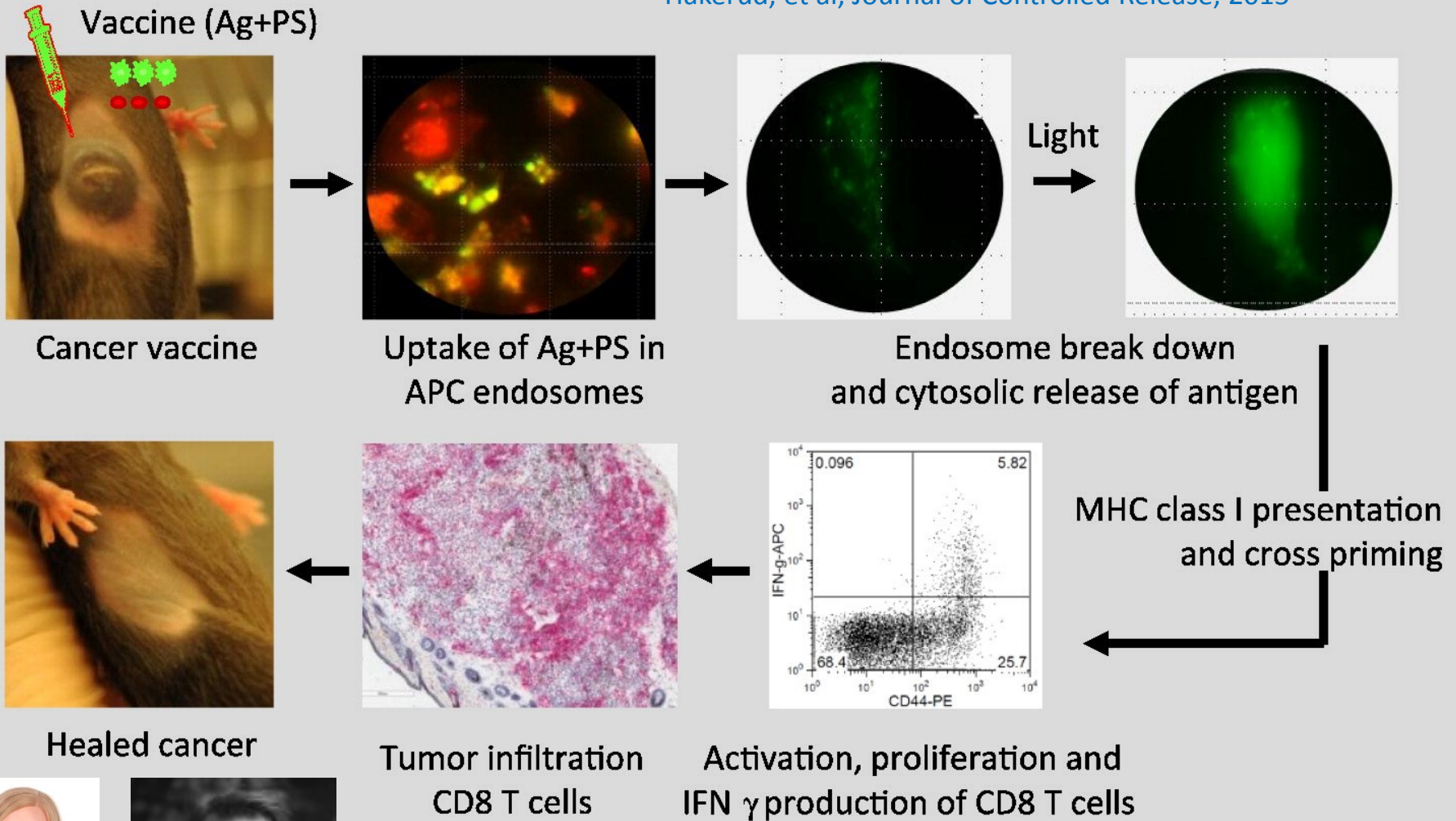


Antigen uptake, processing, and T-cell presentation in PCI-based vaccination



Photosensitisation facilitates cross-priming of adjuvant-free protein vaccines and stimulation of tumour-suppressing CD8 T cells.

