

Safe Harbour Statement

The following presentation may include predictions, estimates or other information that might be considered forward-looking. The statements regarding the surrounding world and future circumstances in this presentation reflect Cantargia's current thinking with respect to future events and financial performance. Prospective statements only express the assessments and assumptions the company makes at the time of the presentation. These statements are well-considered, but the audience should note that, as with all prospective assessments, they are associated with risks and uncertainties.



Agenda

Cantargia introduction Göran Forsberg

CANFOUR results Christer Svedman

CANFOUR clinical trial Lars Thorsson

Combination therapies David Liberg

Summary Göran Forsberg



CANO4 phase I clinical data at ESMO

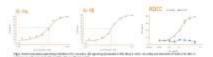
1172P

A first-in-class, first-in-human phase I/IIa trial of CAN04, targeting Interleukin-1 Receptor Accessory Protein (IL1RAP), in patients with solid tumors

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- RESULTS

Patient population

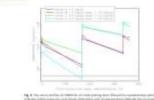
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CONCLUSIONS

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- CAN04 has generally been well tolerated
- 6 mg/kg is safe.
- **Encouraging biomarker results** already after two doses of **CAN04.**
- In a heavily pre-treated patient population, 5 of 13 patients (38%) had SD. One patient with **NSCLC** had SD for 6 months.

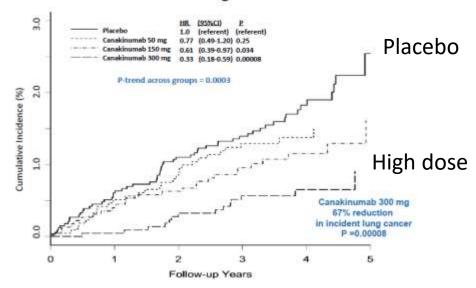


IL-1 blockade in cancer- Recent supportive clinical data

CANTOS trial

- Canakinumab (Novartis)
- Reduced lung cancer incidence by 67 % and death by 77 %.

CANTOS: Additional Non-Cardiovascular Clinical Benefits Incident Lung Cancer



- Clinical validation of IL-1 pathway
- Cantargia's CAN04 has broader MOA

Canakinumab phase 3 trials

Adjuvant NSCLC

After surgery, no mets, placebo control 1500 patients, recruitment ongoing Completion 2021/22

First line (CANOPY-1)

Untreated locally advanced/metastatic Combination Pembro/Platinum doublet 627 patients, start Dec 2018 Completion 2021/22

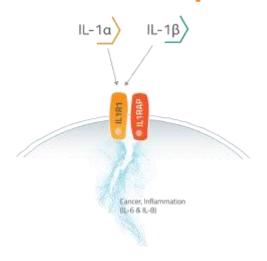
Second line metastatic (CANOPY-2)

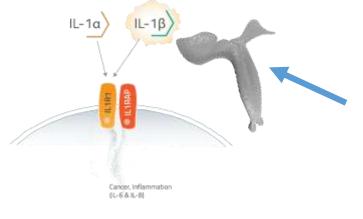
Previously treated loc adv/metastatic Combination Docetaxel 240 patients, start Dec 2018 Completion 2021



CAN04 (nidanilimab) vs Canakinumab

IL-1α





IL-1β

Canakinumab

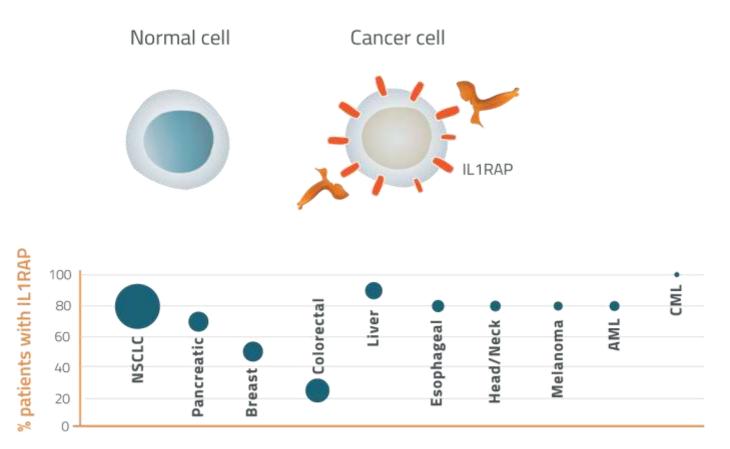
Antibody directed against one of the two IL-1 ligands, IL-1β

CAN04:

- Binds the common signaling receptor and counteracts both ligands
- Induce killing via the immune system (ADCC)



Medical need and IL1RAP



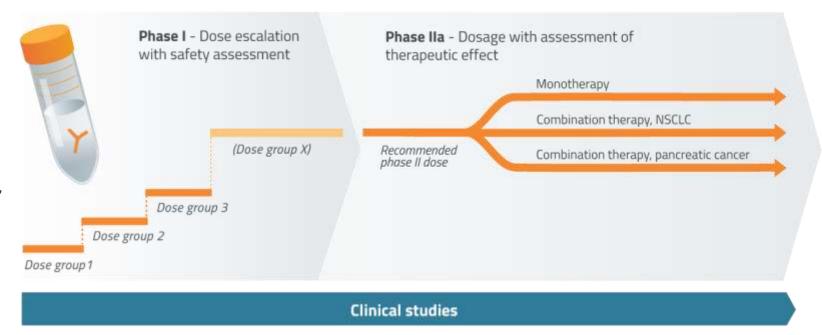
- Cantargia founded based on:
 - Discovery of IL1RAP on cancer cells
 - Antibodies against IL1RAP antitumor effects
 - Patents on antibody therapy against IL1RAP
- Primary indications. NSCLC and pancreatic cancer
- Biomarker studies ongoing, identify patients most likely to respond
- Opportunity to expand development in additional cancer forms



CANO4 – CANFOUR clinical trial

Phase I/IIa trial - NSCLC and pancreatic cancer

- Norway, Denmark, Netherlands and Belgium
- Well renowned centres (Jules Bordet, Brussels; Erasmus Rotterdam, NKI, Amsterdam; Rigshospitalet, Copenhagen; Radiumhospitalet, Oslo)
- 16 patients treated, good safety
 - NSCLC, pancreatic cancer, colon cancer, triple negative breast cancer
- Phase IIa: focused on NSCLC and pancreatic cancer (appr 20 centres)
 - Monotherapy
 - Combination with standard therapy
 - NSCLC Cisplatin/Gemcitabine
 - Pancreatic cancer Gemcitabine/nabpaclitaxel



Q4 2018 Early 2020



Cantargia at a glance

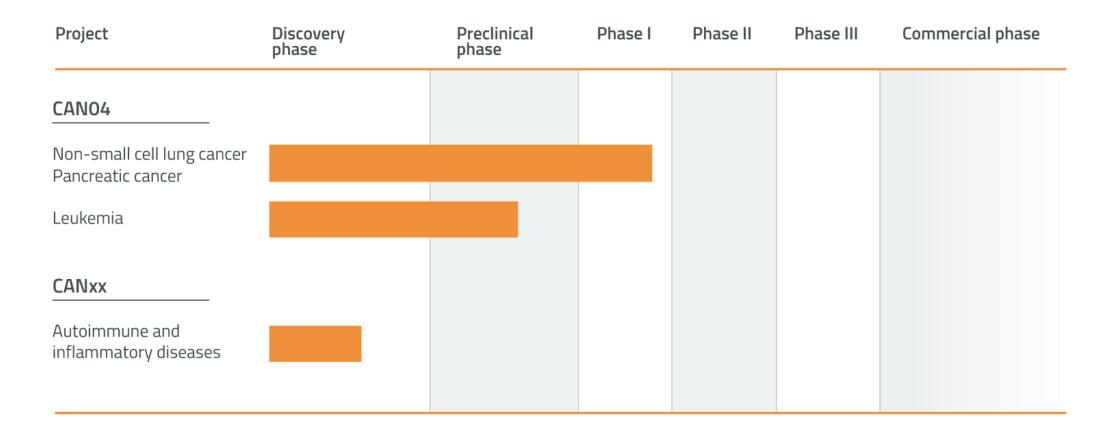
- Specialized in antibody therapy/immunology, with initial focus on oncology
- Granted IP therapeutic target IL1RAP and drug candidate
- Lead antibody CAN04 (nidanilimab) in clinical development
- Strong management team with proven track record in clinical development and business development
- Listed on Nasdaq Stockholm
- Approximately 5000 shareholders
- Based in Lund, Sweden

