Charité Research Organisation

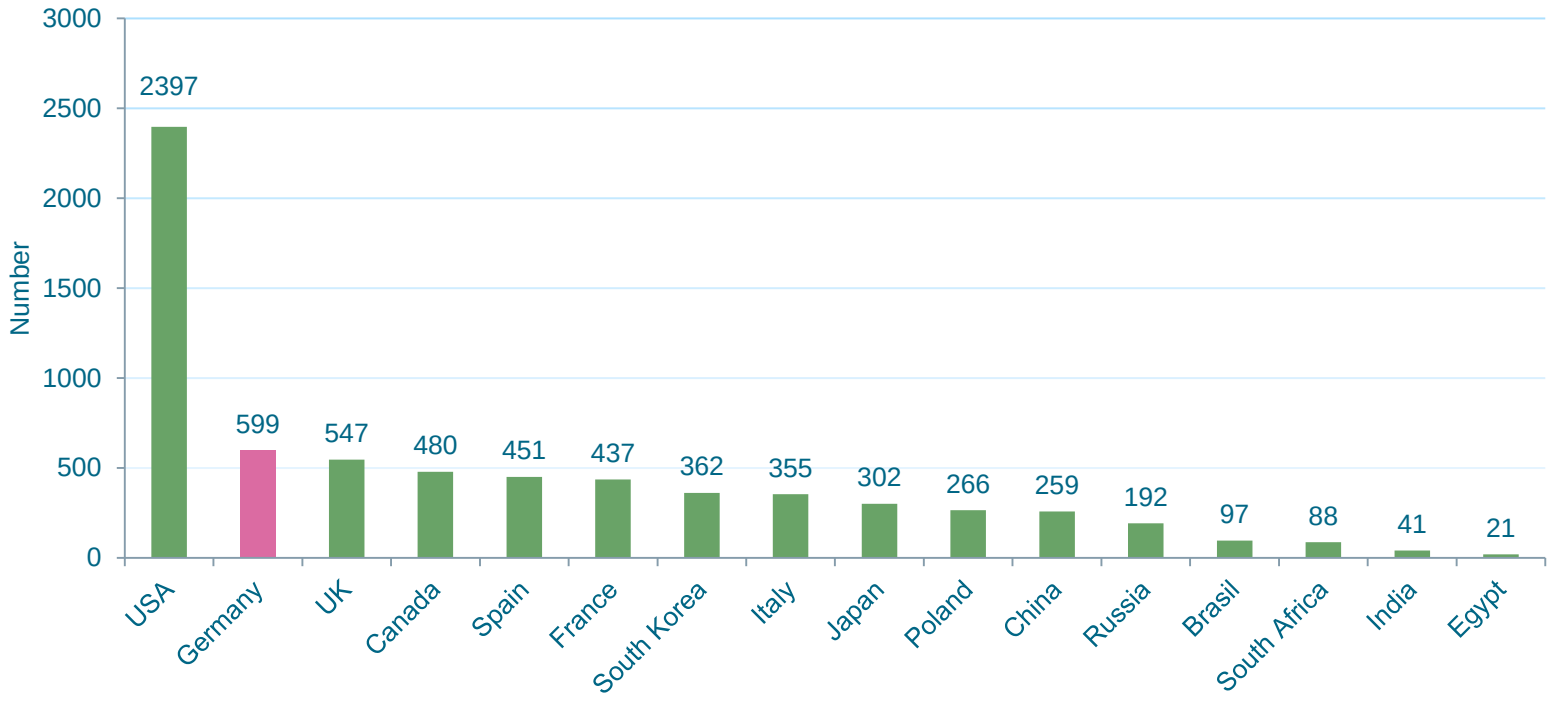
Conducting Clinical Trials in Germany:

