

# PHASE I STUDY WITH PHOTOCHEMICAL INTERNALISATION (PCI)– A NOVEL TECHNOLOGY FOR TREATMENT OF PERIHILAR CHOLANGIOCARCINOMA

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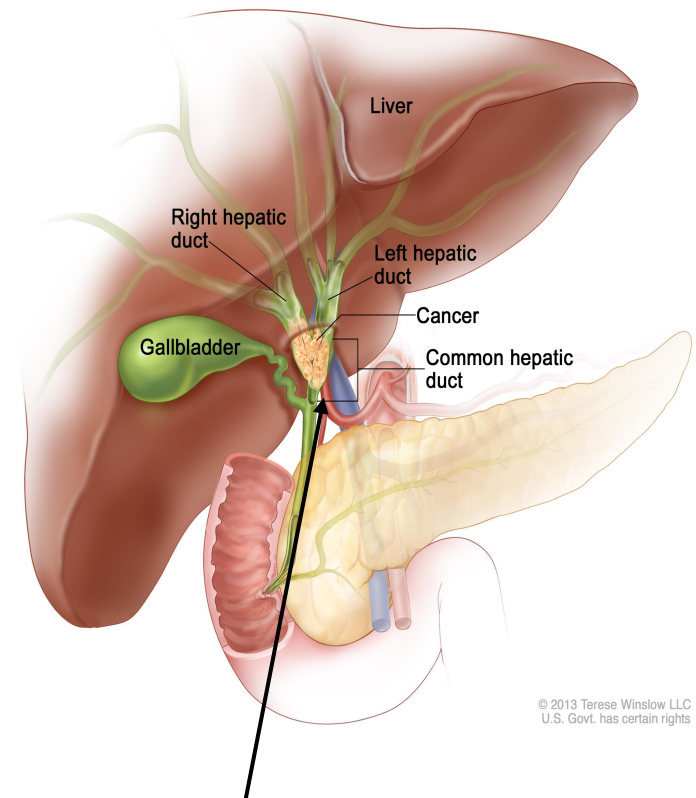
No conflicts of interest



## CHOLANGIOCARCINOMA (CCA)

- ▶ Malignant proliferation of cholangiocytes – the epithelial cells lining the biliary tree
- ▶ ‘Cholangiocarcinoma’ includes
  - Intrahepatic tumours (10%\*)
  - Perihilar tumours (60-70%\*)
  - Distal tumours (20-30%\*)
  - Differences in incidence, pathobiology and management
- ▶ Over 90% of CCA are adenocarcinomas

\* Bile duct cancer, Am Cancer Soc, 10/30/2013



*Perihilar bile duct cancer is the initial target for PCI treatment*



# CCA – CURRENT TREATMENT OPTIONS

- ▶ Yearly incidence of 1-2 per 100,000 in the western world (higher incidences in Asia)
- ▶ Five-year survival rate < 5%
  - ➔ 0% when inoperable – average approx. 12 months survival

## ▶ Current management

### ▪ **Surgery**

- Only potentially curative treatment for CCA.
- Less than 1/3 are resectable at presentation

### ▪ **Endoscopic treatment**

- Palliative endoscopic stenting
- Photodynamic therapy (PDT)

### ▪ **Chemotherapy**

- Most commonly gemcitabine and cisplatin (ABC02 trial)

