



**MEDIZINISCHE
FAKULTÄT
HEIDELBERG**

Ethics Committee of the Med. HD Alte Glockengießerei 11/1 69115 Heidelberg

NCT Study Center Mr.
Lucian Le Cornet
Im Neuenheimer Feld 130/3
69120 Heidelberg

The evaluation shall be carried out in consultation with the ethics committees involved, also listed in Annex 2.

cc:BfArM by e-mail
Involved ethics committees by e-mail
- Final shipment -

20.12.2019
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FAVOURABLE OPINION

EudraCT no: 2018-002675-17
Inspection plan code: NCT-2017-0545 / HeLeNe-18-03-#545
Title: Quizartinib and High-dose Ara-C plus Mitoxantrone in Relapsed/Refractory AML with FLT3-ITD (Q-HAM)
Sponsor: Ruprecht-Karls-University of Heidelberg Medical Faculty represented in law by Heidelberg University Hospital
Applicant: NCT Study Center, Heidelberg
LKP: Prof. Dr. Richard F. Schlenk, Heidelberg
Our sign: **AFmu-576/2019** (Please always specify)

Dear Sir,

The Ethics Committee considered your above request at its meeting on 26/08/2019. The additional information requested was received on **11/25/2019** and **12/10/2019** and **12/20/2019**, respectively.

The Ethics Committee issues a favourable opinion. Reason: There are no grounds for refusal according to Section 42 (1) AMG. The evaluation is based on the documents listed in Annex 1.

The evaluation shall be valid for the inspection bodies listed in Annex 2, together with their inspectors and alternates.

University of Heidelberg Ethics Committee of the Faculty of Medicine

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Chair:

Prof. Dr. med. Dr. h.c. Thomas Strowitzki

Vice Chair:

Prof. Dr. med. Klaus Herfarth

Management:

Dr. med. Verena Pfeilschifter

eFeedback



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The positive assessment cannot yet be given for the trial sites listed in Appendix 3, including investigators and alternates, as we have not yet received a final opinion from the responsible ethics committee involved.

The Commissioners listed in Annex 4 took part in the vote. Yours sincerely

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Dr. Pfeilschifter, Verena
TeleSec PKS eIDAS QES CA 1
German Telekom AG
Friday, 27. December 2019 15:02 CET

Prof. Dr. med. Dr. h.c. Thomas Strowitzki
Chairman

Attachments

Appendix 1-4

General Notes:

- The ethical and legal responsibility for the conduct of this clinical trial remains with the sponsor, the principal investigator, and the investigators.
- The composition and functioning of the Ethics Committee comply with national laws, regulations and the ICH GCP Guideline as amended from time to time.
- An objection to this Opinion may be raised within one month of publication. The objection must be submitted in writing or recorded at the office of the Ethics Committee of the Medical Faculty Heidelberg, Alte Glockengießerei 11/1, 69115 Heidelberg.
- Aspects of research projects relating to data protection law are only examined by the ethics committee in a cursory manner. This vote/assessment therefore does not replace consultation with the responsible data protection officer. Compliance with the relevant data protection laws and the implementation of the data protection concept are the responsibility of the study director/investigator or sponsor.