Opportunities for translational research

24th of April 2017

GERMANY: A LEADING COUNTRY FOR THE CONDUCT OF CLINICAL RESEARCH

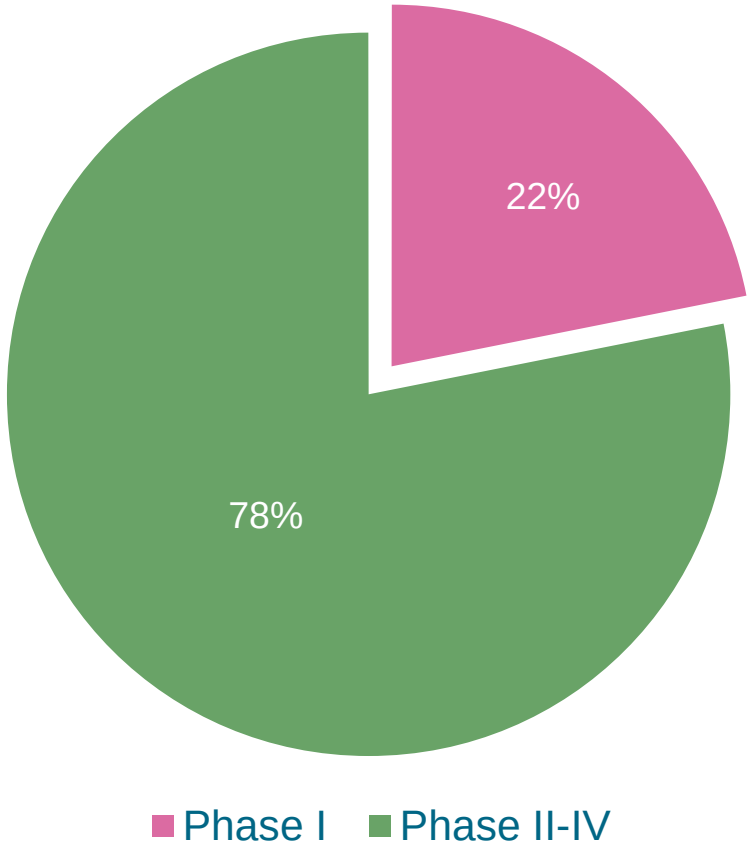
- In 2015, Germany was 2nd in the world for the number of clinical trials performed in the country by the research based pharmaceutical industry



Source: Industry-financed clinical studies based on study registry, clinicaltrials.gov (June 2016)

GERMANY: NUMBER OF CLINICAL STUDIES CONDUCTED

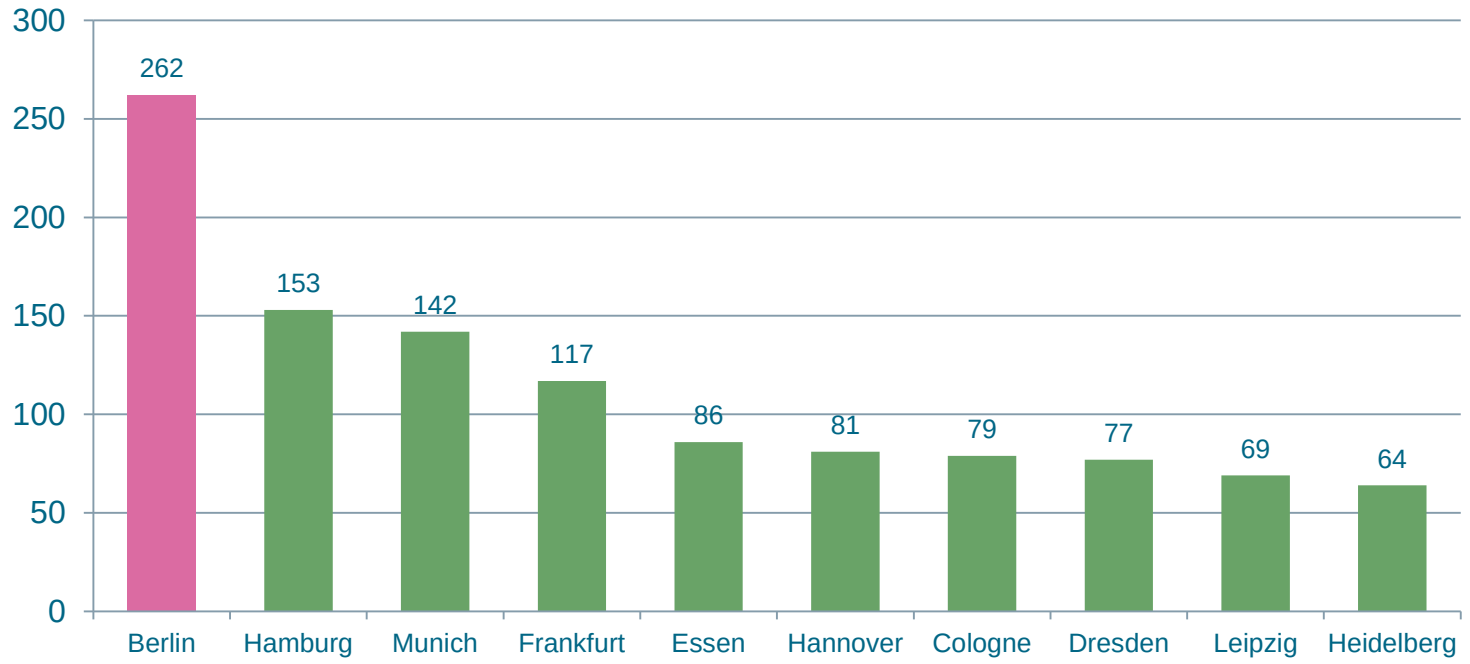
- A total of 599 studies conducted in Germany in 2015
- 131 Phase I studies
- 468 Phase II-III studies