### *Key components of PCI*

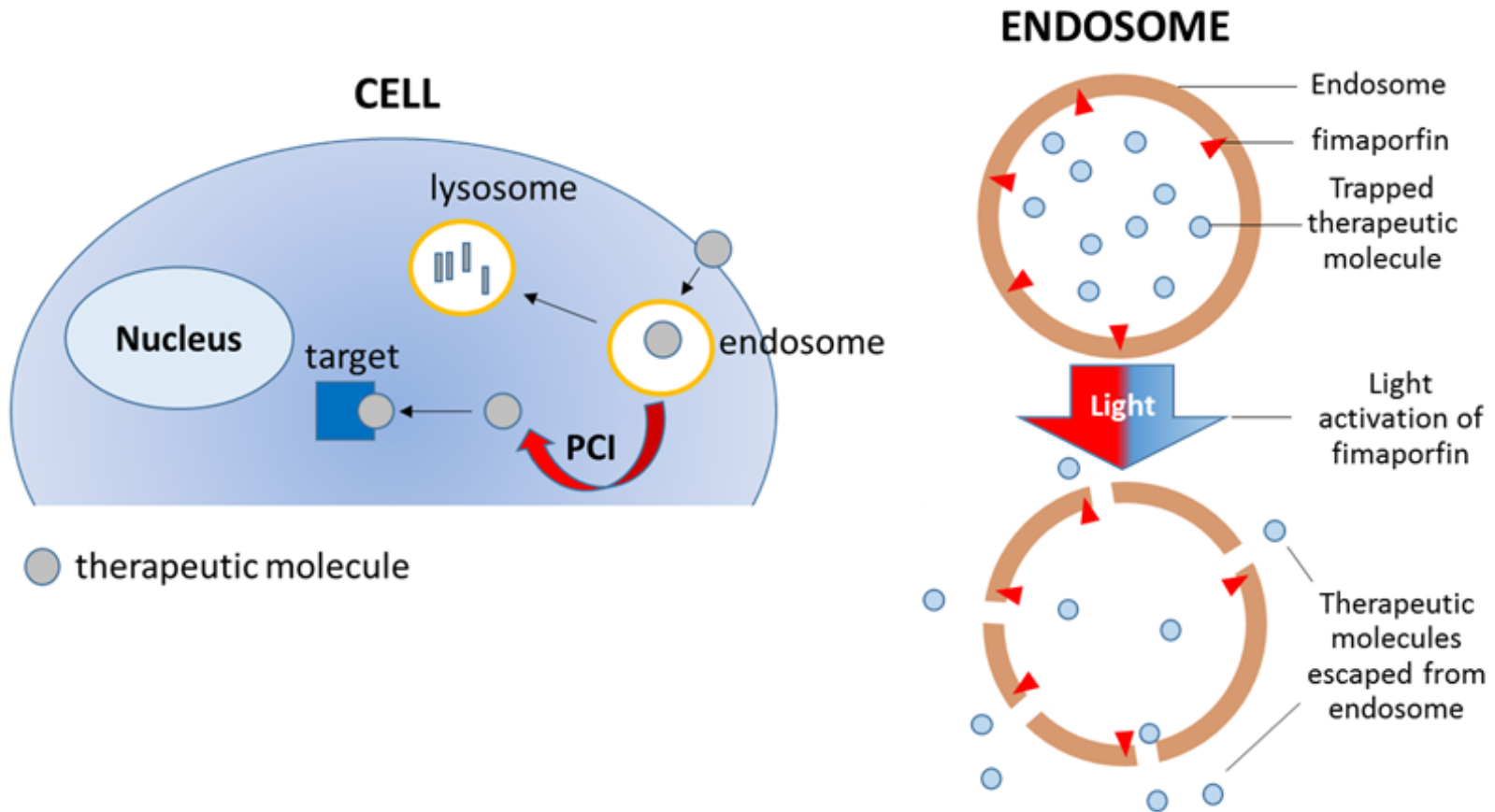
Targeted illumination is done using standard endoscopic procedure

Gemcitabine effect enhanced by PCI



# PHOTOCHEMICAL INTERNALISATION (PCI)

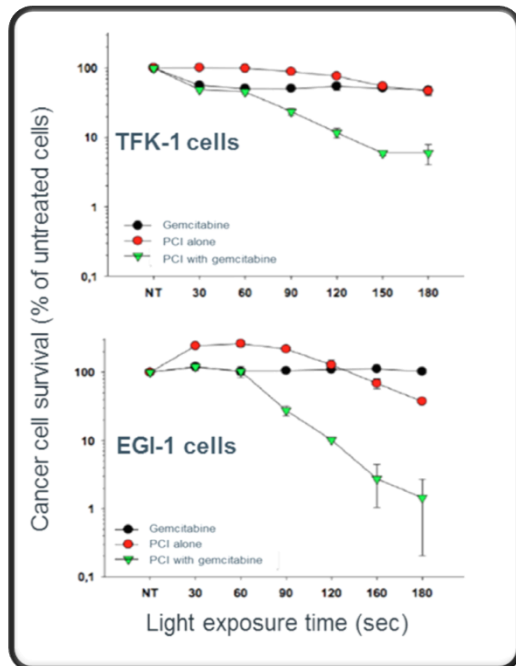
- ▶ Endosomal release triggered through illumination



