Trial Description

Title

A phase II trial to evaluate safety and efficacy of combined trastuzumab and AUY922 in advanced non-small cell lung cancer (NSCLC) with HER2 - overexpression or -amplification or - mutation.

Trial Acronym

TRY

URL of the trial

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Brief Summary in Lay Language

The main aim of the trial is to evaluate the efficasy and the safety of AUY 922 + Herceptin (in combination). Both medication should block cancer cells growing. Herceptin blocks especially cancer cells with a specific genetic alteration (HER2). Therefore only patients with HER2 alteration in non-small lung cancer can participate in this trial. Herceptin is approved for other diseases. AUY 922 is not approved. The drugs will be given by infusion. During the infusion and after the infusion blood samples will be taken to determine the drug level in the blood.

Brief Summary in Scientific Language

Trastuzumab and AUY922 in HER2-overexpressed or -amplified or –mutated NSCLC

Organizational Data

- DRKS-ID: **DRKS00003301**
- Date of Registration in DRKS: **2012/11/02**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **12-114 , Ethik-Kommission der Medizinischen Fakultät der Universität zu Köln**

Secondary IDs

- EudraCT-Number: **2011-005655-13**
- BfArM-No.: **4038232**
- Sponsor-ID: **TRY (Universität Köln)**

Health condition or Problem studied

- ICD10: **C34 - Malignant neoplasm of bronchus and lung**
- Free text: **HER2-overexpression or -amplification or -mutation**

Interventions/Observational Groups

- Arm 1: **Part 1: Trastuzumab (Herceptin®) Monotherapy, once weekly. Loading dose 4 mg/ kg, subsequently 2 mg/ kg. In case of progression:**
  Part 2: Trastuzumab (Herceptin ®) once weekly, 2 mg/ kg + AUY922 once weekly, 70 mg/m2 - until progression.

  Both Infusions are given the same day.

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Single arm study**
- Blinding: **Open (masking not used)**
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Treatment**
- Assignment: **Single (group)**
- Phase: **II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **No**

Primary Outcome

Response rate (RR) of the combination therapy with Trastuzumab and AUY922, determined by CT every 6 weeks

Secondary Outcome

• To evaluate the response rate in patients treated with trastuzumab monotherapy by CT (every 6 weeks)
• To evaluate the tolerability of trastuzumab and AUY922 in combination (endpoints: assessment of adverse events (AEs) according to CTC-AE V4.0, ongoing)
• To evaluate the clinical efficacy of trastuzumab monotherapy and the combination descriptively (endpoints: progression-free survival (PFS) determined by CT every 6 weeks, overall survival (OS) determined by contact every 6 months)
• To correlate clinical efficacy of trastuzumab monotherapy and the combination with HER2 overexpression or mutational or amplification status

descriptively. Response and HER 2 status will be compared. Her 2 Status will be analyzed before start of study medication
- **To assess pharmacokinetics of AUY922 and trastuzumab (PK blood samples will be taken weekly)**
- **To establish a pharmacokinetic / pharmacodynamic model with regard to response rate and adverse events**

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Klinik I für Innere Medizin, Köln**
- University Medical Center **Essen**

Recruitment

- Planned/Actual: **Planned**
- (Anticipated or Actual) Date of First Enrollment: **2012/12/01**
- Target Sample Size: **29**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

- **Stage IV NSCLC patients after failure of at least one standard therapy with HER2 protein overexpression or gene amplification (FISH-positive) or mutation**
- **Age > 18 years**
- **ECOG performance status 0 to 2**
- **Life expectancy of at least 12 weeks**
- **Evaluable disease or disease measurable per Response Evaluation Criteria in Solid Tumors (RECIST)**
- **Adequate bone marrow, liver and renal function and adequate electrolyte balance as assessed by**

following laboratory requirements conducted 14 days prior to treatment:
- **Hemoglobin ≥ 9.0 g/dL**
- **Absolute neutrophil count (ANC) ≥ 1500 /mm3**
- **Platelet count ≥ 100,000/µL**
- **Total bilirubin ≤ 2 x ULN**

- **ALT, AST and alkaline phosphatase (AP) ≤ 2.5 x ULN or ≤ 5.0 x ULN, if liver metastasis are present**
- **PT-INR/PTT < 1.5 x ULN**
- **Creatinine clearence (CrCl) ≥ 60ml/min calculated by either MDRD-formel or by 24 hours urine collection**
- **Total calcium (corrected for serum albumin) within normal limits or correctable with supplements**
- **Magnesium within lower normal limits or correctable with supplements**
- **Potassium within normal limits or correctable with supplements**
- **Written informed consent (after adequate explanation of the trial) to participate in the trial and to adhere to trial procedures, as well as consenting to data protection procedures**
- **In case of females with childbearing potential (definition of menopause is no bleeding at least 12 months after last menstruation):**
- **negative serum pregnancy test in women with childbearing potential**
- **efective method of contraception (Pearl-Index not greater than 1%)**

Exclusion criteria

- **Known hypersensitivity to any study medication**
- **Other history of ongoing malignancy that would potentially interfere with the interpretation of efficacy**
- **Previous treatment with Hsp90 inhibitors (e.g.17-AAG)**
- **Treatment with therapeutic doses of coumarin derivatives..Low doses of coumarin derivatives (e.g. < 2mg/day) are permitted**
- **Pregnant or lactating women**
- **Patients with concurrent severe and/or uncontrolled medical conditions (e. g. uncontrolled diabetes mellitus, active untreated of uncontrolled infection, chronic obstructive or chronic restrictive pulmonary disease including dyspnea at rest from any cause) that could cause unacceptable safety risks or compromise compliance with the protocol**
- **Impaired cardiac function including any of the following:**
  - **History (or family history) of long QT syndrome**
  - **Mean QTcF ≥ 450 msec on screening ECG**
  - **History of clinically manifested ischemic heart disease ≤ 6 months prior to study start**
  - **History of heart failure or left ventricular (LV) dysfunction (LVEF ≤ 45%) by transthoracal echocardiography**
  - **Clinically significant ECG abnormalities including one or more of the following: left bundle brunch block (LBBB), right bundle brunch block (RBBB) with left anterior hemiblock (LAHB), ST segment elevations or depressions > 1 mm or 2nd (Mobitz II) or 3rd degree AV block**
  - **History or presence of atrial fibrillation, atrial flutter or ventricular arrhythmias including ventricular tachycardia or Torsades de Pointes**
  - **Other clinically significant heart disease (e.g. congestive heart failure, uncontrolled hypertension, history of labile hypertension, or history of poor compliance with an antihypertensive regimen)**
  - **Clinically significant resting bradycardia (< 50 beats per minute)**
  - **Patients who are currently receiving treatment with any medication which has a relative risk of prolonging the QTc interval or inducing Torsades de Pointes and cannot be switched or discontinued to an alternative drug prior to commencing AUY 922**
  - **Obligate use of a cardiac pacemarker**
- **Known diagnosis of HIV, active hepatitis B and/or C (testing is not mandatory)**
- **Clinically symptomatic leptomeningeal or brain metastases (patients with clinically stable brain metastases may be enrolled)**
- **Any person being in an institution on assignment of the respective**

authority

Addresses

■ **Primary Sponsor**

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Sources of Monetary or Material Support

- **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

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Status

- Recruitment Status: **Recruiting planned**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*