

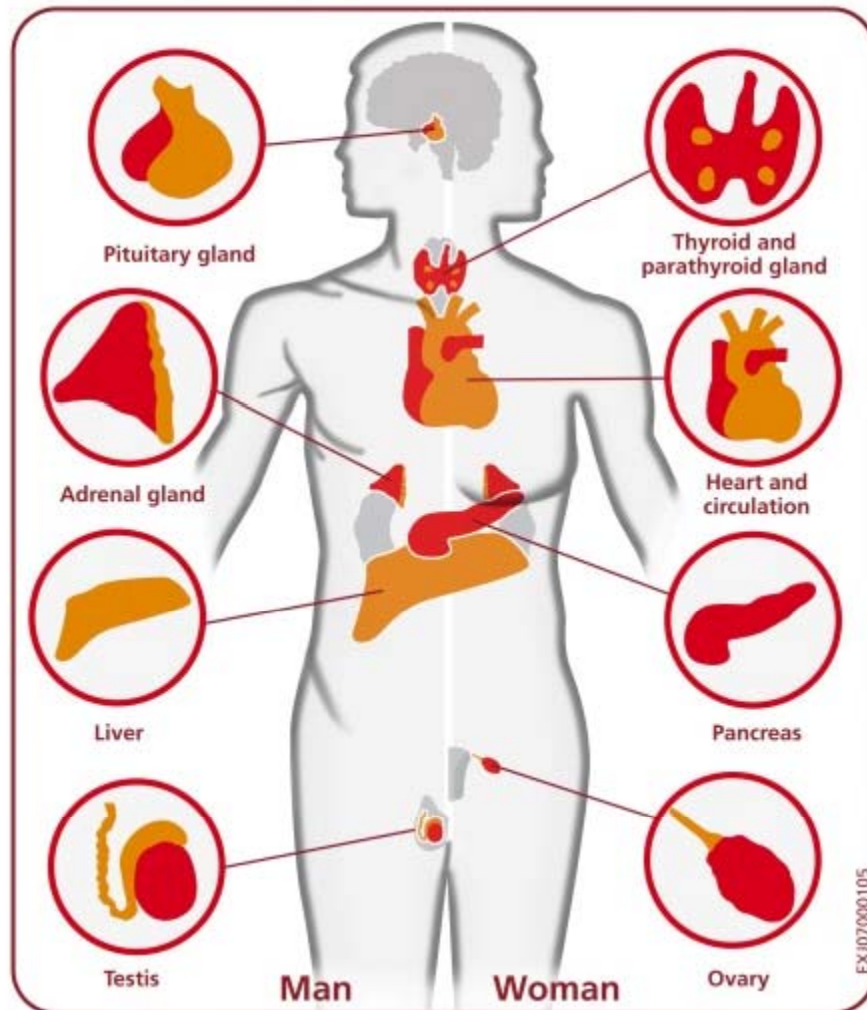
Efficacy of oral iron chelator deferasirox in transfusion dependent anemias

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Introduction

- Repeated blood administration in transfusion dependent anemias leads to excessive iron deposition in vital body organs.
- This leads to considerable morbidity and mortality in these patients.
 - Hypogonadism, diabetes mellitus, hypothyroidism, hypoparathyroidism
 - Cardiac dysfunction
 - Liver dysfunction
 - Joint dysfunction

Organs that may be affected by iron overload



Toxic iron builds up across the body and can cause serious damage to vital organs, including the heart and liver.

Introduction

- 50% of thalassemia major patient die before the age of 35 years due to iron overload associated cardiac failure*.
- Adequate iron chelation can prevent iron overload associated complications and can improve survival in these patients.

* Comparison of effects of oral deferiprone and subcutaneous desferrioxamine on myocardial iron concentrations and ventricular function in beta-thalassaemia. Lisaj, et al. The Lancet. Vol 360. 2002.

Desferrioxamine

■ Advantages:

- Long-term experience
- Effective in maintaining near-normal iron stores
- May be combined with deferiprone.

■ Disadvantages:

- Requires parenteral infusion
- Ear, Eye, Bone toxicity
- Poor Compliance

Deferiprone

■ Advantages:

- Orally active
- Enhanced removal of cardiac iron
- May be combined with desferrioxamine

■ Disadvantages:

- May not achieve negative iron balance in all patients at 75mg/kg per day.
- Risk of agranulocytosis & erosive arthritis.

Deferasirox

- Orally active
- Bioavailability and half life suitable for once daily dosing.
- Shown to be effective in various clinical trials.
- The most common side effects reported with deferasirox:
 - gastro-intestinal events
 - skin rash
 - mild dose-dependent increase in creatinine and alanine transaminase levels

Objective

- To evaluate the efficacy and safety of deferasirox in patients with transfusion dependent anemias

Patients & Methods

- Study design: Descriptive study.
- Study period: December 2008 – August 2009
- Study setting: Aga Khan University Hospital, Karachi.