Håkerud, et al, Journal of Controlled Release, 2015



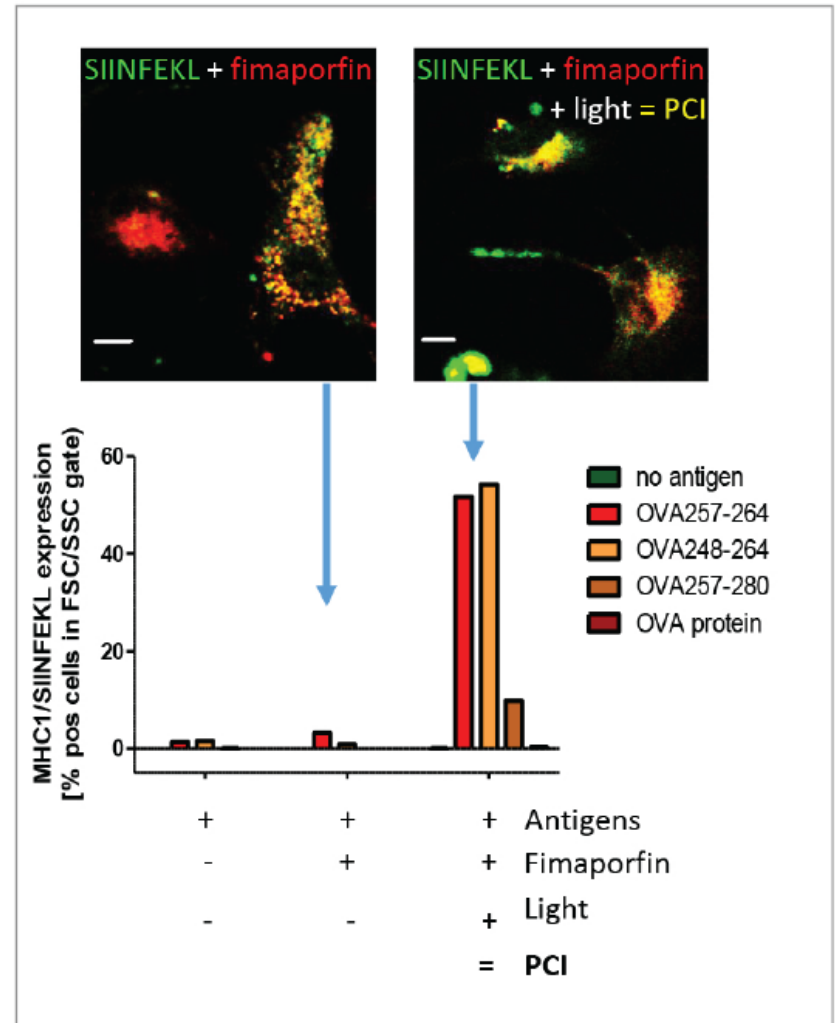
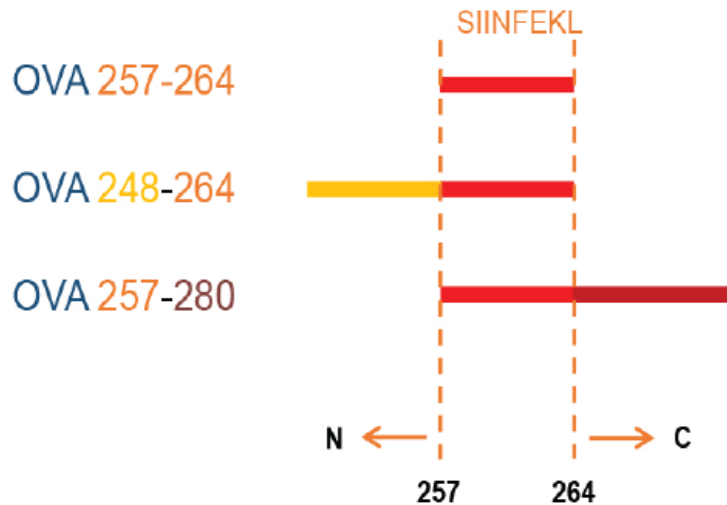
Hjálmsdóttir Á et al. Mol Pharm, 2016

Bruno C. Et al. J Immunol, 2015

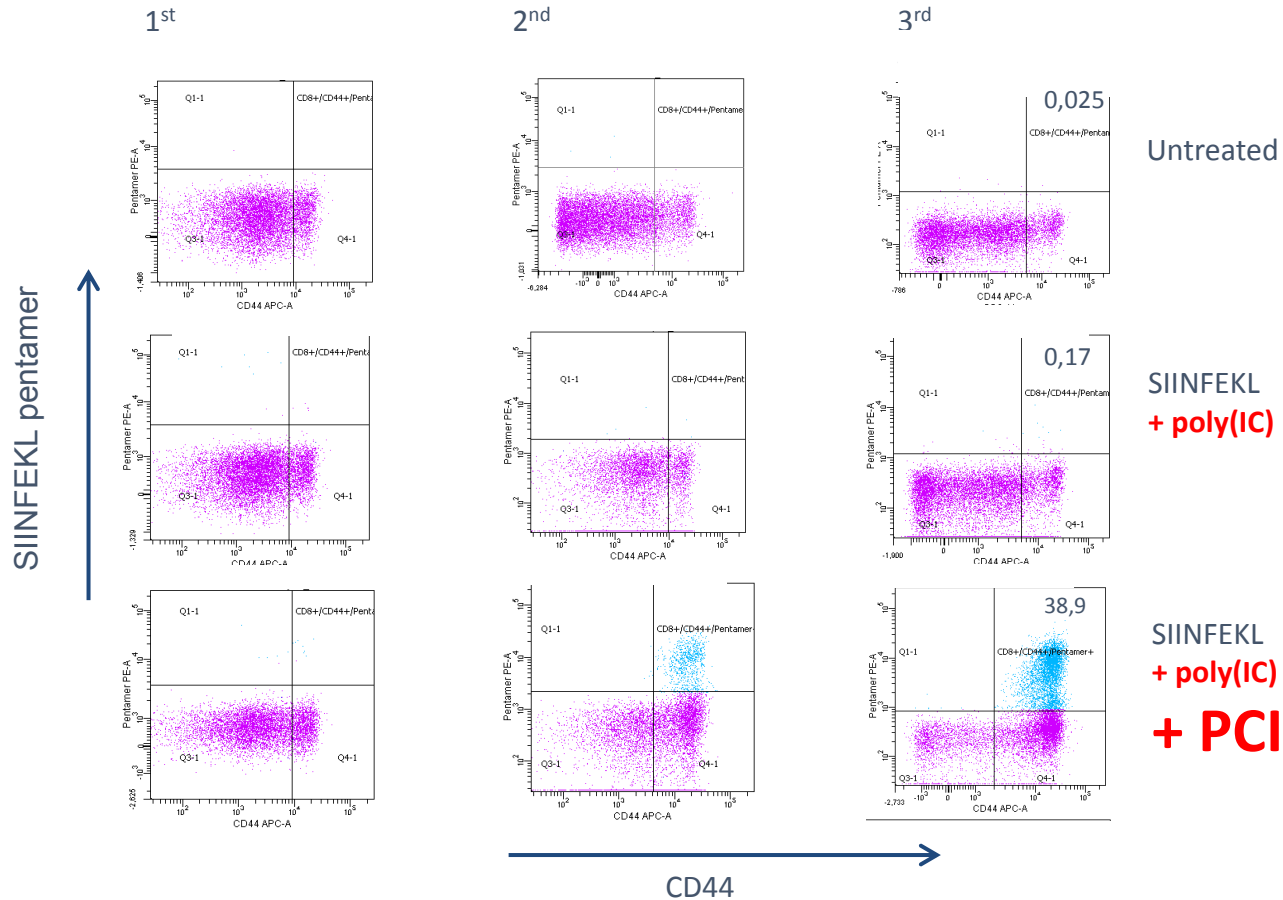
Waeckerle-Men Y et al. Eur J Pharm Biopharm. 2013

