KURZPROTOKOLL
DSMM XV

Öffentlicher Titel	Phase II Studie zu Pomalidomid/Ixazomib/Dexamethason bei refraktärem oder rezidiviertem Multiplen Myelom
Wissenschaftl. Titel	Pomalidomid, Ixazomib, und Dexamethason (PId) mit oder ohne Intensivierung durch Cyclophosphamid (PICd): Phase II Studie bei refraktärem oder rezidivierendem Multiplen Myelom
Kurztitel	DSMM XV
Studienart	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase II
Erkrankung	Blut: Multiples Myelom: rezividiert/refraktär
Einschlusskriterien	- Male or female patients >= 18 years of age at the time of signing the informed consent form - Patients capable to understand the purposes and risks of the study, who are willing and able to participate in the study and from whom written and dated informed consent to participate in the study has been obtained prior to any study related assessments/ procedures being conducted - Patients with relapsed or refractory, histologically confirmed multiple myeloma - Patients must have received at least two but not more than four prior anti-myeloma regimens including lenalidomide and bortezomib and have demonstrated disease progression on the last therapy - Prior treatments must have included both lenalidomide and bortezomib: at least two consecutive cycles of lenalidomide and bortezomib (alone or in combination) and adequate prior alkylator exposure. This is either as part of a stem cell transplant or at least 6 consecutive cycles of an alkylator-based therapy - Patients must have failed bortezomib and lenalidomide therapy: progression within 60 days; PR or better with progression within 6 month and/or bortezomib intolerant after >= 2 cycles and achieving <= MR - Relapsed from or refractory to at least one regimen (induction, autologous stem cell transplantation (or allogenic stem cell transplantation) and consolidation/maintenance are considered one “regimen”) - Measurable levels of serum and/or urine M-protein: serum M-protein >= 5 g/L and/or urine M-protein >= 200 mg/24h or serum free light chain (sFLC) concentration of > 100 mg/L of the involved FLC, provided sFLC ratio is abnormal (sFLC K/Lambda ratio (< 0.26 or > 1.65) - Life expectancy >= 3 months - ECOG performance status of 0, 1, or 2 - Patients must be able to adhere to the study visit schedule and other protocol requirements - All women and men must acknowledge to have understood the hazards and necessary precautions associated with the use of pomalidomide and ixazomib - All subjects must agree in writing to strictly adhere to the Pomalidomide Pregnancy Prevention Plan as given in Appendix C - Females of childbearing potential (FCBP) must: - -> Understand the potential teratogenic risk to the unborn child - -> Agree to utilize two reliable forms of contraception simultaneously without interruption for at least 28 days before starting study drug, while participating in the study (including dose interruptions), and for at least 90 days after study treatment discontinuation - -> Be capable of complying with effective contraceptive measures

- -> Be informed and understand the potential consequences of pregnancy and the need to notify her study doctor immediately if there is a risk of pregnancy
- -> Understand the need to commence the study treatment as soon as study drug is dispensed following a negative pregnancy test
- -> Understand the need and accept to undergo pregnancy testing based on the frequency outlined in this protocol
- Females must agree to abstain from breastfeeding during study participation and for at least 28 days after study drug discontinuation
- Males must agree to use a latex condom during any sexual contact with FCBP while participating in the study and for 90 days following discontinuation from this study, even if he has undergone a successful vasectomy
- Males must also agree to refrain from donating semen or sperm while on the study drugs and for 90 days after discontinuation from this study treatment
- Subjects must agree to refrain from donating blood while on study therapy and for 28 days after discontinuation from this study treatment
- Subjects must agree not to share medication
- Patients must meet the following clinical laboratory criteria:
- -> Absolute neutrophil count (ANC) >= 1 x 109/L
- -> Platelet count >= 75/nl for patients in whom < 50% of bone marrow nucleated cells are plasma cells
- -> Platelet count >= 30/nl for patients in whom >= 50% of bone marrow nucleated cells are plasma cells. (Platelet transfusions to help patients meet eligibility criteria are not allowed within 3 days before study enrollment)
- -> Total bilirubin <= 1.5 x the upper limit of the normal range (ULN)
- -> Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) <= 3 x ULN
- -> Calculated creatinine clearance >= 30 mL/min