Patients & Methods

■ Inclusion Criteria:

- Patients with transfusion dependent anaemias
 - Thalassaemia Major, Myelodysplastic Syndrome, Aplastic Anemia
- Serum Ferritin Levels > 1000ng/ml.

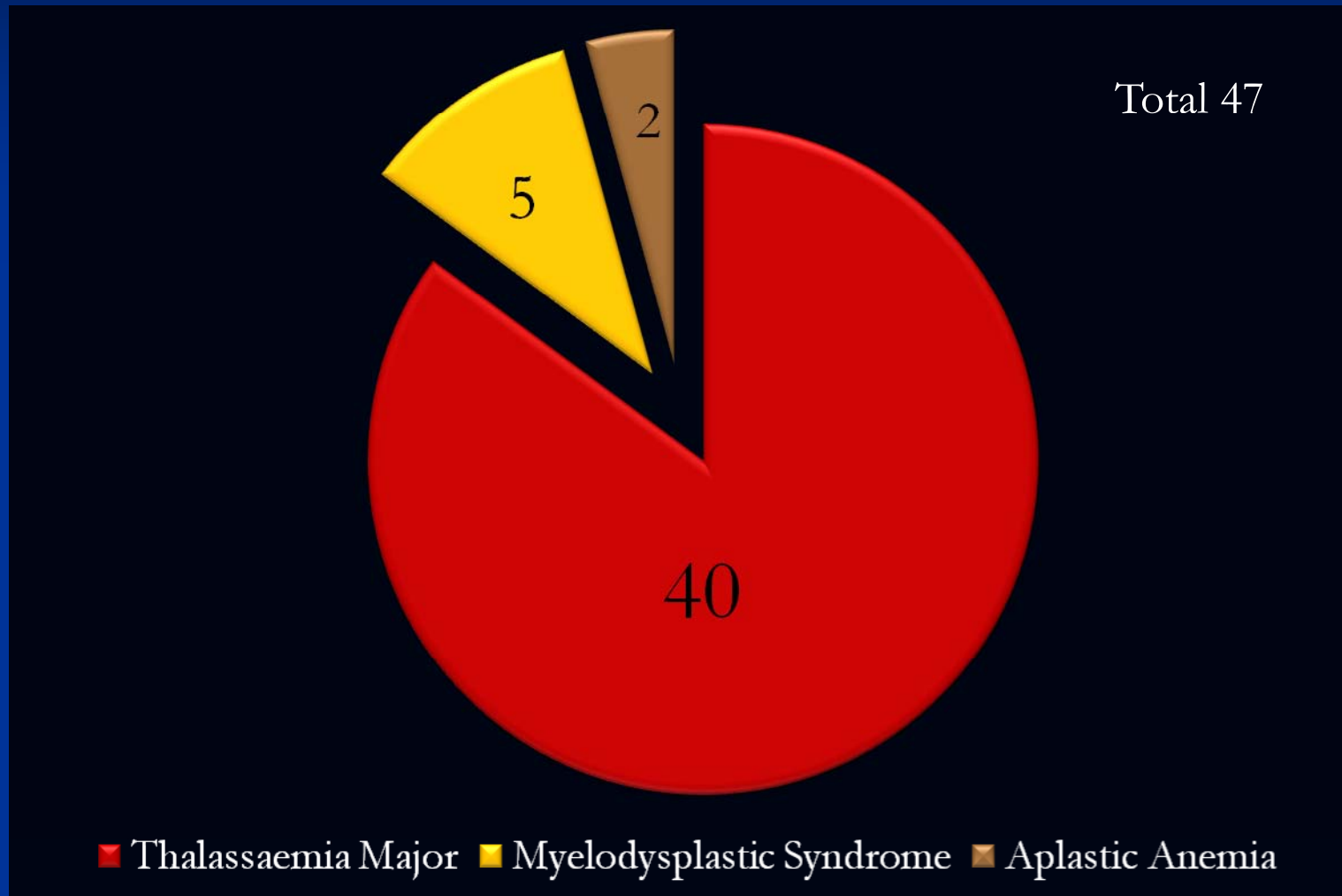
■ Exclusion Criteria:

- Patients < 2 years.
- Patients with baseline level of Alanine aminotransferase (ALT) >300 U/l (including patients with known hepatitis B/C)
- Patients with serum creatinine above >2.0 mg/dl