Håkerud, et al, Journal of Controlled Release, 2014

PCI induces cytosolic release of peptide antigen and strongly enhances its MHC-I presentation in APCs



PCI of OVA peptide SIINFEKL trigger robust activation of antigen-specific CD8+ T-cells



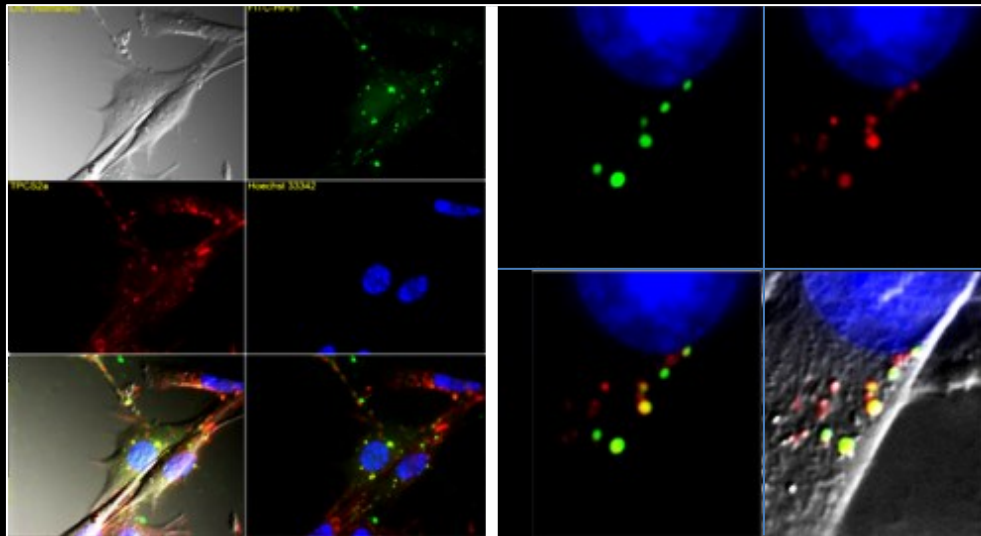
PCI-enhanced peptide- or protein-based vaccination

Clinical relevant vaccine antigen:
Human papilloma virus (HPV cancers)
TRP-2 (malignant melanoma)

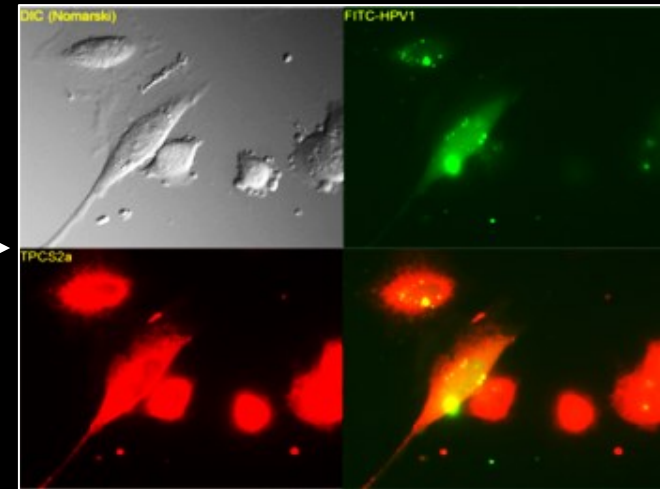


PCI-induced cytosolic release of HPV₄₃₋₇₈ long vaccine peptide

Before PCI

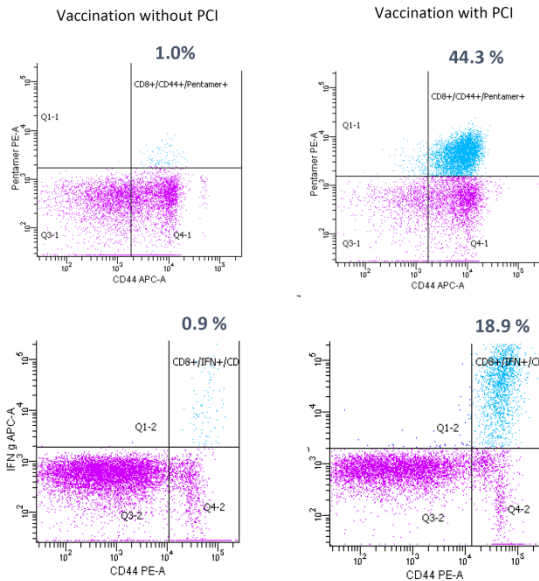


After PCI



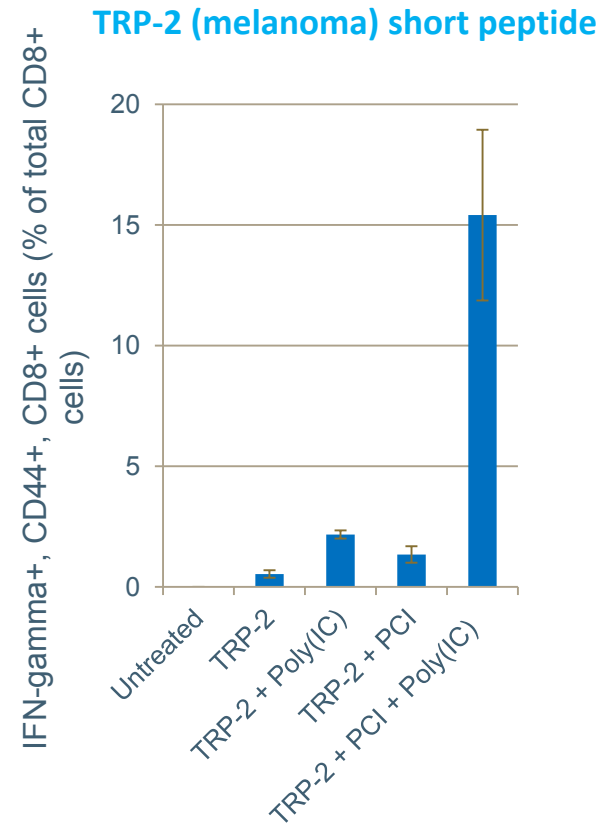
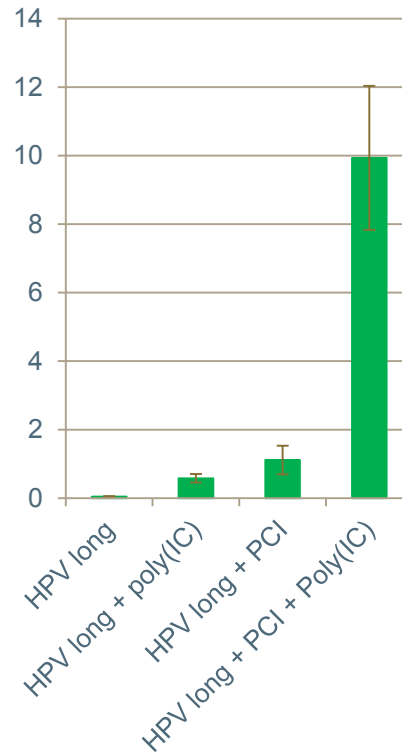
TPC52a FITC-HPV1 Hoechst 33342

