



Crenolanie

A next-gen tyrosine kinase inhibitor for use in FLT3-mutated AML

THE ROLE OF FLT3 MUTATIONS IN AML

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Roughly one-third of AML patients harbor an internal tandem duplication (ITD) in FLT3, a receptor tyrosine kinase. Mutations of FLT3 at D835, a point mutation in the tyrosine kinase domain (TKD), have also been observed in AML patients. Both ITD and TKD mutations lead to constitutive activation of the tyrosine kinase function, making FLT3 an attractive drug target in AML patients. Both ITD and TKD mutations render FLT3 resistant to currently approved inhibitors. Moreover, novel activating FLT3 mutations are being identified in patients with AML. As the clinical development of FLT3 inhibitors proceeds into advanced phase trials, FLT3 mutations will represent a new obstacle in the care of FLT3-mutated AML patients.

CRENOLANIB IS A SELECTIVE TYPE I PAN-FLT3 INHIBITOR

Crenolanib, a type I TKI, is a potent inhibitor of FLT3-ITD and secondary KD mutants. Crenolanib represents the first TKI to exhibit both kinase selectivity and invulnerability to resistance-conferring KD mutations. Crenolanib, which spares cKIT, represents a promising therapy for achieving deep and durable responses in FLT3-mutant AML.

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CRENOLANIB APART FROM OTHER THERAPEUTIC OPTIONS 1. Crenolanib, whether delivered by itself or as part of a drug combination, has shown benefit in FLT3 mutant AML.

2. Patients who progress after treatment with prior TKIs may still remain sensitive to crenolanib.

3. Crenolanib has favorable pharmacokinetics and does not accumulate with repeated dosing.

4. Crenolanib is a selective type I TKI that does not inhibit wild-type cKIT.



Arog Pharmaceuticals Presents Crenolanib Clinical Data at the 2018 European Hematology Association Meeting

Arog Pharmaceuticals Presents Crenolanib Clinical Data at the 2017 American Society of Clinical Oncology Annual Meeting

Arog Pharmaceuticals Presents Crenolanib Clinical Data at 57th American Society of Hematology Annual Meeting

Arog Pharmaceuticals Receives Orphan Drug Designation in the European Union for Crenolanib for the Treatment of Acute Myeloid Leukemia and Soft Tissue Sarcoma

AROG Pharmaceuticals to Present Clinical Data on Crenolanib at the 2016 American Society of Hematology Annual Meeting

Arog Pharmaceuticals Receives FDA Fast Track Designation for Crenolanib for Advanced Gastrointestinal Stromal Tumors with a D842V Mutation in the PDGFRA Gene

Arog Pharmaceuticals Presents Crenolanib Clinical Data at the 2016 American Society of Clinical Oncology Annual Meeting

recent conference presentations

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- 3. Fathi AT. Emergence of Crenolanib for FLT3-Mutant AML. Blood 2013; 122(22): 3547-8.
- 4. Smith CC, Lasater EA, Lin KC, et al. <u>Crenolanib is a Selective Type I Pan-FLT3 Inhibitor</u>. Proc Natl Acad Sci U S A 2014; 111(14): 5319-24.
- 5. Zhang W, Gao C, Konopleva M, et al. Reversal of Acquired Drug Resistance in FLT3-Mutated Acute Myeloid Leukemia

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