Source: Industry-financed clinical studies based on study registry, clinicaltrials.gov (June 2016)

BERLIN: A LEADING CITY FOR THE CONDUCT OF CLINICAL RESEARCH

- In 2015, Berlin was 1st amongst German cities for the number of clinical trials performed



CHARITÉ – UNIVERSITÄTSMEDIZIN BERLIN

CHARITÉ
UNIVERSITÄTSMEDIZIN BERLIN

- Founded in 1710
- Largest university hospital in Germany
- 17 centres with over 100 clinics

CHARITÉ RESEARCH ORGANISATION

CHARITÉ OWNED - OPERATIONALLY INDEPENDENT – SCIENTIFCALLY DRIVEN

Charité Research Organisation

scientifically driven

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

UNDERSTANDING THE CHALLENGE

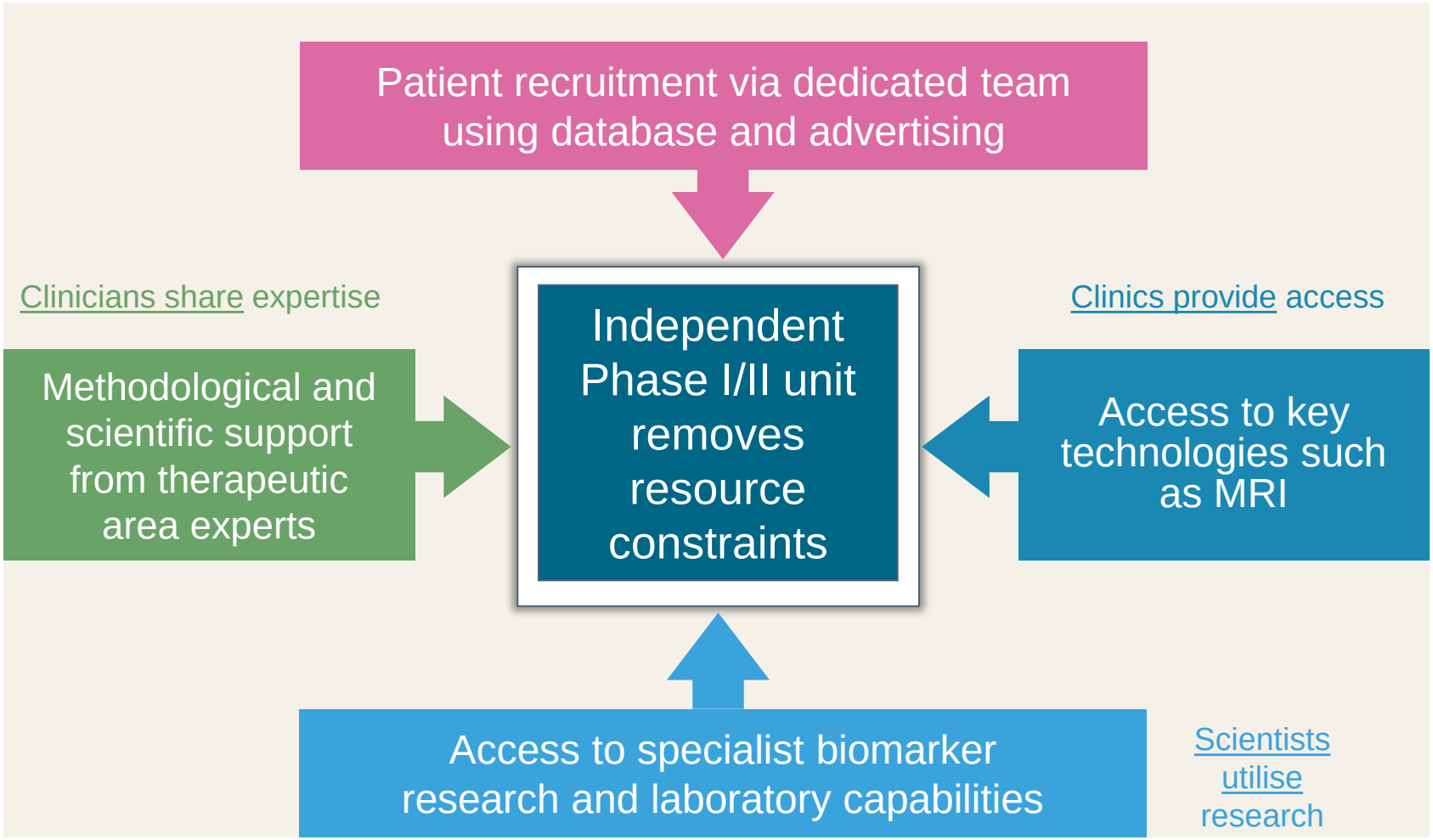
Translate pre-clinical results into the clinic as efficiently as possible