PCI with clinically relevant vaccine antigens trigger robust activation of antigen-specific CD8 T-cells



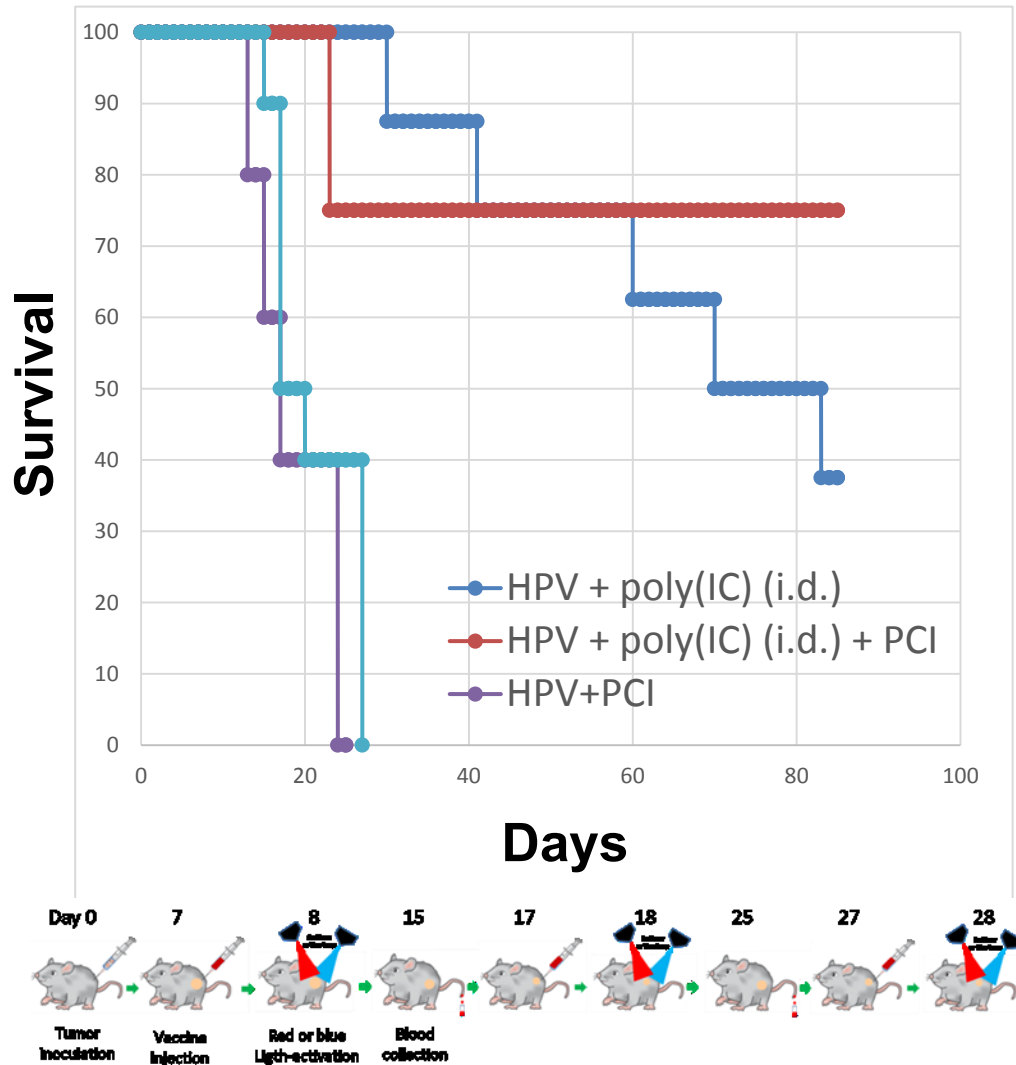
Pentamer+, CD8+, CD44+ cells in blood (% of total CD8 cells)

HPV long peptide



*PCI = fima VACC

Intradermal PCI vaccination of long HPV-peptide in combination with Poly(I:C) enhance immunity and anti-tumor responses in the HPV-based cancer model TC-1 in C57BL/6 mice.



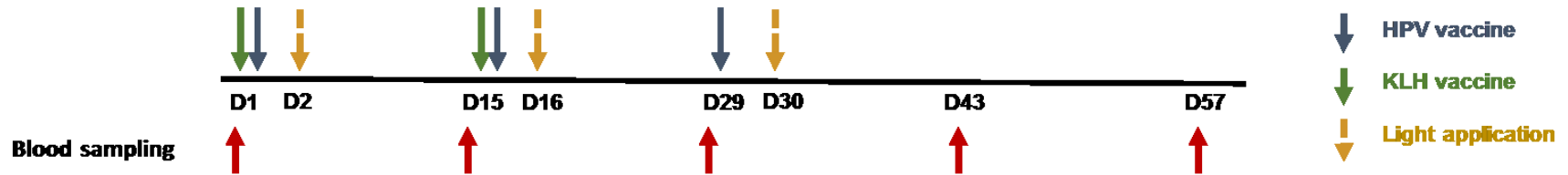
PCI-enhanced vaccination is safe, and gives promising cellular immune responses to an HPV peptide-based vaccine in a phase I clinical study in healthy volunteers

