



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, lymphopenia 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 inter-

actions. Additive adverse effects with drugs causing gastrointestinal or hepatic disorders and lymphopenia 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 lymphopenia. 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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