Financial highlights

- Share price: 19.90 SEK (2.22 USD), Oct 22, 2018
- Market cap: 1317 MSEK (147 MUSD), Oct 22, 2018
- Cash: 213 MSEK (23.3 MUSD), Jun 30 2018

Current owners (Sep 30, 2018)		
Sunstone	9.0%	
1st AP fund	6.9%	
Avanza Pension	5.2%	
4th AP fund	4.6%	
2nd AP fund	3.3%	
Öhman Bank S.A.	3.3%	
SEB S.A. clients	3.2%	
Mats Invest AB	2.0%	
Tibia konsult	1.9%	
Kudu AB	1.9 %	
Others	58.6%	

Cantargia pipeline





CANFOUR – ESMO poster

1172P

A first-in-class, first-in-human phase I/IIa trial of CAN04, targeting Interleukin-1 Receptor Accessory Protein (IL1RAP), in patients with solid tumors



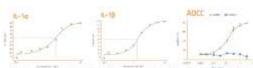
BACKGROUND

influentation has been advancedged as an important part of the development of tumors! interleakin-1 (it-1) is a assist "alasm" inflammatory cytokine upstream in the cytokine cascade and there is a robust body of evidence supporting that II-1 signaling is involved in career progression!. The relevance of targeting 6-1 has recently been highlighted by an exploratory analysis of the CANTOS study where partients treated with canalinemals in the highest dose are had a significantly reduced incidence of long career (HR 6.53, p-0.0001) and long career specific restality (HR 0.23, p-0.0000)³. Interbolin-1 receptor associated protein (0.19AP) is a co-recuptor of the IL-2 receptor (0.191) and is required for IL-1 signaling (Fig. 1). IL19AP is expressed in multiple bematitiogical and solid turner indications. Non-small cell long surcer (MSCIC) and partiriodic cancer (PCAC) represent key indications due to high supression of RIBAP (NSCIC 80% and PCAC 20%), high sernet residual resol and widorce supporting that R-L signaling is of relevance in those indications, not least as a resistance mechanism to

CANGE is a fully humanized artificity directed applied 0.00AP that in one climal readels potently inhibits it has and ti-15 and also triggers antibody dependent cytotrality (ADCC) (Fig. 2). The current ongoing CANFOLIR pinese. liftle study [MCT03267316] is designed to assess safety/interability of CANDA.



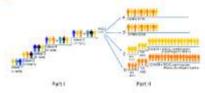
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The primary objective was to assess rafety (CTCAE v4.03) and toterability of weekly administration of CAMON in order to define the Maximum Telerated Dave (MTD)/Necosameroled Phase 2 Dove (NP2O). Patients with reliqued or refractory recovaried cell lung cancer, perconatic durtal adenocarcinoma, breast (TRBC) or colorectal (CRC) cancer were included in the initial part of the trial using a 3-1 done excalation design. Key eligibility criteria were ECDG (1), normal argan function and no bleeding disprijer or couplingstfu. Tutour responses were involved according to BEC every 8 works. Serven samples were obtained for pharmocolitectic evaluation and for assessment of sinulatory biomarkers of relevance for the mechanism of action (e.g. 8. 6.

Study design



Patient population

- Monatalia Spess to accordance to monate misted Sequence Criteria (MC) be computed conceptable (ET) or magnetic recommon imaging (MW) year, no more than it works pror to screening.
- At least 4 weeks since the last days of characteristic radiation therapy immunitarists, or supers, at least 6 weeks for framer which is Ensure to have delayed towards; of least it weeks toke treatment with bodgsc/largered therapies.
- Barless Conjunction Oncology brough (ECOC) performance status, CL.

National Programme of the Control of therapy or for which there is no standard therapy, CRC and TNSC on not allowed in second part of the trial.

- Subjects recoking any other investigational agents sturing or pust prior to (within 26 days of first study strug edministration) participation in this must.
- Clinical continues of an active second malignancy. hulgorts with a life reporture of 2 weeks
- Uncontrolled on agenthaest cardiovascular disease defined as New York Hoart Accession Classification III, or W.
- . Other tracked conditions that in the convent of the investments observable the subsect for inclusion

RESULTS

Patient population

May characteristics of the patient population are summarized in Table 1, Switcer subjects were excelled and There were 5 sincer failures across the four motest colours, (5-6 mg/kg). Falsons, were heavily pool-treated with a resear of £3 grow breas of thereby live as 1-11)



CANON has generally been well tolerated (Table 2 and 3). The most operation AC was infusion inteled maction (WA) (so Adm of all published will associated events with the infusion regulation in the first drive and combining within a few bocas. To reduce the risk of IFE, a greeing dose, promedication with ambistanines paracetariol and continuous colds and prolonged duration of infusion have been implemented for the first dose. A slight patient reprincipal on infusion resultion on the second dose, otherwise no influsion related reactions have been seen at later times. A dose lenting toxistly demography textropered that was reversible was seen in 127 patients at 0 mg/kg. Cohort 5 has recordly fewn withstail at 15 ing/kg. A magniture tolerated time has not set been reached

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Biomarkers

An extension biomarker analysis will be performed at the end of the study, intentin analysis of a unlect set of garanteens of relevance in serior showed a decrease versus baseline in 6-6 in (1 of 34 patients with a strong trend (prot.06) and a decrease in CRF in 9 of 11 patients (prot.04) after law dozes of CANOS, consistent with the CANOS made of action and supporting target engagement.

Of the patients that had received at least one (1) time of CANDA, 13 patients had everlable pre- and post-treatment assumment by imaging at the tale of data just off COLEP), New (C) patients (Afre) had chable decision (SD) by official it weeks follow up: NOCLC (1), CRC (6), and PEAK (1), Eight (5) patients had progressive thinks (PC). The patient with NOCLC hall 50 of 8 weeks.

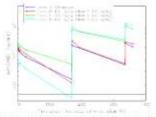


Fig. 1. This secure profites of CARDIA from an instancement does followed the represented does advantables includes instance higher registeries and desentables with revise stage before all though ma-formations are does not provide a finish and an employment and allowed or 47 personners.

CONCLUSIONS

- + CAMOA has generally been well tolerated, the most common treatment related AC is an infusion inlated resetting during the first infusion and receiving within a few hours, a side effect often observed with webbody therapy.
- + Engylig is sale and tolerable. MTD has not liven reached and the study is now enrolling patients in cohort 5 et 10 mg/kg
- Signature results support target organizated already after two down of CANOS.
- In a hourly pre-treated patient population, 5 of 13 patients (36%) that had received at least 1 does of CAMON had 50 by ERC. at 8 weeks follow up. One patient with NSCLC had 50 for 6 months.
- The next stop after the recommended phase if dose has been established will be to evaluate CWMM in a dose expansion. phase as repretherapy as well as is combination with standard of care therapy in the target indications MESS (15 and 24 Brief and PDRC (\$1" line) in separate treatment arms

References

- Females D-et al. Cell 2003 Nette M-et al. Ret Nomenat 2017
- Ballet Firt & James Street 2017 Wang et al. Gazers Res 2014
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Acknowledgements

In total of the mady team, the authors thent the patients and that facility for their participation in the blade.





