Conducting Clinical Trials in Germany:
Opportunities for translational research

24th of April 2017
In 2015, Germany was 2nd in the world for the number of clinical trials performed in the country by the research based pharmaceutical industry.

Source: Industry-financed clinical studies based on study registry, clinicaltrials.gov (June 2016)
A total of 599 studies conducted in Germany in 2015
- 131 Phase I studies
- 468 Phase II-III studies

Source: Industry-financed clinical studies based on study registry, clinicaltrials.gov (June 2016)
In 2015, Berlin was 1st amongst German cities for the number of clinical trials performed.
Founded in 1710

Largest university hospital in Germany

17 centres with over 100 clinics
Deliver Proof of Concept faster via more effective use of university hospital resources

Phase I/II unit with 30+ beds and a dedicated team of around 100 FTEs and 50 support staff

Facilitate a single center solution for early clinical studies in HVs and patients whenever possible
Translate pre-clinical results into the clinic as efficiently as possible

- Evaluate safety
- Explore efficacy
- Demonstrate POC

HVs/Patients…Patients….Patients….Patients….Patients….Patients….Patients

Faster
### Requirements for Effective Translational Clinical Research

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<th>Expertise</th>
<th>Medical and scientific staff with extensive clinical background</th>
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<td>Experience</td>
<td>An in-depth understanding of operational challenges (e.g. high frequency sampling)</td>
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<td>Facilities and Equipment</td>
<td>State of the art, dedicated, Phase I unit and staff</td>
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<td>Access to Patients</td>
<td>Effective recruitment of HVs and patients</td>
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<td>5</td>
<td>Access to Biomarkers</td>
<td>Imaging, other diagnostics and advanced lab capabilities to explore effects in humans</td>
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CRO’s CENTERS OF EXCELLENCE APPROACH

- Independent Phase I/II unit removes resource constraints
  - Methodological and scientific support from therapeutic area experts
  - Access to key technologies such as MRI
  - Access to specialist biomarker research and laboratory capabilities

- Patient recruitment via dedicated team using database and advertising
  - Clinicians share expertise
  - Clinics provide access

Scientists utilise research
IMAGING CENTER OF EXCELLENCE

MRI with central scoring services,
PD Dr. med. Kay-Geert Hermann

Ultrasound expertise via Prof. Dr. med.
Marina Backhaus, developed US 7 score

Leading the way in use of Florescence Optical Imaging in rheumatology
BIOMARKER CENTER OF EXCELLENCE

Immunological Study Laboratory (ISL)

DIN EN ISO 15189
DIN EN ISO/IEC 17025

Off the shelf assays
Transfer and validation of sponsor assays
Research laboratory

10 colour flow cytometer
Hematology analyzer
Multiplex ECL
Multi-analyte ELISA
Multiplex Luminex
ELISA-Reader

Prof. Hans-Dieter Volk
Scientific Director

PD Dr. Gerald Grütz
Head of Laboratory
EFFECTIVE RECRUITMENT IS CRITICAL TO STUDY TIMELINES

30% of a typical clinical study timeline directly relates to the recruitment of subjects

70%

90% of clinical trials are delayed because of patient recruitment problems.

“Online recruitment is streamlining clinical trials”, Datamonitor, 2008
Patients Enrolled Per Clinical Site: 0 - 5

% of Sites Contributing Zero Patients: 20-30%
A SINGLE CENTER APPROACH IS POSSIBLE: EXAMPLES

**MS:**
FTIH study in n=44 progressive MS patients with MRI imaging

**Crohn’s:**
FTIH study in n=60 HV and n=24 Crohn’s patients with endoscopy and immunology markers analysed locally

**Sjögren’s Syndrome**
Phase I study in n=27 Sjögren’s patients with ESSDAI scoring, salivary flow assessment, gland ultrasound and biopsy.

**RA:**
FTIH study in n=92 RA patients with DAS28 ≥ 3.2 combining SAD i.v., SAD s.c. and MAD s.c. dosing.
CRO RECRUITMENT APPROACH: FACILITATING SINGLE CENTER PATIENT STUDIES

Appeal directly to the patient + Have the resources to treat the patient with utmost respect + Financially compensate the patient properly
INNOVATION: A NATIONAL SINGLE CENTER
ONE CENTER, GERMAN WIDE SJÖGREN PATIENT RECRUITMENT

- 250 telephone contacts
- 100 information sessions
- 54 screenings
- 27 enrolled patients
- Referral 6
- Google 21

11 patients from Berlin, 16 from the rest of Germany

INNOVATION: PRE-SCREENING STUDIES
ENROLMENT OF 54 ASTHMA PATIENTS IN TWO MONTHS

Pre-screening study approved by local ethics
Core block of patients identified to push to main study
Ultimately n=98 retained for main study screening
n=54 enrolled

n=244 asthma patients identified and pre-screened against key study inc/exc. criteria before and during conduct of HV part

n=108 considered to be “probably” eligible for main study

n=98 entered into main study screening

n=54 enrolled in just over 2 months in 2 parallel cohorts of 27
Leading Ethic committee
EC responsible for the so-called LKP (leading PI) is the leading EC issuing a central vote for Germany

Timeline
30 days ethics timeline for single site in Germany, 60 days for multicenter studies
14 day timeline available for Phase I trials if part of a development program.

Submission requirements
According to German drug law and EU regulations. Patient information, summary of protocol and patient questionnaires need to be in German language
Two Health Authorities

**BfArM** (Bundesamt für Arzneimittel und Medizinprodukte): responsible for small molecules and medical devices

**PEI** (Paul Ehrlich Institute): responsible for biological products, vaccines, allergens and more

**Timeline**

30 to 60 days depending on investigational product (e.g. 60 days for PEI if biologic with human or animal origin)

**Open for innovative trial designs**

PEI approves very innovative trial designs for early clinical trials (e.g. multipart studies combining healthy volunteers and multiple different patient populations, adaptive designs)
Clinical trial support:
all major contract research organisations are placing late phase studies in Germany for their clients; several local CROs available to support late phase studies

Large number of qualified clinics and investigators:
41% of the studies initiated in 2015 were Phase III trials

All indications covered:
206 different indications were investigated in Phase II to III in 2015 in a broad variety of indications: 150 x Oncology, 124 x Inflammation (e.g. Asthma, MS, Morbus Crohn), 53 x Infectiology (e.g. Hep C, HIV), 34 x Cardiology
Germany is 2nd in the world for the number of clinical trials performed

Berlin is 1st amongst German cities for the number of clinical trials performed

Translational Research: A national single center approach is possible

Regulatory framework allowing innovative study designs
“The future depends on what you do today”  
Mahatma Ghandi (1869-1948)