Primary objectives

- Assess the safety and local tolerance of PCI mediated vaccination
- Identify a safe dose for later clinical studies

Secondary objective

- Analyze the immunological responses to the vaccination

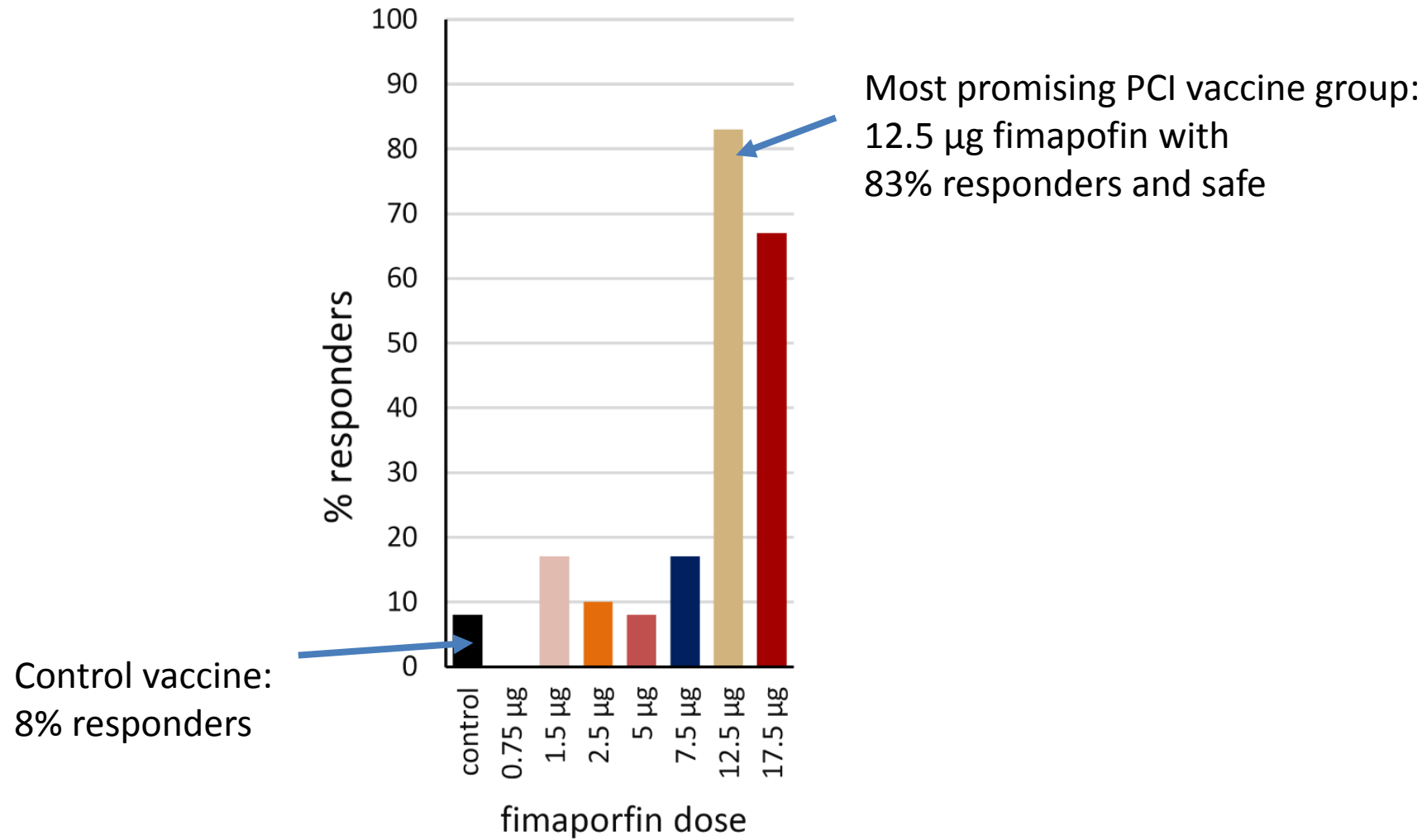


The subjects were vaccinated with two HPV16 E7 peptides and Keyhole Limpet Hemocyanin (KLH) protein, serving as model antigens for peptide- and protein-based vaccines.

PCI groups received fimaporfin + vaccine + adjuvant (Hiltonol) + light
 A control group received Hiltonol and vaccine antigens only

