



PANHELLENIC ASSOCIATION FOR THE PROTECTION OF THALASSAEMIA
PATIENTS

THALASSAEMIA SESSION 18th JANUARY 2020, HOTEL TITANIA
“New Therapies in Thalassaemia”

SUMMARY OF THALASSAEMIA UPDATE

Coordinator: Prof. Vasili Berdoukas

1. Treatment of Hepatitides. Dr. Dimitris Kountouras.



With the current medications now available for the treatment of both Hepatitis B and C practically all patients with thalassaemia, who had been infected by either of these viruses have now be cleared of circulating virus. In addition, there is a total eradication programme for these viruses for the whole of Greece.

2. Cardiological findings in 600 Greek patients with haemoglobinopathies. Dr. Dimitris Kotsionis



With the purchase of a high resolutions portable ultrasound and a portable ECG machine, Dr. Kotsionis and his team have travelled to smaller cities and Thalassaemia treatment centres throughout Greece offering a comprehensive evaluation to patients both with respect to their general condition with respect to iron overload, but in particular their cardiac evaluation. The patients from these centres do not always have easy access to visit the larger centres and many have not been able to have similar evaluations. The main findings have been heavy hepatic iron load, cardiac arrhythmias, strokes resulting from thrombi that arise from the atria because of atrial fibrillation and pulmonary hypertension. Recommendations for management were made. Where centres have been visited more than once, the recommendations made at earlier visits have resulted in significant improvements in the patients' status.

3. Iron Chelation Therapy in Children– Dr. Antonis Kattamis



Dr. Kattamis presented the current available chelators and their application to their use in childhood. He showed that transfusion dependent children load much earlier with iron than

was originally thought and suggested we need to consider different criteria for when to start. He showed efficacy data for the chelators and in particular presented data from the DEEP study that was a study in children evaluating the efficacy of deferiprone in children and also a large comparison study that showed that deferiprone was not inferior to deferasirox in efficacy with respect to ferritin, liver and cardiac iron reduction. There were no unexpected adverse events and other than neutropenia being a little more common for deferiprone, even though there was neutropenia in the deferasirox group as well. Rash and renal dysfunction was more common for deferasirox. Overall, the incidence of adverse events were not significantly different.

4. Gene Therapy. Dr. George Kaltsounis



Dr. Kaltsounis presented information on the current status of gene therapy. Using viral vectors that contain a new beta globin gene and can infect a single cell and are then inactive, there have been two major trials, that were more effective in patients with beta plus thalassaemia major, though not IVS 110 mutations and for a small number of patients with beta zero thalassaemia. A subsequent study with new technology allowed better success with beta zero thalassaemia. The newer technology with a more natural process without using viruses called CRISPR-Cas 9 is now being developed for inducing Hb F production that provides the possibility of improving all severe haemoglobinopathies. There are concerns about the cost and the availability to patients.

5. **Hepatic Cancer, Liver transplant, medical follow up - Dr. Aileen Marshall**



Dr. Marshall presented data on the causes of hepatic cirrhosis and hepatic cancer. She described the approach to treatment of hepatic cancer and that this could involve chemoembolism, surgery and liver transplantation. She explained the criteria for eligibility for liver transplantation and exclusion criteria, in particular comorbidities. She discussed the waiting list and approximately how many days a patient usually had to wait for the transplant. She demonstrated how liver transplant is done surgically. Then she presented the intraoperative and post operative complications and how these are managed, in particular the use of immunosuppressive treatment.

6. **The experience of a patient with liver transplantation – George Konstantinou**



George, who is a patient with thalassaemia and who is now one of the older patients with thalassaemia alive, discussed his experience with liver transplantation that took place over 5 years ago. Initially George had hepatitis C infection that was treated with a number of unsuccessful regimes and he had liver cirrhosis. Over 5 years ago he developed liver cancer. He was evaluated in depth for eligibility and was subsequently put on the agonizing waiting list for a liver transplant. He waited for XXX days. He was not allowed to leave the UK

during the waiting period and also once he was called he had to be admitted immediately. The surgery itself was uneventful. He did have a hepatic artery thrombosis that was managed relatively successfully, but he then had numerous episodes of serious infections that required admission to hospital for many long term admissions. He has now been well for a long period of time and other than that needed to continue all his thalassaemia treatments and his immune suppressive therapy he remains very well and active.

7. Iron load in Thalassaemia: how low should it be?– Dr. Fernando Tricta



Dr. Tricta presented data on the toxicity of iron and how early it starts. Transferrin saturation should become an important test to determine the efficacy of iron chelation. He showed data from Egypt that showed that children starting deferiprone at a low dose as soon as their ferritin reached 400 took longer than patients taking placebo to show labile plasma iron, increase their transferrin saturation and to reach a ferritin of over 1000. He also showed that in the normal population high transferrin saturations were detrimental to general health and survival. He presented data from thalassaemia patients who had been on intensive chelation therapy for about 5-7 years and who reached normal ferritin levels and normal liver iron concentrations who also showed improvement in cardiac and endocrine function. He presented information on how deferiprone shuttles iron from cells onto deferoxamine, if it is present and then reenters cells and takes out more iron. Overall he stresses that we should be aiming for normal iron levels in patients and that chelators should be circulating 24 hours per day.

8. Luspatercept – Dr. Antonio Piga



Dr. Piga discussed the different research areas that may lead to improved erythropoiesis in patients with thalassaemia. Luspatercept and Sotatercept were developed as activin trap inhibitors. Their action allows the improvement in red cell maturation in the marrow of patients. Luspatercept was subjected to Phase I, II and III studies in thalassaemia major and Phase I and II in thalassaemia intermedia with ongoing studies in the latter. In thalassaemia intermedia, it has effected an increase in Hb between 1-2gm/dl. The patients feel clinically better. In thalassaemia major, in the majority of patients it has allowed a significant increase in the transfusion interval and also a reduction in ferritin and liver iron levels. The side effects are minimal and transitory. The medication has been approved by the FDA for its use in thalassaemia major and it is now being considered by the EMEA for European licencing. There are concerns about the cost.



President Costa Papageorgiou



Coordinator Prof. Vasili Berdoukas

