immutep

LAG-3 IMMUNOTHERAPY

A Novel IO Therapy (eftilagimod alpha) in Metastatic Breast Cancer and other settings

KOL call – 26th June 2019

(ASX: IMM, NASDAQ: IMMP)

KOL Biographies

Luc Y. Dirix, MD, PhD

Dr. Luc Dirix is Head of Medical Oncology at the Oncology Center at AZ Sint-Augustinus Hospital in Antwerp, Belgium

Principal investigator of the AIPAC trial

Prof. Salah-Eddin Al-Batran

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Principal investigator of the INSIGHT trial

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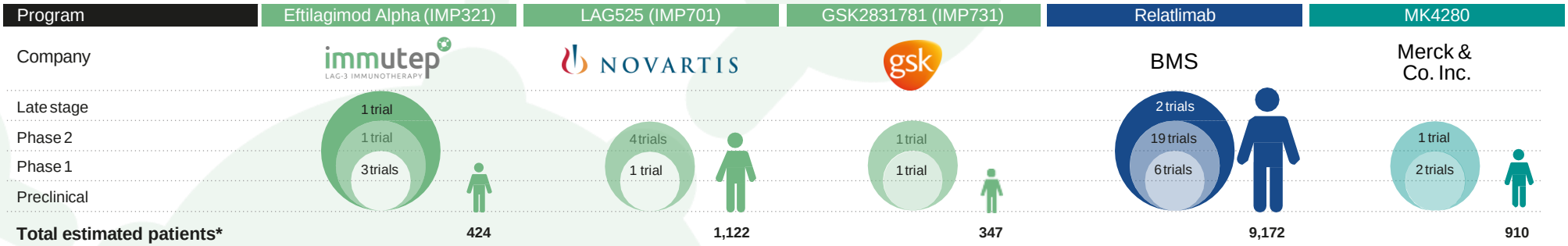
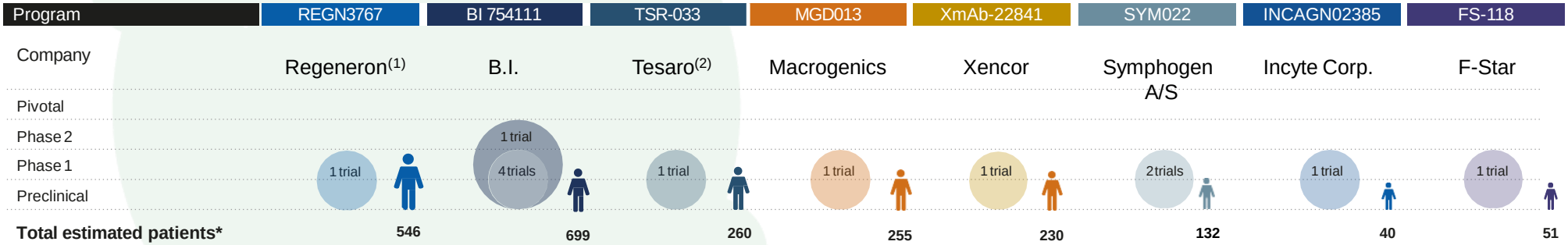
LAG-3 Clinical Development Overview

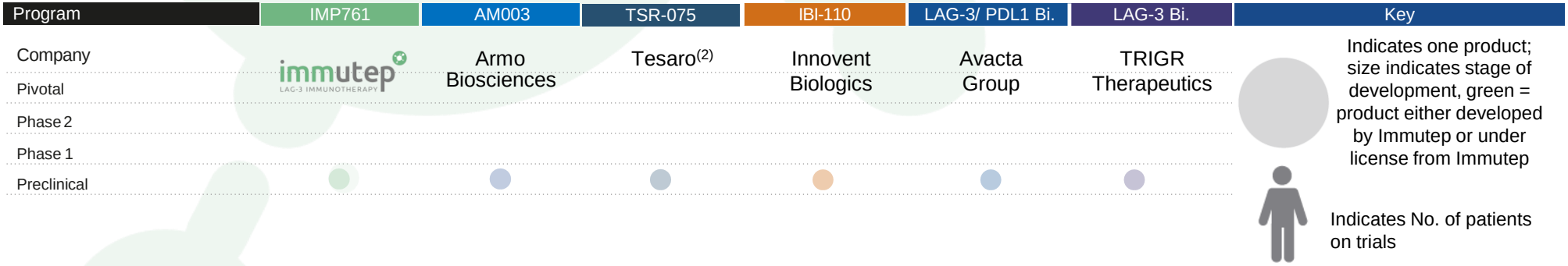
Frédéric Triebel, MD, PhD

LAG-3 Therapeutic Landscape Overview

Immutep is the leader in developing LAG-3 modulating therapeutics







Notes:

Sources: GlobalData, company websites, clinical trials.gov, and sec.gov

Information as of June 14, 2019, includes planned and completed trials, includes trials where the company may not be the sponsor

(1) As of January 7, 2019 Regeneron is in full control of program and continuing development

(2) Tesaro was acquired by and is now part of GSK

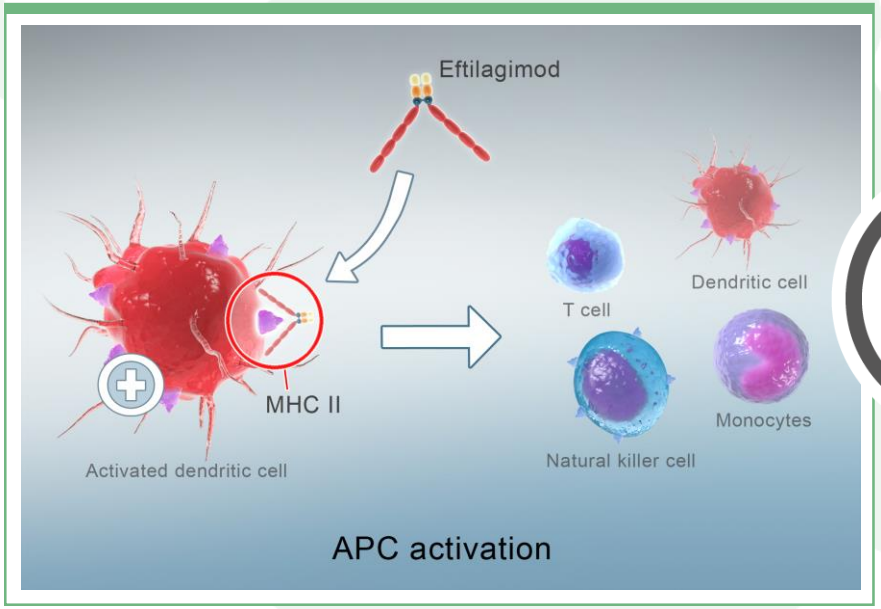
Eftilagimod Alpha

(Efti, IMP321)

