We want to save patients with severe cancer and autoimmune diseases

Clinical investigations with our lead antibody CAN04 to our proprietary target

Göran Forsberg, CEO

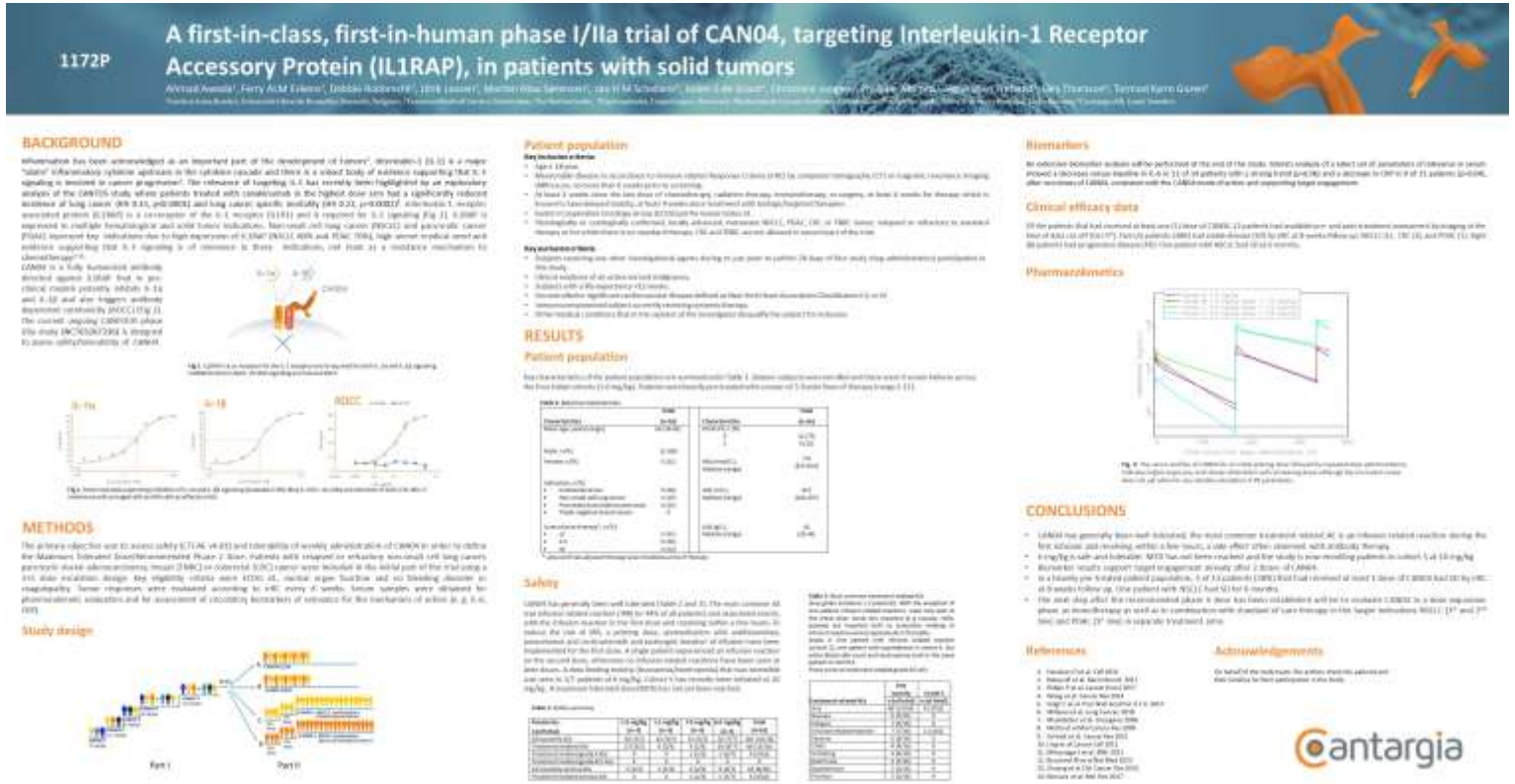
Safe Harbour Statement

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

CAN04 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

BACKGROUND

METHODS

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Pharmacokinetics

CONCLUSIONS

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Acknowledgements

cantargia

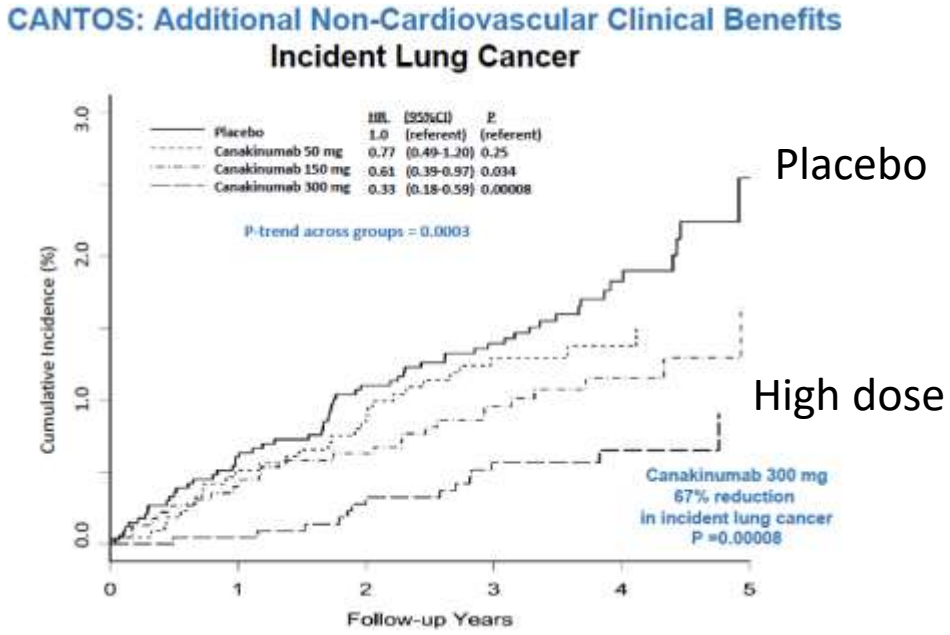
- **CAN04 has generally been well tolerated**
- **6 mg/kg is safe.**
- **Encouraging biomarker results already after two doses of CAN04.**
- **In a heavily pre-treated patient population, 5 of 13 patients (38%) had SD. One patient with NSCLC had SD for 6 months.**

cantargia

IL-1 blockade in cancer- Recent supportive clinical data

CANTOS trial

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



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

Canakinumab phase 3 trials

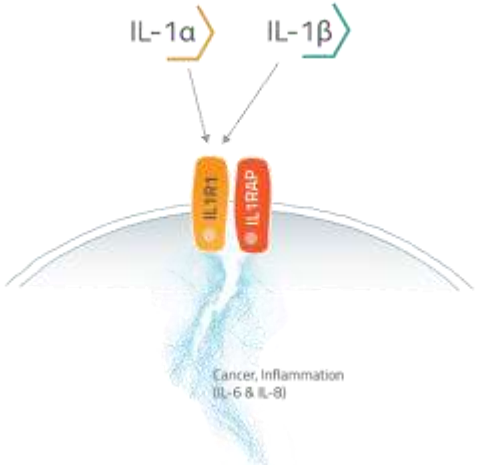
Adjuvant NSCLC
After surgery, no mets, placebo control
1500 patients, recruitment ongoing
Completion 2021/22

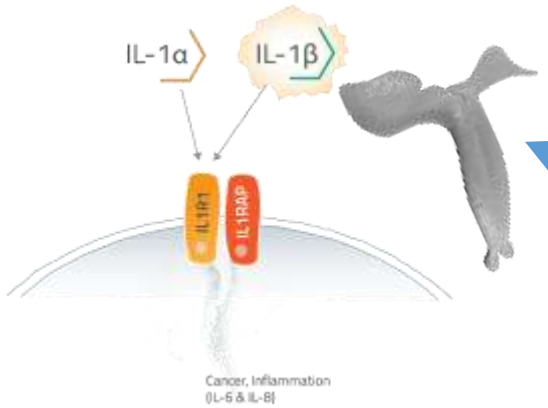
First line (CANOPY-1)
Untreated locally advanced/metastatic
Combination Pembro/Platinum doublet
627 patients, start Dec 2018
Completion 2021/22

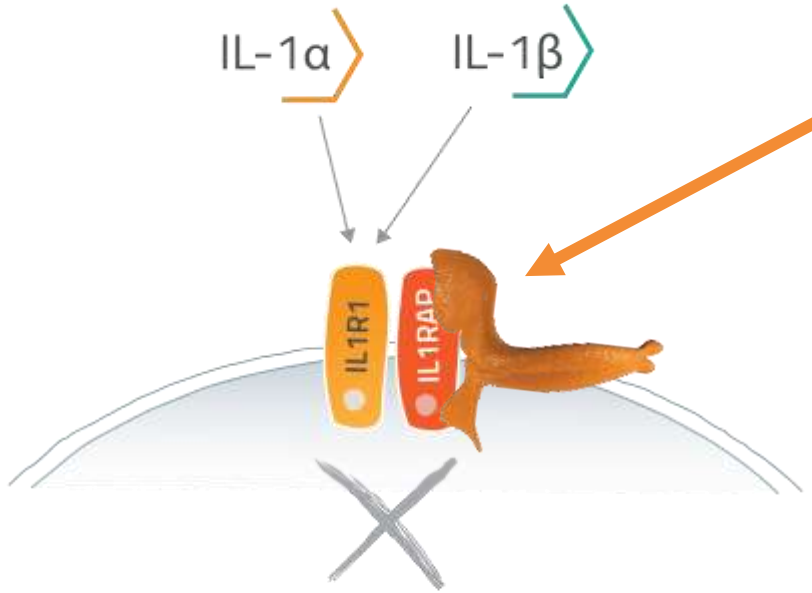
Second line metastatic (CANOPY-2)
Previously treated loc adv/metastatic
Combination Docetaxel
240 patients, start Dec 2018
Completion 2021

Source clinicaltrials.gov

CAN04 (nidanilimab) vs Canakinumab





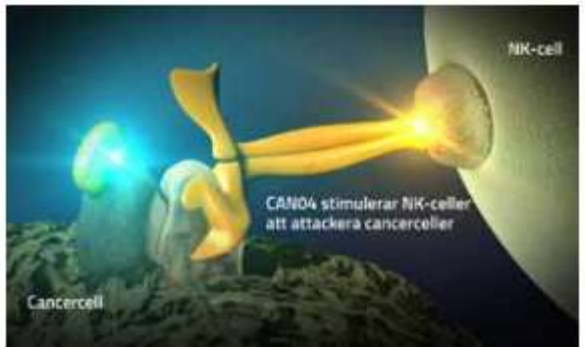


Canakinumab

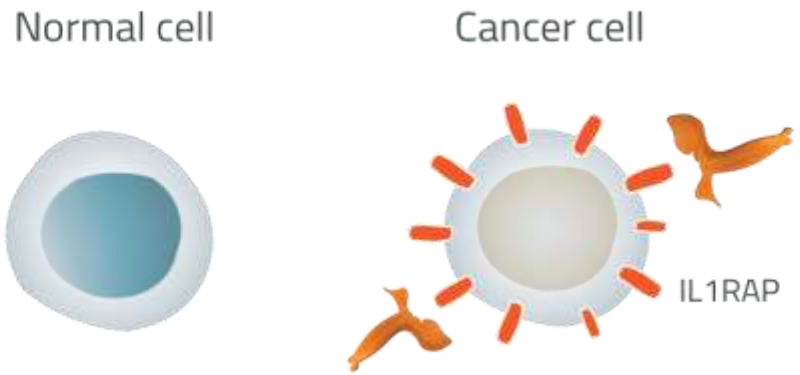
- Antibody directed against one of the two IL-1 ligands, IL-1β

