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Olutasidenib demonstrates promising tolerability and efficacy in *IDH1* mutated accelerated / blast phase myeloproliferative neoplasms

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INTRODUCTION

- Progression of myeloproliferative neoplasms (MPN) to accelerated phase (AP) or blast phase (BP) is associated with an aggressive course and dismal prognosis.
- Intensive treatment is poorly tolerated and low-intensity therapy with hypomethylating agents is associated with a median survival of 8 months.
- Mutations involving *IDH1* or *IDH2* often accompany such progression raising the potential for targeted therapy with IDH inhibitors.
- Enasidenib and ivosidenib, the first approved IDH2 and IDH1 inhibitor, respectively, have demonstrated favorable outcomes in several small series.
- Olutasidenib is an IDH1 inhibitor approved for the treatment of relapsed/refractory acute myeloid leukemia with an *IDH1* mutation.

AIM

- To evaluate the use of olutasidenib in patients with accelerated and blast phase MPNs.

METHOD

- Using prescribing records cross-referenced with institutional databases, we identified all patients with accelerated or blast phase MPN who received olutasidenib.
- Electronic medical record was utilized to assess baseline clinical, demographic, and genomic information.
- Treatment history and clinical outcome was assessed with a data cut-off of 5/1/2024.

RESULTS

- 4 patients were identified who received olutasidenib for *IDH1*-mutated AP/BP MPN.
- Median age 68 years.
- Three patients with relapsed/refractory disease. One received olutasidenib as initial therapy for AP MPN.
- Two patients received olutasidenib in combination with ruxolitinib.
- One patient experienced differentiation syndrome managed with brief interruption in treatment and administration of steroids.
- Three patients experienced normalization of peripheral blasts. (Pre-treatment peripheral blast % was 59%, 11%, and 11%, respectively for those patients.)
- The patient who did not experience normalization in peripheral blasts experienced normalization of hematologic values.
- Molecular responses were unable to be evaluated at data cut-off.
- Median duration of therapy was 4 months.
- All patients remain alive and on olutasidenib

Patient	Accelerated or Blast Phase	Mutations	Cytogenetics	Prior Therapy	Clincial Outcome
1	AP	JAK2/ASXL1/SRSF1/ IDH1	46,XY	none	Blast clearance, remained transfusion independent
2	BP	JAK2/SRSF2/IDH1/ ASXL1/ RUNX1/STAG2	46,XY, i(21), del20q	HMA/Ven	Normalization of hgb, plt, neutrophils; persistent peripheral blasts.
3	BP	MPL/IDH1/SRSF2/ RUNX1	46,XY,add(6)(q27)	HMA/Ven; CLAG	AML complete response – marrow reversion to chronic phase MPN --> transplant
4	BP	CALR/IDH1/SETBP1	46,XX,del(13)(q12 q14)	7+3	Normalization of peripheral blasts, WBC, plt. Continued transfusion dependency

CONCLUSIONS

- In a small cohort of patients with AP/BP MPN and IDH1 mutations, olutasidenib was well tolerated and associated with favorable clinical outcomes

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