The "INSIGHT" Trial:

Two new strata of an explorative, single center, open-labeled, phase I study to evaluate the feasibility and safety of subcutaneous injections with IMP321 (LAG-3Ig fusion protein, eftilagimod alpha) combined with either standard-of-care drug therapy or combined with PD-L1 inhibition (avelumab) in advanced stage solid tumor entities

Daniel W. Mueller[1,5], Thorsten O. Goetze[1,5], Akin Atmaca[2], Mohammad-Reza Rafiyan[2], Elke Jäger[2], Christian Brandts[3], Urs Pabst-Giger[4], Markus Düx[2], Thomas W. Kraus[2], Simon Stahn[2], Regina Eickhoff[5], Salah-Eddin Al-Batran[1,5]

(Authors' affiliations: [1]Institute of Clinical Cancer Research (IKF) at Krankenhaus Nordwest, UCT-University Cancer Center, Frankfurt, Germany; [2]Krankenhaus Nordwest, Frankfurt, Germany; [3]Universitätsklinikum Frankfurt, Germany; [4]Universitätsklinikum Münster, Germany; [5]IKF Klinische Krebsforschung GmbH am Krankenhaus Nordwest, Frankfurt, Germany)

Background

The two new strata of the INSIGHT trial evaluate feasibility and safety of s.c. IMP321 injections (eftilagimod alpha) in combination with either SOC 1st / 2nd line drug therapy (Stratum C) or in combination with an PD-L1 inhibitor (avelumab; Stratum D) in advanced stage solid tumors as well as to generate first efficacy data. IMP321 is a MHC class II agonist that activates antigen-presenting cells (primary target cells) and then CD8 T cells (secondary target cells). Activation of the dendritic cell network and subsequent T cell recruitment at the tumor site with IMP321 may lead to enhanced anti-tumor CD8 T cell responses. Thus, especially combinations with PD-1/PD-L1 inhibitors might display interesting effects by activating immune cells and disabling immune inhibitory mechanisms at the same time.

Methods

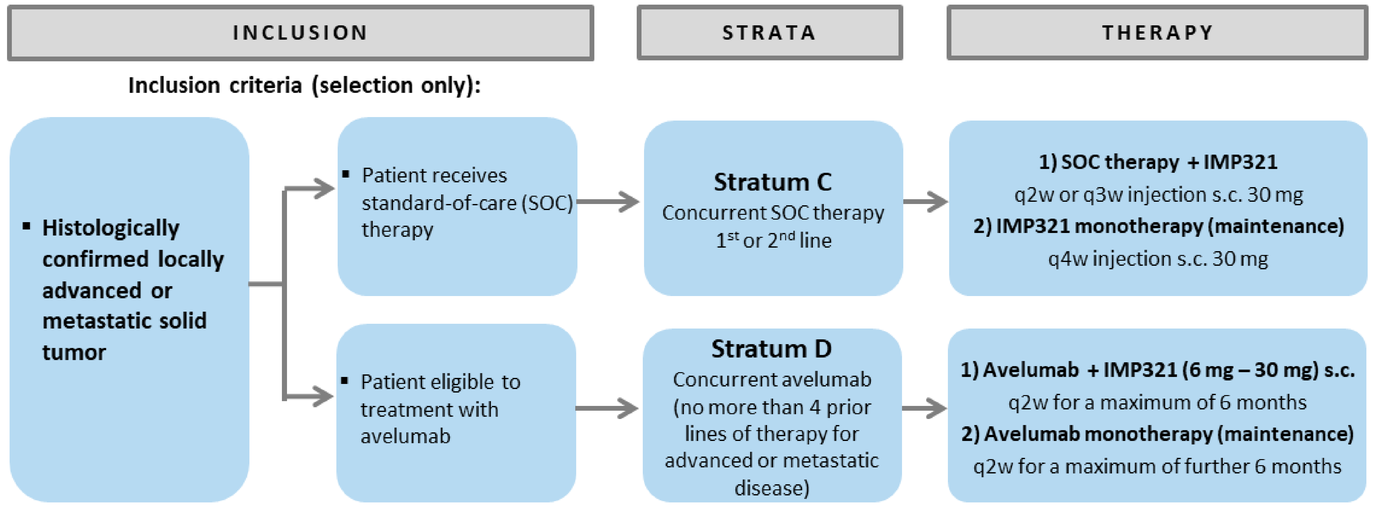
This is a prospective investigator initiated phase I trial consisting of four strata, two of which have recently been opened for recruitment:

New **Stratum C:** Patients with solid tumors treated with SOC chemo- or targeted therapy in first or second line receive concomitant s.c. IMP321 (30mg) injections. This combination is aimed to enhance the immune response against tumor cells compared to chemo-/ targeted SOC therapy alone.

New **Stratum D:** Patients will receive avelumab i.v. q2w (800mg) along with s.c. IMP321 injections (6mg or 30mg) for up to 12 cycles. Patients may continue receiving avelumab monotherapy for further 12 cycles. The recommended phase 2 dose of avelumab plus IMP321 will be determined and the activity of IMP321 in combination with avelumab evaluated.

The combination of IMP321 and avelumab is aimed to enhance efficacy by combining IMP321's activating effects on immune cells with the release of immune inhibitory effects caused by interruption of the PD-1/PD-L1 axis by avelumab.

Study Scheme (Strata C + D only)



- **Primary endpoint: Feasibility** (*rate of pts. receiving protocol treatment without occurrence of a DLT)*
  - Safety, tolerability and recommended phase 2 dose of IMP321 when combined with avelumab
  - Safety and tolerability of IMP321 when added to SOC drug therapy
- **Primary efficacy endpoint:** Overall response rate (RECIST 1.1)
- **Translational endpoints:** Immune response in whole blood and tumor tissue

Study is open for recruitment; as of mid-May 2019, 14 pts have been recruited in total (all strata).

Outlook

If patients treated in course of this phase I study display immune and clinical responses, this POC data will build the basis to evaluate the safety and efficacy of IMP321 in combination treatment in larger sets of patients with defined tumor entities.

KRANKENHAUS NORDWEST

Study management contact information:

Dr. Daniel Mueller
mueller.daniel@ikf-khnw.de

Study identifiers:

EudraCT-No.: 2016-002309-20
clinicaltrials.gov: NCT03252938

IKF Klinische Krebsforschung am Krankenhaus Nordwest