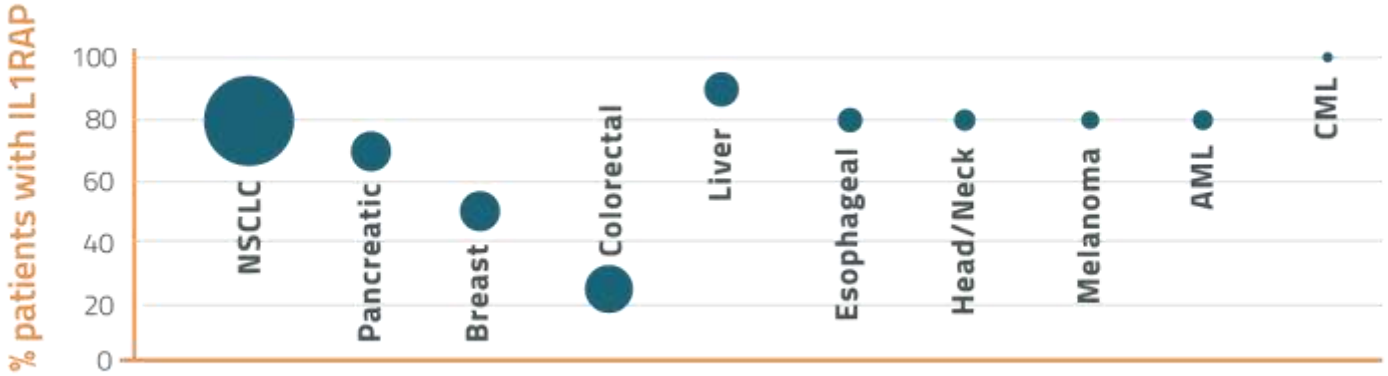
CAN04:

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



Medical need and IL1RAP





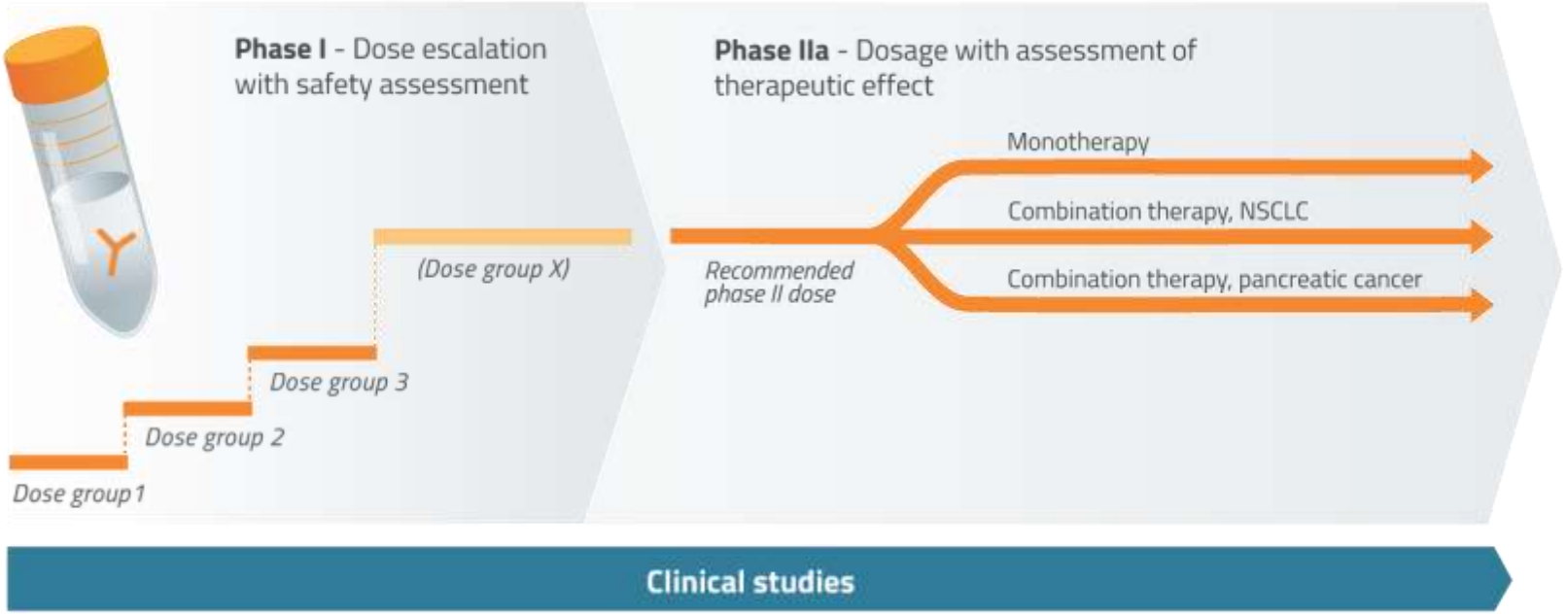
Size of each indication corresponds to annual deaths in USA

- 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

CAN04 – 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/nab-paclitaxel



Q4 2018

Early 2020

Details on www.clinicaltrials.gov

Cantargia at a glance

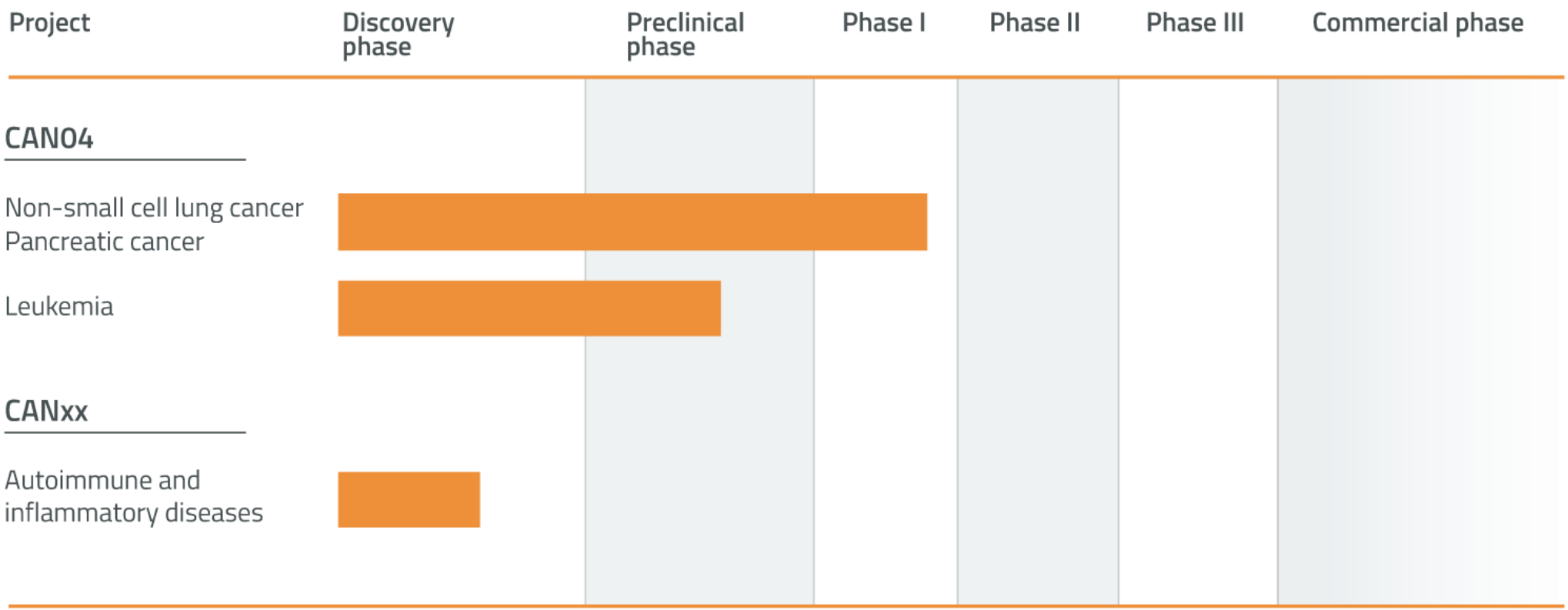
- Specialized in antibody therapy/immunology, with initial focus on oncology
- Granted IP - therapeutic target IL1RAP and drug candidate
- Lead antibody CAN04 (nidanilimab) in clinical development
- Strong management team with proven track record in clinical development and business development
- Listed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

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

Ahmad Awada[1], Ferry ALM Eskens[2], Debbie Robbrecht[2], Ulrik Lassen[3], Morten Mau Sørensen[3], Jan H M Schellens[4], Jolien S de Groot[4], Christiane Jungels[5], Philippe Aftimos[5], Sophie Blum Feniland[6], Lars Thorsson[6], Tormod Kyrre Guren[7]

BACKGROUND

Inflammation has been acknowledged as an important part of the development of tumors[1]. Interleukin-1 (IL-1) is a major "alarm" inflammatory cytokine upstream in the cytokine cascade and there is a robust body of evidence supporting that IL-1 signaling is involved in cancer progression[2]. The relevance of targeting IL-1 has recently been highlighted by an exploratory analysis of the CANTOS study where patients treated with canakinumab in the highest dose arm had a significantly reduced incidence of lung cancer (HR 0.33, p<0.0001) and lung cancer specific mortality (HR 0.23, p<0.0002)[3]. Interleukin-1 receptor associated protein (IL1RAP) is a co-receptor of the IL-1 receptor (IL1R1) and is required for IL-1 signaling (Fig 1). IL1RAP is expressed in multiple hematological and solid tumor indications. Non-small cell lung cancer (NSCLC) and pancreatic cancer (PDAC) represent key indications due to high expression of IL1RAP (NSCLC 80% and PDAC 70%), high unmet medical need and evidence supporting that IL-1 signaling is of relevance in these indications, not least as a resistance mechanism to chemotherapy[3,4].

CAN04 is a fully humanized antibody directed against IL1RAP that in pre-clinical models potently inhibits IL-1α and IL-1β and also triggers antibody dependent cytotoxicity (ADCC) (Fig 2). The current ongoing CANFOUR phase I/IIa study (NCT03267316) is designed to assess safety/tolerability of CAN04.

Fig 1. IL1RAP is a co-receptor for the IL-1 receptor and is required for both IL-1α and IL-1β signaling. CAN04 binds to IL1RAP, inhibits signaling and induces ADCC

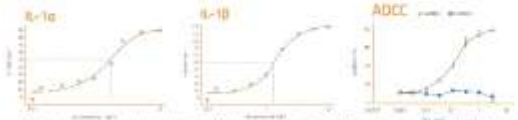
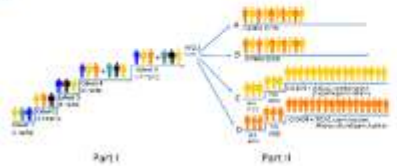


Fig 2. Preclinical data supporting inhibition of IL-1α and IL-1β signaling (assessed in HEK-Blue IL-1/33, Ca-acid) and induction of ADCC (SK-MEL-3 melanoma cells as target cells and NK cells as effector cells)

METHODS

The primary objective was to assess safety (CTCAE v4.03) and tolerability of weekly administration of CAN04 in order to define the Maximum Tolerated Dose (MTD)/Recommended Phase 2 Dose (RP2D). Patients with relapsed or refractory non-small cell lung cancer, pancreatic ductal adenocarcinoma, breast (TNBC) or colorectal (CRC) cancer were included in the initial part of the trial using a 3+3 dose escalation design. Key eligibility criteria were ECOG ≤1, normal organ function and no bleeding disorder or coagulopathy. Tumor responses were evaluated according to irRC every 8 weeks. Serum samples were obtained for pharmacokinetic evaluation and for assessment of circulatory biomarkers of relevance for the mechanism of action (e. g. IL-6, CRP).

Study design



Patient population

Key inclusion criteria:

- Age ≥ 18 year
- Measurable disease in accordance to immune related Response Criteria (irRC) by computed tomography (CT) or magnetic resonance imaging (MRI) scan, no more than 4 weeks prior to screening.
- At least 4 weeks since the last dose of chemotherapy, radiation therapy, immunotherapy, or surgery, at least 6 weeks for therapy which is known to have delayed toxicity, at least 2 weeks since treatment with biologic/targeted therapies.
- Eastern Cooperative Oncology Group (ECOG) performance status ≤1.
- Histologically or cytologically confirmed, locally advanced, metastatic NSCLC, PDAC, CRC or TNBC tumor, relapsed or refractory to standard therapy or for which there is no standard therapy. CRC and TNBC are not allowed in second part of the trial.

