The clinical management of thalassaemias can be considered under three concepts namely: prevention, treatment and cure. This lecture will focus mainly on clinical treatment aspects, while recognizing that prevention and cure are equally important goals. Indeed while bone marrow transplantation from a healthy sibling donors has been the mainstay of curative treatment for over two decades, the extension of this approach to matched unrelated donors using high-resolution HLA typing has been associated with results in some centres comparable with those obtained employing an HLA-identical sibling, with estimated probabilities for obtaining thalassaemia-free survival between 85 and 87%.(Gaziev, et al 2008). Furthermore, a recent successful report of an E/b0-thalassaemia patient treated by gene therapy, shows that the applications and reach of curative therapy are likely to extend further. This latter approach (Cavazzana-Calvo, et al) used heavy pre-treatment conditioning and a lentiviral vector that carried transcriptional control elements that were specific for red-blood-cell precursors. Two years after treatment, the patient is synthesizing 10-20% adult Hb. The long term safety needs to be established and the significance and safety implications development of a clonal expansion of haemopoietic cells bearing a vector insertion in the HMGA2 gene, with significantly increased expression of HMGA2 need to be established.

The risks and benefits of potentially curative therapy need to be balanced against the improving outcomes with non-curative therapy. Standard treatment of thalassaemia major (TM), consists of the transfusion of safe blood combined with effective iron chelation. The range of therapies for iron overload have increased in recent years, as have the diagnostic tools for estimating iron overload and its distribution. The risk of death from cardiomyopathy in TM has fallen considerably in recent years, so that other morbidities and causes of mortality are becoming increasingly important. Key question with modern chelation are to understand how low iron overload can be effectively reduced without the risks of chelator toxicities and whether endocrinopathies can be prevented with the adoption of more ambitious chelation regimes. The use of MRI techniques (eg mT2*) has helped to identify those at the greatest risks of cardiomyopathy, so that intensive chelation treatment can be targeted for those most at risk: a recent audit of over 100 patients at UCLH and Whittington Hospitals, monitored with cardiac MRI for the last decade has shown that those with evidence of increased myocardial iron has fallen from 60% to 20% of patients. Furthermore, in this cohort, cardiac iron overload is no longer the leading cause of mortality (Thomas et al, 2010). These patients received a range of chelation therapies including monotherapies of desferrioxamine, deferiprone or deferasirox or combinations of deferiprone and desferrioxamine, with about one third of patients switching therapies at least once. No clear difference in outcome was seen between different regimes, except that patients who had more than 2 switches of therapy were less likely to have achieved significant improvement in myocardial iron. The optimal treatment of milder forms of homozygote or compound heterozygote thalassaemias (thalassaemia intermedia) is less clear, due to the increased risk of red cell allo-immunisation in patients who begin transfusion relatively late in life. With the exception of small numbers of impressive cases, the response to HbF modulators in intermedia syndromes is unpredictable and thus far often dissapointing.
