Mocravimod improves overall survival in AML patients undergoing allogeneic hematopoietic cell transplantation

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INTRODUCTION

Mocravimod (MOC) is a sphingosine-1-phosphate (S1PR) modulator in late stage clinical development for potentially preventing relapse in acute myeloid leukemia (AML) patients undergoing allogeneic hematopoietic cell transplantation (allo-HCT). The success of allo-HCT is limited by leukemia relapse, which is closely related to overall survival (OS), and graft-versus-host disease (GvHD). Graft-versus-leukemia (GvL) effect is essential to prevent disease relapse. Pharmacological modulation of S1PR signaling by MOC efficiently sequesters T cells in lymphoid organs and thus enables a therapeutic benefit of MOC via donor T cell-mediated GvL against the leukemic cells whilst reducing GvHD due to fewer alloreactive T cells infiltrating peripheral tissue. Study CKRP203A2105 (NCT01830010) investigated the safety and tolerability of MOC in patients with hematological malignancies undergoing allo-HCT.[1]

OBJECTIVE(S)

The aim of this study was to explore relapse and survival outcomes for a subgroup of AML patients included in the CKRP203A2105 study in comparison to a matched-pair control group of AML patients undergoing allo-HCT who did not receive MOC treatment during the same time at one study site.

METHOD(S)

Seven AML patients were included in CKRP203A2105 across three treatment arms: 3mg MOC+cyclosporine A/methotrexate (CsA/MTX) (part 1), 1mg MOC+CsA/MTX and 3mg MOC+tacrolimus (Tac)/MTX (part 2; Figure 1). During the same period nine AML patients underwent allo-HCT at one of the study sites outside of the trial, thus without MOC. These nine patients were selected based on the same inclusion criteria as study patients and were used as a matched-pair control group. Follow-up period was up to 1 year in part 1 and up to 2 years in part 2. Further follow-up information for individual patients could be collected after obtaining informed consent for this follow-up study. Bayesian comparison of OS of MOC-treated AML patients and controls was performed.

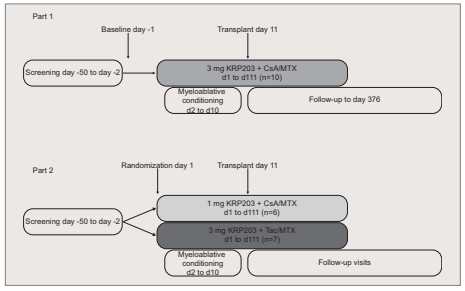

Figure 1. Study design CKRP203A2105 (NCT01830010)

RESULT(S)

Patients demonstrated comparable baseline characteristics with a median age of 51 years in the MOC arm versus 46 years in the control arm, and a pre-allo-HCT remission state of complete remission (CR) in 4 (57.1%) patients in the MOC-treated arm versus 4 (44.4%) patients in the control arm (Table 1). Due to limited size of study population, more patients were male in the MOC group; 5 (71.4%) versus 3 (33.3%) in the controls. Only two out of seven patients in the MOC arm died prior to censoring (approximately at 2.5- and 5-years post allo-HCT), compared to six out of nine patients in the control group (Figure 2). One of these two patients in the MOC group relapsed after two years and died four months later, while the other patient died without relapse. In the control group, all patients, but one, died due to disease progression. A Bayesian comparison of the survival curves of the MOC patients and the control group suggested a 93% probability that MOC increased the OS compared to the control group (Figure 3).

	Mocravimod (n=7)	Controls (n=9)
Age		
Mean (SD)	47.4 (12.1)	44.4 (14.1)
Median	51	46
Min-Max	26-63	23-62
Sex - n(%)		
male	5 (71.4)	3 (33.3)
Remission state pre allo-HCT - n(%)		
CR	4 (57.1)	4 (44.4)
Persistence	1 (14.3)	4 (44.4)
Relapse	2 (28.6)	1 (11.1)

Table 1. Baseline patients' characteristics

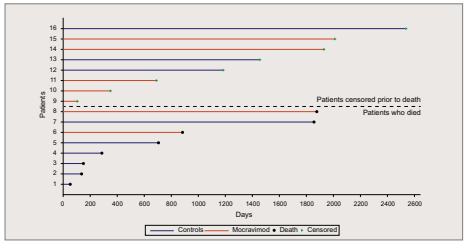

Figure 2. Individual survival times of Mocravimod AML patients and control patients who did not receive Mocravimod

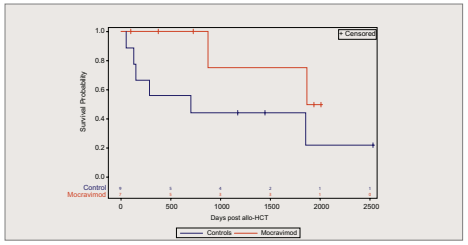

Figure 3. Overall survival probabilities of Mocravimod AML patients compared to control patients. Mocravimod patients (n=7): AML receiving 3mg MOC+CsA/MTX (n=3), 1mg MOC+CsA/MTX (n=2), or 3mg MOC+Tac/MTX (n=2), Follow-up period was approximately 2000 days for selected patients. Control AML patients (n=9) had a follow-up time of up to 2500 days after allo-HCT. 2/7 patients died in MOC arm, 6/9 patients died in control arm. Modelling Estimate: 93% probability that MOC increases OS compared to control treatment.

CONCLUSION(S)

- Patient characteristics were comparable between the two groups with a high percentage of patients receiving allo-HCT in persistent or relapsing AML
- Only 1 AML patient relapsed while being on mocravimod treatment
- Only 2 out of 7 mocravimod-treated patients died, compared to 6 out of 9 control patients
- This post hoc analysis demonstrates a survival benefit for AML patients underoing allo-HCT who receive treatment with mocravimod on top of their standard treatment
- This further supports the development of mocravimod as adjunctive and maintenance treatment in AML patients undergoing allo-HCT and provides a rationale for a mocravimod treatment period of 12 months which is currently investigated in an ongoing Phase III trial, the MO-TRANS trial (NCT05429632)

ACKNOWLEDGEMENTS

We would like to thank all patients who participated in this study.

REFERENCES

[1]Dertschnig et al., TCT 29 (2023) 41.e1-41.e9

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