Ausschlusskriterien

- Concomitant cancer chemo- or radiotherapy (except for local radiation therapy for preexisting lytic lesions)
- Treatment with any investigational product within 60 days prior to first administration of pomalidomide and ixazomib
- Patients eligible for autologous and / or allogeneic stem cell transplantation
- Abnormal/inadequate organ or bone marrow function as defined below (any single parameter to fulfill condition):
- -> ANC < 1 /nl
- -> Hemoglobin < 8.0 g/dL (prior RBC transfusion or recombinant human erythropoietin use is permitted)
- -> Platelet count < 75 /nl for patients in whom < 50% of bone marrow nucleated cells are plasma cells
- -> Platelet count < 30/nl for patients in whom >= 50% of bone marrow nucleated cells are plasma cells
- -> Estimated GFR (MDRD) < 45 ml/min
- -> AST/ALT > 3 x upper limit of normal (ULN)
- -> Serum (total) bilirubin > 1.5 x ULN
- -> Corrected serum calcium > 14 mg/dL (> 3.5 mmol/L); or free ionized calcium > 6.5 mg/dL (> 1.6 mmol/L)
- -> Serum creatinine > 1.5 x ULN
- Prior pomalidomide based therapy

- Prior ixazomib based therapy
- Baseline peripheral neuropathy > Grade 1 on clinical examination within 14 days before enrollment
- Active HIV, hepatitis B (including patients who are tested Anti-HBc-positive and / or HBsAg-positive) or hepatitis C infection after serologic testing
- Any other concurrent disease or medical conditions that are deemed to interfere with the conduct of the study as judged by the investigator
- Known hypersensitivity to pomalidomide and its analogues in general and/or to ixazomib and its analogues or to any other component of study drugs
- Prior malignancy excluding adequately treated with curative intent basal cell or squamous cell skin cancer, in situ cervical, breast or prostate cancer without any evidence of residual disease or requiring anti-cancer treatment < 2 years prior to initiating study treatment
- Patients with congestive heart failure NYHA Class III and IV, cardiac arrhythmias (except atrioventricular block type I and II, atrial fibrillation/flutter, bundle brunch block) or other signs and symptoms of relevant cardiovascular disease
- Pregnant women, nursing mothers, lactating women, and women of childbearing potential as well as male subjects who are unwilling to adhere to the guidelines of the treatment-specific pregnancy prevention program
- Unwilling or unable to follow protocol requirements
- Systemic treatment with strong inhibitors of CYP1A2 (fluvoxamine, enoxacin,ciprofloxacin), strong inhibitors of CYP3A (clarithromycin, telithromycin, itraconazole, voriconazole, ketoconazole, nefazodone, posaconazole) or strong CYP3A inducers (rifampin, rifapentine, rifabutin, carbamazepine, phenytoin, phenobarbital), or use of Ginkgo biloba or St. John’s wort within 14 days before randomization in the study
- Known gastrointestinal (GI) disease or GI procedure that could interfere with the oral absorption or tolerance of the study drugs including difficulty swallowing
- Inability or unwillingness to receive thromboembolism prophylaxis

Alter	18 Jahre und älter
Prüfzentren	**Innere Medizin 2** (Rekrutierung beendet) Hämatologie / Medizinische Onkologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Beate Kienzler-Sach beate-ursula.kienzler-sach@unimedizin-ffm.de
Sponsor	GWT TUD Gmbh
Registrierung in anderen Studienregistern	EudraCT 2014-001757-16
Links	Studiendokumente zum Download (roXtra)