**Ivosidenib (AG-120) in patients with IDH1-mutant relapsed/refractory myelodysplastic syndrome: Updated enrollment of a phase 1 dose escalation and expansion study**

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**BACKGROUND**

Several compounds that selectively inhibit histone deacetylase (HDAC) or inhibit histone methyltransferase (HMT) have been approved for the treatment of advanced hematologic malignancies. We have previously reported updated results of the first phase 1 dose escalation and expansion study of ivosidenib (AG-120), an oral inhibitor of IDH1 (NCT02704058). The results of this study included a total of 126 patients with relapsed/refractory (R/R) acute myeloid leukemia (AML), and 25 patients with relapsed/refractory (R/R) advanced hematologic malignancies (R/R AML or R/R MDS). The study was ongoing (NCT02074839) enrolled adults with mIDH1 advanced hematologic malignancies, including R/R MDS. The study is ongoing (Figure 1).  

**OBJECTIVES**

The objectives of this study are:

- To assess the safety, tolerability, and clinical activity of ivosidenib in patients with R/R AML or R/R MDS.
- To evaluate the pharmacokinetics of ivosidenib in patients with R/R AML or R/R MDS.
- To characterize the pharmacokinetics of ivosidenib and to evaluate the pharmacodynamic relationship of ivosidenib and 2-HG.
- To assess the pharmacodynamic effects of ivosidenib.

**SUB-STUDY DESIGN**

- This is a sub-study of the phase 1 dose-escalation and expansion study, enrolling patients with mIDH1 R/R MDS only.
- In this population of patients with mIDH1 R/R MDS, the primary objectives of this study are:
  - Primary: to assess the safety, tolerability, and clinical activity of ivosidenib 550 mg.
  - Secondary: to characterize the pharmacokinetics of ivosidenib and to evaluate the pharmacodynamic pharmacokinetic relationship of ivosidenib and 2-HG.
- Exploratory: to assess the pharmacodynamic effects of ivosidenib.

**SUMMARY AND CURRENT STATUS**

**Summary**

- The favorable efficacy and safety of ivosidenib in the small population of patients with mIDH1 R/R MDS in the phase 1 clinical study of patients with mIDH1 hematological malignancies supports further evaluation in this sub-study.
- This sub-study will evaluate the efficacy and safety of ivosidenib in ≥23 patients with mIDH1 R/R MDS.
- Further information on CR is available at https://clinicaltrials.gov/ct2/show/NCT02704058.

**Study status**

- Patients are being recruited from 22 sites in the US and France.
- Contact medinfo@agios.com.

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**CONFLICTS OF INTEREST**

JMF: Agios – honoraria and research funding. CDD: AbbVie, Agios, Celgene, Daiichi Sankyo – honoraria and research funding. MJS: AbbVie, Actinium, Agios, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – research funding; AbbVie, Actinium, Agios, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – consultant. RMS: AbbVie, Actinium, Agios, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – research funding; AbbVie, Actinium, Agios, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – consultant. HMK: AbbVie, Agios, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – research funding; AbbVie, Agios, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – consultant. DAD: Agios, Celgene, Daiichi Sankyo – research funding; AbbVie, Actinium, Arog, Astellas, BMS, Cyclacel, Daiichi Sankyo, Delta Fly, Jazz, KAHR, Nohla, Oncolyze, Orsenix, Rigel, Tetraphase – consultant. NA: AbbVie, Actinium, Arog, Astellas, BMS, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – research funding; AbbVie, Actinium, Arog, Astellas, BMS, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – consultant. RMS: AbbVie, Actinium, Agios, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – research funding; AbbVie, Actinium, Agios, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – consultant. HMK: AbbVie, Agios, Celgene, Daiichi Sankyo – honoraria and research funding. CDD: AbbVie, Agios, Celgene, Daiichi Sankyo – consultant. RMS: AbbVie, Actinium, Agios, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – speaker. NA: AbbVie, Actinium, Arog, Astellas, BMS, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – consultant. DAD: Agios, Celgene, Daiichi Sankyo – honoraria and research funding; AbbVie, Actinium, Arog, Astellas, BMS, Cyclacel, Daiichi Sankyo, Delta Fly, Jazz, KAHR, Nohla, Oncolyze, Orsenix, Rigel, Tetraphase – consultant. NA: AbbVie, Actinium, Arog, Astellas, BMS, Celgene, Daiichi Sankyo, Genentech, Gilead, Kite, MedImmune, Novartis, Pfizer – consultant. DAD: Agios, Celgene, Daiichi Sankyo – honoraria and research funding; AbbVie, Actinium, Arog, Astellas, BMS, Cyclacel, Daiichi Sankyo, Delta Fly, Jazz, KAHR, Nohla, Oncolyze, Orsenix, Rigel, Tetraphase – consultant. Brianna Schmitt, John DiNardo, Sarah Hamamoto, and Sarah Spera contributed to the preparation of the manuscript. This study was funded by Agios Pharmaceuticals, Inc., Cambridge, MA, USA.

**REFERENCES**