Appendix 1

List of documents submitted

Primary Submitted Documents:	<p>Letter dated 05.08.2019</p> <p>Anl 34_Summary dt, undated</p> <p>Checklist of the working group of the ethics committees of 02.08.2019</p> <p>Module 1 of 06.08.2019</p> <p>Module 2 from 05.08.2019</p> <p>Confirmation letter EudraCT number dated 04.07.2018</p> <p>Cost absorption statement dated 15.07.2019.</p> <p style="text-align: right;">Versicherungsbestätigung vom 08.03.2019, Versicherungsschein-Nr.: 5701031003018</p> <p>Contribution invoice dated 08.03.2019, policy number: 81940702 03078 390 2668001 (incl. attachment to invoice).</p> <p>Asset Register</p> <p>Patient information and consent form, version _V1_1 of 05.08.2019 Anl 17_Risk_Benefit_Weighing, undated.</p> <p>Protocol, version 1.2 as of 05.08.2019</p> <p>INVESTIGATOR'S BROCHURE Quizartinib, version 12.0 as of 04/26/2019</p> <p>Annex 08_Name and Characterization Active Substances, undated.</p> <p>CV Prof. Dr. Richard F. Schlenk as at Aug 05, 2019</p> <p>Certificate "Study Update Hematology and GCP Training" Prof. Dr. Richard F. Schlenk from 11.03.2017 (incl. agenda)</p> <p>Certificate of Participation "GCP/AMG Training" (Basic Course) Prof. Dr. Richard F. Schlenk from 07.10.2015 (incl. training contents)</p> <p>Certificate "Study Leader Course" Prof. Dr. Richard F. Schlenk from 23.11.2018 CV Dr. med. Tim Sauer from 05.08.2019</p> <p>Study Experience Tim Sauer, MD Aug 05, 2019</p> <p>Certificate "AMG Advanced Course for Examiners / Deputies (Ä2) " Dr. med. Tim Sauer from 02.07.2019</p> <p>Certificate of attendance "Investigator Course" Dr. med. Tim Sauer from 07.03.2009 (incl. content)</p> <p>FDS Prof. Dr. Richard F. Schlenk from 07.08.2019 FDS Dr. med. Tim Sauer from 07.08.2019</p> <p>Site Qualification Form for Examiners, Substitutes (Heidelberg) from 05.08.2019 (P/Deputy)</p> <p>Centre-specific documents</p> <p>KKS compulsory consultation notice of 03.07.2019 KKS compulsory consultation notice of 07.08.2019</p> <p>Contract on the Support of a Clinical Trial (IIT) between Heidelberg University Hospital and Medical Clinic V dated 15.05.2019 (LKP / Medical Director) resp. 27.05.2019 (Commercial Director Uniklinik HD) Responsibility Split dated 27.05.2019 (LKP/IMBI/ QoL DKFZ) resp. 07.06.2019 (KKS Heidelberg) resp. 28.05.2019 (LAB Dept. Internal Medicine V)</p> <p>Annex 20_Financing, undated</p> <p>(Sample) contract, submission dated June 12, 2019, undated.</p> <p>Statement on number of paper-based documents to the participating ethics committees dated 05/08/2019.</p> <p>Anl 09_Subject of the clinical trial, undated</p> <p>Annex 10_Number, age and sex of persons concerned, undated Annex 11_Criteria for selection, undated</p> <p>Annex 12_Justification of gender distribution, undated</p> <p>Annex 13_Treatment plan, undated</p> <p>Attachment 15_disclosure of pseudonymised data from 01.08.2019</p>
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(LKP) Attachment 16_meaning of clinical trial, undated
Annex 25_Methods of investigation envisaged, undated
Annex 26_Simultaneous participation in study, undated

Annex 29_Compensation of auditors and compensation of data subjects, undated
 Annex 30_ Data protection compliance of 15.07.2019 (LKP)
 Annex 32_Criteria for suspension or early termination, undated
 Annex 05_Institutions involved, undated
 Annex 33_List of ECs involved, undated
 Annex 04_name and address of sponsor, undated
 CD-ROM

Formal Submission:

Letter from Prof. Richard F. Schlenk dated 08/21/2019 Letter from LKP regarding funding dated 06/28/2019.
 Cooperation Agreement between Study Center of the Dept. of Internal Medicine V and Institute of Medical Biometry and Informatics (IMBI) (version of 06/27/2019) dated 06/27/2019 (LKP) and 06/28/2019 (Director IMBI), respectively.
 Clinical Trial Agreement between Study Center of the Dept. of Internal Medicine V and Institute of Medical Biometry and Informatics (IMBI) (version of 06/27/2019) dated 06/27/2019 (LKP) and 06/28/2019 (Director IMBI), respectively.
 Agreement on the Support of an Investigator Initiated Trial between Heidelberg University Hospital and Daiichi Sankyo Europe GmbH (version of 16.05.2018) dated 27.08.2018 (Kaufmann Direktorin Uni Heidelberg / Daiichi Sankyo Europe GmbH) resp. 20.08.2018 (LKP) resp. 21.08.2018 (ärztl Direktor Innere Medizin V)
 AMENDMENT No. 1 TO Investigator Initiated Study AGREEMENT between Heidelberg University Hospital and Daiichi Sankyo Europe GmbH (version of 14.08.2018) dated 12.09.2018 (Kaufmann Direktorin Uni Heidelberg) resp. 21.08.2018 (Daiichi Sankyo Europe GmbH) resp. 07.09.2018 (ärztl Direktor Innere Medizin V) resp. 06.09.2018 (LKP)
 Sponsor obligations in drug trials in IITs dated 24.06.2019 (LKP)
 Budget plan Q-HAM, version dated 02.07.2019.
 Annex 00_0_list of facilities, version 01HD dated 21/08/2019
 Annex 05_involved facilities dated 21/08/2019.
 Annex 33_List of ECs involved as of 15.08.2019
 Special agreements for proband annual insurance for universities / university hospitals for clinical trials / studies to be carried out in Germany ("Uni-Jahresvertrag"), as of: undated
 General Insurance Conditions for Insurable Clinical Trials of Medicinal Products/Annual Contract (AVB-Prob/AMG-JV) - U 199 -, as at: 1.16
 Privacy compliance statement dated 08/22/2019 Your email dated 08/23/2019.