Patients & Methods

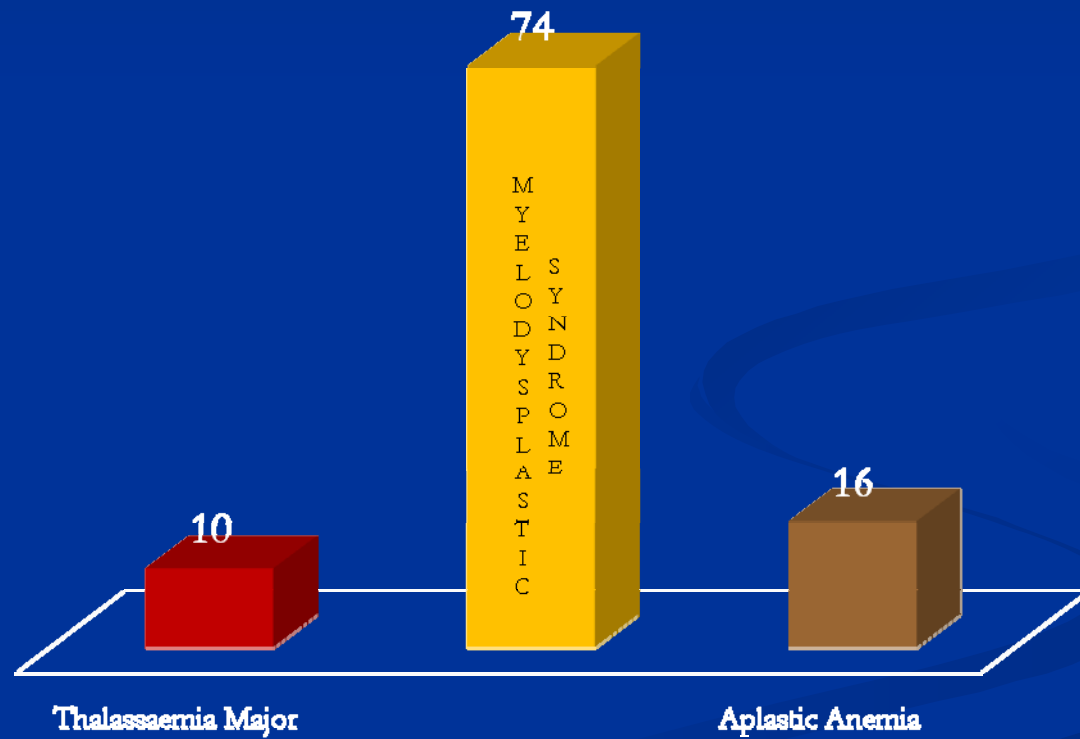
- Baseline serum ferritin, SGPT & creatinine levels.
- Deferasirox 20mg/kg/po/daily
- Serum ferritin, SGPT & Creatinine levels at 6 months.
- Efficacy was measured in terms of reduction in serum ferritin levels
- Safety was measured by measuring serum creatinine and SGPT levels as indicators of renal and hepatic toxicity respectively.