Key exclusion criteria:

- Subjects receiving any other investigational agents during or just prior to (within 28 days of first study drug administration) participation in this study.
- Clinical evidence of an active second malignancy.
- Subjects with a life expectancy <12 weeks.
- Uncontrolled or significant cardiovascular disease defined as New York Heart Association Classification III, or IV.
- Immunocompromised subject currently receiving systemic therapy.
- Other medical conditions that in the opinion of the investigator disqualify the subject for inclusion.

RESULTS

Patient population

Key characteristics of the patient population are summarized in Table 1. Sixteen subjects were enrolled and there were 9 screen failures across the four initial cohorts (1-8 mg/kg). Patients were heavily pre-treated with a mean of 3.9 prior lines of therapy (range 1-11).

Table 1. Baseline characteristics

Characteristics	Total (n=16)	Characteristics	Total (n=16)
Mean age, years (range)	63 (39-81)	ECOG PS, n (%)	
		0	11 (73)
		1	4 (25)
Male, n (%)	11 (69)		
Female, n (%)	5 (31)		1 (6)
		HB (mmol/L), Median (range)	8.9 (6.9-10.9)
Indication, n (%)			
• Colorectal cancer	5 (56)		
• Non-small cell lung cancer	5 (56)		
• Pancreatic ductal adenocarcinoma	4 (25)		
• Triple-negative breast cancer	0	LDH (U/L), Median (range)	217 (161-475)
Lines of prior therapy*, n (%)			
• 1	5 (31)		
• 2-3	9 (56)	ALB (g/L), Median (range)	41 (29-46)
• 4+	2 (13)		

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

Safety

CAN04 has generally been well tolerated (Table 2 and 3). The most common AE was infusion related reaction (IRR) (in 44% of all patients) and associated events, with the infusion reaction in the first dose and resulting 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. A dose limiting toxicity (leucopenia/neutropenia) that was reversible was seen in 1/7 patients at 8 mg/kg. Cohort 5 has recently been initiated at 10 mg/kg. A maximum tolerated dose has not yet been reached.

Table 2. Safety summary

Parameters, n (of total)	1.0 mg/kg (n=3)	1.3 mg/kg (n=3)	2.0 mg/kg (n=3)	5.0 mg/kg [n=7]	Total (n=16)
All casuality AEs	18 (3/3)	40 (3/3)	33 (3/3)	67 (7/7)	189 (16/16)
Treatment related AEs	17 (3/3)	6 (2/3)	9 (2/3)	26 (6/7)	68 (13/16)
Treatment related grade 1 AEs	0	0	1 (1/3)	3 (1/7)	4 (1/16)
Treatment related grade ≥3 AEs	0	0	0	0	0
All casuality serious AEs	3 (1/3)	0 (0/3)	4 (2/3)	8 (4/7)	26 (6/16)
Treatment related serious AEs	0	0	1 (1/3)	5 (1/7)	6 (1/16)

Table 3. Most common treatment related AEs

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

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 a decrease versus baseline in IL-6 in 11 of 14 patients with a strong trend (p=0.06) and a decrease in CRP in 9 of 11 patients (p=0.04) after two doses of CAN04, consistent with the CAN04 mode of action and supporting target engagement.

Clinical efficacy data

Of the patients that had received at least one (1) dose of CAN04, 13 patients had available pre- and post-treatment assessment by imaging at the time of data cut off (Oct 1st). Five (5) patients (38%) had stable disease (SD) by irRC at 8 weeks follow up: NSCLC (1), CRC (3), and PDAC (1). Eight (8) patients had progressive disease (PD). One patient with NSCLC had SD at 8 months.

Pharmacokinetics

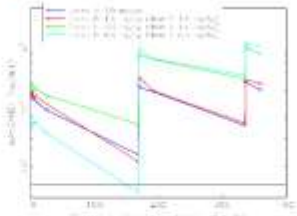


Fig. 3. The serum profiles of CAN04 from an initial priming dose followed by repeated dose administrations indicates higher exposure and slower elimination with increasing doses although the accumulation curves does not yet allow for any reliable calculation of PK parameters

CONCLUSIONS

- CAN04 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.
- 8 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 two doses of CAN04.
- 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 CAN04 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.

References

1. Hanahan D et al. Cell 2011
2. Netea-M et al. Nat Immunol 2017
3. Ridker P et al. Lancet Oncol 2017
4. Wang et al. Cancer Res 2014
5. Voigt C et al. Proc Natl Acad Sci U S A. 2017
6. Mildner et al. Lung Cancer. 2018
7. Muenkler et al. Oncogene 2008
8. Mellor et al Mol Cancer Res 2009
9. Schmid et al. Cancer Res 2011
10. Ling et al Cancer Cell 2012
11. Mbeunkui S et al. BMC 2010
12. Brochard M et al Nat Med 2013
13. Zhuang et al Clin Cancer Res 2005
14. Roessner et al. Mol Res 2017

Acknowledgements

On behalf of the study team, the authors thank the patients and their families for their participation in the study.

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CANFOUR – baseline characteristics

Characteristics	Total (n=16)
Mean age, years (range)	63 (39-81)
Male, n (%)	11 (69)
Female, n (%)	5 (31)
Indication, n (%)	
• Colorectal cancer	9 (56)
• Non-small cell lung cancer	3 (19)
• Pancreatic ductal adenocarcinoma	4 (25)
• Triple-negative breast cancer	0
Lines of prior therapy*, n (%)	
• ≤2	5 (31)
• 3-5	9 (56)
• ≥6	2 (12)

Characteristics	Total (n=16)
ECOG PS, n (%)	
0	12 (75)
1	4 (25)
HB (mmol/L), Median (range)	7.6 (6.0-10.0)
LDH (U/L), Median (range)	217 (162-475)
ALB (g/L), Median (range)	41 (29-45)

* 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

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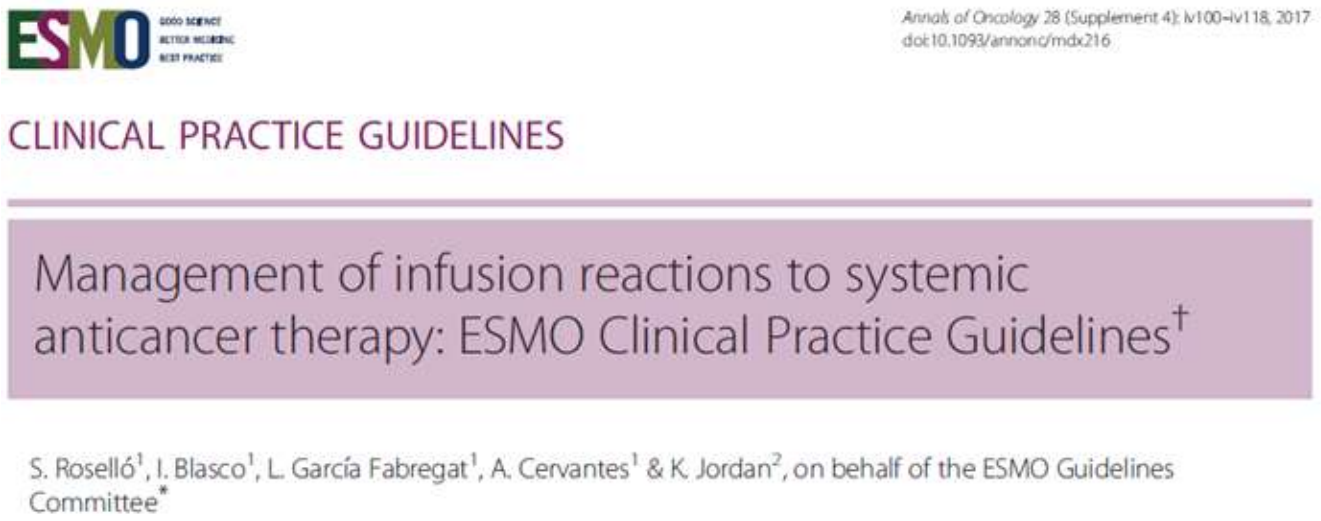


ESMO

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. Roselló[1], I. Blasco[1], L. García Fabregat[1], A. Cervantes[1] & K. Jordan[2], on behalf of the ESMO Guidelines Committee*

Rosell et al. Annals of Oncology 2017

CANFOUR – treatment related adverse events (AE)

Treatment related AEs	Any toxicity n (of total)	Grade 3 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%

1. Reck et al. N Engl J Med 2017. 2. Lopes et al. Abstract LBA4 2018. 3. Socinski et al. N Engl J Med 2018. 4. Gandhi et al. N Engl J Med 2018

CANFOUR – biomarkers

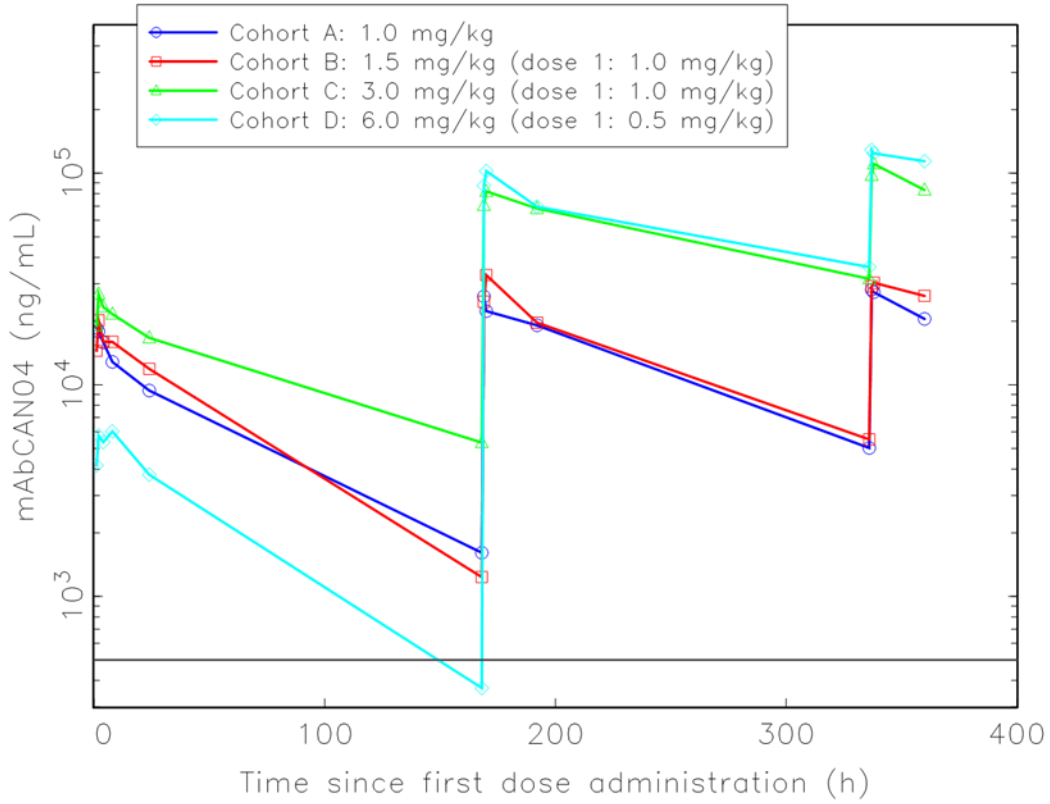
- An extensive biomarker analysis will be performed at the end of the study.