CANFOUR – baseline characteristics

	Total		Total
Characteristics	(n=16)	Characteristics	(n=16)
Mean age, years (range)	63 (39-81)	ECOG PS, n (%)	
		0	12 (75)
		1	4 (25)
Male, n (%)	11 (69)		
Female, n (%)	5 (31)	HB (mmol/L),	7.6
	3 (82)	Median (range)	(6.0-10.0)
Indication, n (%)			
Colorectal cancer	9 (56)	LDH (U/L),	217
Non-small cell lung cancer	3 (19)	Median (range)	(162-475)
Pancreatic ductal adenocarcinoma	4 (25)		
Triple-negative breast cancer	0		
Lines of prior therapy*, n (%)		ALB (g/L),	41
• ≤2	5 (31)	Median (range)	(29-45)
• 3-5	9 (56)	(13.182)	(== :=)
• ≥6	2 (12)		

^{*} adjuvant/neo-adjuvant therapy was included as a line of therapy



CANFOUR – safety

- CAN04 has generally been well tolerated
- The most common AE was infusion related reaction (IRR) at the first dose resolving within a few hours
 - To reduce the risk of IRR, a priming dose, premedication with antihistamines, paracetamol and corticosteroids and prolonged duration of infusion have been implemented for the first dose.
- A single patient experienced an infusion reaction on the second dose, otherwise no infusion related reactions have been seen at later doses.
- Three patients with grade 3 events.
- Cohort 5 has recently been initiated at 10 mg/kg.
- A maximum tolerated dose has not yet been reached.



Infusion reactions (IRR)

Infusion related reactions are common with some of the most commonly used antibodies:¹

- 77% with rituximab,
- 61% with ofatumumab
- 15% with cetuximab



Annals of Oncology 28 (Supplement 4): Iv100-iv118, 2017 doi:10.1093/annonc/mdx216

CLINICAL PRACTICE GUIDELINES

Management of infusion reactions to systemic anticancer therapy: ESMO Clinical Practice Guidelines[†]

S. Roselló¹, I. Blasco¹, L. García Fabregat¹, A. Cervantes¹ & K. Jordan², on behalf of the ESMO Guidelines Committee^{*}



CANFOUR – treatment related adverse events (AE)

	Any toxicity	Grade 3
Treatment related AEs	n (of total)	n (of total)
Any	68 (13/16)	4 (3/16)
Nausea	8 (5/16)	0
Fatigue	7 (5/16)	0
Infusion related reaction	7 (7/16)	1 (1/16)
Pyrexia	6 (6/16)	0
Chills	4 (4/16)	0
Vomiting	4 (4/16)	0
Diarrhoea	3 (3/16)	0
Hypotension	2 (2/16)	0
Pruritus	2 (2/16)	0

With the exception of a single infusion related reaction at the 2nd dose, all infusion related reactions occured at the first dose.

Grade 3: one patient with infusion related reaction (cohort 3) one patient with hypokalemia in (cohort 4) one patient with low white blood cells count and neutropenia (cohort 4).

There were no treatment-related grade 4/5 AEs



For comparison: Immune checkpoint inhibitor safety profile in lung cancer

Study and regimens	Treatment related AEs grade 3-5
Keynote 024 ¹ Pembro vs pembro+chemo doublet	26 vs 53%
Keynote 042 ² Pembro vs Pembro+chemo (single agent)	18 vs 42%
IMPower 150 ³ Atezo+bev+chemo doublet vs chemo doublet	59% vs 50%
Keynote 189 ⁴ Pembro+ chemo doublet vs chemo doublet	67 vs 65%



CANFOUR – biomarkers

- An extensive biomarker analysis will be performed at the end of the study.
- Interim analysis of a select set of parameters of relevance in serum showed:
 - 1. a decrease versus baseline in IL-6 in 11 of 14 patients with a strong trend (p=0.06)
 - 2. a decrease in CRP in 9 of 11 patients (p=0.04) after two doses of CAN04 consistent with the mode of action and supporting target engagement

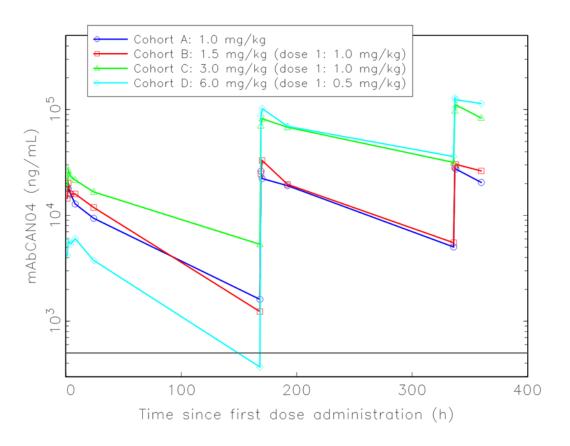


CANFOUR – clinical efficacy data

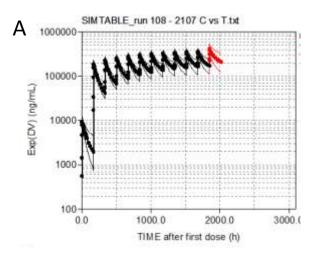
- Of the patients that received at least one (1) dose of CANO4, 13 patients had available pre- and post-treatment assessment by imaging at the time of data cut off (Oct 5th).
- Five (5) patients (38%) had stable disease (SD) by irRC at 8 weeks follow up: non-small cell lung cancer (1), colorectal cancer (3), and pancreatic cancer (1). 8 patients had progressive disease. 1 pt with lung cancer had SD at 6 months.

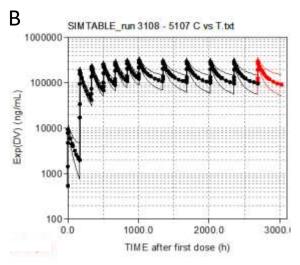


CANFOUR – cohort 1-4 - PK



Individual time-plasma profiles on log-lin scale for mAbCAN04





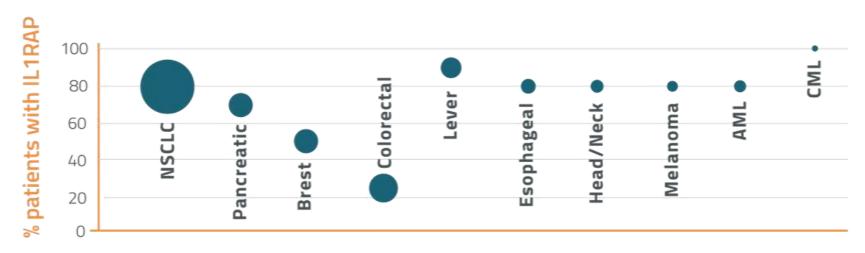
Predicted serum concentration of CAN04 vs time curves in human

Predicted serum concentration of CAN04 vs time curves in human illustrating the 5th, 50th, and 95th percentiles of the median in 2000 simulated studies of 12 patients after an initial priming dose of 0.5 mg/kg, followed by 5 weekly (Q1W) doses of 10 mg/kg, followed by 6 doses of CAN04 (10 mg/kg) weekly (**A**) or every second week (Q2W) (**B**).

