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Universitätsklinik für
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Final Report: HDMM Trial

- **Study-Title, Investigators etc.**

  HDM201 and midostaurin (HDMM) in relapsed/refractory AML with FLT3mut and TP53wt, a phase I study.

  Sponsor Investigator: Prof. Dr.med. Thomas Pabst; Department of Medical Oncology; University Hospital/Inselspital; 3010 Bern; Switzerland

- **Objectives**

  Overall Objective
  To determine the maximum tolerated dose (MTD) and to characterize dose-limiting toxicities (DLTs) of HDM201 when added to midostaurin in relapsed/refractory AML patients with TP53 wildtype and FLT3mut.

  Primary Objective
  The primary objective of this phase I study is to establish feasibility and to determine the MTD of HDm201 and its recommended dose that will be used in a later phase II study (recommended phase II dose; RP2D) when added to midostaurin combination for first-line treatment in relapsed/refractory AML patients with TP53 wildtype and FLT3mut

  Secondary Objectives
  • assess the rate of morphologic complete remission (CR) with HDMM treatment
  • assess the toxicities observed in AML patients treated with HDMM
  • assess overall survival (OS) in AML patients treated with HDMM
  • assess progression free survival (PFS) in AML patients treated with HDMM
  • assess infectious complications in AML patients treated with HDMM

  Safety Objectives
  Among other secondary objectives listed above, this study aims to assess toxicities of HDM201 in combination with midostaurin in AML patients. Accordingly, adverse events will be recorded.

- **Number of Patients (planned)**
  A target of minimum 3 and maximum 24 subjects will be enrolled in this phase I study.

- **Screening: how many patients, screening failure, reasons for not entering the study**
  Enrolled patients: 2
  Screening Failures: 0

Pre-Screening Failures: 10
AML, but FLT-3 negative: 5
Not willing to participate in a study: 1
therapy with another FLT-3 Inhibitor: 1
not fit elderly, enrolment in another trial: 1
death before ASCT: 1
AML not confirmed: 1

- **Study Period (years): Date of First Enrolment, Date of Last Completed**
  First enrolled: 19.8.2021 / Last off-study: 12.1.2022 (date reported to Swissmedic and EC)

- **Patient characteristics: 2 enrolled patients**
  HDMM-01 - relapsed AML (first diagnosis 05/2020; relapse 11.8.2021)
  HDMM-02 – relapsed AML (first diagnosis 04/2021; relapse 25.11.2021)

- **Treatment duration, dose, reason for discontinuation**
  HDMM-01:
  Study treatment: 24.8.2021 until 16.9.2021
  Dose: 50 mg Midostaurin BID on days 1 to 28 and 40 mg HDM201 at dose level 1 (days 1-3)
  reason for discontinuation: progression

  HDMM-02:
  Study treatment intake: 16.12.2021 until 17.1.2022
  Note: official study end 12. 01.2022 was notified to health authorities but according to patient`s diary the intake of 50 mg Midostaurin occured until 17.1.2022 in the morning
  Dose: 50 mg Midostaurin BID on days 1 to 28 and 40 mg HDM201 at dose level 2 (days 1-5: 16.12.2021 until 20.12.2021 and 13.1.2022 to 16.1.2022)
  reason for discontinuation: progression

- **Safety summary**
  No DLT occured
  See SAE overview and «Notification Study End» (attachment)

- **Overall Conclusion**
  No dose limiting toxicities were observed at the dose levels investigated in this trial. The trial, nevertheless, needed to be stopped by the sponsor (Novartis) due to accrual below the anticipated accrual rate. No definite conclusions can be drawn from this trial.

Berne, January 19th 2023

Prof. Dr.med. Thomas Pabst

Attachments:
Notification Study End, 14.09.2022
SAE overview