- 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

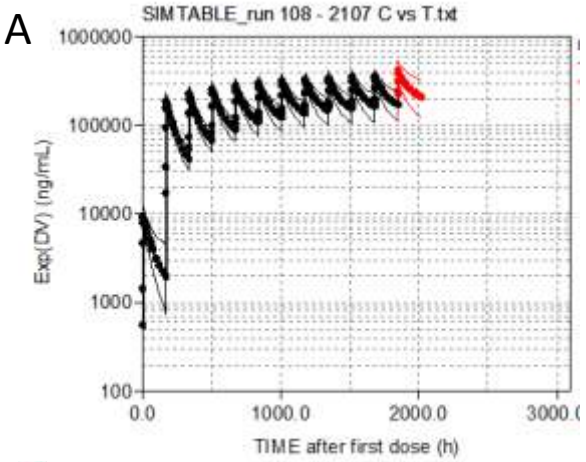
- Of the patients that received at least one (1) dose of CAN04, 13 patients had available pre- and post-treatment assessment by imaging at the time of data cut off (Oct 5th).
- Five (5) patients (38%) had stable disease (SD) by irRC at 8 weeks follow up: non-small cell lung cancer (1), colorectal cancer (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

A



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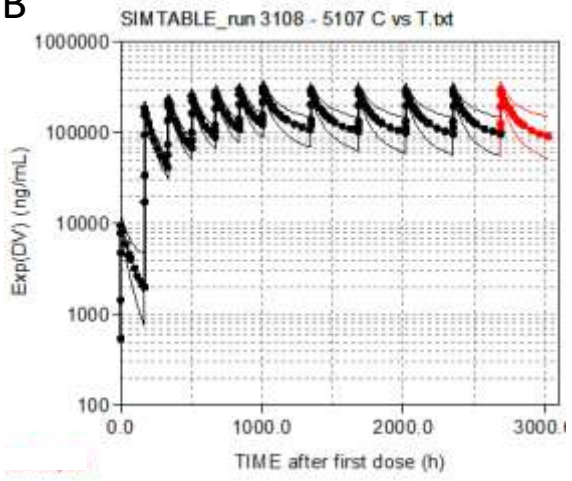
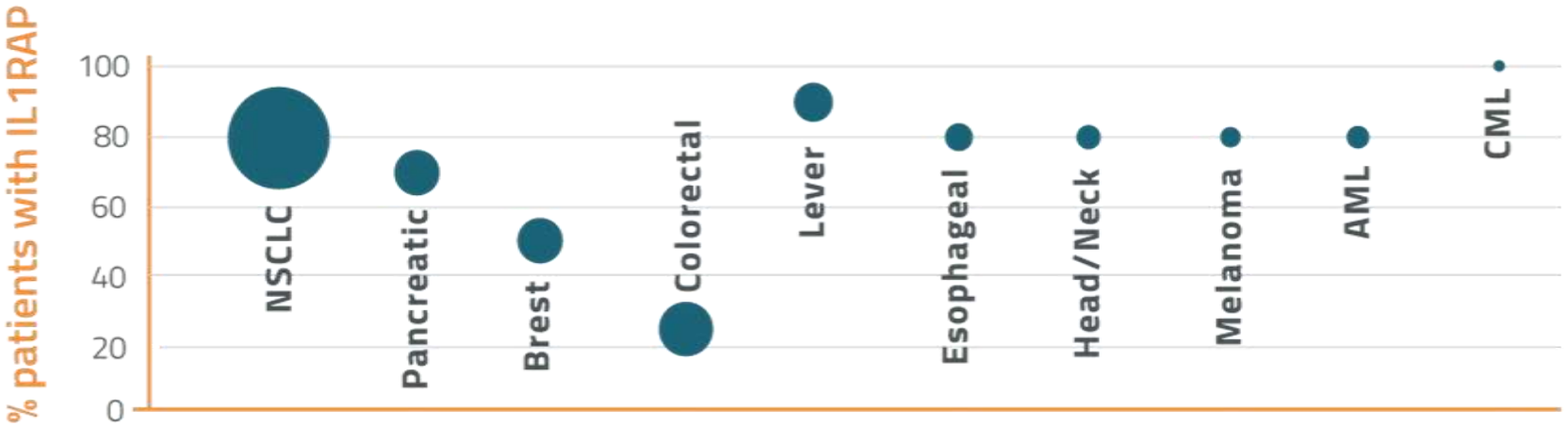


Predicted serum concentration of CAN04 vs time curves in human
Predicted serum concentration of CAN04 vs time curves in human illustrating the 5th, 50th, and 95th percentiles of the median in 2000 simulated studies of 12 patients after an initial priming dose of 0.5 mg/kg, followed by 5 weekly (Q1W)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

CANFOUR – CONCLUSIONS

- CAN04 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 CAN04 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

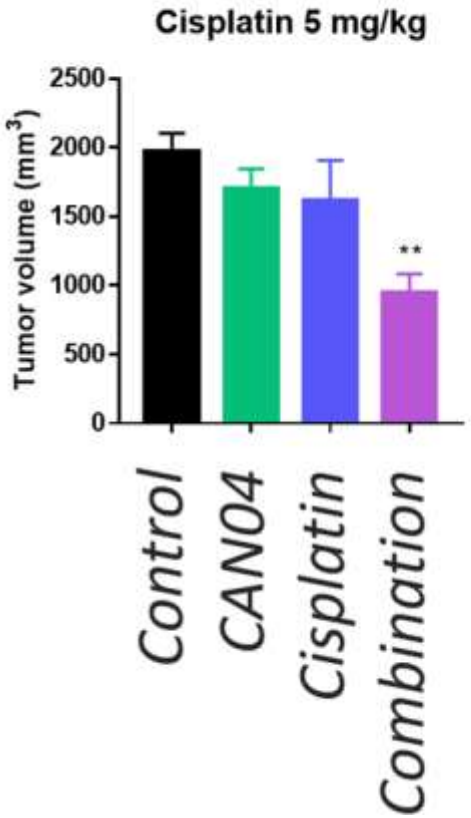
NSCLC and pancreatic cancer: our target indications in combination with chemotherapy



IL1RAP expression and size of indications

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

CAN04 in combination with Cisplatin is superior to either agent alone and less toxic in pre-clinical models

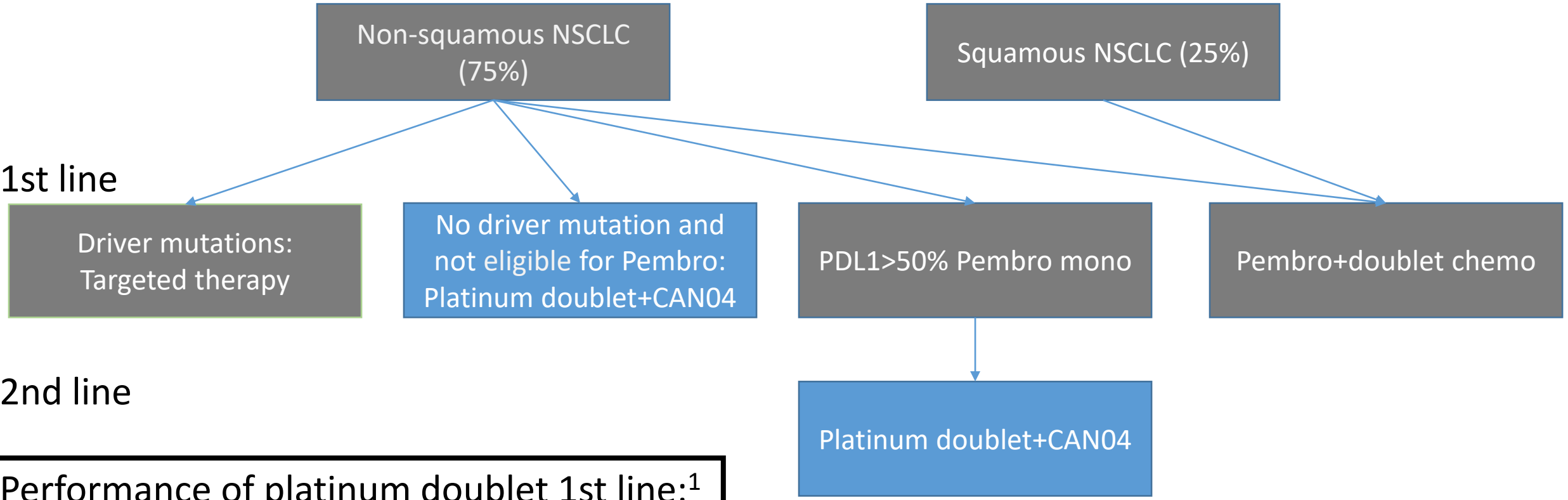


	Control	CAN04	Cisplatin	Combination
Animals withdrawn	20 % (Tumor)	0 %	50 % (Toxicity)	20 % (Toxicity)
Tumor reduction	N/A	14%	18%	52 %
Comment	*Highest tumor burden*	*Best safety*	*Highest toxicity*	*Superior efficacy and reduced toxicity*

Combination CAN04/Cisplatin superior to individual agents

- **Reduction in severe toxicity**
- **Increased efficacy**

Positioning of CAN04 in NSCLC (metastatic disease) in CANFOUR



Performance of platinum doublet 1st line:[1]

- 25% response rate
- progression free survival: 5-6 months

1. Scagliotti et al. J Clin Oncol 2008

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

1st line

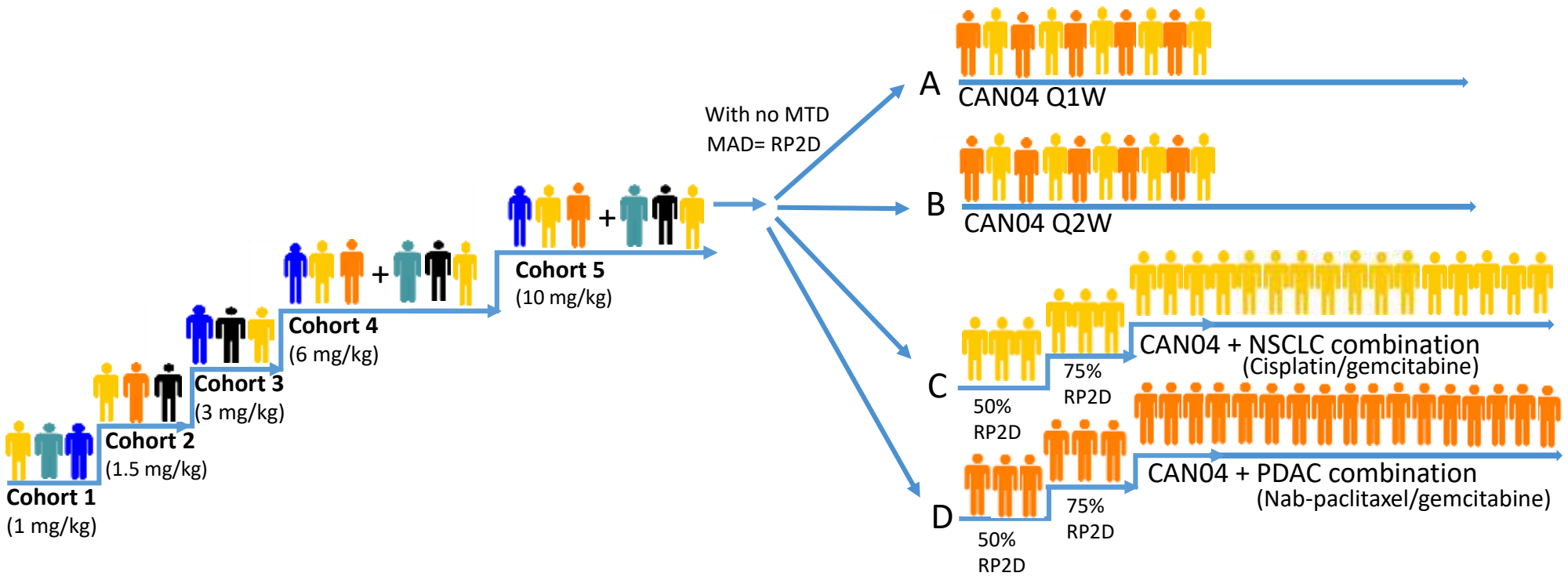
Gemcitabine+nab-paclitaxel+CANO4	FOLFIRINOX	Gemcitabine (very frail patients)

Performance gemcitabine+ nab pactlitaxel 1st line:[1]

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

1. von Hoff et al. Lancet 2013

CANFOUR – study design



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.