CANFOUR - CONCLUSIONS

- CANO4 has generally been well tolerated, the most common treatment related AE is an infusion related reaction during the first infusion and resolving within a few hours, a side effect often observed with antibody therapy.
- 6 mg/kg is safe and tolerable. MTD has not been reached and the study is now enrolling patients in cohort 5 at 10 mg/kg
- Biomarker results support target engagement already after 2 doses of CAN04 (week 3)
- In a heavily pre-treated patient population, 5 of 13 patients (38%) that had received at least 1 dose of CAN04 had SD by irRC at 8 weeks follow up. One patient with NSCLC had SD for 6 months.
- The next step after the recommended phase II dose has been established will be to evaluate CANO4 in a dose expansion phase as monotherapy as well as in combination with standard of care therapy in the target indications NSCLC (1st and 2nd line) and PDAC (1st line) in separate treatment arms

NSCLC and pancreatic cancer: our target indications in combination with chemotherapy

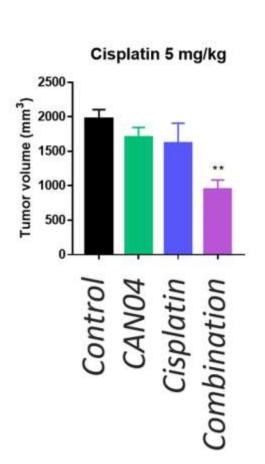


IL1RAP expression and size of indications

1st and 2nd line NSCLC and 1st line pancreatic cancer represents significant opportunities with high unmet need



CANO4 in combination with Cisplatin is superior to either agent alone and less toxic in pre-clinical models



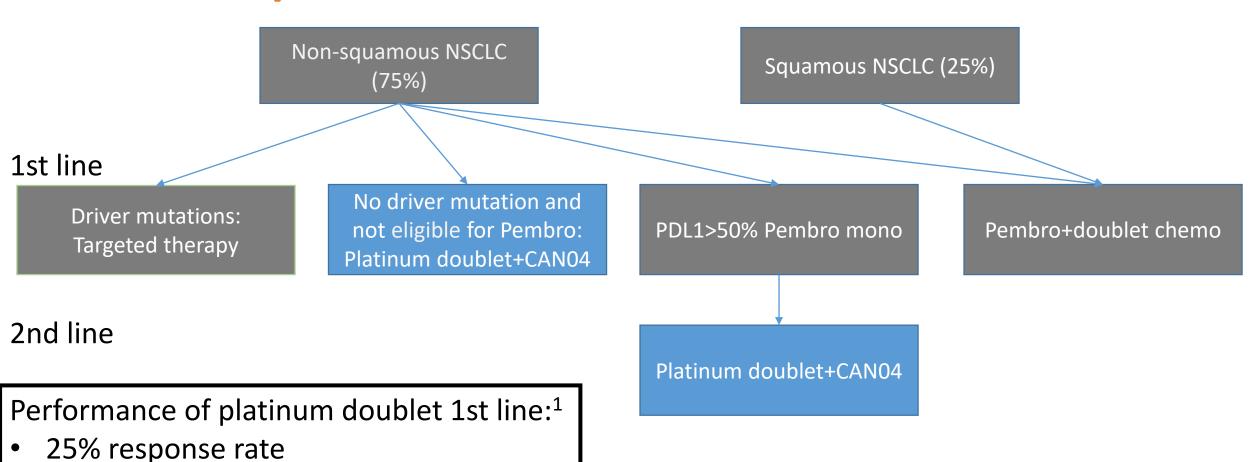
	Control	CAN04	Cisplatin	Combination
Animals withdrawn	20 % (Tumor)	0 %	50 % (Toxicity)	20 % (Toxicity)
Tumor reduction	N/A	14%	18%	52 %
Comment	Highest tumor burden	Best safety	Highest toxicity	Superior efficacy and reduced toxicity

Combination CAN04/Cisplatin superior to individual agents

- Reduction in severe toxicity
- Increased efficacy



Positioning of CAN04 in NSCLC (metastatic disease) in CANFOUR





progression free survival: 5-6 months

Positioning of CAN04 in pancreatic cancer (locally advanced or metastatic) in CANFOUR

1st line

Gemcitabine+nab-paclitaxel+CANO4

FOLFIRINOX

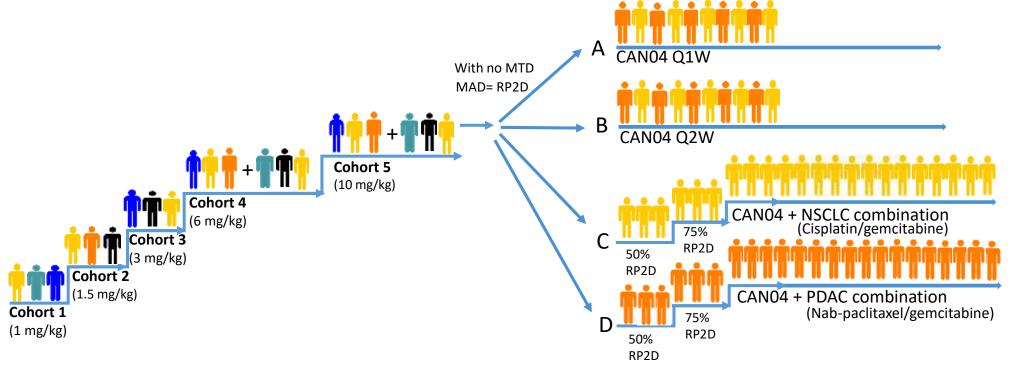
Gemcitabine (very frail patients)

Performance gemcitabine+ nab pactlitaxel 1st line:1

- 25% response rate
- progression free survival: 5 months



CANFOUR – study design



Part I Part II



CANFOUR

An open label, dose escalation followed by dose expansion, safety and tolerability trial of CAN04, a fully humanized monoclonal antibody against IL1RAP, in subjects with solid malignant tumors.

Primary Objective	 Part I To define the MTD or RP2D of CAN04, given Q1W in subjects with relapsed or refractory NSCLC, PDAC, TNBC or CRC. Part II To determine the safety and tolerability of CAN04 in subjects with NSCLC or PDAC tumors, when given as monotherapy or in combination with standard
	chemotherapy regimen.

Secondary Objectives

- To assess pharmacokinetic (PK) parameters of CAN04.
- To assess anti-drug antibody (ADA) formation against CAN04.
- To determine preliminary signs of clinical efficacy of CAN04 as a single agent.

Additional secondary objectives for Part II

- To assess health-related Quality of Life (QoL)
- To determine preliminary signs of clinical efficacy of CAN04 when given in combination with standard chemotherapy regimen

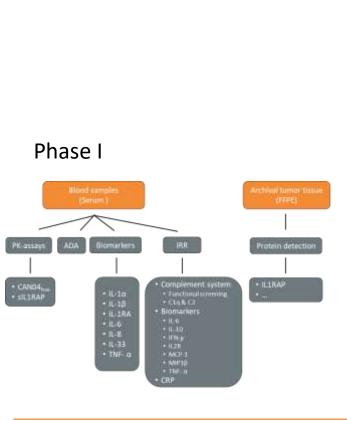


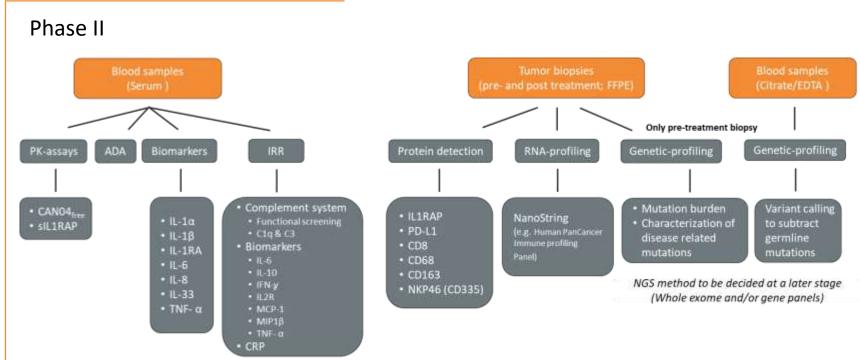
CANFOUR – additional assessments

Endpoint	Assessment			
Secondary endpoints	 Pharmacokinetics, including sIL1RAP Anti-drug antibodies (ADA) Preliminary signs of efficacy (ORR, DoR, PFS, OS) Additional endpoint for Part II: Health-related QoL (EORTC QLQ C30) 			
Exploratory	 IL1RAP expression and other disease-related, inflammatory, immune or microenvironment-related biomarkers (protein, RNA, genomic or other in tumor tissue Part I – archival tumor tissue Part II – paired pre- and during/post treatment biopsies Other disease-related, inflammatory, immune or microenvironment-related emerging biomarkers in circulation Serum levels of CRP Volumetric assessment of tumor size 			
Evaluation of IRRs	Complement factors, cytokines and CRP			



