See also p. 38



midostaurin (RYDAPT°) for some types of acute myeloid leukaemia

Improved survival, but adverse effects underestimated

Abstract

● The standard treatment for patients with acute myeloid leukaemia is a combination of *daunorubicin + cytarabine* as induction therapy, followed by consolidation therapy with chemotherapy or bone marrow transplantation. Maintenance therapy has not been shown to be of benefit in prolonging survival. About one-third of patients have tumour cells carrying a mutation in the FLT3 gene, which is an adverse prognostic factor.

● *Midostaurin* (Rydapt°, Novartis) is an inhibitor of multiple tyrosine kinases, including the FLT3 kinase. It has been authorised in the European Union for patients with newly diagnosed acute myeloid leukaemia who carry a FLT3 mutation.

● In a randomised, double-blind, placebo-controlled trial in 717 patients aged less than 60 years, addition of *midostaurin* to the *daunorubicin + cytarabine* combination in the induction phase, then to high-dose *cytarabine* in the consolidation phase, with continuation of *midostaurin* in a maintenance phase, increased the proportion of patients alive at 5 years to 51% compared to 43%. However, *midostaurin* was not evaluated in patients aged over 60 years, who generally have a poor prognosis.

● Assessment of the adverse effects of *midostaurin* in the main trial was incomplete. According to available data, *midostaurin* carries at least a risk of gastrointestinal disorders, catheter infections, lymphopoenia and elevated liver transaminase levels.

● *Midostaurin* is metabolised by cytochrome P450 isoenzyme CYP 3A4 and may be an inducer of various cytochrome P450 isoenzymes and an inhibitor of P-glycoprotein, creating the potential for numerous pharmacokinetic interactions. Additive adverse effects with drugs causing gastrointestinal or hepatic disorders and lymphopoenia can also be expected.

● *Midostaurin* is toxic to the embryo and fetus.

OFFERS AN ADVANTAGE

In a trial in 717 patients with acute myeloid leukaemia and a FLT3 mutation, *midostaurin* (a multi-tyrosine kinase inhibitor) added to induction and consolidation therapy, and then continued as maintenance monotherapy, increased the proportion of patients alive at 5 years by 8%. It was not evaluated in patients aged over 60 years, who generally have a worse prognosis. According to an incomplete assessment of its adverse effects, *midostaurin* mainly carries a risk of gastrointestinal disorders, elevated transaminase levels and lymphopoenia. In practice, *midostaurin* can be offered to patients aged less than 60 years with careful monitoring of adverse effects. It is important to report these adverse effects.

RYDAPT° - *midostaurin* soft capsules

- **25 mg** of *midostaurin* per soft capsule

antineoplastic; inhibitor of tyrosine kinases including FLT3 and KIT

Indication: "*in combination with standard daunorubicin and cytarabine induction and high-dose cytarabine consolidation chemotherapy, and for patients in complete response followed by midostaurin single agent maintenance therapy, for adult patients with newly diagnosed acute myeloid leukaemia (AML) who are FLT3 mutation-positive*". [EU centralised procedure – orphan drug].

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▶ Translated from *Rev Prescrire* **November 2018**
Volume 38 N° 421 • Pages 814-815

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