**TOSEDOSTAT PLUS LOW DOSE CYTARABINE COMBO INDUCES A HIGH RATE OF RESPONSES THAT CAN BE PREDICTED BY GENETIC PROFILING IN AML: FINAL RESULTS OF A PHASE II MULTICENTER STUDY**

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**BACKGROUND**
- Tosedostat is a new, orally bioavailable inhibitor of members of the M1 and M17 classes of aminopeptidases.
- Tosedostat is effective as single agent, with a manageable safety profile, in AML.

**AIMS**
We assumed that the addition of Tosedostat to Low-Dose Cytarabine may improve the response rate and remission duration over what is expected with chemotherapy or tosedostat alone.

**PATIENTS & METHODS**

**Objectives of the Study (EudraCT number: 2012-000334-19):**
- **Primary objective:** To assess the CR rate of combination regimen
- **Secondary objective:** To assess the safety and the toxicity of the combination regimen; the response rate of stable disease or better: the OS and PFS; possible biomarkers associated to sensitivity/resistance by GEP

**Study treatment:**
- Oral Tosedostat (120 mg daily on days 1-240) and subcutaneous cytarabine (20 mg BID daily on days 1–10 of each cycle).
- Courses were repeated every 4 weeks up to 8 cycles
- Patients achieving CR after 8 cycles receive maintenance with Tosedostat, 60 or 120 mg/day, until disease progression.

**Efficacy:**
- **Induction period mortality 12% (4 death in aplasia)**
  - Complete response rate: 45.4% (15/33)
  - Overall response rate: 54.4% (15 CR, 3 PR)
  - No Response: 7/33 PD and 4/33 SD
  - 10/18 (55%) responding patients are **STILL IN REMISSION** after a median follow up of 319 days

**Overall Survival according to response**

**GEP:**
- Based on the differentially expressed genes (N=212), samples were clearly divided according to the clinical response (CR vs. no CR):

**CONCLUSIONS**
- Tosedostat and Low-dose Cytarabine combo produced a CR rate superior to what expected (45.4% versus 25%)
- The achievement of CR could be efficiently predicted by GEP
- Potential biomarkers were identified by GEP