CANFOUR -Molecular profiling of tumors and serum samples







CANFOUR

Part I

Principal Investigator: Professor Ahmad Awada Jules Bordet Institute, Brussels, Belgium

Belgium

Institut Jules Bordet, Brussels

Denmark

Rigshospitalet, Copenhagen

The Netherlands

Netherlands Cancer Institute, Amsterdam Erasmus MC, Rotterdam

Norway

Oslo University Hospital, Radiumhospitalet, Oslo



Part II

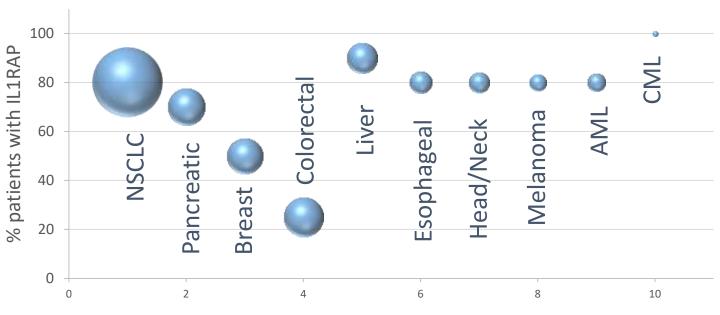
- Austria
- Belgium
- Denmark
- Germany
- The Netherlands
- Norway
- Sweden



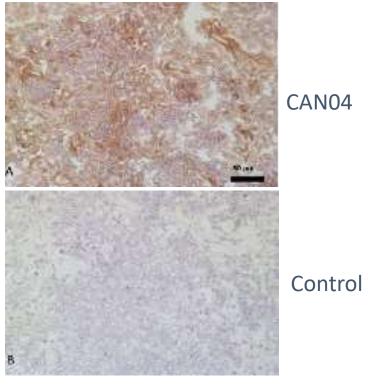
Tumor inflammation – key to cancer features

Intrinsic pathway Genome instability Tumor-promoting and mutation inflammation

IL1RAP is highly expressed in several cancers



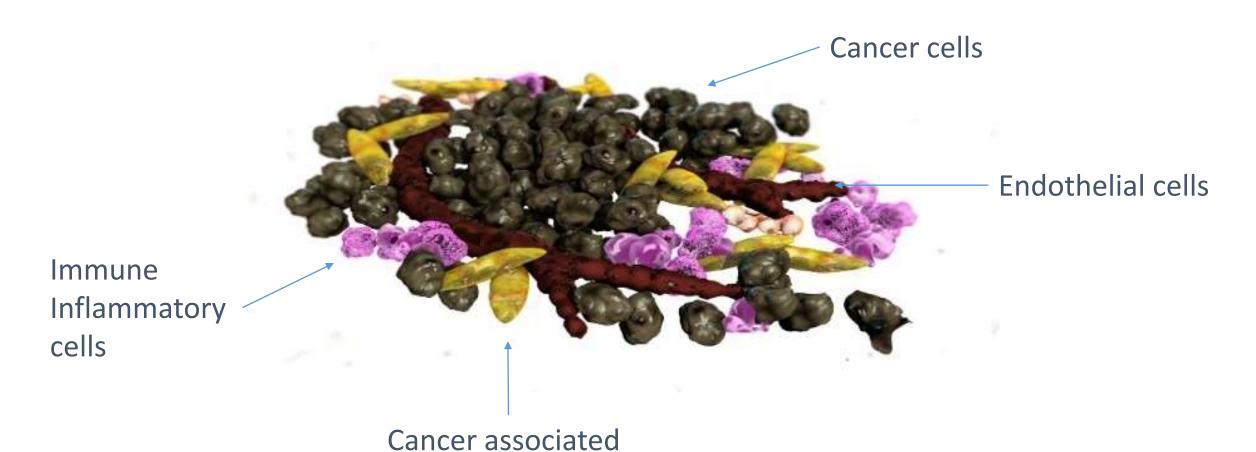
Size of each indication corresponds to annual deaths in USA



Pancreatic cancer

Targeting the tumor microenvironment

fibroblasts

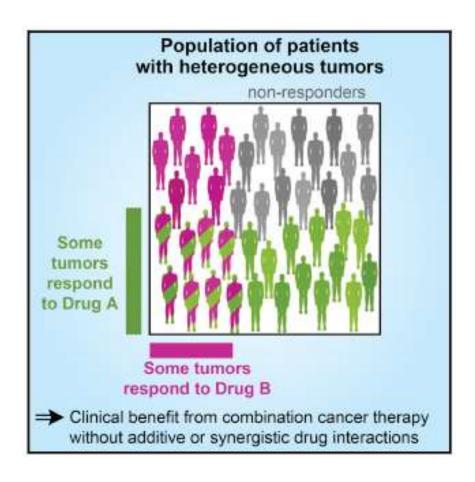


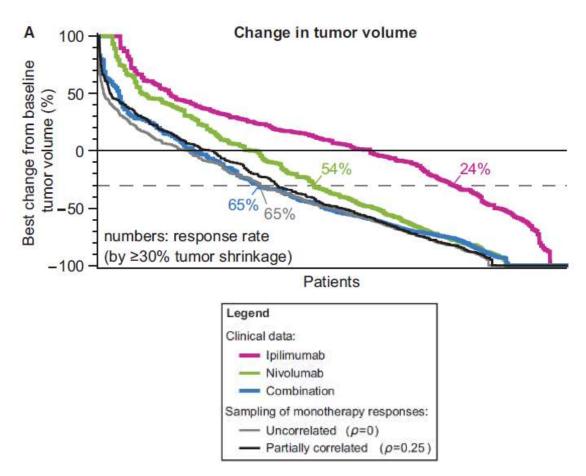
Combination therapy

- Synergistic effects: 1 + 1 = 3
- Additive effects: 1 + 1 = 2
- Variability effects: 1 + 1 = 1,5



Combination therapy







Combination therapy

- Synergistic effects: 1 + 1 = 3
- Additive effects: 1 + 1 = 2
- Variability effects: 1 + 1 = 1,5



IL-1 and resistance to therapy

Interleukin-1 blockade overcomes erlotinib resistance in head and neck squamous cell carcinoma

Aditya Stanam^{1,2}, Katherine N. Gibson-Corley^{2,5,6}, Laurie Love-Homan², Nnamdi Ihejirika3, Andrean L. Simons1,2,4,5,6

[CANCER RESEARCH 62, 910-916, February 1, 2002]

Autocrine Production of Interleukin 1B Confers Constitutive Nuclear Factor &B

Activity and Chemoresistance i A Novel Role for the Interleukin-1 Receptor Axis in

Resistance to Anti-EGFR Therapy

Alexander Arlt,2 Jens Vorndamm,2 Susanne Heiner Schäfer

Mattia Lauriola 1,2,*

IRAK1 is a therapeutic target that drives preast

cancer Neutrophil-Derived IL-1β Impairs the Efficacy

Zhen Ning Wee of NF-kB Inhibitors against Lung Cancer Puay Leng Lee1

Dave S.B. Hoon Allyson G. McLoed, Taylor P. Sherrill, Dong-Sheng Cheng, Wei Han, Jamie A. Saxon, Linda A. Gleaves, 2 Pingsheng Wu,³ Vasiliy V. Polosukhin,² Michael Karin,⁴ Fiona E. Yull,^{1,5} Georgios T. Stathopoulos,^{2,6,7} Constitutive Vassilis Georgoulias, 8 Rinat Zaynagetdinov, 2,11,* and Timothy S. Blackwell 1,2,5,9,10,11