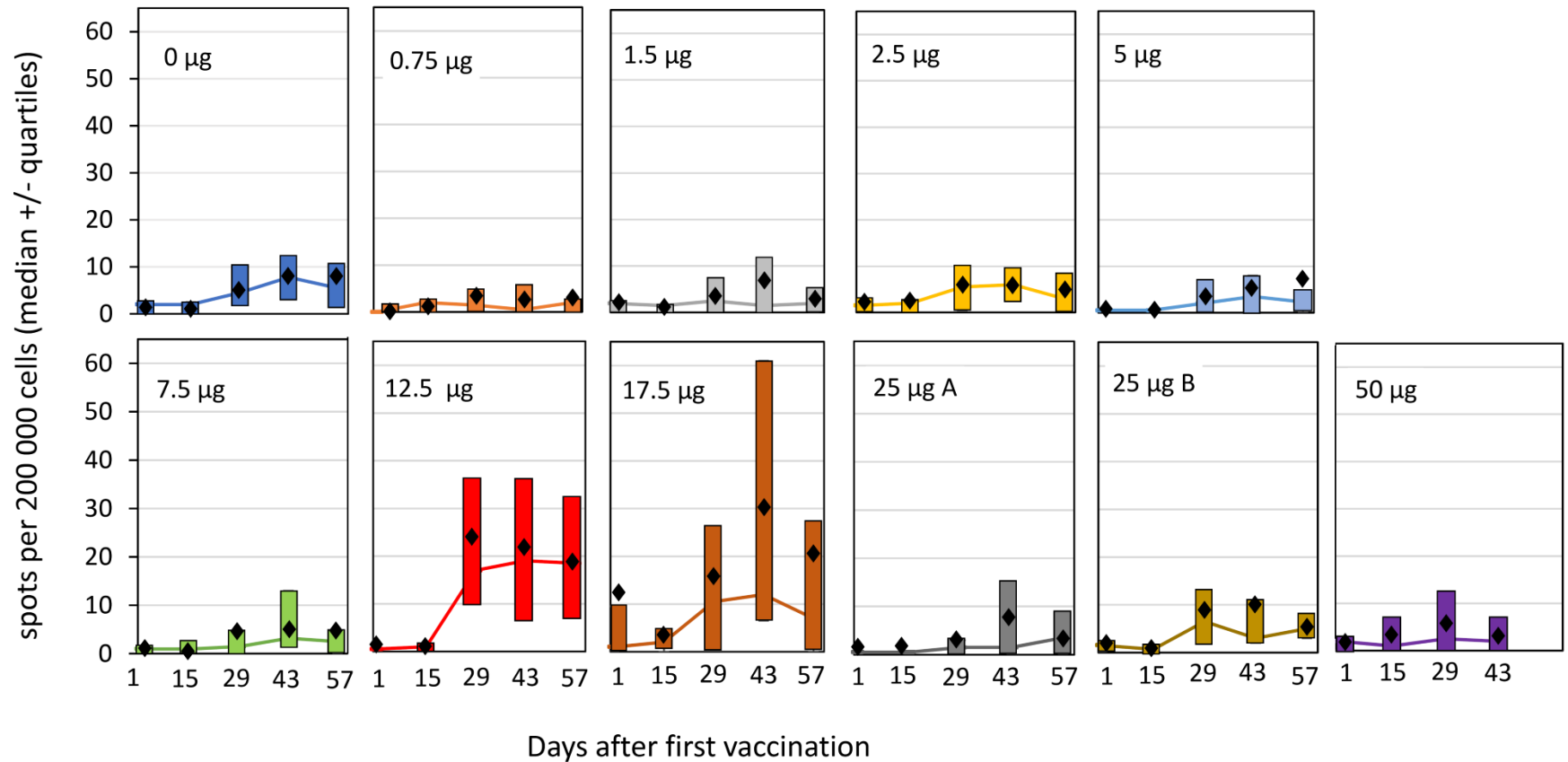
Fimaporfin doses below 17.5 μg were identified as safe and tolerable

Responders to HPV vaccination in the different dose groups was assessed based on the ELISpot results = CD4 and CD8T-cell responses