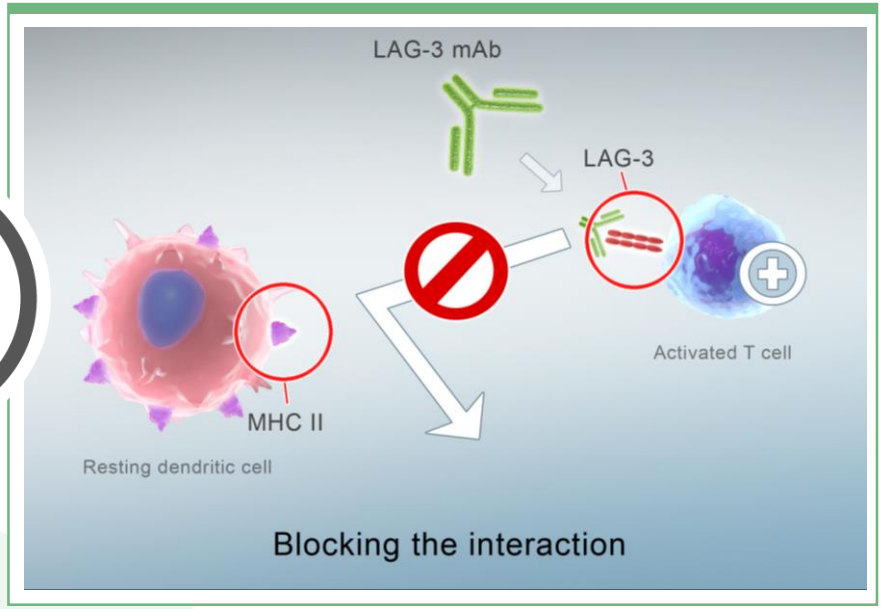
Efti - Innovative LAG-3 IO Product Candidate

- Only APC targeting LAG-3 product candidate currently in clinical development
- A unique approach (“turning cold tumors into hot tumors” with LAG-3)
- Synergistic with other therapeutic agents and modalities e.g. IO agents, chemotherapy

“PUSHING THE ACCELERATOR ON IMMUNE RESPONSES”



“RELEASING THE BRAKE ON THE T CELL”



Efti is a MHC II **agonist**

APC activator

- Boost and sustain the $CD8^+$ T cell responses
- Activate multiple immune cell subsets

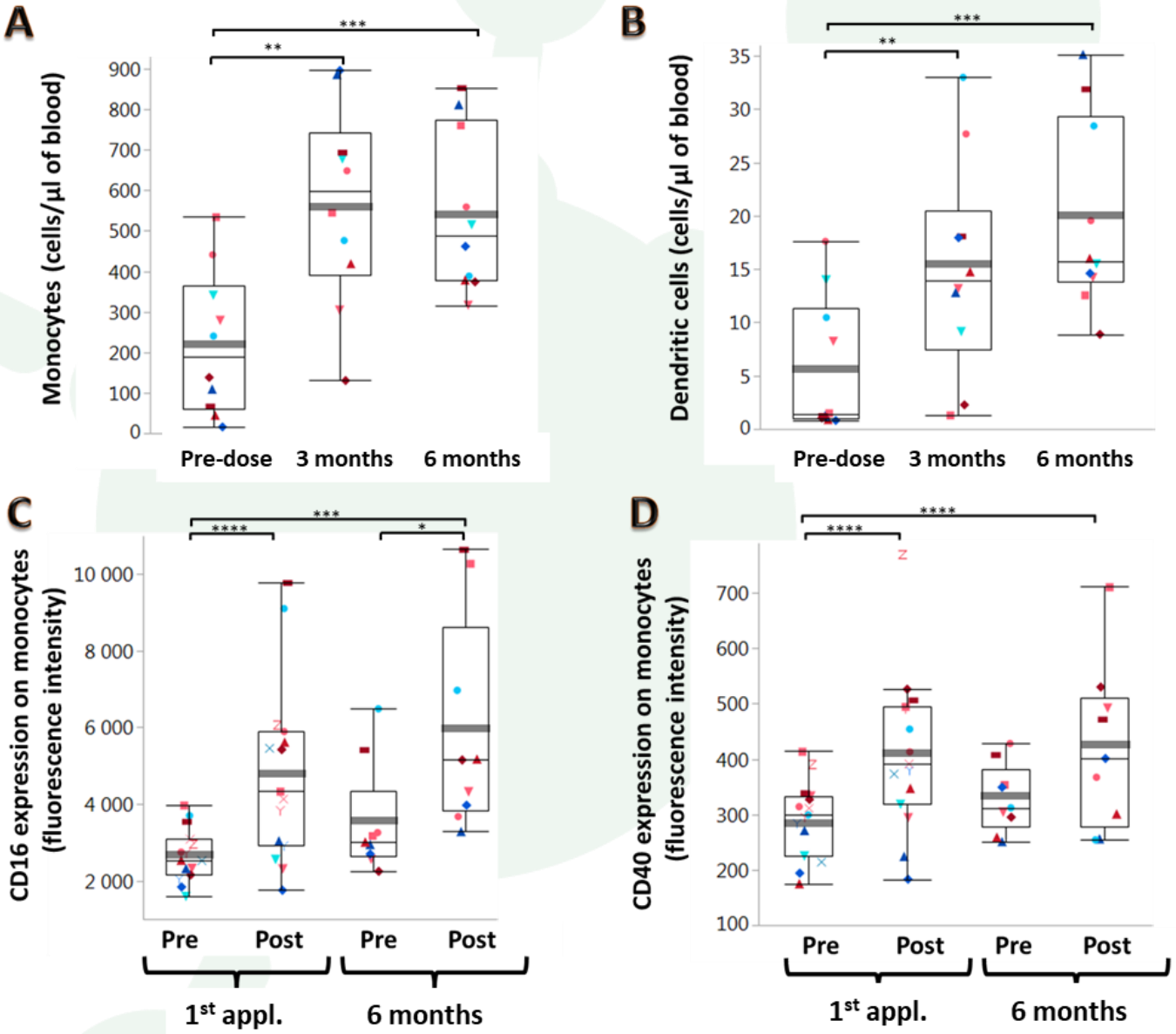
LAG-3 antagonist, or blocking, antibodies:

Immune checkpoint inhibitor

- Increase cytotoxicity of the pre-existing CD8 T cell response

Efti Pharmacodynamic Effect (AIPAC Immunomonitoring)

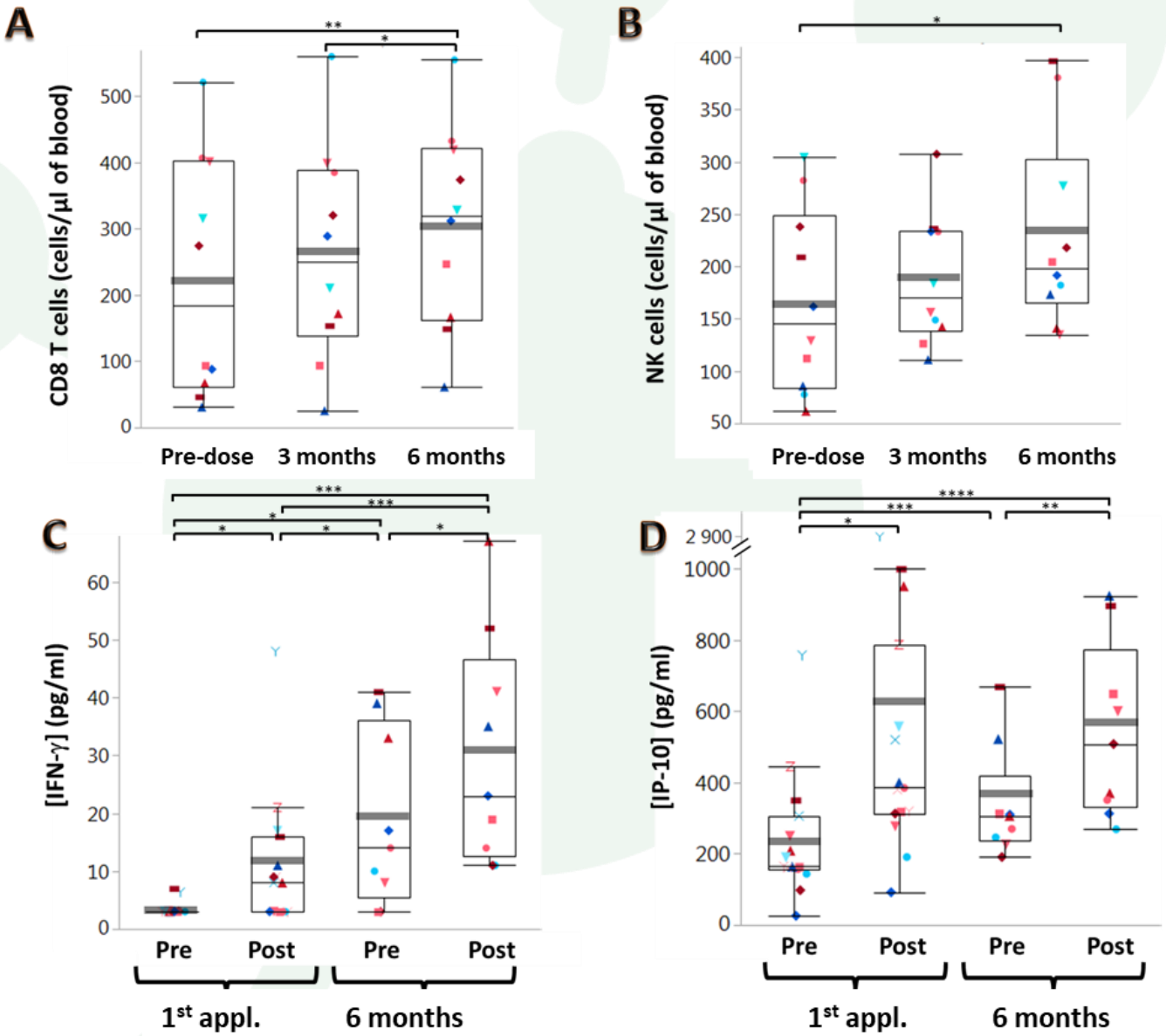
Primary Target Cells



Primary target cells: Sustained increase of circulating Antigen-Presenting Cells (APCs) like monocytes (A) and dendritic cells (B). Rapid activation of monocytes (CD16 (C) and CD40 (D)).

Efti Pharmacodynamic Effect (AIPAC Immunomonitoring)