Prognosis and Chemoresistance in Pancreatic Ductal Adenocarcinoma

Daoxiang Zhang¹, Lin Li¹, Hongmei Jiang¹, Brett L. Knolhoff¹, Albert C. Lockhart¹, Andrea Wang-Gillam¹, David G. DeNardo¹, Marianna B. Ruzinova², and Kian-Huat Lim¹ Serum levels of IL-6 and IL-1 β can predict the efficacy of gemcitabine in patients with advanced pancreatic cancer

S Mitsunaga*1,2, M Ikeda1, S Shimizu1, I Ohno1, J Furuse3, M Inagaki4, S Higashi5, H Kato5, K Terao6 and A Ochiai2

Valerio Gelfo 1,2,†, Martina Mazzeschi 1,†, Giada Grilli 1, Moshit Lindze Chemotherapy-triggered cathepsin B release in Gabriele D'Uva 60, Balázs Győrffy 7,8, Andrea Ardizzoni 1, Yosef Yarden myeloid-derived suppressor cells activates the Nlrp3 inflammasome and promotes tumor growth

> Mélanie Bruchard^{1,2,8}, Grégoire Mignot^{1,2,8}, Valentin Derangère^{1,2}, Fanny Chalmin^{1,2}, Angélique Chevriaux^{1,3}, an1,2, Wilfrid Boireau4, Benoit Simon4, Bernhard Ryffel5, Jean Louis Connat6, los7, François Martin1,2, Cédric Rébé1-3, Lionel Apetoh1-3,8 & François Ghiringhelli1-3,8

ory cytokines defines resistance of inhibitors

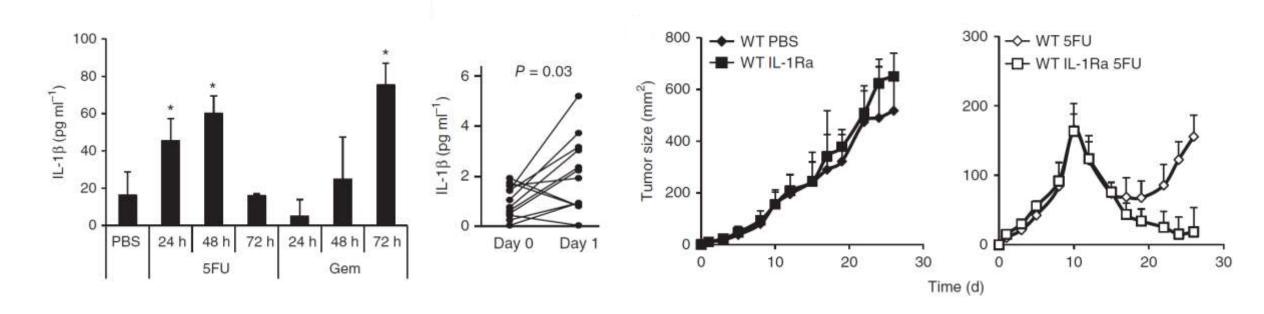
Maria Teresa Rodia^{1,*}, Michela Pucci¹, Massimiliano Dall'Ora¹, 4, Rossella Solmi1, Lee Roth5, Moshit Lindzen5, Massimiliano a Bertotti⁶, Elisabetta Caramelli¹, Pier-Luigi Lollini¹, Livio Trusolino⁶, Fabriele D'Uva^{7,**}, Mattia Lauriola^{1,2,**}



IL-1 and resistance to therapy, via MDSC

Gemcitabine and 5FU induce IL-1 release by MDSC

IL-1 blockade counters chemoresistance

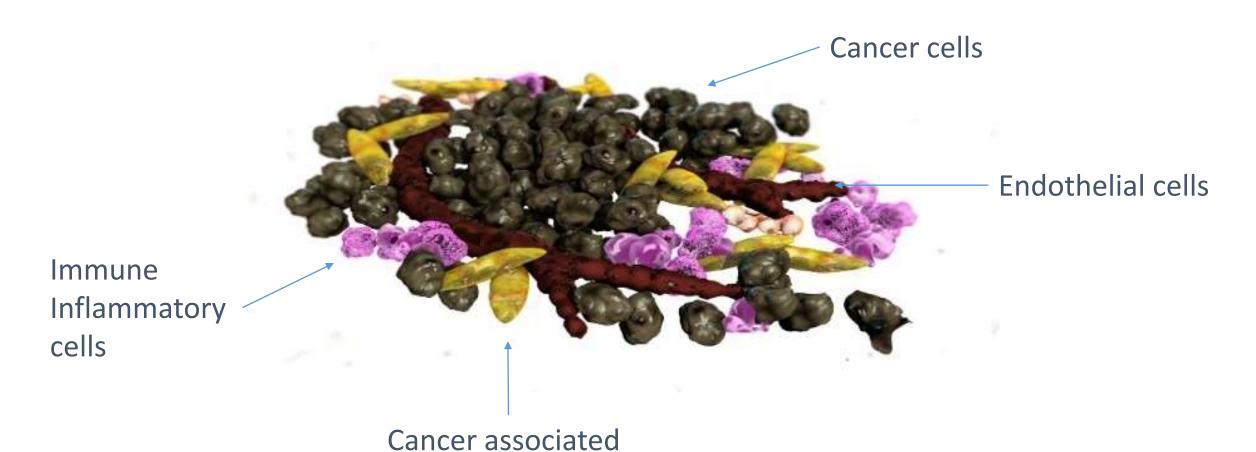


Gemcitabine and 5FU triggers IL-1 in tumor associated myeloid cells (Myeloid Derived Suppressor Cells) that counteract therapeutic effects



Targeting the tumor microenvironment

fibroblasts



Pancreatic ductal adenocarcinoma (PDAC)

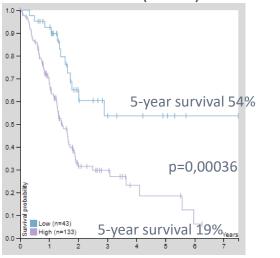
Propensity to metastasize, resistance to chemo- and radiotherapy, 5-year survival < 6%

KRAS mutated (75-90%)

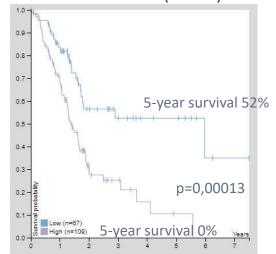


Constitutive NFkB activation

KRAS mRNA (TCGA) vs survival

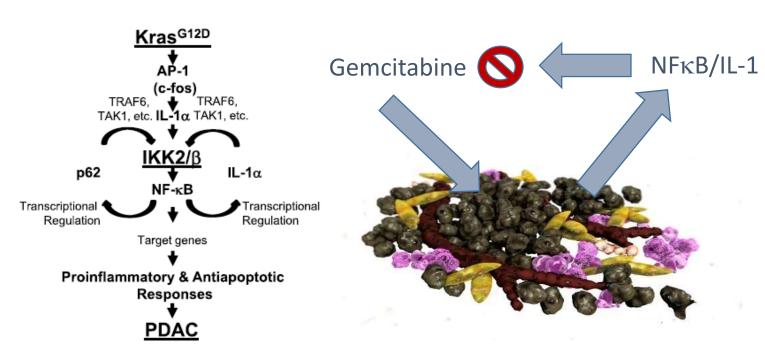


IL1RAP mRNA (TCGA) vs survival



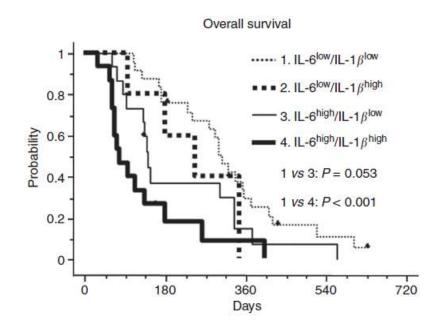


Pancreatic ductal adenocarcinoma (PDAC)



Ling et.al, KRAS^{G12D}-Induced IKK2/ β /NF- κ B Activation by IL-1 α and p62 Feedforward Loops is Required for Development of Pancreatic Ductal Adenocarcinoma, Cancer Cell 2012 Zhuang et.al; IL1 Receptor Antagonist Inhibits Pancreatic Cancer Growth by Abrogating NF-kB Activation, Clinical Cancer Res 2016

Zhang et.al; Constitutive IRAK4 Activation Underlies Poor Prognosis and Chemoresistance in Pancreatic Ductal Adenocarcinoma, Clinical Cancer Res 2017



Mitsanuga et.al; Serum levels of IL-6 and IL-1 β can predict the efficacy of gemcitabine in patients with advanced pancreatic cancer, Br J Cancer 2013



IL-1 combinations in pancreatic cancer

Treatment:

MABp1 (anti-IL1 α mAb) in combination with Onivyde® (Irinotecane liposome injection) and 5-fluorouracil/folinic acid

Objectives:

Phase I single arm trial to evaluate MTD, safety and tolerability.