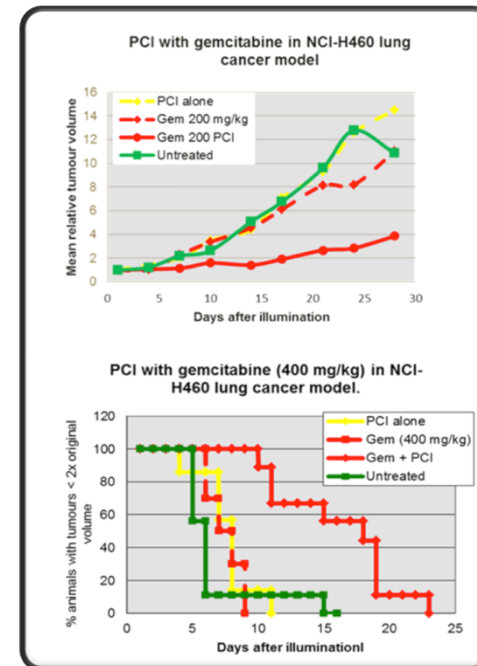
# PRE-CLINICAL DATA

Photochemical internalisation (PCI) enhances the effect of gemcitabine *in vitro* and *in vivo*

- ▶ PCI enhances the effect of gemcitabine in bile duct cancer cells *in vitro*



- ▶ PCI enhances the effect of gemcitabine in animal cancer *in vivo* model



# CHOLANGIOCARCINOMA (CCA)- CLINICAL PHASE I TRIAL

**A Phase I/II Dose Escalation Study to Assess the Safety, Tolerability and Efficacy of Amphinex<sup>®</sup>-induced Photochemical Internalisation (PCI) of Gemcitabine followed by Gemcitabine/Cisplatin Chemotherapy in Patients with Advanced Inoperable Cholangiocarcinomas**

## ► Phase I

- Determination of tolerable dose and safety profile of *Amphinex-induced PCI of gemcitabine followed by cis/gem chemotherapy*
  - PCI + up to 8 cycles of cis/gem
  - 3+3 dose escalation design (light and/or Amphinex (fimaporfin) dose)
  - Cohort review committee evaluates each cohort
  - DLT window until d21 of 1st cycle cis/gem
  - Endpoints: DLTs, safety (AEs, labs, physical findings), PK



## ▶ Phase I

### ▪ Dose escalation completed

- 11 European study sites (UK, Germany, Norway)
- 16 patients treated in 4 dose cohorts (4<sup>th</sup> cohort expanded)

- ▶ 11/16 patients completed 8 cycles of chemotherapy
- ▶ No mortality *on-study*
- ▶ No Dose Limiting Toxicity (DLT) observed
- ▶ Adverse Events seen during the DLT window
  - Photosensitivity reactions (mostly mild)
  - Abdominal pain
  - Cholangitis





# TRIAL RESULTS

## ► Response at target tumour level

### ► 6 months radiology data: Cohort III & IV – response at single lesion level

Measurable lesions	Lesion shrinkage		Stable lesion	Lesion growth
19 (total number of targets selected across the two independent readers)	17	12 (lesion not detectable)	1 (<20% reduction & <10% increase)	1 (>10% mass increase)
		5 (>20% mass reduction)		

- Independent radiological evaluation of all patient images (Cohort III and IV)
- Images evaluated separately by two expert radiologists
- ***Shrinkage of near 90% of selected target lesions, with more than 60% being undetectable at 6 months***

➤ *“Change in tumor size by RECIST correlates linearly with overall survival in Phase I oncology studies”*  
(analysis of 24 phase I studies) <sup>1</sup>

<sup>1</sup> Jain et al 2012 – JCO 30:2684–90



## ► 6 months radiology data: Cohort III & IV - (n=7 evaluable perihilar tumours)

RECIST	PD	SD	PR	CR
	2	1	2	2

PD: Progressive disease (>20% growth)

SD: Stable Disease

PR: Partial Response (>30% shrinkage)

CR: Complete Response (no visible tumour)

- Independent evaluation of patient images from Cohort III and IV per RECIST
- Images evaluated separately by two experts in bile duct cancer/cholangiocarcinoma
- **Response rate exceeding 50%** –  
far above expected results with standard treatment (Cis/Gem chemotherapy\*)

Valle J. et al.

N Engl J Med. 2010 Apr 8;362(14):1273-81

and personal communication



# CONCLUSIONS

- ▶ **PCI boosts the effect of gemcitabine locally in the bile duct**
- ▶ **Maintenance of biliary drainage is critical in this patient population  
survival benefit through local tumour control**
- ▶ **Phase-I includes low number of patients,  
nevertheless results indicate high objective tumor response rate**
- ▶ **Early indicators of efficacy using PCI treatment with fimaporfin and gemcitabine  
are encouraging**