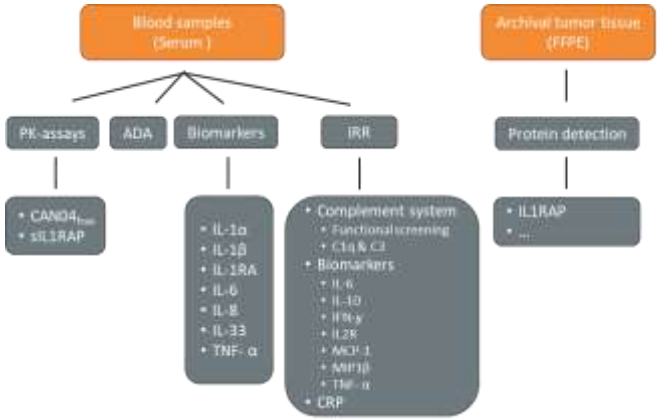
Secondary Objectives	• To assess pharmacokinetic (PK) parameters of CAN04. • To assess anti-drug antibody (ADA) formation against CAN04. • To determine preliminary signs of clinical efficacy of CAN04 as a single agent. **Additional secondary objectives for Part II** • To assess health-related Quality of Life (QoL) • To determine preliminary signs of clinical efficacy of CAN04 when given in combination with standard chemotherapy regimen

CANFOUR – additional assessments

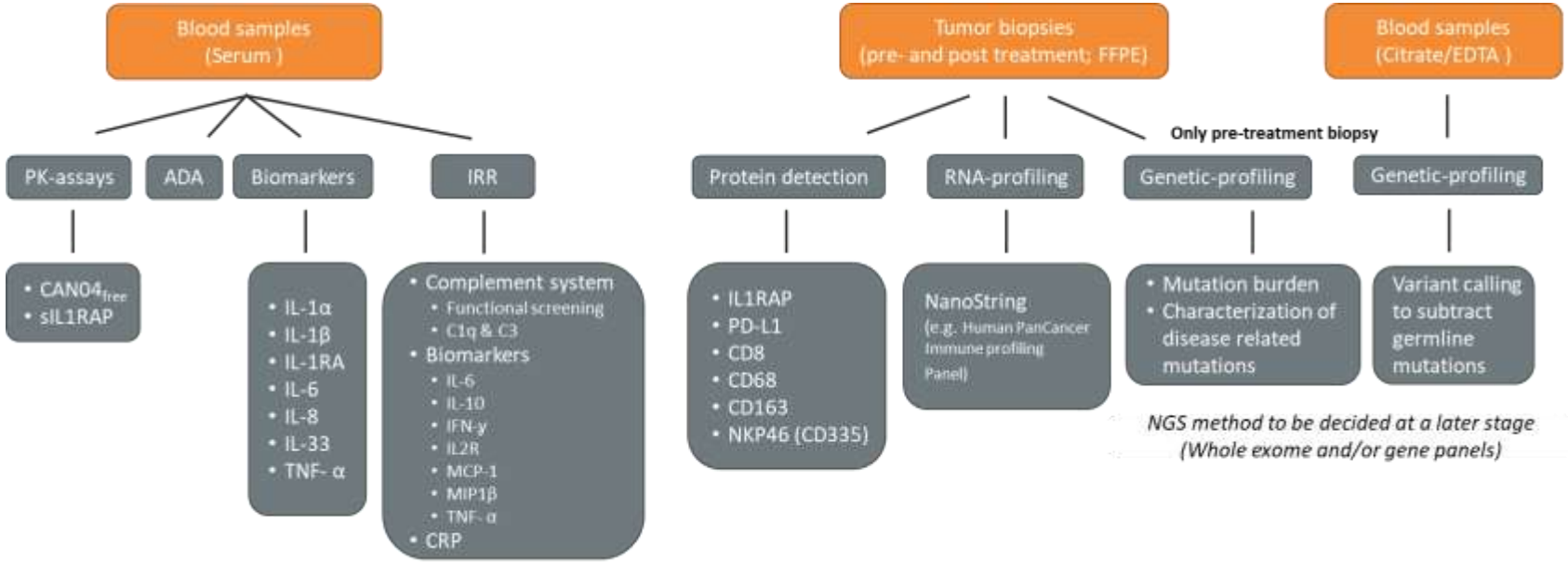
Endpoint	Assessment
Secondary endpoints	• Pharmacokinetics, including sIL1RAP • Anti-drug antibodies (ADA) • Preliminary signs of efficacy (ORR, DoR, PFS, OS) • Additional endpoint for Part II: Health-related QoL (EORTC QLQ C30)
Exploratory	• IL1RAP expression and other disease-related, inflammatory, 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