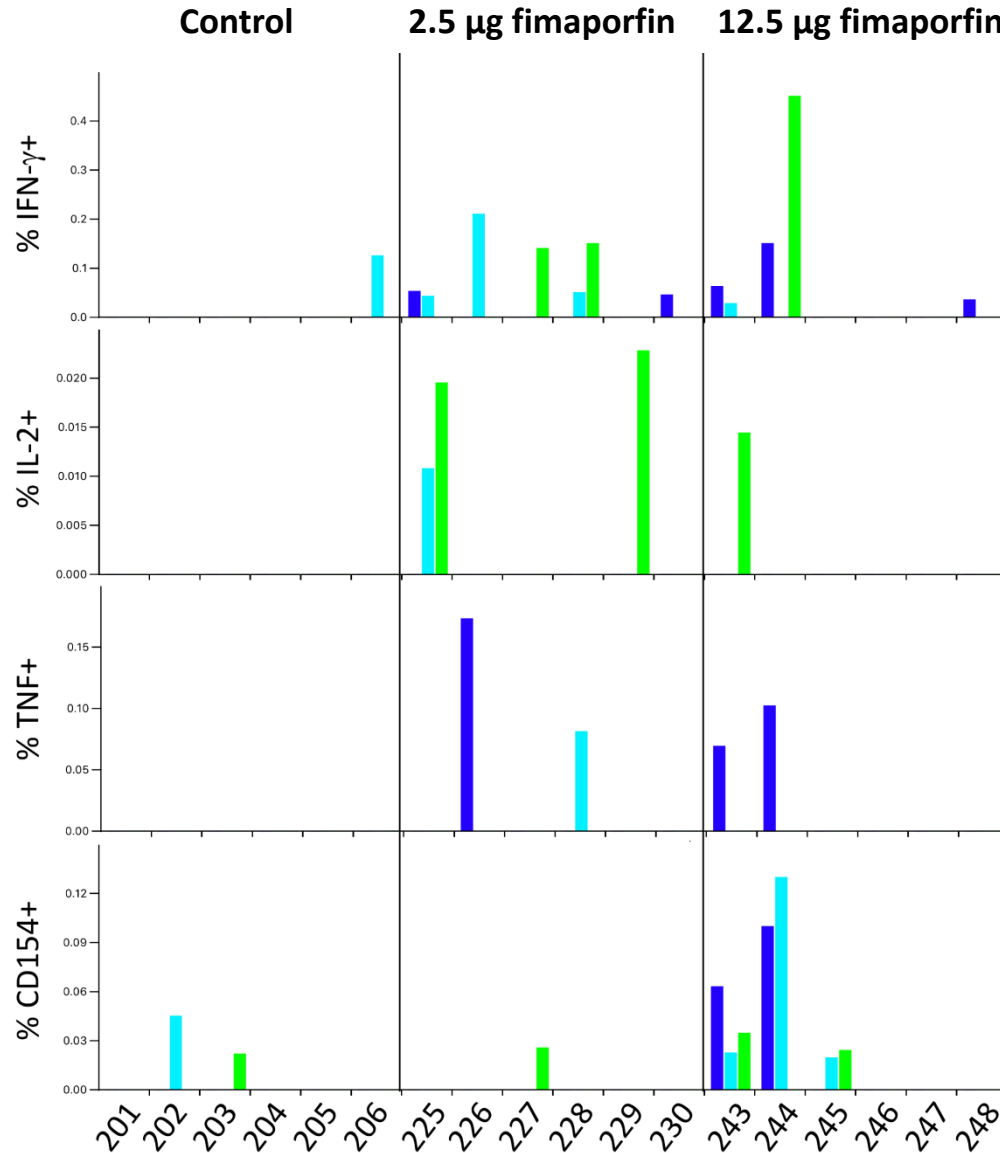


T-cell activation after PCI vaccination

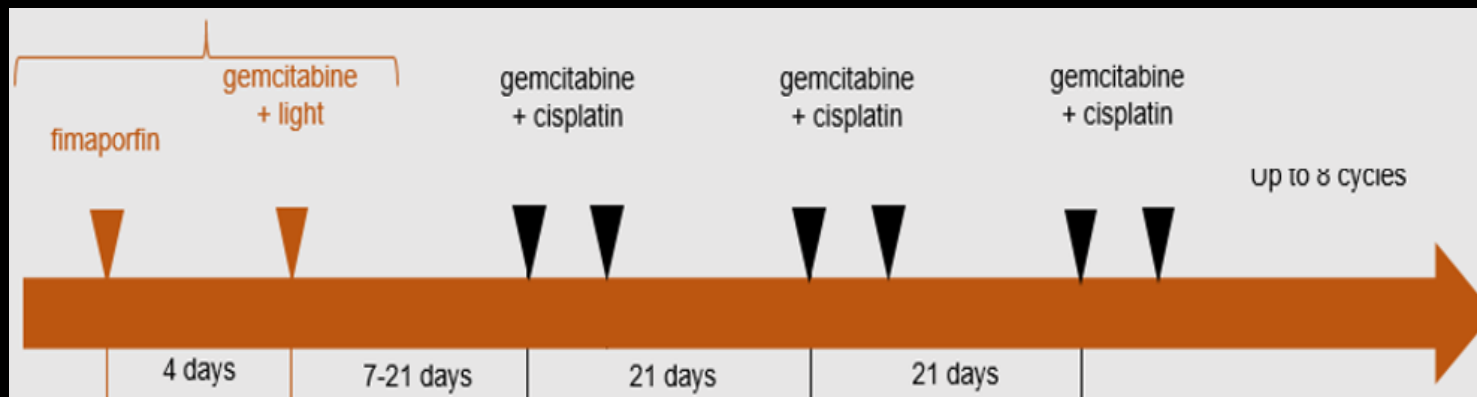
ELISpot responses against HPV16 E7 by cohorts and timepoint.

