**Scientific Title**
A Phase I/II Clinical Trial of PXD101 in Combination with Idarubicin in AML Patients not suitable for Standard Intensive Therapy

**Short Title**
PXD101-CLN-15

**Id KN/ELN** LN_NN_0007_300

**Trialgoup**
NN

**Type of Trial**
multicentric, open-label

**Phase**
Phase I/II

**Disease**
Acute myeloid leukemia (AML) AML all subtypes without FAB M3

**Stage of Disease**
de novo/non-treated relapsed/refractory

**Aim**
- To determine the safety and tolerance (Maximum Tolerated Dose, Dose Limiting Toxicity) and explore efficacy (Response rate (CR or PR)), using the response criteria of the International Working Group (Cheson et al 2003)
- To examine the time to response, response duration, overall survival, relapse-free survival, event-free survival and remission duration following PXD101 combination therapy.
- To examine aspects of PK and PHDY of PXD101 in combination with idarubicin in the two PXD101 schedules.

**Inclusion Criteria**
- Signed consent of an IEC-approved informed consent form.
- patients above 60 years in first relapse or refractory.
- patients 18-60 years 2nd relapse or refractory to at least two intensive chemotherapy cycles.
- patients above 60 years with high risk features (cytogenetics, secondary or treatment related AML).
- patients above 60 years with myelodysplastic syndrome with > 10% blasts in bone marrow (WHO RAEB-2). For patients below 60 years potential curative treatments should have been exhausted.
- Performance status (ECOG) 2.
- Age ≥18 years.
- Acceptable liver, renal and bone marrow function including the following:
  - a. Bilirubin ≤1.5 times upper limit of normal (ULN)
  - b. AST (SGOT) or ALT (SGPT) and Alkaline Phosphatase ≤3 times upper limit of normal.
  - c. Serum creatinine ≤1.5 times upper limit of normal (ULN).
- Serum potassium within normal range.
- Acceptable coagulation status: APTT and PT or INR within ≤1.5 times upper limit of normal or in the therapeutic range if on anticoagulation.
- Female patients with reproductive potential with a negative pregnancy test within the last 7 days before trial enrollment and must use a safe contraceptive during and for a period of 60 days after the trial. Fertile female partners to male participants must likewise use contraceptive for the same period.

**Exclusion Criteria**
- Treatment with investigational agents within the last 4 weeks.
- Prior treatment with HDAC inhibitors including valproic acid.
- Prior antileukemic therapy, within the last 3 weeks before trial dosing including chemotherapy, radiotherapy, endocrine therapy or immunotherapy. Cytoreduction with hydroxyurea for high blood counts is allowed during the pre-trial investigation phase but the treatment should be discontinued at least 3 days before the PXD101 treatment.
- Co-existing active infection (including HIV) or any co-existing medical condition likely to interfere with trial procedures, including significant cardiovascular disease (New York Heart Association Class III or IV) cardiac disease, myocardial infarction within the past 6 months, unstable angina, congestive heart failure requiring therapy, unstable arrhythmia or a need for anti-arrhythmic therapy, uncontrolled hypertension, bradycardia with heart rate <50/min or evidence of ischemia on ECG, marked baseline prolongation of QT/QTcF interval, e.g., repeated demonstration of a QTcF interval > 450 msec; Long QT Syndrome; the required use of concomitant medication on PXD101 infusion days that may cause Torsade de Pointes.
- Altered mental status precluding understanding of the informed consent process and/or completion of the necessary study procedures.
- Concurrent second malignancy
- History of hypersensitivity to idarubicin.
- Cumulative idarubicin dose above 100 mg/m2 (or with respect to cardiotoxicity) corresponding doses of other anthracyclines.
- LVEF below normal range (< 45%)
- Known CNS leukaemia.

Age
>= 18 years

Status
Closed

start of Recruitment
22.08.0007

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