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

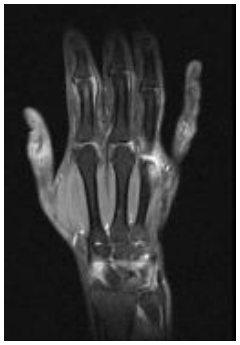
REQUIREMENTS FOR EFFECTIVE TRANSLATIONAL CLINICAL RESEARCH

1	**Expertise** Medical and scientific staff with extensive clinical background
2	**Experience** An in-depth understanding of operational challenges (e.g. high frequency sampling)
3	**Facilities and Equipment** State of the art, dedicated, Phase I unit and staff
4	**Access to Patients** Effective recruitment of HVs and patients
5	**Access to Biomarkers** Imaging, other diagnostics and advanced lab capabilities to explore effects in humans

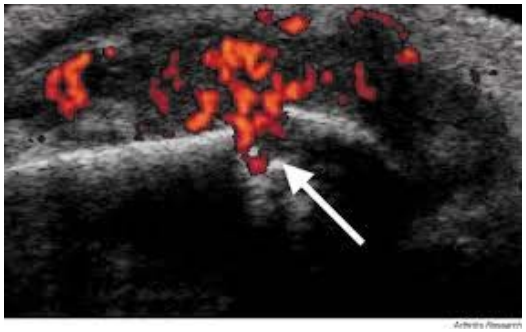
CRO's CENTERS OF EXCELLENCE APPROACH



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)