Phase I



Phase II



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

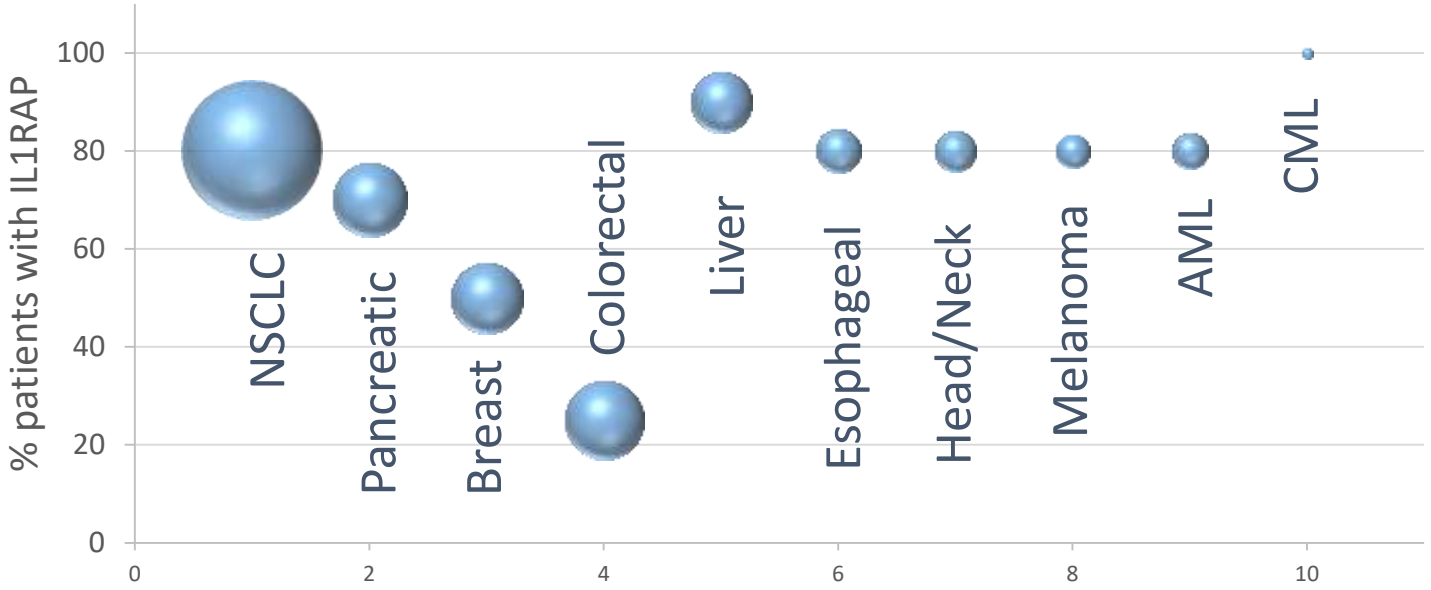
Intrinsic pathway

Genome instability and mutation

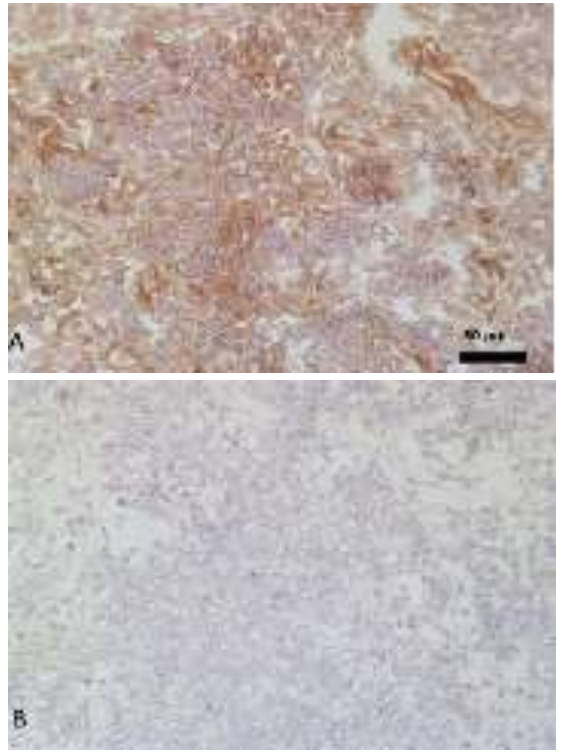
Tumor-promoting inflammation

Extrinsic pathway

IL1RAP is highly expressed in several cancers



Size of each indication corresponds to annual deaths in USA



CAN04

Control

Pancreatic cancer

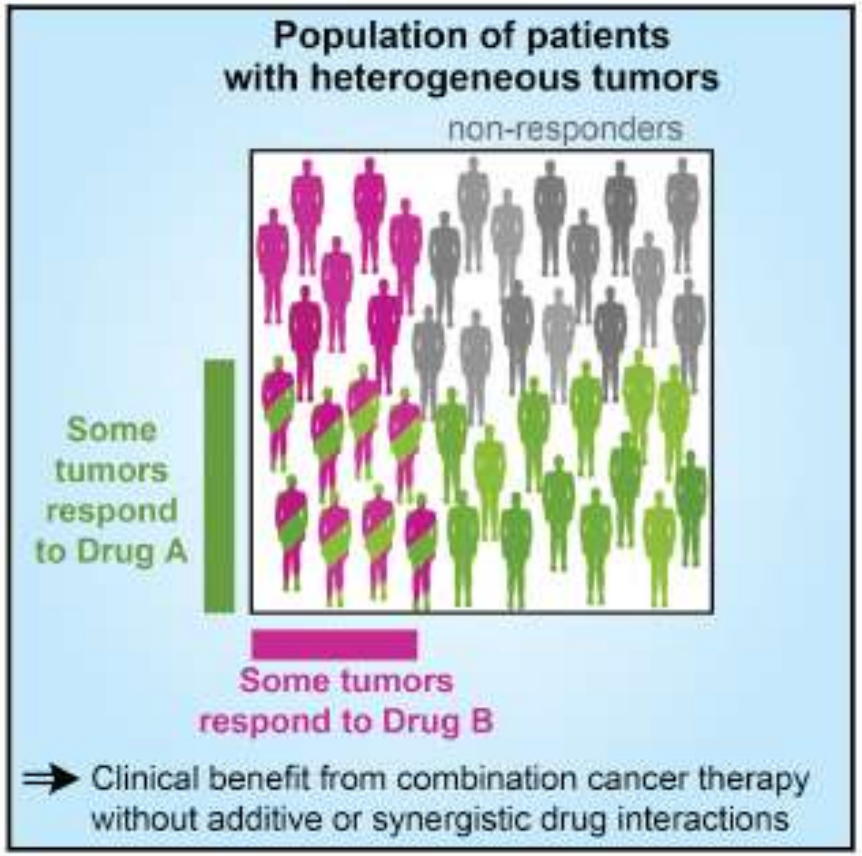
Cantargia

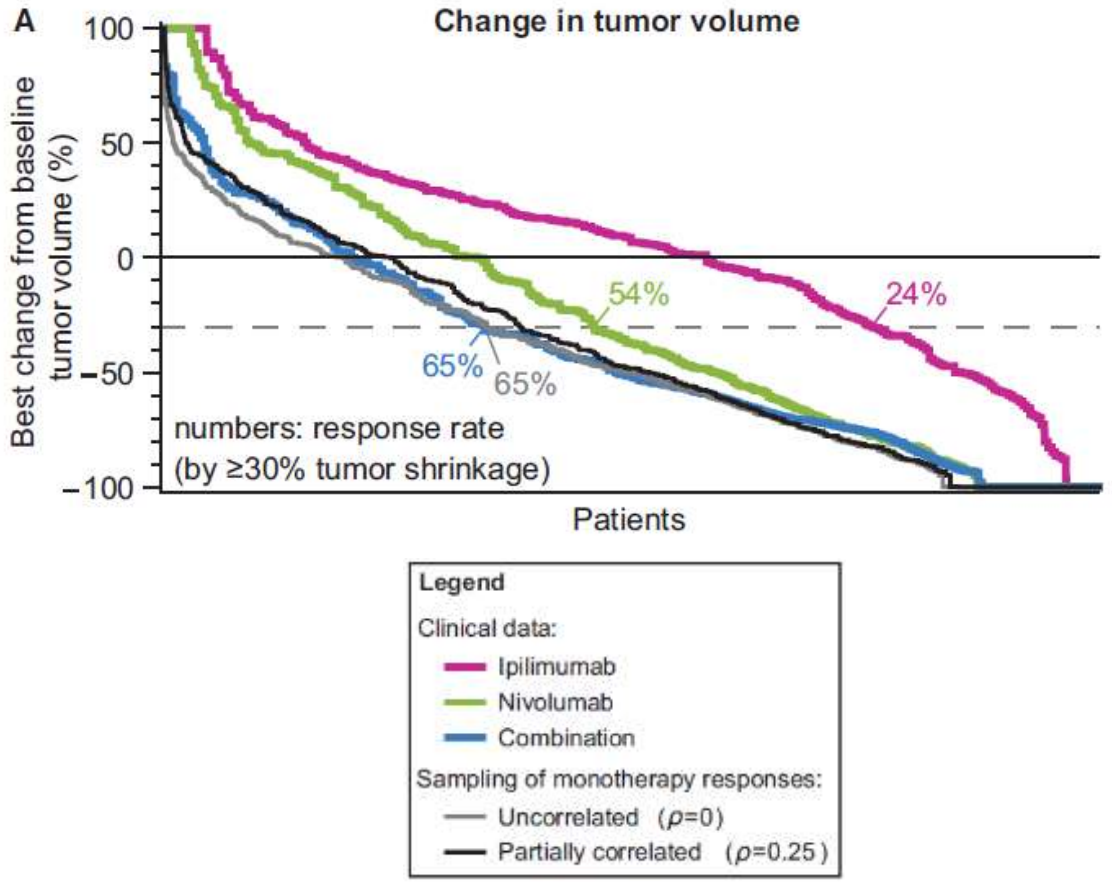
Targeting the tumor microenvironment

Combination therapy

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

Combination therapy





Palmer and Sorger, Combination Cancer Therapy Can Confer Benefit via Patient-to-Patient Variability without Drug Additivity or Synergy, Cell 2017

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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-Homan[2], Nnamdi Ihejirika[3], Andrean L. Simons[1,2,4,5,6]

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

Autocrine Production of Interleukin 1β Confers Constitutive Nuclear Factor κB Activity and Chemoresistance i

Alexander Arlt,[2] Jens Vorndamm,[2] Susanne Heiner Schäfer[3]

Serum levels of IL-6 and IL-1β can predict the efficacy of gemcitabine in patients with advanced pancreatic cancer

S Mitsunaga*[,1,2], M Ikeda[1], S Shimizu[1], I Ohno[1], J Furuse[3], M Inagaki[4], S Higashi[5], H Kato[5], K Terao[6] and A Ochiai[2]

A Novel Role for the Interleukin-1 Receptor Axis in Resistance to Anti-EGFR Therapy

Valerio Gelfo [1,2,†], Martina Mazzeschi [1,†], Giada Grilli [1], Moshit Lindze
Gabriele D'Uva [6], Balázs Győrffy [7,8], Andrea Ardizzoni [1], Yosef Yarden
Mattia Lauriola [1,2,*]

Vassilis Georgoulias,[8] Rinat Zaynagetdinov,[2,11,*] and Timothy S. Blackwell[1,2,5,9,10,

IRAK1 is a therapeutic target that drives breast cancer

Zhen Ning Wee
Puay Leng Lee[1]
Dave S.B. Hoon

Chemotherapy-triggered cathepsin B release in 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], an[1,2], Wilfrid Boireau[4], Benoit Simon[4], Bernhard Ryffel[5], Jean Louis Connat[6], los[7], François Martin[1,2], Cédric Rébé[1–3], Lionel Apetoh[1–3,8] & François Ghiringhelli[1–3,8]

Neutrophil-Derived IL-1β Impairs the Efficacy of NF-κB Inhibitors against Lung Cancer

Allyson G. McLoed,[1] Taylor P. Sherrill,[2] Dong-Sheng Cheng,[2] Wei Han,[2] Jamie A. Saxon,[1] 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] Vassilis Georgoulias,[8] Rinat Zaynagetdinov,[2,11,*] and Timothy S. Blackwell[1,2,5,9,10,11]

ory cytokines defines resistance of inhibitors

, Maria Teresa Rodia[1,*], Michela Pucci[1], Massimiliano Dall'Ora[1], ,4], Rossella Solmi[1], Lee Roth[5], Moshit Lindzen[5], Massimiliano a Bertotti[6], Elisabetta Caramelli[1], Pier-Luigi Lollini[1], Livio Trusolino[6], Gabriele D'Uva[7,], Mattia Lauriola[1,2,**]**

Constitutive [illegible] Prognosis and Chemoresistance in Pancreatic Ductal Adenocarcinoma

Daoxiang Zhang[1], Lin Li[1], Hongmei Jiang[1], Brett L. Knolhoff[1], Albert C. Lockhart[1], Andrea Wang-Gillam[1], David G. DeNardo[1], Marianna B. Ruzinova[2], and Kian-Huat Lim[1]

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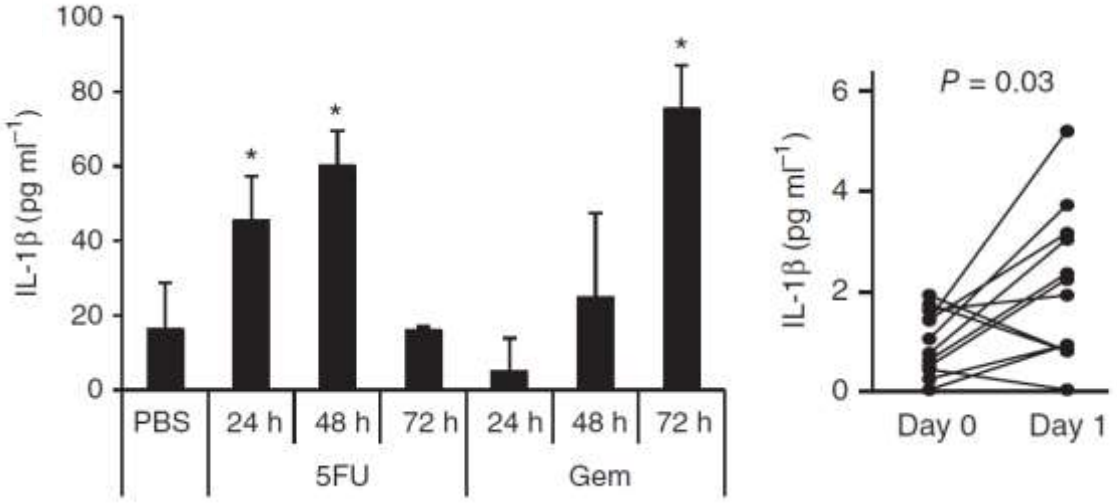
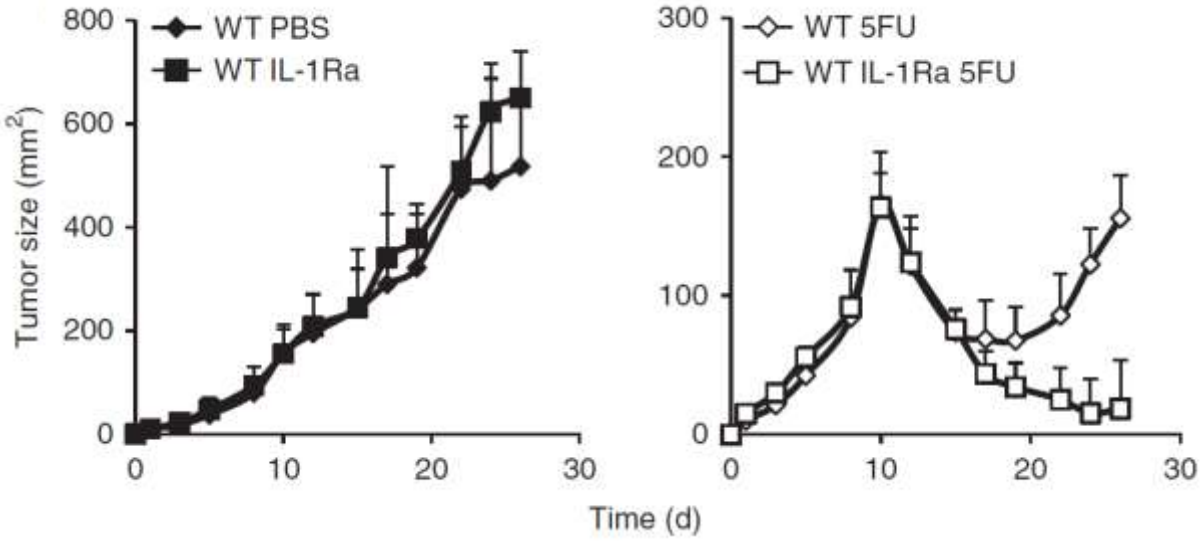
IL-1 and resistance to therapy, via MDSC

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

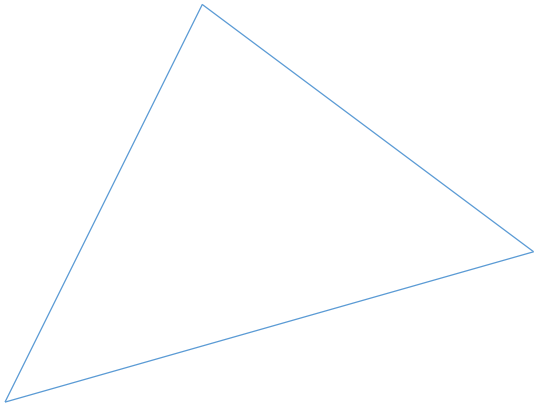
Bruchard et.al, Chemotherapy-triggered cathepsin B release in myeloid-derived suppressor cells activates the Nlrp3 inflammasome and promotes tumor growth, Nat Med 2013

Targeting the tumor microenvironment

Pancreatic ductal adenocarcinoma (PDAC)

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

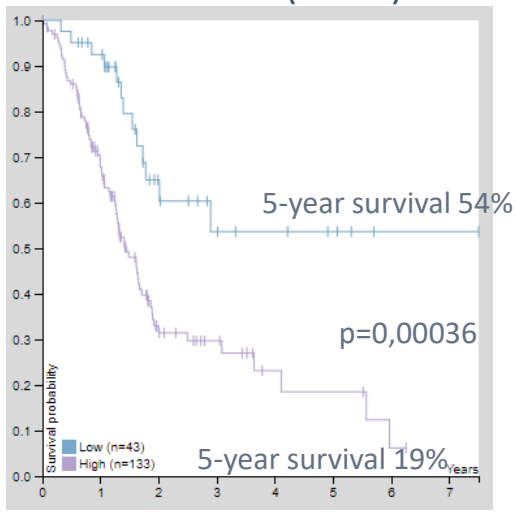
KRAS mutated (75-90%)