Secondary measures:

- LBM
- Weight stability
- Levels of systemic inflammation

Patients: Pancreatic cancer and cachexia

Size: N=16 Regimen: Q2W

Treatment:

Anakinra (IL1-RA) in combination with gemcitabine, nab-paclitaxel and cisplatin

Objectives:

Pilot study to evaluate improved survival (DFS) by the addition of anakinra to chemotherapy combo.

Secondary measures:

- Overall survival (OS)
- Quality of life (QoL)
- Safety and tolerability

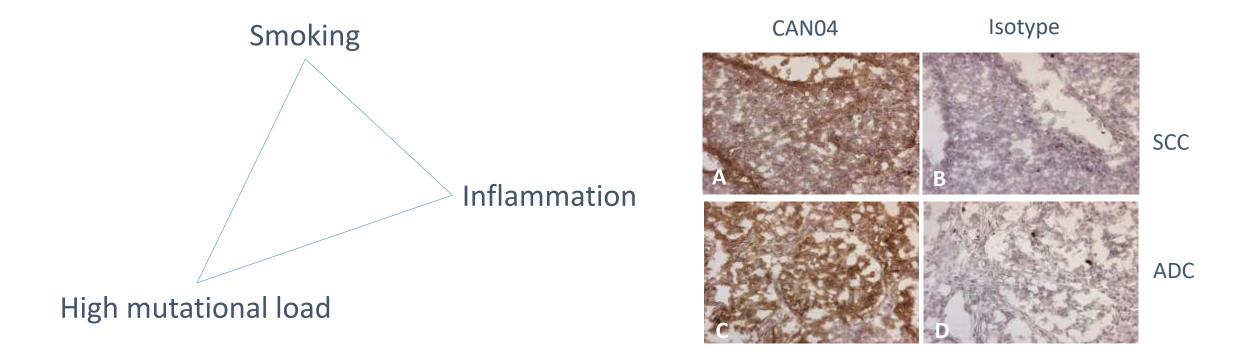
Patients: Pancreatic cancer

Size: N=16

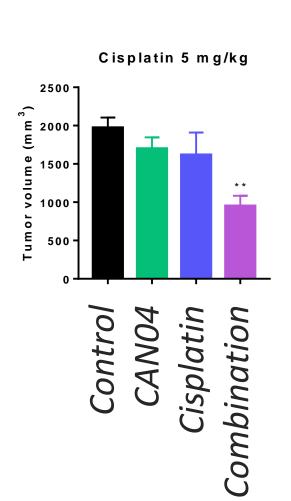
Regimen: Day 1, 8 and 21 cycle – 6 cycles



Non-small cell lung cancer (NSCLC)



CANO4 in combination with Cisplatin is superior to either agent alone and less toxic in pre-clinical models



	Control	CAN04	Cisplatin	Combination
Animals withdrawn	20 % (Tumor)	0 %	50 % (Toxicity)	20 % (Toxicity)
Tumor reduction	N/A	14%	18%	52 %
Comment	Highest tumor burden	Best safety	Highest toxicity	Superior efficacy and reduced toxicity

Combination CAN04/Cisplatin superior to individual agents

- Reduction in severe toxicity
- Increased efficacy

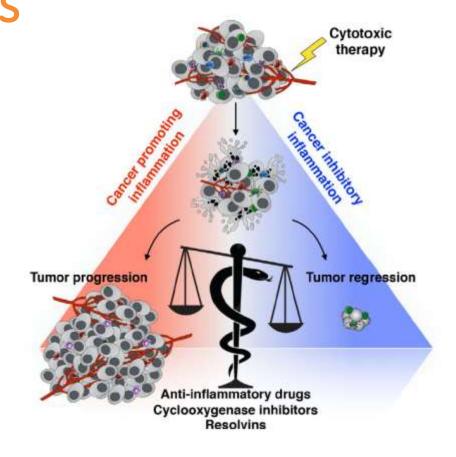


Summary

- Tumor inflammation contributes to many of the hallmarks of cancer, is required for tumor development and contributes to resistance to therapy
- IL-1 is involved in tumor growth, metastasis and resistance to therapy
- Therapy resistance can be cancer cell intrinsic or via cells in the TME
- Evidence support the relevance of targeting IL1 in combination with Gemcitabine in PDAC
- Internal preclinical data provides strong support for combining CAN04 with cisplatin in NSCLC