Prof. Hans-Dieter Volk
Scientific Director

PD Dr. Gerald Grütz
Head of Laboratory

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

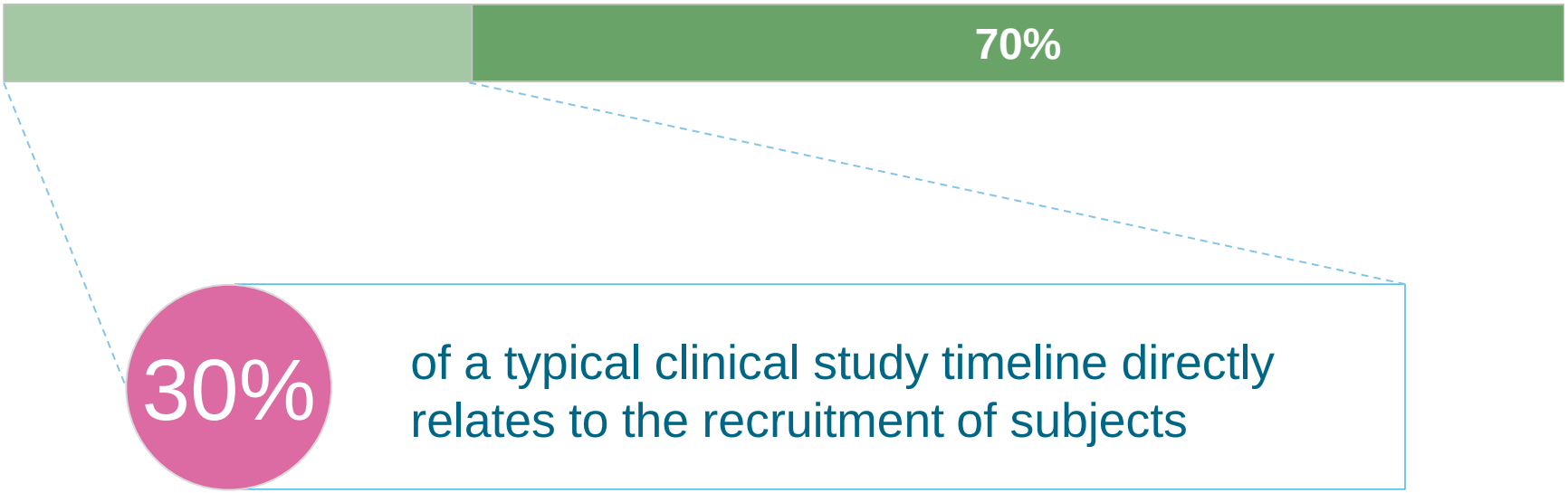
Multiplex ECL

Multi-analyte ELISA

Multiplex Luminex

ELISA-Reader

EFFECTIVE RECRUITMENT IS CRITICAL TO STUDY TIMELINES



Reinventing Patient Recruitment: Revolutionary Ideas for Clinical Trial Success, J.F. Bachenheimer, B.A. Brescia, Gower Publishing, 2007