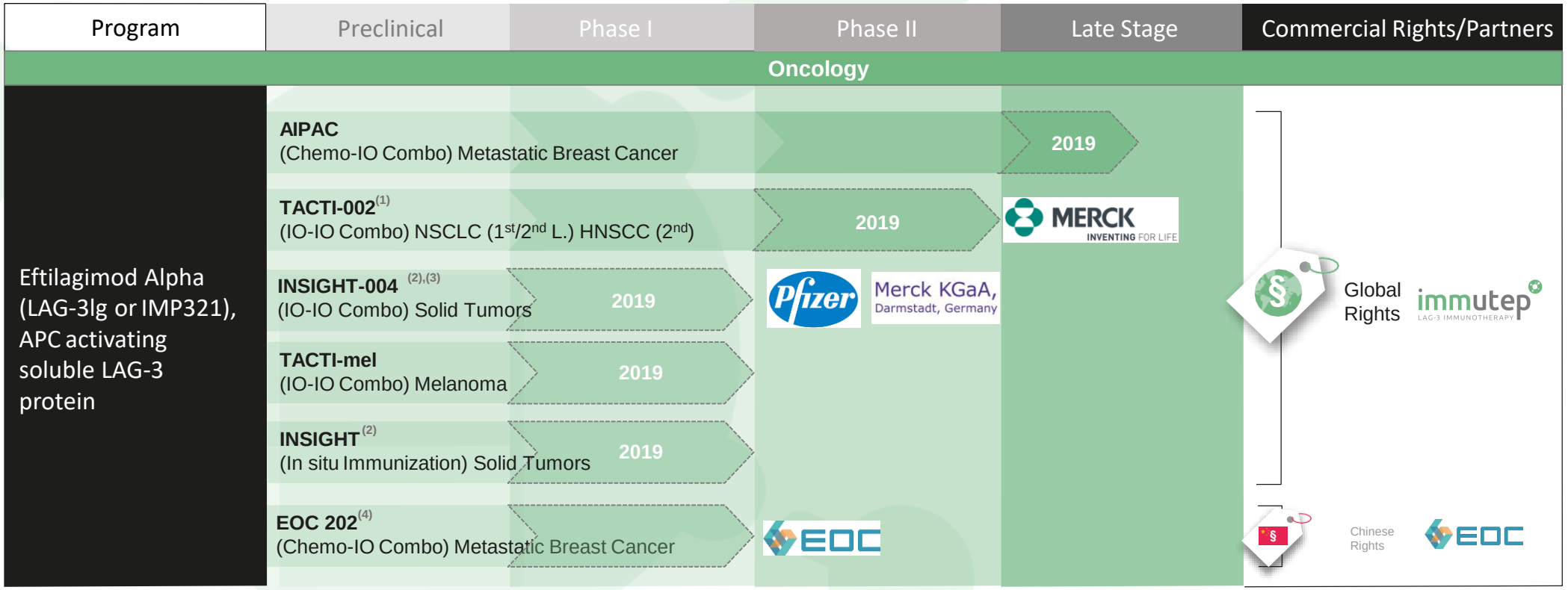
Secondary Target Cells



Secondary target cells: Sustainable increase in absolute numbers of effector cells like i.e. CD8 T cells (A) and Natural Killer cells (B). IMP321 induces early and sustainable increase of Th1 biomarkers like IFN-γ (C) and IP-10 (CXCL10, D).

Eftilagimod Alpha Clinical Trials*

*Expecting multiple data readouts throughout H2 2019**



Notes

* Actual timing of data readouts may differ from expected timing shown above. Information in pipeline chart current as at 25 June 2019

(1) In combination with KEYTRUDA® (pembrolizumab) in non-small cell lung carcinoma ("NSCLC") or head and neck carcinoma ("HNSCC")

(2) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this clinical trial

(3) In combination with BAVENCIO® (avelumab)

(4) EOC Phama is the sponsor of the EOC 202 clinical trial which is being conducted in the People's Republic of China

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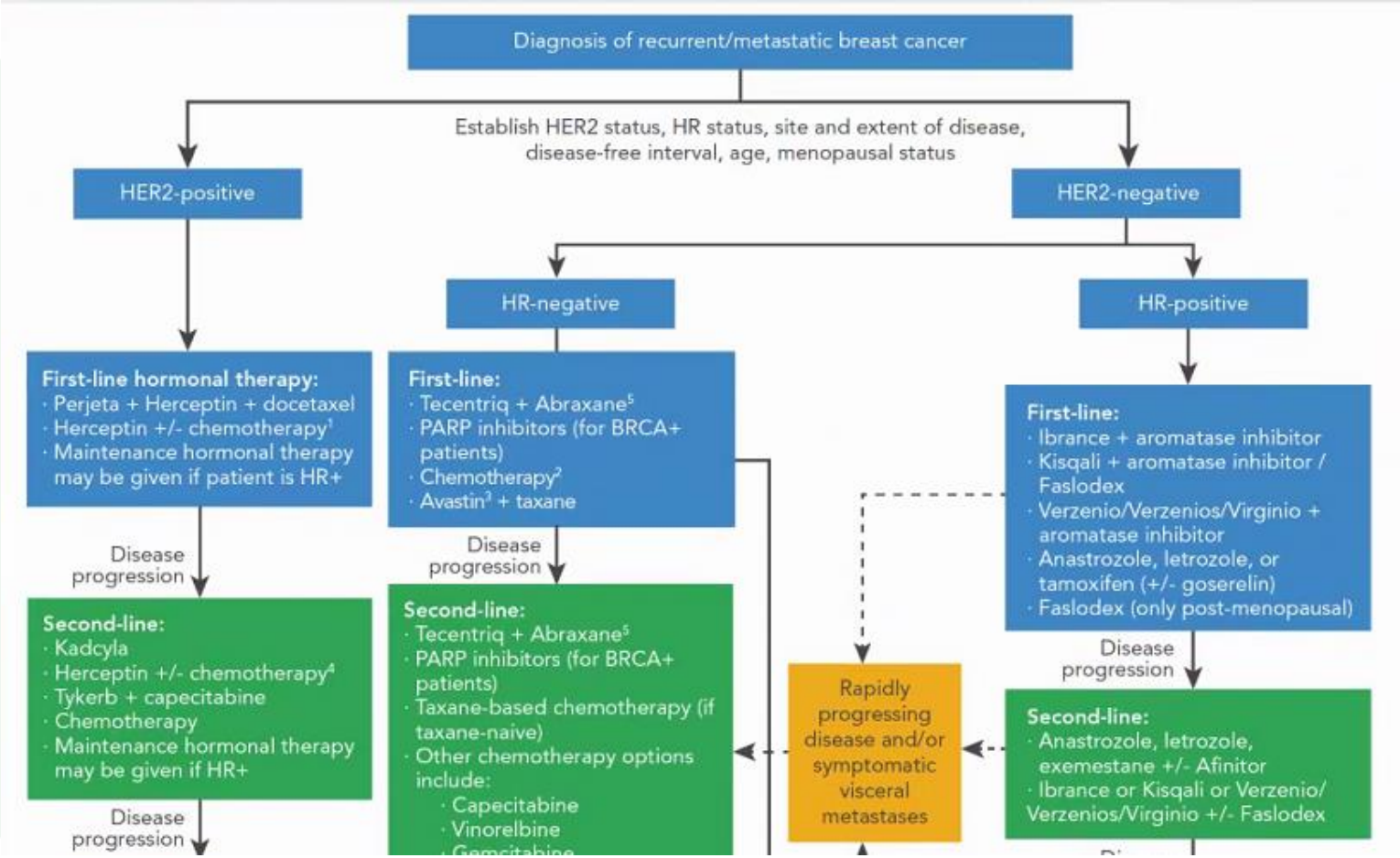
Metastatic Breast Cancer
An Overview