Your email dated 2019-09-02
 Confirmation disclosure of pseudonymous data dated 31/08/2019 (LKP).

Your email dated 09/27/2019
 Center specific documents.

Your email dated 02/10/2019
 Center specific documents.

Letter from Prof. Dr. Schlenk dated 25.11.2019 Centre-specific documents
 CD-ROM

Letter from Prof. Dr. Schlenk dated 09.12.2019 List of Annexes
 Module 1 from 09.12.2019
 Centre-specific documents CD-ROM

**Substantive
Submission:**

Letter from Prof. Dr. Schlenk dated 25.11.2019 List of Annexes
Insurance policy accident insurance no. 50079192101 dated 24.09.2019 General conditions for the SV accident insurance (SVAUB 2017), version January 2017.
Supplementary conditions for group accident insurance (ZB Gruppen-UV), version September 2014
Data protection information, version 01.10.2018 CD-ROM

Letter from Prof. Dr. Schlenk dated 09.12.2019 List of Annexes
Protocol, version 1.2ek as of 09.12.2019 (with and without changes marked).
Patient information and consent form, version 1.1ek as of 09.12.2019 (with and without changes marked).
Module 1 from 09.12.2019 CD-ROM

Letter from Prof. Dr. Schlenk dated 18.12.2019
Patient information and consent form, version 1.1ekV2 of 18.12.2019 (with and without marking of the changes)
Your email on 12/20/2019

Annex 2

The positive evaluation is valid for the following inspection bodies including examiners and deputies:

Ethics Committee	Examiner/Deputy Examiner/Testing Unit
Ethics Committee of the Medical Faculty Heidelberg Old bell foundry 11/1 69115 Heidelberg	Prof. Dr. Richard F. Schlenk (P) Dr. med. Tim Sauer (Deputy) Heidelberg University Hospital Dept. of Internal Medicine V Im Neuenheimer Feld 410 69120 Heidelberg
Ethics Committee at the TU Dresden Fetscherstraße 74 01307 Dresden (letter dated Sep. 16, 2019)	PD Dr. med. Christoph Röllig (P) Dr. med. Jan Moritz Middeke (Deputy) University Hospital Carl Gustav Carus Dresden Medical Clinic and Polyclinic I Fetscherstr. 74 01307 Dresden
Ethics Committee at the Saxon State Medical Association Schützenhöhe 16 01099 Dresden (letter, Sept. 20, 2019)	PD Dr. med. Mathias Hänel (P) Dr. med. Regina Herbst (Deputy) Klinikum Chemnitz gGmbH Clinic for Internal Medicine III Haematology/Oncology Bürgerstr. 2 09113 Chemnitz
Ethics Committee of the Medical Faculty of the Martin Luther University Halle-Wittenberg Magdeburger Straße 16 06112 Halle (Saale) (letter dated Sep 04, 2019)	Maxi Wass, MD (P)* PD Dr. med. Lutz Müller (Deputy) University Hospital Halle (Saale) Clinic and Polyclinic for Internal Medicine IV Ernst-Grube-Str. 40 06120 Halle (Saale)
Ethics Committee of the Friedrich Schiller University Jena Bachstraße 18 07743 Jena (letter dated Sep 04, 2019)	PD. Dr. med. Sebastian Scholl (P) Dr. Ulf Schnetzke (Deputy) University Hospital Jena Clinic for Internal Medicine II Haematology and Internal Oncology, Am Klinikum 1 07747 Jena
Ethics Committee at the Medical Association of Baden-Württemberg Liebknechtstr. 33 70565 Stuttgart (letter dated Aug. 28, 2019) (letter dated 08 Oct. 2019)	Dr. med. Thomas Geer (P) Dr. med. Ulrike Sokoll (Deputy) Diakoneo Diakonie Klinikum Schwäbisch Hall gGmbH Internal Medicine III Clinic for Hematology, Oncology and Palliative Medicine Diakoniestrasse 10 74523 Schwäbisch Hall
Ethics Committee of the Bavarian Medical Association Mühlbauerstraße 16 81677 Munich (letter dated Aug. 27, 2019)	Dr. med. Kerstin Schaefer-Eckart (P) Dr. med. Knut Wendelin (Deputy) Paracelsus Medical Private University Nuremberg North Hospital Clinic for Internal Medicine 5 Focus on Oncology / Hematology Prof.-Ernst- Nathan-Str. 1 90419 Nuremberg