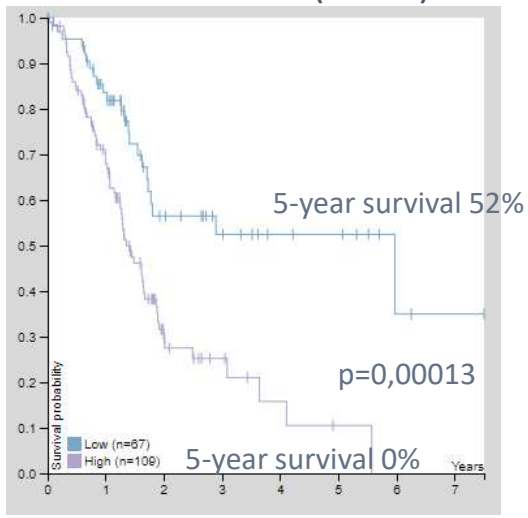
IL1 expression

Constitutive NFκB activation

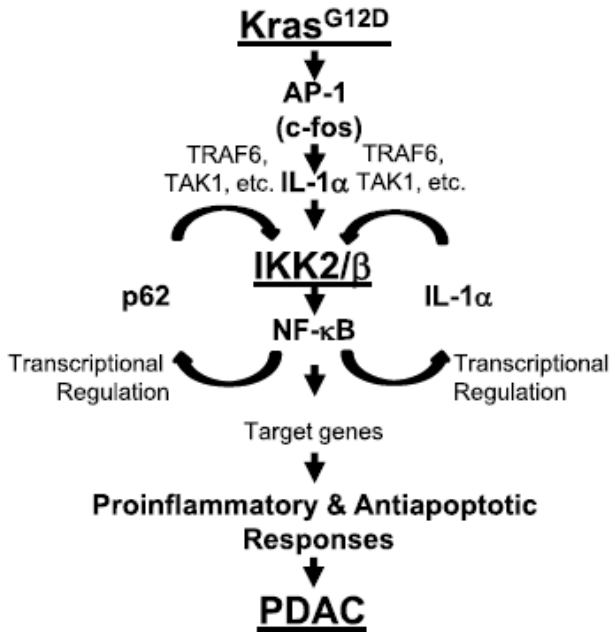
KRAS mRNA (TCGA) vs survival



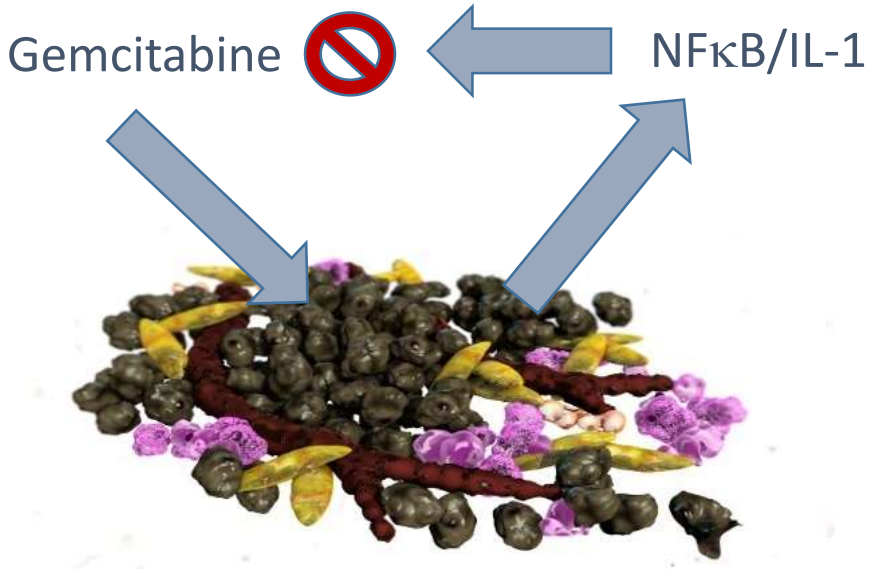
IL1RAP mRNA (TCGA) vs survival



Pancreatic ductal adenocarcinoma (PDAC)

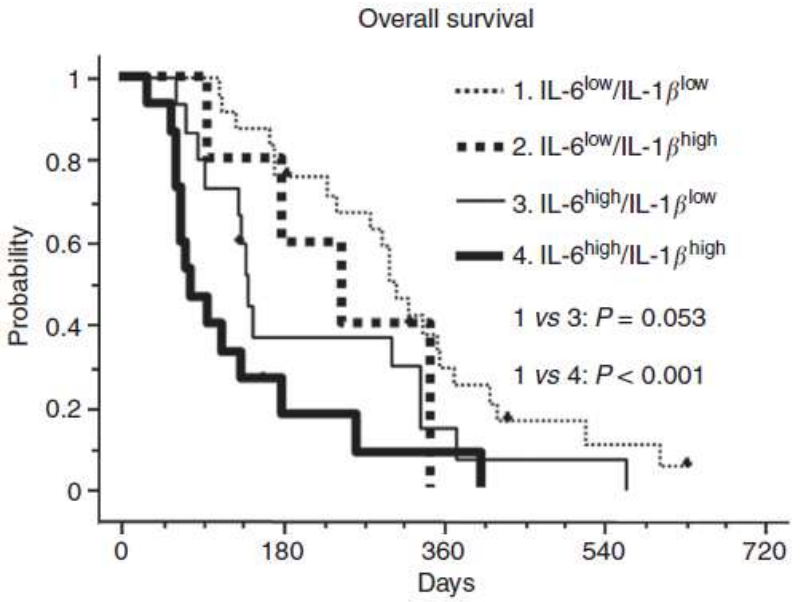


Ling et.al, KRAS^{G12D}-Induced IKK2/β/NF-κB Activation by IL-1α and p62 Feedforward Loops is Required for Development of Pancreatic Ductal Adenocarcinoma, Cancer Cell 2012



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-1β can predict the efficacy of gemcitabine in patients with advanced pancreatic cancer, Br J Cancer 2013

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IL-1 combinations in pancreatic cancer

Treatment:
MABp1 (anti-IL1α 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

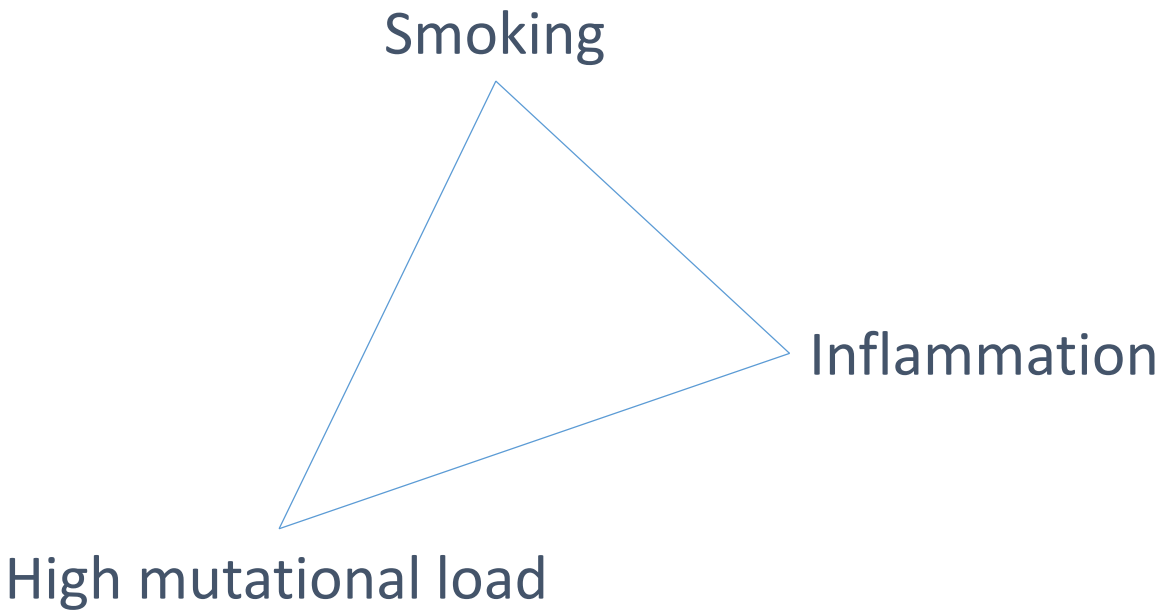
Treatment:
Anakinra (IL1-RA) in combination with gemcitabine, nab-paclitaxel and cisplatin

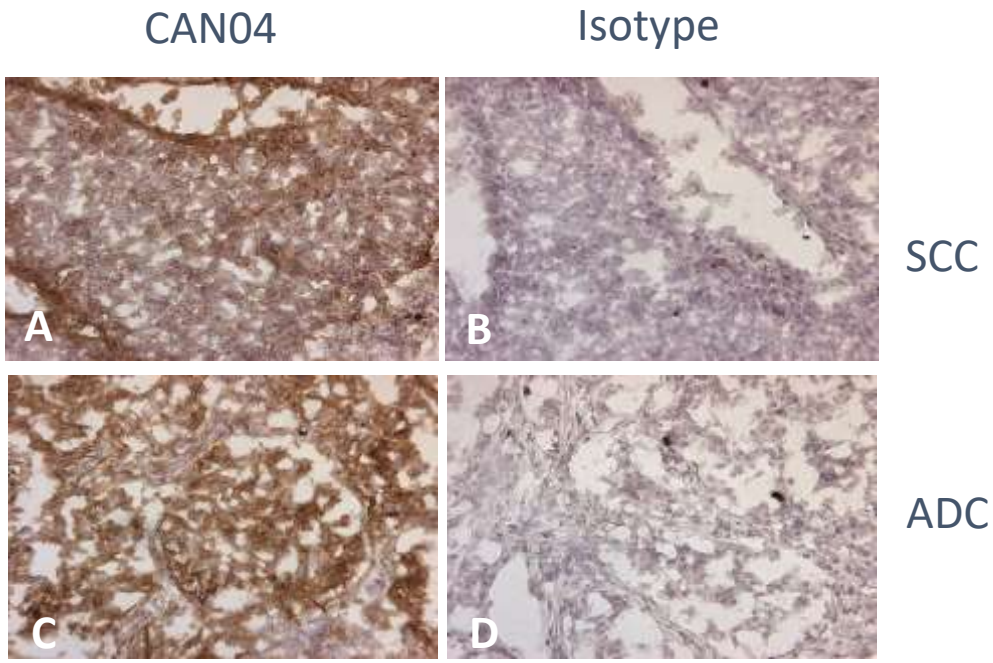
Objectives:
Pilot study to evaluate improved survival (DFS) by the addition of anakinra to chemotherapy combo.
Secondary measures:

- 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)





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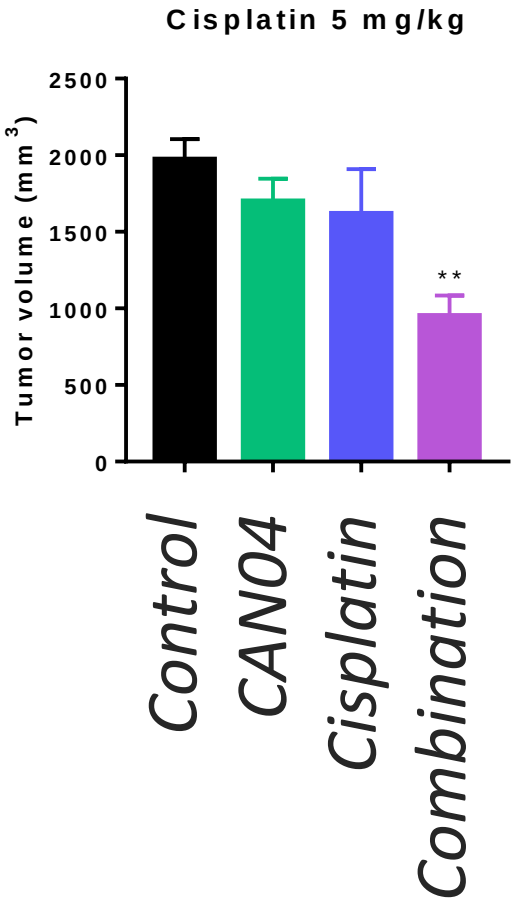

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Combination CAN04/Cisplatin superior to individual agents

