

Trial Description

Title

First in man study to evaluate the safety, tolerability and preliminary efficacy of the Fc-optimized FLT3 antibody FLYSYN for the treatment of acute myeloid leukemia patients with minimal residual disease

Trial Acronym

FLYSYN-101

URL of the trial

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Brief Summary in Lay Language

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Brief Summary in Scientific Language

The purpose of this study is to characterize the safety profile and preliminary efficacy of FLYSYN as monotherapy in adult subjects with NPM1 positive acute myeloid leukemia (AML), ineligible for allogeneic hematopoietic stem cell transplantation in complete remission (CR) with molecular detection of minimal residual disease (MRD)

Organizational Data

- DRKS-ID: **DRKS00011887**
- Date of Registration in DRKS: **2017/03/17**
- Date of Registration in Partner Registry or other Primary Registry: **2016/05/13**
- Investigator Sponsored/Initiated Trial (IST/IIT): **no**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **184/2016AMG1 , Ethik-Kommission an der Medizinischen Fakultät der Eberhard-Karls-Universität und am Universitätsklinikum Tübingen**

Secondary IDs

- EudraCT-No.
(for studies acc. to Drug Law): **2016-000236-17**
- Primary Registry-ID: **NCT02789254 (clinicaltrials.gov)**

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Health condition or Problem studied

- ICD10: **C92.0 - Acute myeloblastic leukaemia [AML]**

Interventions/Observational Groups

- Arm 1: **Cohort 1:**
Patient 1-3: FLYSYN 0.5 mg/m² body surface area (BSA) day 1
Cohort 2:
Patient 4-6: FLYSYN 0.5 mg/m² body surface area (BSA) day 1 FLYSYN 1.0 mg/m² BSA day 2
Cohort 3:
Patient 7-9: FLYSYN 0.5 mg/m² body surface area (BSA) day 1, FLYSYN 4.5 mg/m² BSA day 2
Cohort 4:
Patient 10-12 and 13-28*: FLYSYN 0.5 mg/m² body surface area (BSA) day 1, FLYSYN 14.5 mg/m² BSA day 2**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: [---]*
- Allocation: **Single arm study**
- Blinding: [---]*
- Who is blinded: [---]*
- Control: **Uncontrolled/Single arm**
- Purpose: **Treatment**
- Assignment: **Single (group)**
- Phase: **I-II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **No**

Primary Outcome

Incidence and severity of adverse events (AE) (CTCAE V4.03) until 28 days (i.e. Visit 7, day 29) after dosing

Secondary Outcome

Incidence and severity of adverse events (AE) (CTCAE V 4.03) until 180 days (i.e. Visit 11, day 180) after dosing

- **Pharmacokinetics and pharmacodynamics**
- **Immunogenicity of FLYSYN based on both absolute (number and percentage of subjects who develop HAMA/HAHA) and semi-quantitative (HAMA/HAHA titer determination of confirmed positive samples) assessments**
- **Absolute and percent change from baseline in measurements of B, T, and NK cell populations and activation**
- **Absolute changes from baseline in laboratory parameters**
- **Change in cytokines from baseline**
- **Overall response rate, defined as MRD negativity or at least one log step reduction**
- **Duration of response, time to MRD progression (log step), time to relapse**
- **Absolute change from baseline in overall quality of life scores (EORTC QLQ C-30)**

Countries of recruitment

- **DE Germany**

Locations of Recruitment

- Medical Center **Universitätsklinikum Tübingen - Medizinische Klinik II, Tübingen**
- Medical Center **Universitätsklinikum Heidelberg - Medizinische Klinik V, Heidelberg**
- Medical Center **Universitätsklinikum Ulm - Klinik für Innere Medizin III, Ulm**
- Medical Center **Medizinische Hochschule Hannover - Klinik für Hämatologie, Hämostaseologie, Onkologie und Stammzelltransplantation, Hannover**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2017/02/15**
- Target Sample Size: **28**
- 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

- **Age ≥ 18 years at the time of voluntarily signing an IEC-approved informed consent, there is no upper age limit**
- **Diagnosis of AML with NPM1 mutation according to WHO criteria**
- **Confirmed FLT3 expression on leukemic cells**
- **Known mutational status of FLT3 (FLT3-ITD, FLT3-TKD, FLT3 wild type)**
- **Hematological CR (ANC count $> 1.000/\mu\text{L}$, Thrombocytes $> 100.000/\mu\text{L}$), but MRD positivity after any therapy except allogeneic stem cell transplantation**
- **Life expectancy of > 3 months**
- **ECOG performance status ≤ 2**
- **Subject must be willing to receive transfusion of blood products**
- **Be willing and able to comply with the study protocol for the duration of the study**
- **Females of childbearing potential (FCBP) must undergo repetitive pregnancy testing (serum or urine) and results must be negative**
- **Reliable contraception should be maintained throughout the study and for 6 months after study treatment**
- **Unless practicing complete abstinence from heterosexual intercourse, sexually active FCBP must agree to use adequate contraceptive methods**
- **Males (including those who have had a vasectomy) must use an effective barrier method of contraception throughout the study and for 6 months after study treatment if sexually active with a female of childbearing potential**
- **All subjects must:**
 - **understand that the investigational product could have a potential teratogenic risk.**
 - **be counseled about pregnancy precautions and risks of fetal exposure.**
 - **be able to comply with all study-related procedures, medication use, and evaluations.**

Exclusion criteria

The presence of **ANY** of the following criteria will exclude a patient from study enrollment:

- **Patients proceeding to hematopoietic stem cell transplantation (suitable candidate and donor available, informed consent of patient)**
- **Pregnant or breast feeding females**
- **$> 5\%$ blasts in bone marrow or extramedullary disease**
- **Treatment with monoclonal antibody within 3 months before treatment with FLYSYN or known immunoglobulin intolerance**
- **Known positivity for HIV, active HBV, HCV, or Hepatitis A infection**
- **No consent for registration, storage and processing of the individual disease-characteristics and course as well as information of the family physician and/or other physicians involved in the treatment about study participation**
- **No consent for biobanking**
- **Presence of any medical/psychiatric condition or laboratory abnormalities which may limit full compliance with the study, increase the risk associated with study participation or study drug administration, or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the patient inappropriate for entry into this study**
- **Prior history of malignancies, other than AML/myelodysplastic syndrome (MDS), unless the subject has (i) been free of the disease for ≥ 2 years. (ii) Exceptions include the following: Basal cell carcinoma of the skin, carcinoma in situ of the cervix, carcinoma in situ of the breast, incidental histological finding of prostate cancer (TNM stage of T1a or T1b)**
- **Patients receiving any medication listed in the Appendix IV "Prohibited"**

Medications" (within 14 days prior to the first dose of study drug)

- **Uncontrolled infection, e.g. infection progressing under adequate antimicrobial/antifungal/antiviral treatment**
- **Patients under ongoing treatment with another investigational medication or having been treated with an investigational medication within 14 days of screening**
- **Current treatment with immunosuppressive agents**
- **Systemic diseases (cardiovascular, renal, hepatic, etc.) that would prevent study treatment (e.g., creatinine >1.5x upper normal serum level; bilirubin, AST or AP >2.5x upper normal serum level; heart failure NYHA III/IV; severe obstructive or restrictive ventilation disorder)**

Addresses

■ Primary Sponsor

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■ Contact for Scientific Queries

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Sources of Monetary or Material Support

- **Commercial (pharmaceutical industry, medical engineering industry, etc.)**

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Status

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

Trial Publications, Results and other documents

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Please note:

There are additional attributes available concerning this trial. To open an extended view please [click here](#).