Luc Dirix, MD, PhD

Treatment Landscape for MBC

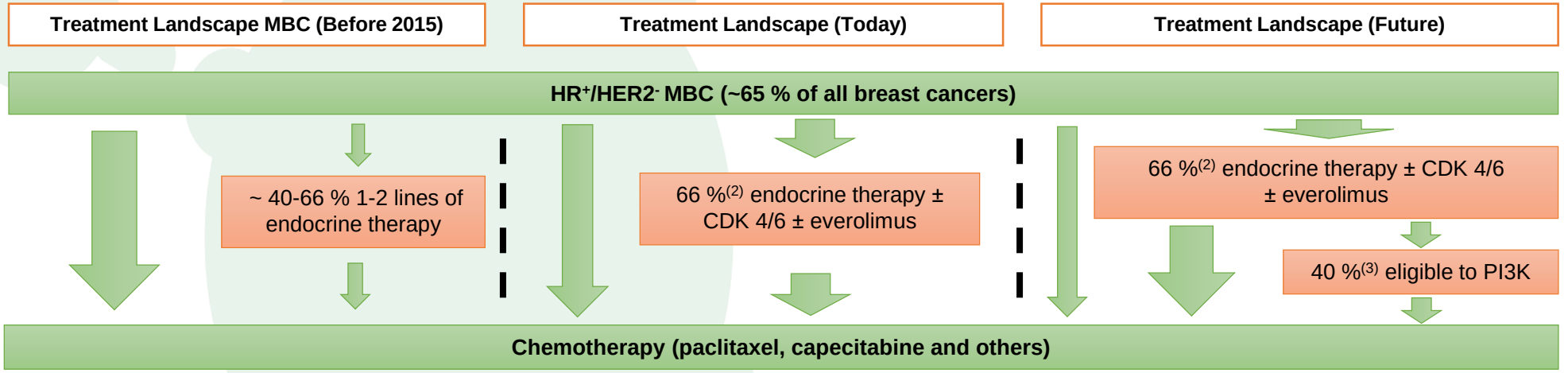
- Current SOC
  - ❖ $HR^{+/-}/HER2^{+}$ MBC: chemo + passive immunotherapy (e.g. anti-HER2 trastuzumab)
  - ❖ TNBC: chemo + active immunotherapy (e.g. anti-PD-L1 atezolizumab)
  - ❖ $HR^{+}/HER2^{-}$: combined endocrine therapy followed by single agent chemo (details next slide)



Treatment Landscape for HR+/HER2- MBC

Epidemiology:

- 812,500 HR+/HER2- diagnoses p.a. worldwide(1)
- ~ appr 250.000 develop metastatic disease and are eligible to chemotherapy



- Despite all changes → no improvement for patients receiving chemotherapy
- Paclitaxel one of the most widely used chemotherapies
- No active IO in this setting thus far
- No active development of any IO agent or other game changer in late stage clinical trials

Notes

(1) Source: GlobalData 2019 MBC – metastatic breast cancer BC – breast Cancer
(2) Caldeira et al Oncology and therapy 2016; 4:189-197
(3) https://www.ascopost.com/News/59389 ; Usage to be determined as not yet approved by EMA
(4) https://www.onclive.com/insights/mbc-endocrine-partner/role-of-pi3k-inhibitors-in-hr-positive-metastatic-breast-cancer

HR+/HER2- MBC Treatment Landscape Comment on Recent Changes

- Introduction of CDK4/6 therapies in the EU:
  - Longer stay on reinforced endocrine therapies (6 months to >12 months)
  - 10-20% remain insensitive
  - 80-90% become resistant after 12 to 36 months
  - No impact on the randomized AIPAC trial results
  - Patients receive more treatment lines before they enter chemotherapy --> effects on efficacy not know thus far
- New agents since CDK4/6
  - PI3Kα inhibitor alpelisib + fulvestrant in second line endocrine therapy (for patients with PI3K mutations) → ~ 40 % (1)
  - Increases PFS from 6 to 11 months
- HR+/HER2- MBC: remains an incurable disease (median OS 24 months at start of chemotherapy) (2),(3)

Sources
(1) https://www.ascopost.com/News/59389
(2) https://www.ncbi.nlm.nih.gov/pubmed/29174181/
(3) https://www.ncbi.nlm.nih.gov/pubmed/19720913

What Are Medical Needs for $HR^+/HER2^-$ MBC?

Ultimate Goal: identify safe therapies prolonging survival with a good QoL

1. Find the right sequence of endocrine + CDK4/6 therapy

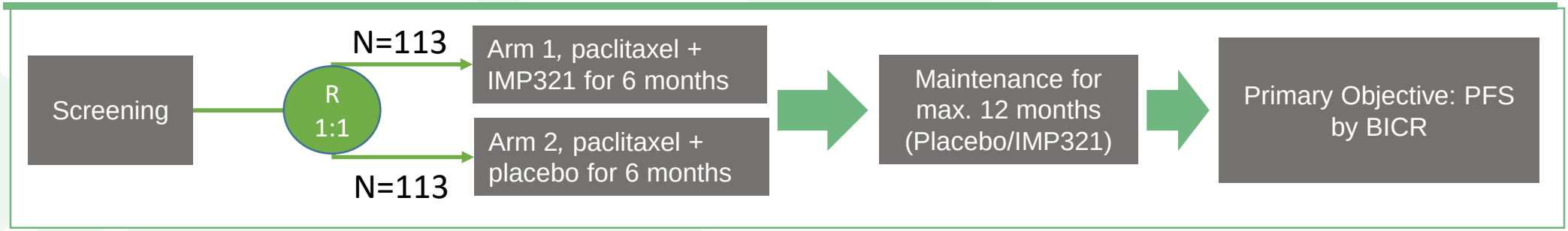
2. When and how to use selective PI3K inhibitors in patients with mutations

3. Adding an active immunotherapy to first-line single agent chemotherapy:
   - PD-1/PD-L1 antibodies have not been successful to date in $HR^+/HER2^-$ patients with cold tumors which need first APC activation to induce CD8 T cells
   - Eftilagimod alpha is an APC activator injected s.c. with a good safety profile

R2PD – recommended phase 2 dose, ORR – overall response rate, PFS – progression free survival, OS – overall survival, PK –pharmacokinetics

AIPAC – Randomized Part

AIPAC: Active Immunotherapy PAClitaxel in MBC



Other Objectives	Anti-tumor activity, safety and tolerability, PK, immunogenicity, quality of life, overall survival
Patient Population	Advanced $HR^+/HER2^-$ MBC with measurable disease indicated to receive 1^{st} line weekly paclitaxel
Treatment	Arm 1: Paclitaxel + IMP321 (30 mg) Arm 2: Paclitaxel + Placebo
Location	>30 sites in 7 (GB, DE, PL, HU, FR, BE, NL) EU countries

- ✓ Double blinded, randomized, potentially pivotal trial
- ✓ Fully recruited Jun 2019
- ✓ Read-out expected Q1 2020
- ✓ Designed to unequivocally demonstrate the efficacy of an APC activator
- ✓ EU conditional marketing authorization possible with single phase IIb trial depending on HR ratio and safety

R2PD – recommended phase 2 dose, ORR – overall response rate, PFS – progression free survival, OS – overall survival, PK –pharmacokinetics