EFFECTIVE RECRUITMENT IS CRITICAL TO STUDY TIMELINES

"Online recruitment is streamlining clinical trials", Datamonitor, 2008

CHALLENGING THE CONVENTIONAL PATIENT STUDY APPROACH

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

facebook

Google

BERLINER KURIER

Berliner Morgenpost

Appeal directly to the patient

+

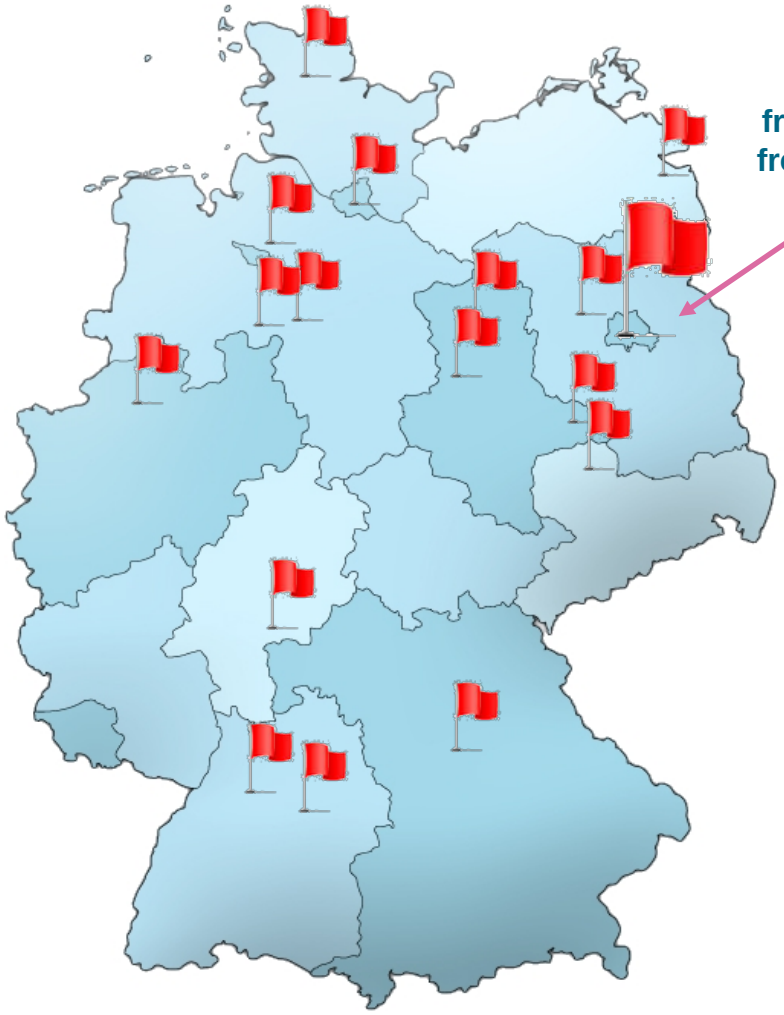
Have the resources to treat the patient with utmost respect

+

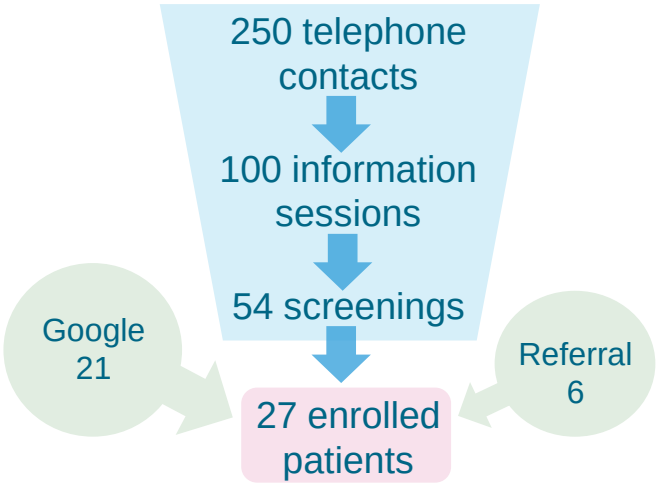
Financially compensate the patient properly