<p>Ethics Committee of the Medical Association of Westphalia-Lippe and the Westphalian Wilhelms University Münster Gartenstr. 210 - 214 48147 Münster</p> <p>(letter dated Aug. 22, 2019)</p>	<p>PD Dr. med. Martin Görner (P) Dr. med. Kai Wegehenkel (Deputy) Bielefeld Municipal Hospital Clinic for Hematology, Oncology and Palliative Medicine Teutoburger Str. 50 33604 Bielefeld</p>
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The Ethics Committee involved points out the following:

* Certificate of successful attendance at the advanced course on 27/09/2019 is to be submitted for the examiner in a timely manner.

Appendix

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The positive evaluation cannot yet be given for the following inspection bodies, including examiners and deputies:

Ethics Committee	Examiner/Deputy Examiner/Testing Unit
Ethics Committee at the Saxon State Medical Association Schützenhöhe 16 01099 Dresden (letter dated Sept. 11, 2019)	Prof. Dr. med. Jörg Schubert (P) Kathrin Petzold (Deputy) Elblandklinikum Riesa Clinic for Internal Medicine II Haematology, oncology, gastroenterology and palliative medicine Vineyard road 8 01589 Riesa*
Ethics Committee at the Medical Association of Baden-Württemberg Liebknechtstr. 33 70565 Stuttgart (letter dated Aug. 28, 2019)	Prof. Dr. med. Mark Ringhoffer (P)** Dr. med. Lukas Kuendgen (Deputy)** Städtisches Klinikum Karlsruhe gGmbH Medical Clinic III Moltke Street 90 76133 Karlsruhe
Ethics Committee at the Medical Association of Baden-Württemberg Liebknechtstr. 33 70565 Stuttgart (letter dated Aug. 28, 2019)	Alexander Reichart, MD (P) Prof. Dr. med. Markus Schaich (Deputy)** Winnenden Hospital Haematology, Oncology and Palliative Medicine Am Jakobsweg 1 71364 Winnenden
Ethics Committee of the Medical Association of Westphalia-Lippe and the Westphalian Wilhelms University Münster Gartenstr. 210 - 214 48147 Münster	Jan-Henrik Mikesch, MD (P) Prof. Dr. Christoph Schliemann (Deputy) University Hospital Münster Medical Clinic A Hematology, Oncology and Pneumology Albert Schweitzer Campus 1 Building A1 48149 Münster

The competent ethics committee involved informs the following:

*As per our letter dated 14/08/2019, supplementary documents including qualification certificates have been requested from the applicant and hence it is not yet possible to assess the testing agencies.