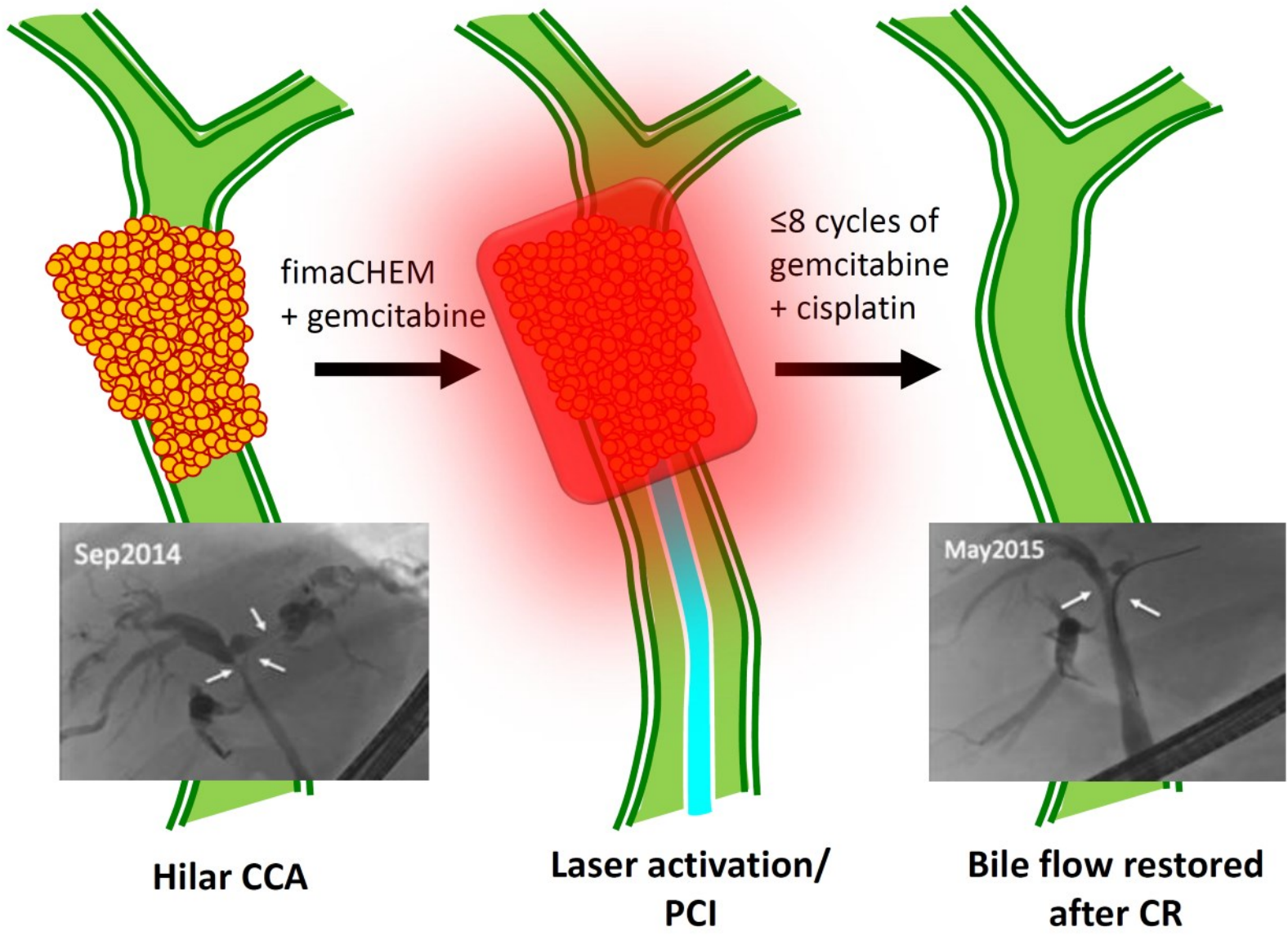


CD8+ T-cell responses to HPV16 E7 peptides

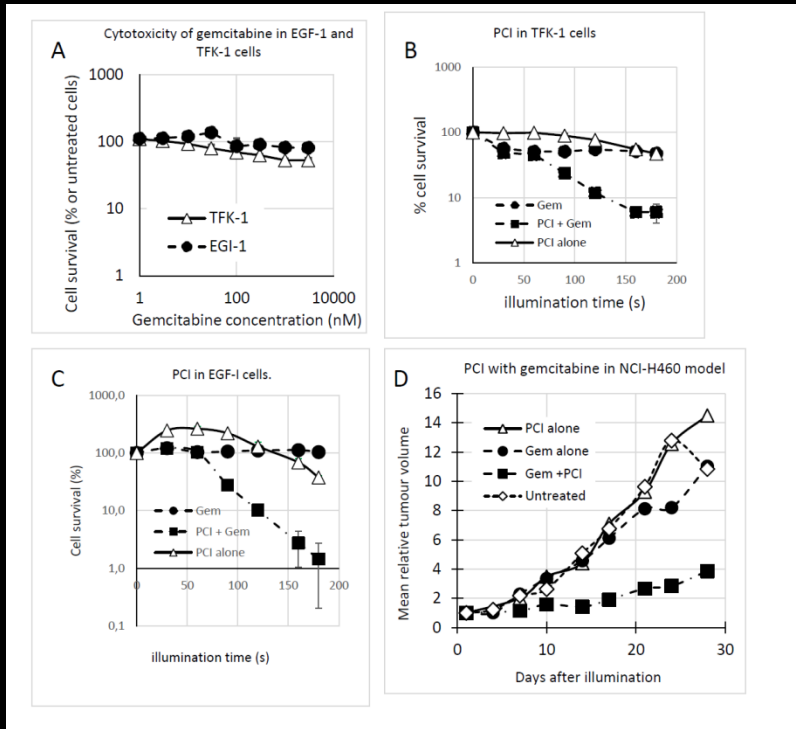


Safety and Efficacy of fimaporfin-induced Photochemical Internalization (PCI) of Gemcitabine followed by Gemcitabine/Cisplatin Chemotherapy in Patients with Locally Advanced Inoperable Cholangiocarcinomas

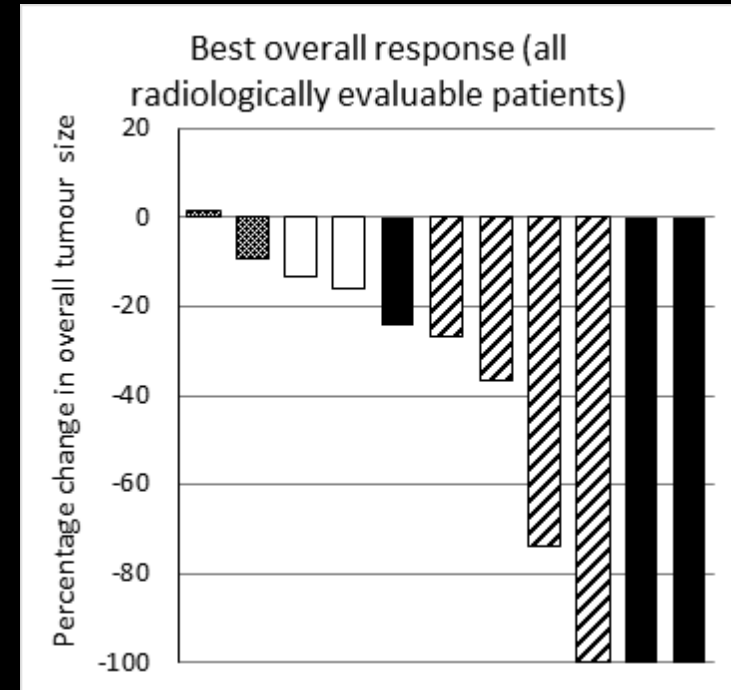




Preclinical results



Clinical results



Based on this , a pivotal world-wide Phase II is ongoing and recruiting

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PCI Treatment/Gemcitabine & Chemotherapy vs Chemotherapy Alone in Patients With Inoperable Extrahepatic Bile Duct Cancer (RELEASE)

ClinicalTrials.gov Identifier: NCT04099888

Recruitment Status: Recruiting
 First Posted: September 23, 2019
 Last Update Posted: October 9, 2020
 See [Contacts and Locations](#)

Sponsor:
 PCI Biotech AS

Information provided by (Responsible Party):
 PCI Biotech AS

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

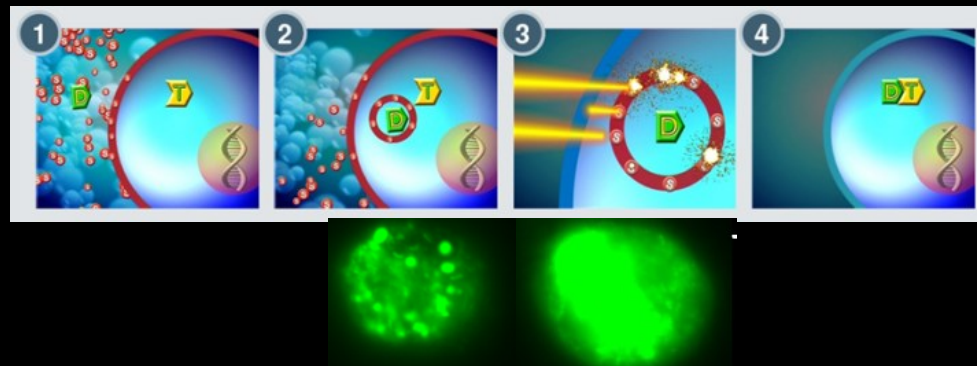
The PCI-based vaccination technology - SUMMARY

Preclinical:

- ▶ PCI enhances MHC class I antigen presentation by releasing antigens into the cytosol of antigen presenting cells
- ▶ PCI enhance CD8-cell immune responses > 100 times
- ▶ Can be used with both protein and peptide antigens

Clinical:

- ▶ Fimaporfin is already tested in clinical trials and has a favourable safety profile both for vaccination and cancer therapy



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