disease. Its application and correlation with clinical outcome may now be evaluated, alongside other approaches, such as multiparametric flow cytometry and *WT1*-expression changes, for its ability to quantify MRD in AML informatively. Applying the same principles mutations in other genes also have potential as appropriate targets that may increase the number of AML patients with normal karyotype amenable to MRD monitoring.

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Keywords: acute myeloid leukaemia, leukaemic stem cell, mutation, quantitative real-time polymerase chain reaction.

Treatment with hydroxycarbamide for intermedia thalassaemia: decrease of efficacy in some patients during long-term follow up

Following the early reports of hydroxycarbamide (HC) efficacy for the treatment of intermedia thalassaemia (Olivieri *et al*, 1997; Rigano *et al*, 1997), many further studies have been published (Bradai *et al*, 2003; Dixit *et al*, 2005; Karimi *et al*, 2005; Singer *et al*, 2005). However, data concerning long-term efficacy are scarce. At our centre, 18 splenectomised untransfused patients with intermedia thalassaemia (median age 37 years, range 18–59 years) and haemoglobin (Hb) levels <8·5 g/dl were treated with HC (median dosage 14·6 mg/kg, range 5–30 mg/kg). We evaluated Hb, mean corpuscular Hb (MCH), haemoglobin F (HbF) and reticulocytes before and after 1 year of treatment. Moreover, we evaluated long-term response to HC in the responders. Overall, after 1 year of treatment we observed an average Hb increase of 1·5 g/dl ($P < 0·001$); 11 of 18 patients had an increase in Hb of >1 g/dl (>1·5 g/dl) in eight patients and were followed further. Four patients had a Hb Lepore genotype; they showed an average Hb increase of 3·1 g/dl (range 2–4·5 g/dl). There was a statistically significant increase of MCH ($P < 0·001$), HbF ($P < 0·001$) and decrease of reticulocytes ($P < 0·05$) after one year of treatment. Mean follow up of the 11 responders was 66 months (range 3–144 months). In seven patients (mean follow up 45 months, range 34–58 months), the 1-year response did not differ significantly from the long-term follow-up response; their Hb level remained stable over the period of observation. In contrast, a progressive trend towards a reduction of response was observed in the other four responders with the longest follow up (mean follow up 104 months, range 70–144 months) (Fig 1). No adverse events were observed during follow up. If confirmed by further studies, our preliminary experience could indicate that the use of HC for the treatment of intermedia thalassaemia could decrease in efficacy over time. If this is because of long-term bone marrow HC toxicity or to bone marrow failure not

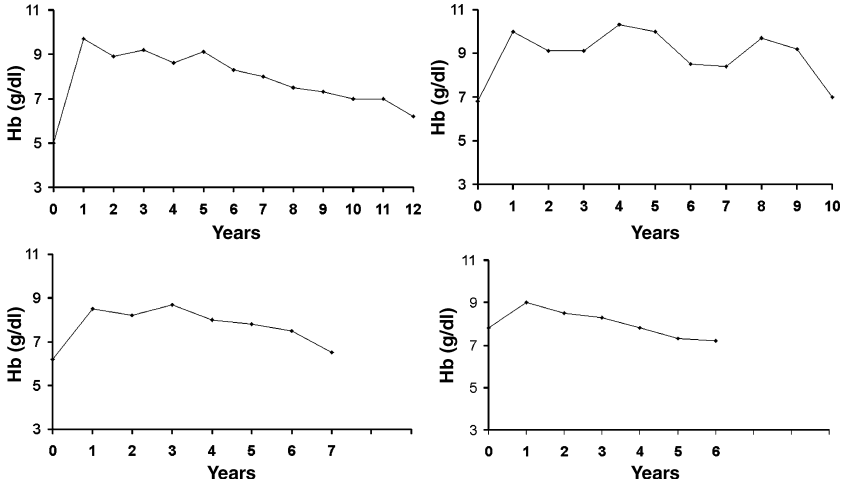

Fig 1. Haemoglobin (Hb) (mean/year) of four patients treated with hydroxycarbamide during long-term follow up. A progressive decrease of Hb was observed in all four patients.

related to HC, remains to be determined. Our centre is currently conducting a trial in which HC is withdrawn and then restarted after 1 month, in one of the four patients with reduced long-term response: a new response after a period of withdrawal could suggest a delayed bone marrow HC toxicity.

In conclusion, our experience confirms that HC can be an effective treatment for patients with thalassaemia intermedia who are not undergoing periodical transfusions. However, clinical response seems to reduce with long-term treatment. Moreover, HC is probably safe after long-term follow up.

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Keywords: thalassaemia, hydroxycarbamide, fetal hemoglobin, therapy, red cell disorders.

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Universal or selected screening for thrombophilia

In an informative meta-analysis and cost-effectiveness analysis, Wu *et al* (2005) examined the fraught area of thrombophilia screening. They provided an invaluable estimate of the cost of preventing a clinical event depending on the strategy employed. Table I (extracted from Table III Wu *et al*, 2005) shows the cost of preventing one venous thromboembolic