The investigators [...] and Dr Ringhofer as well as [...] the deputies Prof. Schaich and Dr Kündgen must provide evidence of an advanced course on clinical trials of medicinal products of at least 8 teaching units of 45 minutes each before the start of the study. The requirements of the German Medical Association of 25.01.2019 must also be taken into account. Evidence of training must be sent to the Commission in a timely manner. Please make sure that the confirmations always contain precise information on the content, time frame and mode of the training (can also be composed of various modules). Proof of participation in a 2-day examiner course that corresponds to the curricular recommendations of the German Medical Association and the Working Group of the Ethics Committees from 2013 can be recognised as equivalent.

Appendix

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The following members participated in the vote:

	Member	Department
<input type="checkbox"/>	Dr. med. Antje Blank Clinical pharmacology	Medical /Clinical Pharmacology u. alClinic Pharmacoepidemiology
<input type="checkbox"/>	Dr. Chobanyan-Jürgens, M.D. Clinical pharmacology	Medical /Clinical Pharmacology u. alClinic Pharmacoepidemiology
<input checked="" type="checkbox"/>	Prof. Dr. med. David Czock Clinical pharmacology	Medical /Clinical Pharmacology u. alClinic Pharmacoepidemiology
<input type="checkbox"/>	Prof. Dr. med. Marc Freichel Pharmacology	Pharmacological Institute Heidelberg
<input type="checkbox"/>	Dr. med. Barbara Grün Clinical pharmacology	..ClinicalPharmacology, NationalCenterforTumorDiseases Heidelberg
<input type="checkbox"/>	Prof. Dr. med. Walter E. Haefeli Clinical pharmacology	Medical /DepartmentClin Pharmacology u. Clinic Pharmacoepidemiology ical
<input type="checkbox"/>	Dr. Nicolas Hohmann Pharmacology	FAf.ClinicalPharmacology, NationalCenterforTumorDiseases Heidelberg
<input type="checkbox"/>	Prof. Dr. phil. Michael Anderheiden qualified lawyer	Univ. Heidelberg / Institute for Constitutional Law, Constitutional Theory and Philosophy of Law
<input checked="" type="checkbox"/>	Prof. Dr. Jens Bülte qualified lawyer	University of Mannheim / Chair of Criminal Law, Criminal Procedure Law, Economic and Fiscal Criminal Law
<input type="checkbox"/>	Prof. Dr. Ralf Müller-Terpitz qualified lawyer	Univ. Mannheim / Chair of Public Law, Law of Economic Regulation and Media
<input type="checkbox"/>	Prof. Dr. jur. Jochen Taupitz qualified lawyer	Institute for German, European and International Medical Law, Health Law and Bioethics of the University of Heidelberg and Mannheim
<input checked="" type="checkbox"/>	Prof. Dr. Justo Lorenzo Bermejo Medical biometry	Institute for Medical Biometry and Informatics
<input type="checkbox"/>	Dipl-Stat. Axel Benner Medical biometry	German Cancer Research Center Heidelberg / Dept. of Biostatistics
<input type="checkbox"/>	Dr. sc. hum., Dipl.-Math. Tom Bruckner Medical biometry	Institute for Medical Biometry and Informatics
<input type="checkbox"/>	Prof. Dr. Meinhard Kieser Medical biometry	Institute for Medical Biometry and Informatics
<input type="checkbox"/>	Prof. Dr. Annette Kopp-Schneider Medical biometry	German Cancer Research Center Heidelberg / Dept. of Biostatistics
<input type="checkbox"/>	Dr. sc. hum. Anja Sander, M. Sc Medical biometry	Institute for Medical Biometry and Informatics
<input type="checkbox"/>	Dipl. Math. Svenja Schüler Medical biometry	Institute for Medical Biometry and Informatics
<input checked="" type="checkbox"/>	Dr. med. Verena Pfeilschifter Medical Ethics	Office of the Ethics Committee of the Medical Faculty Heidelberg
<input type="checkbox"/>	Michael Reichert Medical Ethics	Help for the elderly of the Evang. Stadtmission Heidelberg
<input type="checkbox"/>	Rebekka Steel Nursing service	Center for Orthopedics, Trauma Surgery and Paraplegiology / Dept. of Orthopedics and Trauma Surgery