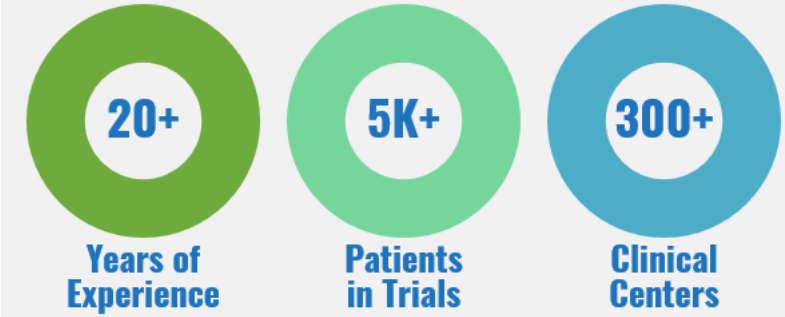
INSIGHT Trial

Salah AL-Batran, MD, PhD

IKF at a Glance (1)

The IKF at a glance

- Location: Frankfurt, Germany
- Founded in 2010 by Prof. Al-Batran MD
- Academic Clinical Research Institution
- Phase I unit and lab and other medical facilities on site
- Network of 500 clinical trial centers
- Several practice changing findings



Nationwide Collaborations /Networks

Bundesministerium für Bildung und Forschung

Hessisches Onkologiekonzept Versorgungsgebiet Frankfurt-Offenbach

UCT Universitäres Centrum für Tumorerkrankungen Frankfurt University Cancer Center

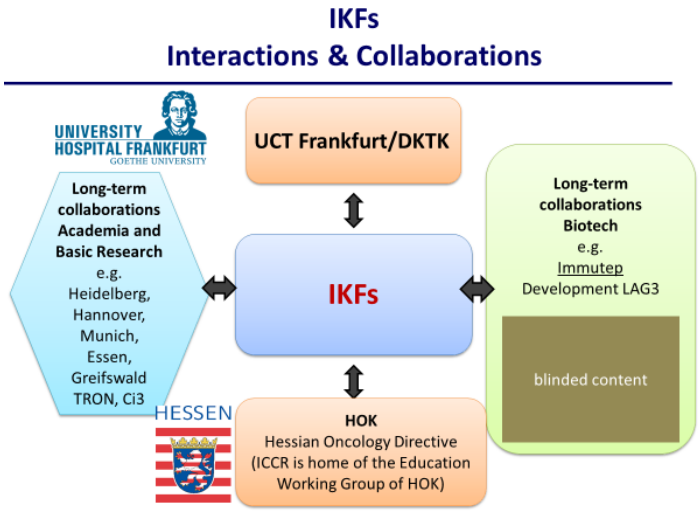
Gefördert durch DFG Deutsche Forschungsgemeinschaft

Deutsche Krebshilfe HELFEN. FORSCHEN. INFORMIEREN.