Good vs bad inflammation – checkpoint inhibitor combinations





Esophagus SCLC Gastric/GEJ Mp TG-02 区 LCL-161 • FOLFOX PD-(L)1 combinations RCC M ramuci Melanoma 🗵 panobinostat 🗵 canakinumeb dsP+5-FU ⊕ ramuci ▼ trametinib ⊠ CIM-112 # ipi + citarinostat ⊠ everolimus ⊠ EGF-816 • bevaci+FOLFOX ₩ PT-2385 # ini+vedolizumah ▼ regorafenib in development trilaciclib M x-4P001 M cavatak # NEOPV-01 • 5-FU/cape+bevaci / ● RG-7461+bevact / +carbo? ₩ TAS-102 ₩ dar ID pegIFN alfa-2b * savolitinib ID crizotinib # rova-T bevaci
 ALX-148 10 PV-10 H NKTR-214 H dorgenmeltucel-L ₩ NKTR-214 TO IMM-101 TO trametinib TO ARRY-382 # CB-839 10 CRS-207 ₩ x-4P001 ₩ 8MS-986026 10 CC-486 # ipi + cobimetinib ☑ LCL-161 ☑ EGF-816 nargetuximab TO getitinib TO IMM-101 • carboP+pac ● IFN alfa-2b ■ PD-0360324 ID ONCOS-102+cyclop ∺ omaveloxolone ∺ indoximo ⊠ cisP+gem M erlotinib M ARRY-382 ⊠ cisP+pemetrexed M entinostat # tivozanib / M Ad/MAGEA3 + MG1-MAGEA3 X LAG-525 IX LAG-525 € O vemurafenib 10 dabrafenib 🗵 LAG-525 treme + etoposide ca bozantinib/ To entinostat To acalabrutinib 器 erlotinib 器 CV-301 器 erlotinib 器 CV-301 器 dasatinib 器 ipi+citarinostat 3€ tucidinostat
3€ mocetinostat
9€ galunisertib 9€ BMS-986016 # AZD-4635 # MEDI-0562 ⊕ olaparib ⊕ treme+AZD-9150 ⊕ epaca +carboP / ID lenvatinib ID carboP+pac/nab-pac # CB-839 ₩ ipi + platinum doublet chemo # dam 舞 SOX 舞 ipi / ● bevard 形 clsP/carboP+pemetrexed ₩ epaca+gem+nab-pac ₩ 8MS-986148/ # sitravatinib ⊕ ramuci ₩ BM5-986179 ₩ veliparib+carboP+pac/pemetrexed ₩ ipi ₩ epaca+mFOLFOX6/ monalizumah # EGF-816 ₩ ceritinib ₩ beward ₩ crizotinib ₽ AZD-6738 ₩ ipi+INCAGN-1876 ₩ ipi+cobjmetinib ₩ epaca # mogamulizumab ₩ APX-005M ● NKTR-214 Dureme+chemo ≋ipi ≋ipi+ # selumetinib+treme ∺ capmatinib + nab-pac ___ ⊕ treme ⊕ osimertinib emo • carboP÷pac/nab-pac ± selumetinib treme +chemo abemaciclib ramud # 8MS-986178 # napabucasin # lirilumah • alectinib 10 ublitudinab + TGR-1202 10 Ti-061 merestinib ₩ INCB-1158 # elotuzumab+pom+de# pom+dex ₩ JTX-2011 ₩ mogamulizumab ☐ REGN-1979 M GSK-3377794 M G100 M epaca ₩ varlilumab ₩ dara ₩ INCAGN-1949 # brent ve dotte # denenicokin # RRX-001 # BMS-986205+ipi # ipi+INCAGN-1949 ₩ ibrutinib ₩ epaca # ONO-4578 ₩ TAK-659 III) azacitidine+epaca III) amcasertib ₩ BMS-988014 10) AFM-13 X GWN-32 ☑ decitabine + MBG-453 m pac m nab-pac ⊕ benda+ritux # galunisertib ⊠ GWN-323 | 10 epaca+carboP+pac | 10 AMG-820 | 10 ARRY-382 ⊕ cc-486 ⊕ len+R-CHOP ₩ TTI-621 ₩ RRX-001 ⊕ dara ♣ AZD-9150 € Hirilumab € cabiralizamab noblituzumab | pl-549 pepaca M demcizumab M cavatak III INCB-24360 III) entinostat IIII lenvatinib M GSK-3174998 M GSK-3359609 M itacitinib X BLZ-945 10 MK-1454 10 MK-1308 ⊠ MCS-110 ⊠ MGB-453 • cabozantinib 10 utomilumab 10 MK-7684 ₩ galunisertib 10 MK-4280 10 SEA-CD40 X BLZ-945 1 BTH-1677 ₩ avadomide azacitidine dara+len M doce + pred emogenovatucei-T M 81-8040 # ipi + cabozantinib ₩ AZD-4547 M ADXS-PSA M acalabriganib Cheme # AZD-1775 NKTR-214 Mp nab-pac+doxor+cyclop M olaparib M CRS-207+epaca 81-8040 ⊕ olaparib ⊕ vistusertib ☑ CJM-112 ☑ panobinostat () carbo P+nab-₩ BMS-986183 Phase I ₩ NEOPV-01 10 ramuci ● PEGPH-20 🗵 trametinib 🗵 canakinumab pac/pac+doxor+cyclop FOLFOX4 " cisP+gem/ ₩ TAK-659 区 EGF-816 区 LCL-161 M mirvetusinab & galunisertib ₩ nab-pac ⊠ everolimus ₩ AZD-6738 ⊠ sorafenib soravtansine • nab-pac+gem Phase II • trastu + pertu + doce Bladder M tenvatinib # TAK-659 / • Ra233Q2 • rucaparib • trastar + pertu • codrituzurhab # PF-06753512 TD olaratumab Phase III gem/iri/5-FU H&NC M ramuci

HCC

Brain Prostate Other

Pancreas

Legend	PD-(L)1 Base	Company	
•	atezolizumab	RHHBY	
	avelumab	MRK.DE	
•	BGB-A317	BGNE	
×	BI-754091	B.I.	
0	CX-072	CTMX	
	durvalumab	AZN	
0	JS-001	SH Junshi	
,000	LY-3300054	LLY	
×	nivolumab	BMY	
×	PDR-001	NVS	
ŋ	pembrolizumab	MRK	
□	cemiplimab	REGN	
	SHR-1210	JS Hengru	
٥	TSR-042	TSRO	
Ж	PF-06801591	PFE	

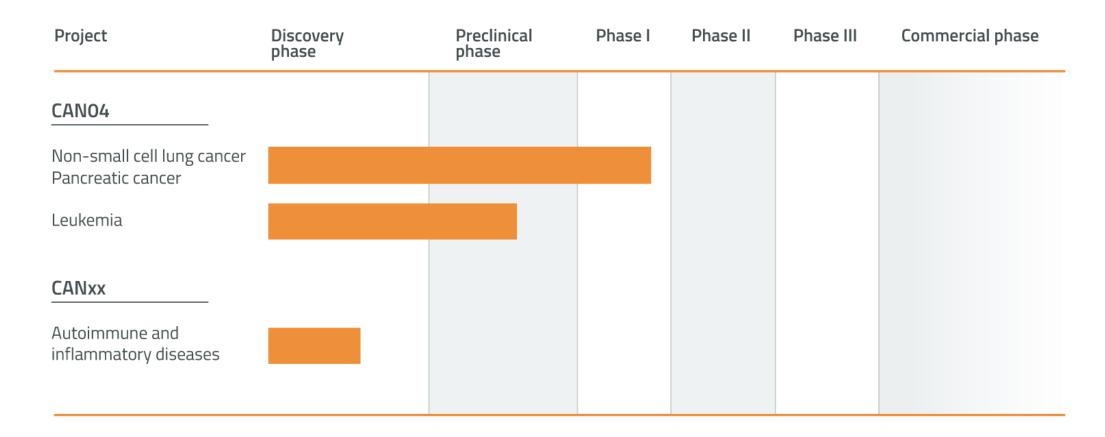


Combination therapy

- Synergistic effects: 1 + 1 = 3
- Additive effects: 1 + 1 = 2
- Variability effects: 1 + 1 = 1,5



Cantargia pipeline

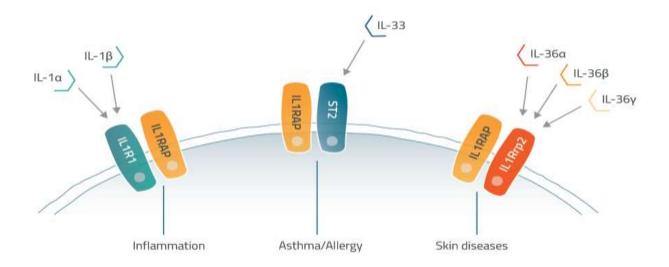


CANTOS additional findings (from Novartis IL-1\beta antibody)

CANCER decreased risk of death with treatment (high dose)						
Lung cancer	77 %	P=0.0002				
Non-lung cancer	37 %	P=0.06				
Decreased incidence of inflammatory disease (all doses)						
Arthritis	32%	p<0.0001				
Ostheoartritis	28%	P=0.0005				
Gout	53%	p<0.0001				
Cardiovascular	12%	P=0.02				
Biomarker levels (reduction)						
CRP	26-41%	P<0.0001				
IL-6	25-43%	P<0.001				

IL1RAP - additional potential indications to leverage the value of our asset

- Three different systems signal through IL1RAP
- These systems contribute to various inflammatory diseases
- Can be blocked by Cantargia's antibodies against IL1RAP



Cantargia partnership with Panorama Res Inc (Sunnyvale, CA) Selection of clinical candidate 2019



Significant value inflection points ahead

2018

- Preclinical data (immuno-oncology effects, combinations etc)
- Phase I clinical data final dose level (Q4 2018)
- Initiation of Phase IIa portion of the clinical trial (Q4 2018)
- US regulatory and clinical strategy

2019/2020

- Clinical progress and Phase IIa results
- Preclinical progress
- CANxx progress



Cantargia summary

- Lead candidate antibody CAN04 in clinical trials against cancer
 - Encouraging interim phase I data
 - Double mechanism of action
 - Initial development in NSCLC and pancreatic cancer (cancer forms with poor prognosis)
 - Direct effects on tumor cells and tumor microenvironment
 - Recent external validation of pathway
- Second generation antibodies for autoimmune disease
- Unique and strong IP
- Strong lead investors with high competence and well known track record
 - Funding through phase IIa until mid 2020.