Appendix

<input type="checkbox"/>	Dr. phil. Nicole Maria Bauer Medical layman	Univ. Innsbruck / Institute for Practical Theology
<input type="checkbox"/>	Christiane Calis Medical layman	Public Relations Office of the City of Heidelberg
<input type="checkbox"/>	Peter Grünewald Medical layman	Theologian, St. Raphael High School Heidelberg
<input checked="" type="checkbox"/>	Renate Walter Medical layman	Housewife
<input type="checkbox"/>	Carina Welsch Medical layman	Special Education Teacher

<input type="checkbox"/>	Prof. Dr. med. Stefan Delorme Radiology	German Cancer Research Center Heidelberg / Dept. of Radiology
<input type="checkbox"/>	PD Dr. med. Monika Eichinger Radiology	Thorax Clinic Heidelberg / Diagnostic and Interventional Radiology
<input type="checkbox"/>	Dr. med. Sabine Haufe Radiotherapy	Radiology Clinic / Dept. of Nuclear Medicine
<input checked="" type="checkbox"/>	Prof. Dr. med. Klaus Herfarth Radiology	Radiology Clinic / Dept. of Radiooncology and Radiotherapy
<input type="checkbox"/>	Angela Paul, MD Radiotherapy	Radiology Clinic / Dept. of Radiooncology and Radiotherapy
<input type="checkbox"/>	Prof. Dr. med. Thomas Strowitzki Gynecology	Gynaecological Clinic/Gynaecological Endocrinology and Fertility disorders
<input type="checkbox"/>	Susanne Picardi, MD Anesthesia	Anaesthesiology Clinic
<input type="checkbox"/>	Prof. Dr. med. Tanja M. Rabsilber Ophthalmology	University Eye Hospital
<input type="checkbox"/>	Prof. Dr. med. Katrin Hoffmann Surgery	Surgical Clinic / Clinic for General, Visceral and Transplant Surgery
<input type="checkbox"/>	Prof. Dr. med. Claudia Sommerer Surgery	Surgical Clinic / Clinic for General, Visceral and Transplant Surgery
<input type="checkbox"/>	Prof. Dr. med. Alexander Scharf Gynecology	Practice for prenatal medicine Darmstadt
<input type="checkbox"/>	PD Dr. med. Johann Greil Pediatrics	Cent. f. Pediatric and Adolescent Medicine / Dept. III Pediatric Hematology and Oncology
<input type="checkbox"/>	PD Dr. med. Peter Ruef Pediatrics	SLK Clinics Heilbronn / Clinic for Paediatrics and Adolescent Medicine
<input type="checkbox"/>	Prof. Dr. med. Claus-Peter Schmitt Pediatrics	Cent. f. Pediatrics and Adolescent Medicine / Dept. of General Pediatrics, Neuropediatrics Metabolism, Gastroenterology, Nephrology
<input type="checkbox"/>	Philipp Ehlermann, MD Cardiology	Medical Clinic / Dept. III Cardiology, Angiology and Pneumology
<input type="checkbox"/>	Dr. med. Jürgen Krauss Oncology	National Center for Tumor Diseases Heidelberg / Dept. of Medical Oncology
<input type="checkbox"/>	Prof. Dr. med. Birgit Friedmann- Bette Sports Medicine	Medical Clinic / Dept. VII Sports Medicine
<input type="checkbox"/>	Dr. med. Dr. med. dent. Julia Katharina Kansy Maxillofacial Surgery	Oral, Dental, Maxillofacial Clinic / Dept. f. Mouth, Jaw & Facial Surgery
<input checked="" type="checkbox"/>	Prof. Dr. med. Peter Ringleb Neurology	Neurological Clinic / Dept. of Neuroradiology and Polyclinic
<input type="checkbox"/>	Prof. Dr. med. Thorsten Steiner Neurology	Klinikum Frankfurt Hoechst / Neurological Clinic
<input type="checkbox"/>	Prof. Dr. med. Wolfgang Wick Neurology	Neurological Clinic / Dept. of Neurology and Polyclinic
<input type="checkbox"/>	Prof. Dr. phil. Beate Ditzen Medical psychology	Institute for Medical Psychology
<input type="checkbox"/>	Joanne Nyarangi-Dix, M.D. Urology	Surgical Clinic / Dept. of Urology
<input type="checkbox"/>	PD Dr. Dr. med. Ute Moog Human Genetics	Institute of Human Genetics