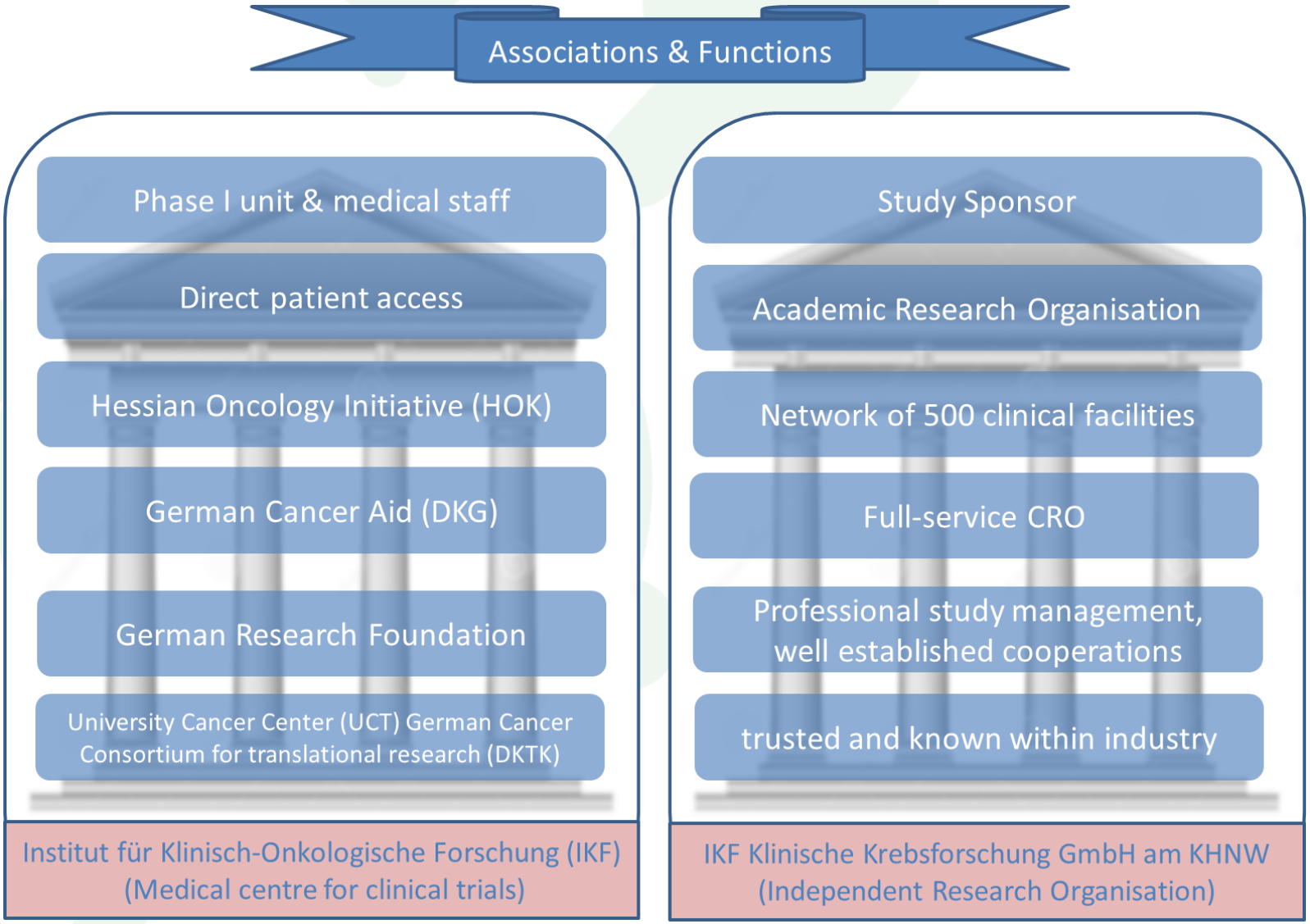
Gemeinsamer Bundesausschuss

Ci3 Cluster für individualisierte Immunintervention – Der Spitzencluster

DKTK Deutsches Konsortium für Translationale Krebsforschung

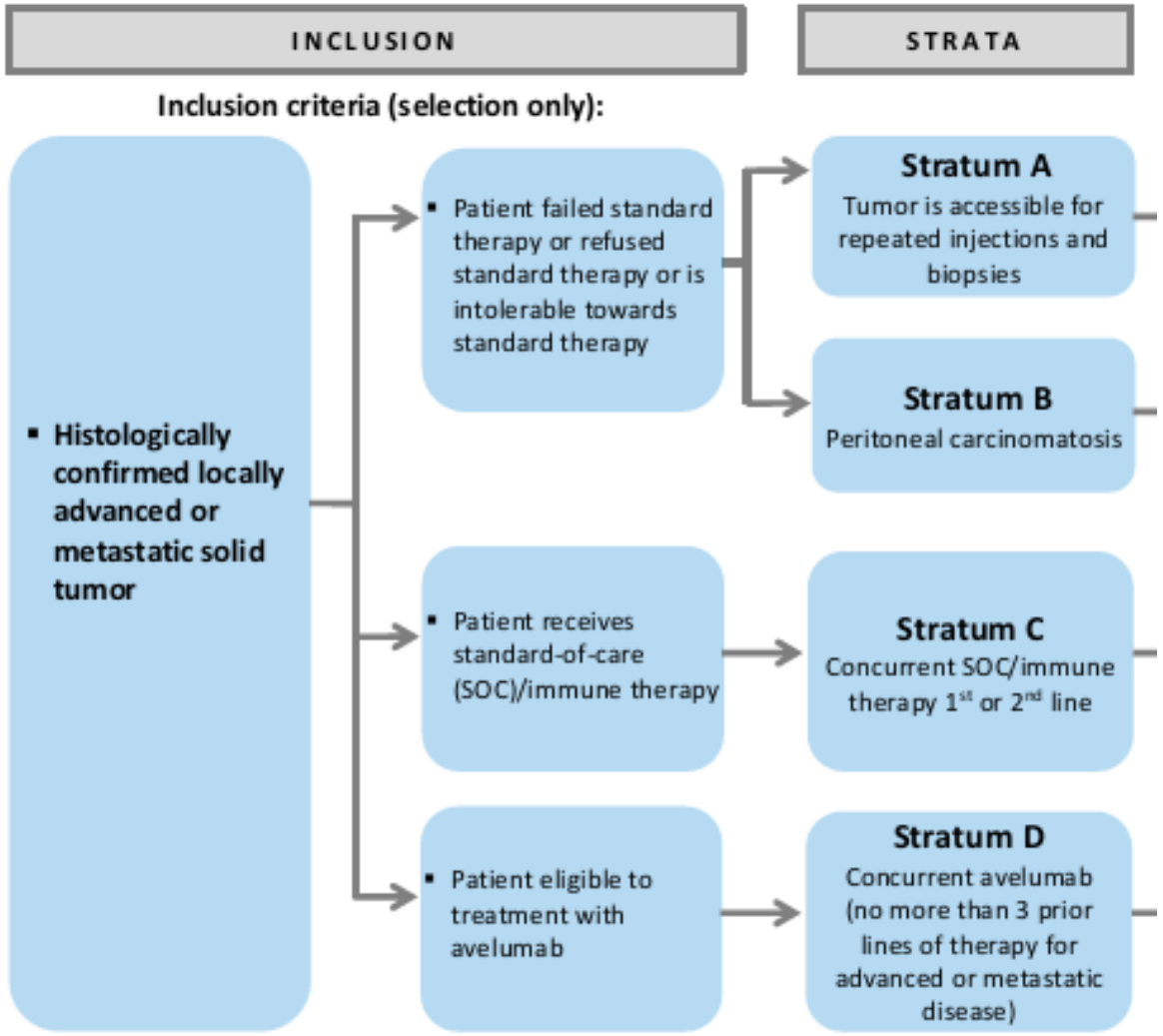


IKF at a Glance (2)

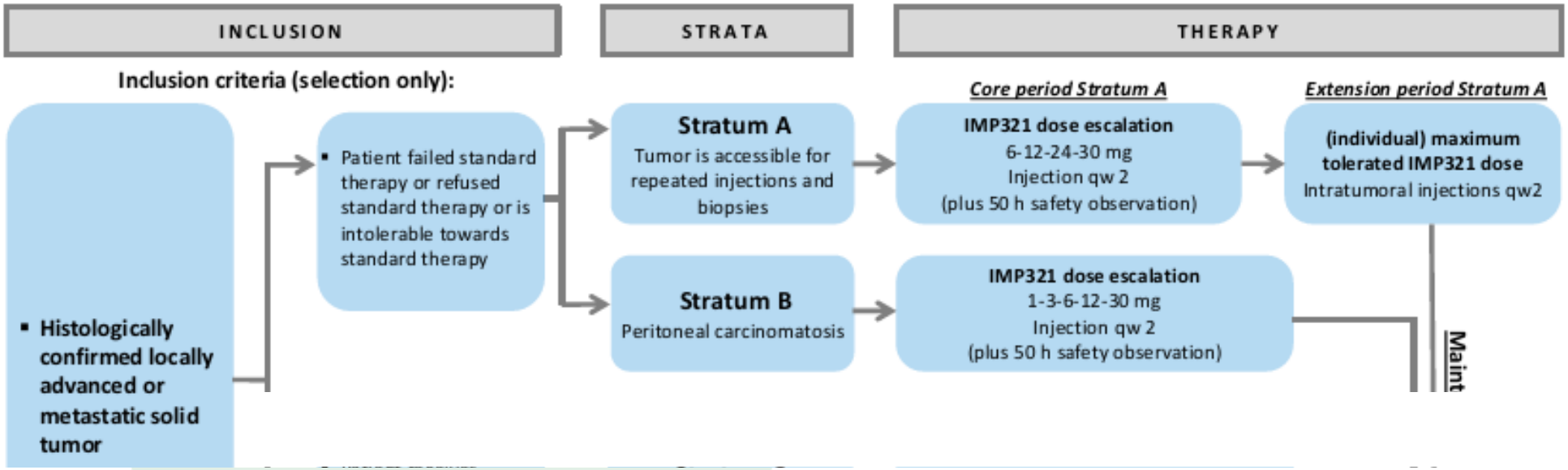


INSIGHT: Design Overview

- INSIGHT is an investigator initiated trial (IIT) with eftilagimod alpha in different settings
- INSIGHT focused on safety and feasibility → dose escalation / confirmation design
- INSIGHT contains 4 different strata:
- Stratum A: Feasibility of intratumoral injection
- Stratum B: Feasibility of intraperitoneal injection
- Stratum C: combination of efti (s.c.) with standard of care
- Stratum D: Feasibility of combination of avelumab (PD-L1 antagonist) with efti (s.c.)

