The “INSIGHT” Trial: An explorative, single center, open-labeled, phase I study to evaluate the feasibility and safety of intra-tumoral, intraperitoneal, and subcutaneous injections with IMP321 (LAG-3Ig fusion protein) for advanced stage solid tumor entities


Study management contact information:
Dr. Daniel Mueller
mueller.daniel@khnw.de
Phone: +49 69 7601 4125
Fax: +49 69 7601 3655

Study Scheme

Inclusion criteria (selection only):
- Patients selected for injection in the first stratum A; patients who no longer meet the inclusion criteria will be automatically included in strata B or C.

Stratum A
- Tumor is accessible for repeated injections and biopsies.
- Patient failed standard therapy or refused standard therapy or is intolerable towards standard therapy.

Stratum B
- Peritoneal carcinomatosis.
- Patient receives standard-of-care (SOC) therapy.

Stratum C
- Concurrent SOC therapy 1st or 2nd line.
- One or more lesions accessible (primary or secondary).

Inclusion

Strata

Therapy

Core period

IMP321 dose escalation
6-12-24-30 mg
Injection qw 2
(plus 50% safety observation)

IMP321 dose escalation
1-3-6-12-30mg
Injection qw 2
(plus 50% safety observation)

1) SOC therapy + IMP321
q2 injection s.c. 30mg
2) IMP321 monotherapy (maintenance)
q4 injection s.c. 30mg

Extension period

(individual) maximum tolerated IMP321 dose
Intratumoral injections qw2

Maintenance

Primary endpoint: Feasibility rate
(rate of pts. receiving protocol treatment according to planned schedule without occurrence of a DLT)

Secondary endpoints: Safety (AEs / SAEs), ORR, individual PFS, individual OS

Translational endpoints: Immune response in whole blood and tumor tissue

Study is open for recruitment; as of mid-May 2018, 7 pts have been recruited into Stratum A (dose escalation accomplished after 3 pts) and 2 pts have been recruited into Stratum B (dose escalation ongoing).

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 direct injection for treatment of the respective tumor entities in larger sets of patients.

Background
The INSIGHT study focuses on evaluation of the feasibility and safety of intratumoral and intraperitoneal injections of IMP321 (mono-agent) for the treatment of advanced stage solid tumors as well as to generate first efficacy data on such treatment. In the later stage, patients treated with a SOC therapy will receive additional s.c. injections with IMP321 to explore safety and efficacy of combined SOC+IMP321-therapy.

Methods
This is an explorative, mono-center, open-label, investigator initiated phase I trial consisting of three strata, two of which have recently been opened for recruitment:

In Stratum A, patients with solid tumors accessible for repeated injections and biopsies receive biweekly intra-tumoral injections with IMP321 (dose escalation 6-12-24-30 mg in first cohort and MTD in consolidation cohort).

In Stratum B, patients with additional peritoneal carcinomatosis receive intraperitoneal injections of IMP321 via a catheter (dose escalation 1-3-6-12-30 mg in first cohort and MTD in consolidation cohort).

In both cohorts, patients showing a treatment benefit after the last direct injection will be offered a maintenance treatment consisting of s.c. IMP321 injections for up to 52 weeks.

IMP321
IMP321 is a soluble form of the LAG-3 T cell surface receptor and represents a highly potent activator of antigen presenting cells (APC). It is a member of a new class of drugs known as "APC activators" (primary mode of action).