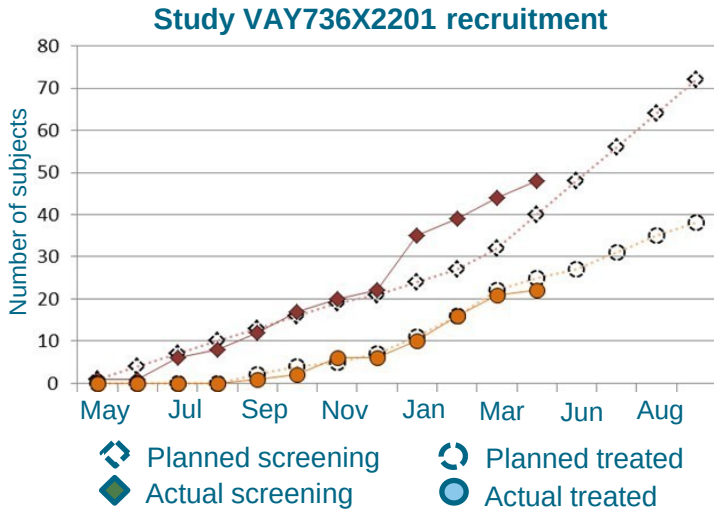
INNOVATION: A NATIONAL SINGLE CENTER

ONE CENTER, GERMAN WIDE SJÖGREN PATIENT RECRUITMENT

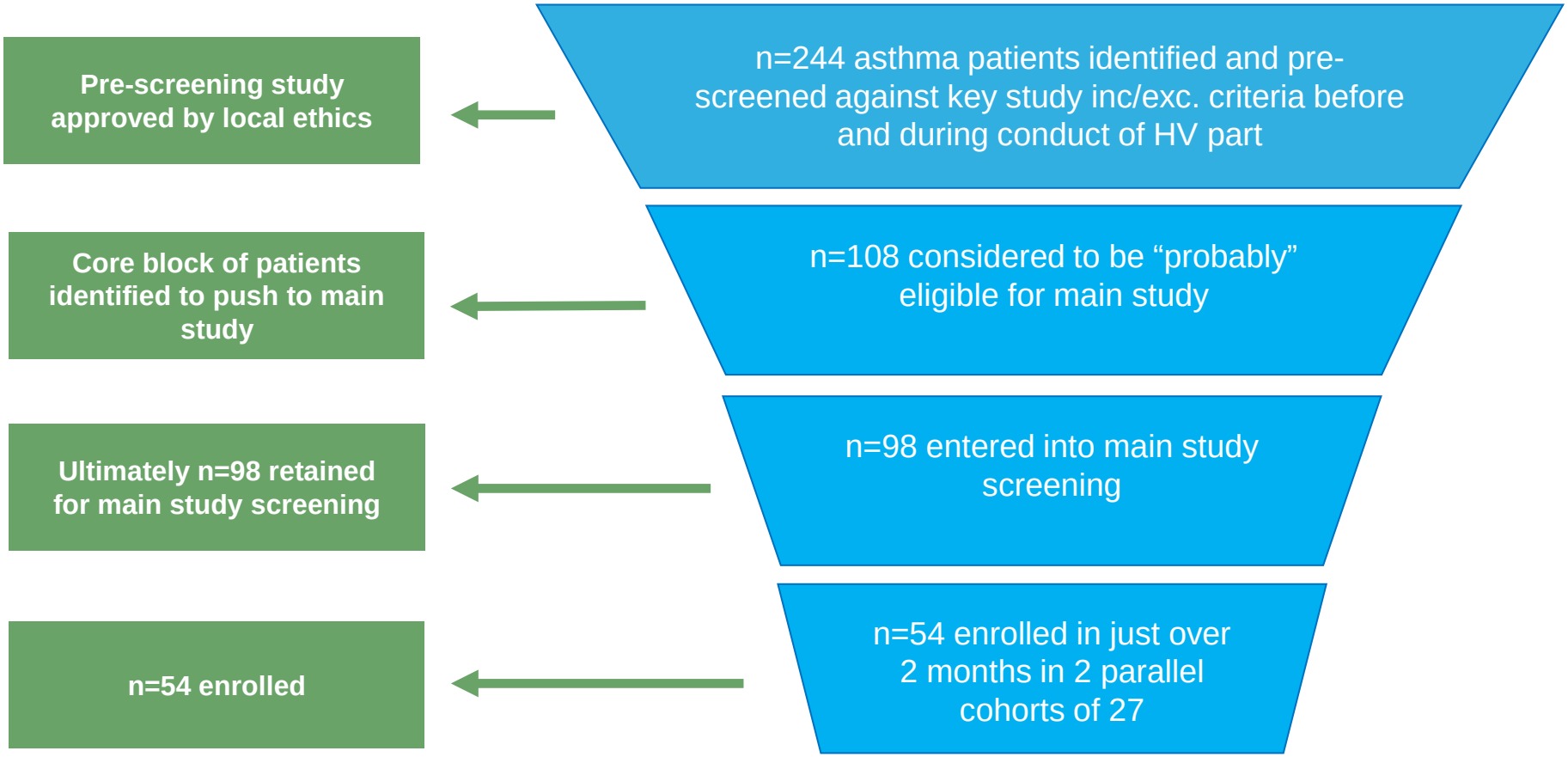


11 patients from Berlin, 16 from the rest of Germany





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



REGULATORY FRAMEWORK: Ethics committee

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

REGULATORY FRAMEWORK: Health Authority

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)

BEYOND PoC – Phase II/III studies in Germany

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

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

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

SUMMARY

- 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)