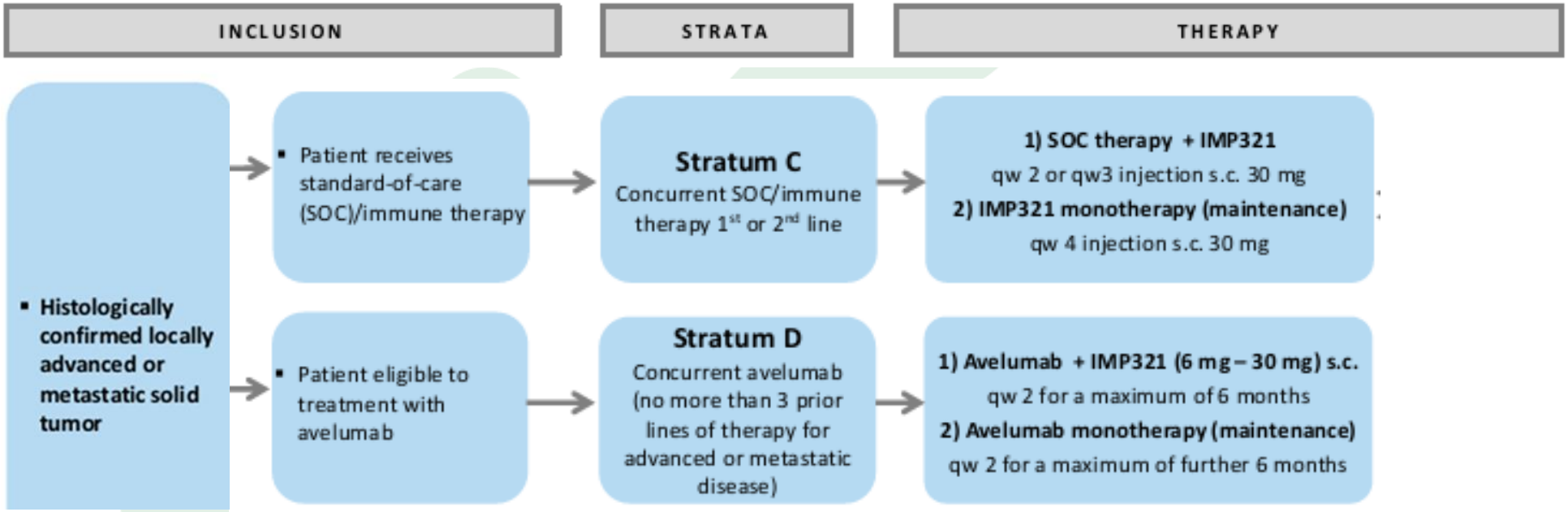


INSIGHT: Design Stratum A + B



- Up to 9 (stratum A) and 9 (stratum B) with interpatient escalations were planned
  - 8 pts completed core period for stratum A
  - 4 pts completed core period for stratum B

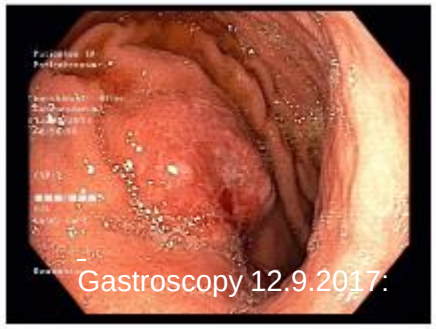
INSIGHT: Design Stratum C + D

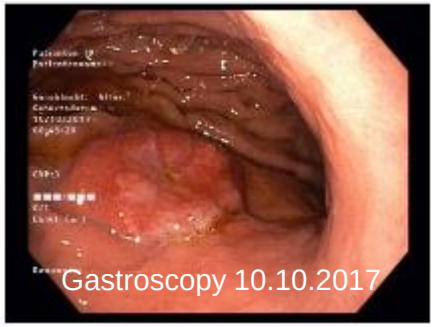


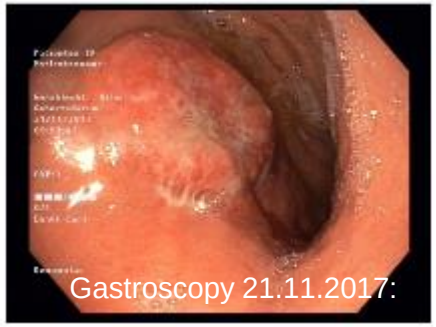
- 20 (stratum C) – not yet recruiting
- Stratum D:
  - Safety + tolerability of avelumab plus efti (6 and 30 mg s.c.)
  - 2 pts enrolled since June 1st 2019

INSIGHT: Single Case

- **Pat 001-001 male, born 1939; metastatic Gastric Cancer of the Corpus, initial diagnosis: 04/2016; Previous therapies 5-FU, Leucovorin, Oxaliplatin, Docetaxel (FLOT) in first line and 5-FU, Leucovorin, Irinotecan (FOLFIRI) in second line**
  - **Stratum A (intratumoral), Escalation cohort**
  - Study Start 08-Sep-2017
  - 7 intratumoral injections: from 08-Sep-2017 (6 mg) to 05-Dec-2017 (30 mg)
  - Multiple assessments with stable disease including 06-Nov-2017: Stable disease
  - 08-Dec-2017: growing lymph node left the kidney
  - PFS: 88 days
  - No SAEs, No DLTs, AEs:
    - Hypertension NCI grade 3 recovered on same day 26-Sep-2017 unrelated
    - 1 AESI: Chills NCI grade 3 recovered on same day 05-Dec-2017 probably related
  - **Current status: Patient still alive: nearly two years+ survival after study entry in a third line therapy setting (usually median survival of 2-4 months)**


Gastroscopy 12.9.2017:


Gastroscopy 10.10.2017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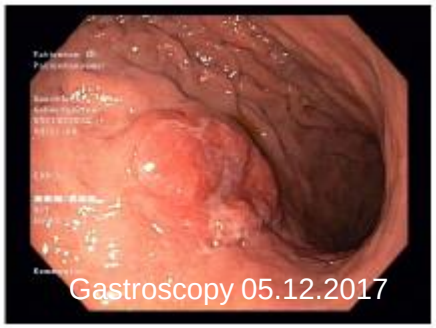
Gastroscopy 05.12.2017

Questions???
Thank you!