ManagingAML

What are the advantages and disadvantages of the different FLT3 inhibitors?

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I'm often asked what are the advantages and disadvantages of one FLT3 inhibitor over another given that there are several treatment options that are FDA approved. We have midostaurin, which is approved in combination with intensive chemotherapy for frontline treatment of patients with FLT3 mutations. We have gilteritinib, which is approved for relapsed and refractory patients as monotherapy. And there's also off-label use of other drugs that inhibit FLT3, for example sorafenib, which has never carried a label for AML. I would first say that gilteritinib is the drug that is probably the most potent and selective of all of these. And certainly that's the drug in the relapse and refractory setting that's really shown the best data as a single agent. In the frontline setting, it's very possible that gilteritinib may improve the results that we're seeing with midostaurin when added to frontline chemotherapy, but we don't know this from an evidence base. And indeed, this is a question that we're trying to answer with frontline randomized trials right now, with both in the US and now in Europe, frontline randomized phase 2 and phase 3 studies comparing which FLT3 inhibitor would be superior in the treatment of newly diagnosed AML. A trial comparing gilteritinib to midostaurin as the third drug added to intensive chemotherapy 7+3 for newly diagnosed patients with FLT3 mutations was just initiated in the US. In terms of their treatment profiles, midostaurin is a less selective drug than gilteritinib and it does not have significant single-agent activity. So really, if the drug is used, midostaurin should be used in the context of combination therapy.

For more information on the trial, please visit:
https://ashpublications.org/blood/article/134/Supplement_1/1309/426901/Phase-II-Randomized-Trial-of-Gilteritinib-Vs