- **Reduction in severe toxicity**
- **Increased efficacy**

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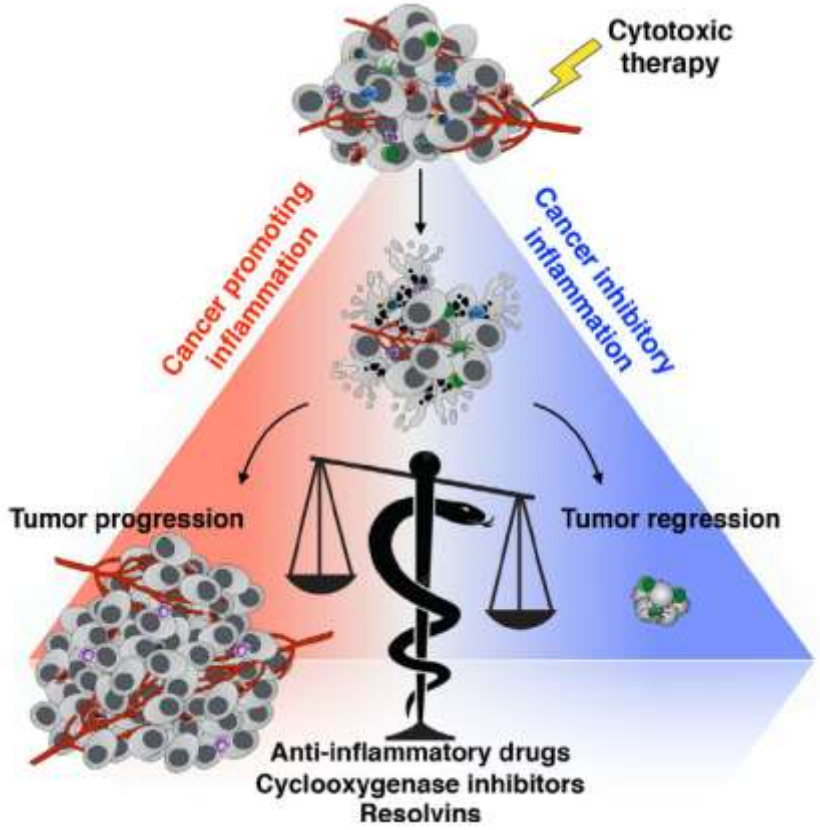
Summary

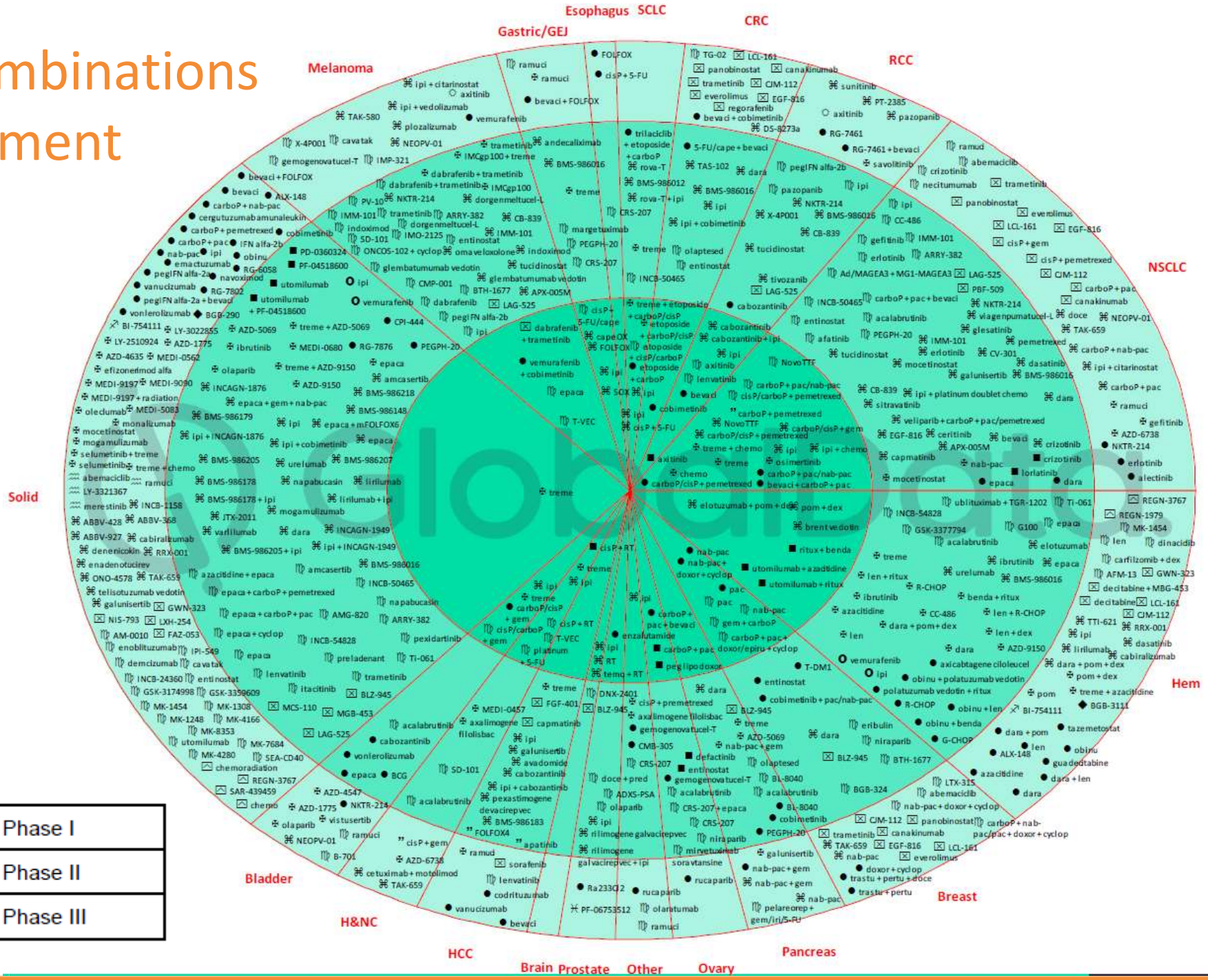
- Tumor inflammation contributes to many of the hallmarks of cancer, is required for tumor development and contributes to resistance to therapy
- IL-1 is involved in tumor growth, metastasis and resistance to therapy
- Therapy resistance can be cancer cell intrinsic or via cells in the TME
- Evidence 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



Bonavita et.al, Resolving the dark side of therapy-driven cancer cell death, JEM 2017
Sulciner et.al, Resolvins suppress tumor growth and enhance cancer therapy, JEM 2017

PD-(L)1 combinations in development



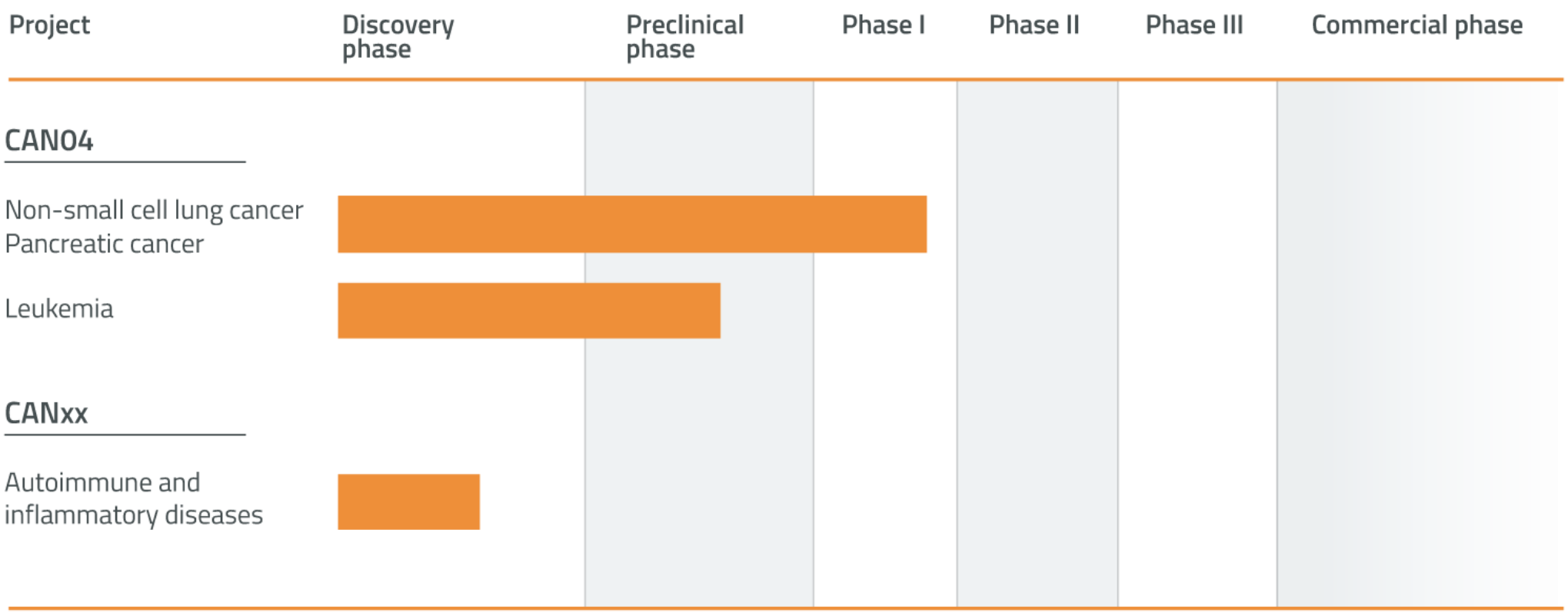
	Phase I
	Phase II
	Phase III

Legend	PD-(L)1 Base	Company
●	atezolizumab	RHHBY
■	avelumab	MRK.DE
◆	BGB-A317	BGNE
⇗	BI-754091	B.I.
O	CX-072	CTMX
♱	durvalumab	AZN
☼	JS-001	SH Junshi
≈	LY-3300054	LLY
⌘	nivolumab	BMY
⊠	PDR-001	NVS
⫛	pembrolizumab	MRK
⊠	cemiplimab	REGN
❞	SHR-1210	JS Hengrui
❒	TSR-042	TSRO
⋕	PF-06801591	PFE

Combination therapy

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

Cantargia pipeline

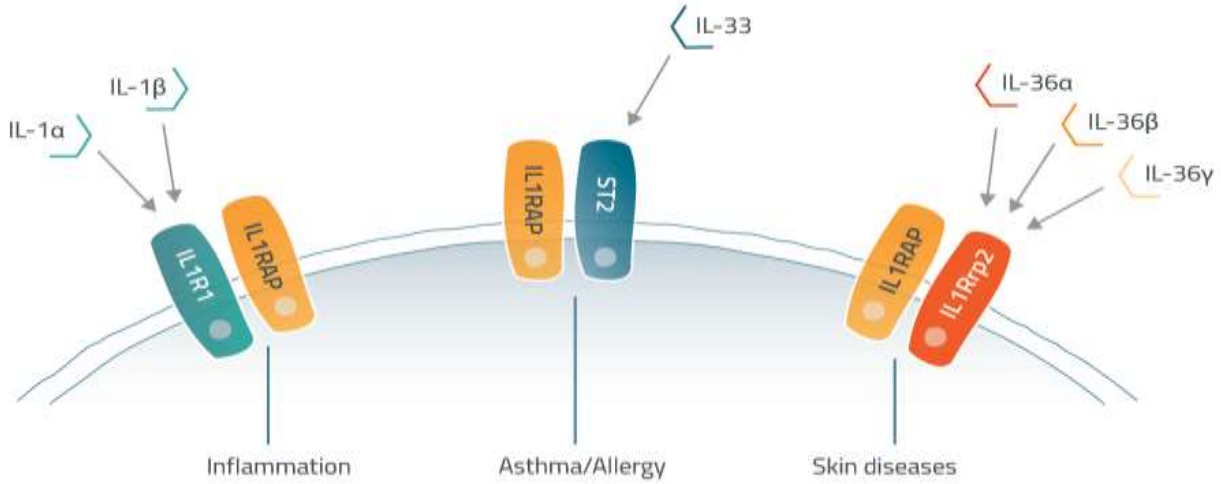


CANTOS additional findings (from Novartis IL-1β antibody)

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.