Results



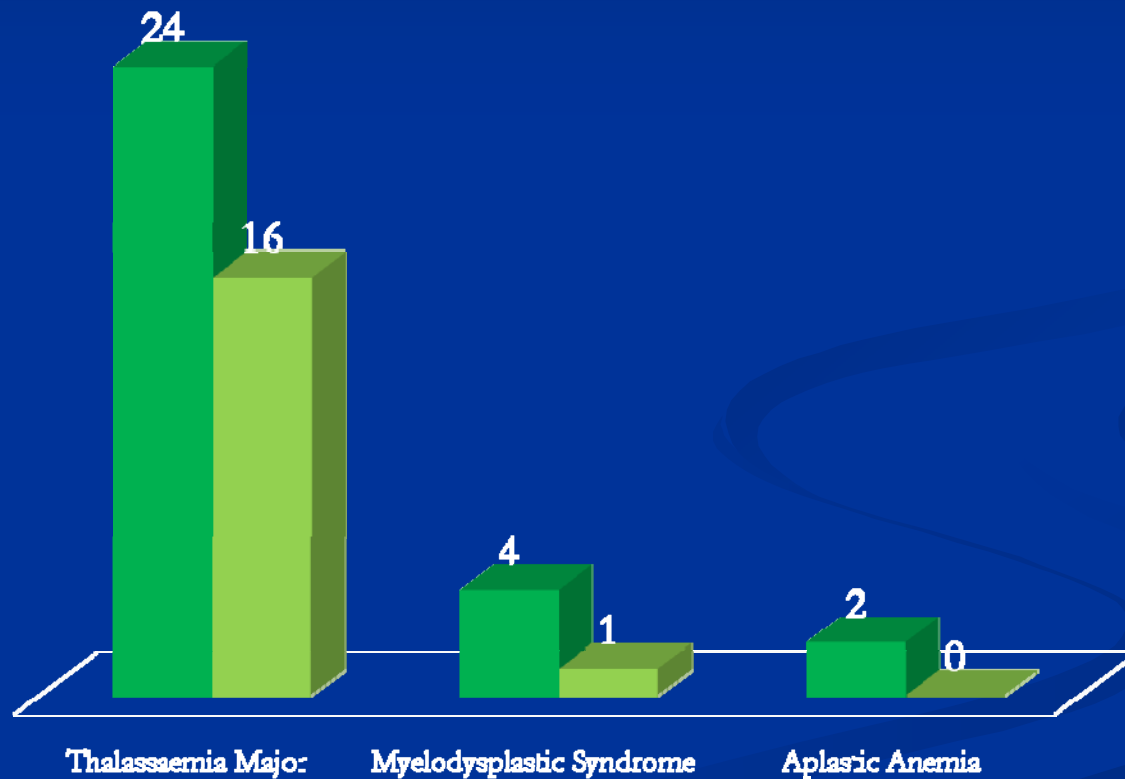
Mean Age

■ Thalassaemia Major ■ MDS ■ Aplastic Anemia

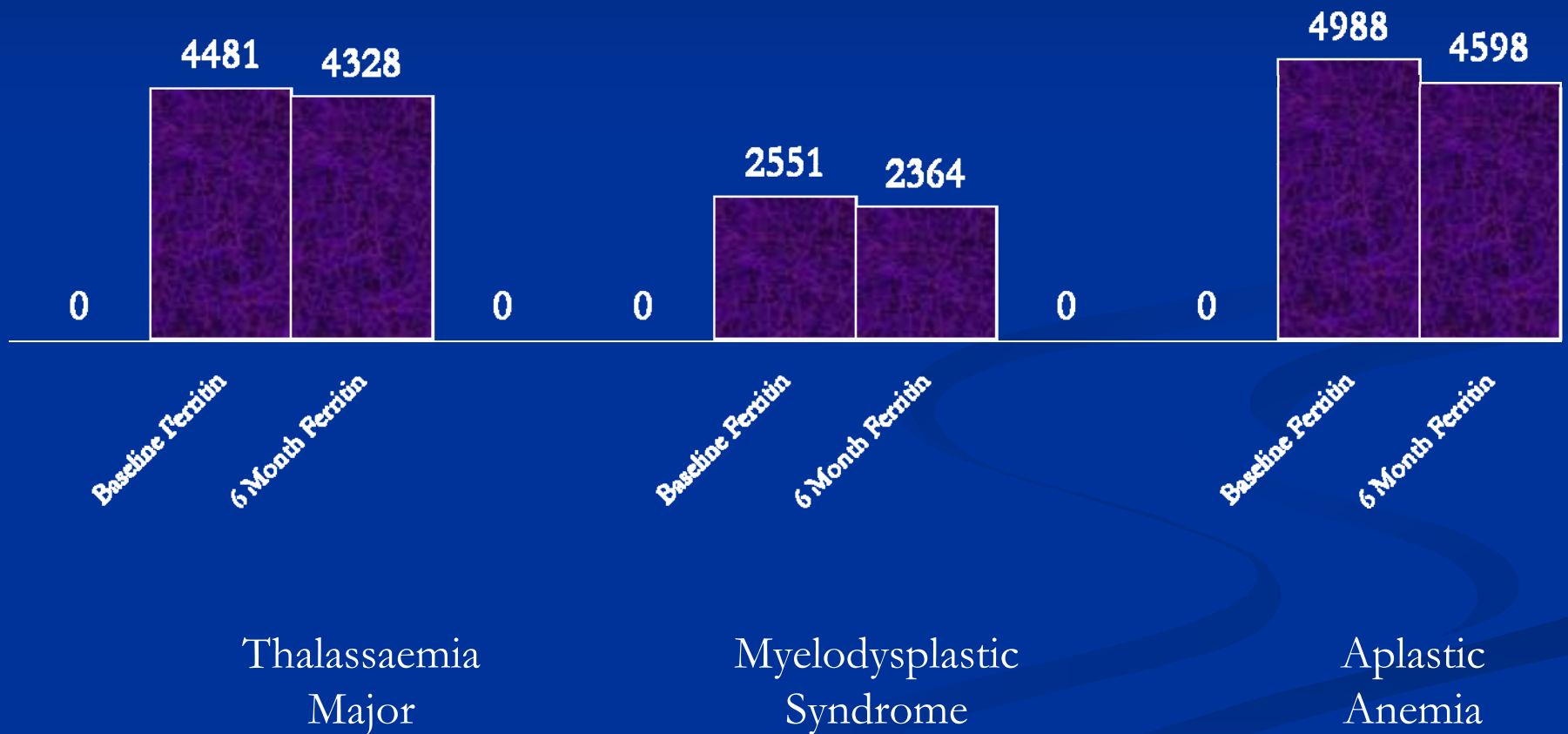


Gender Distribution

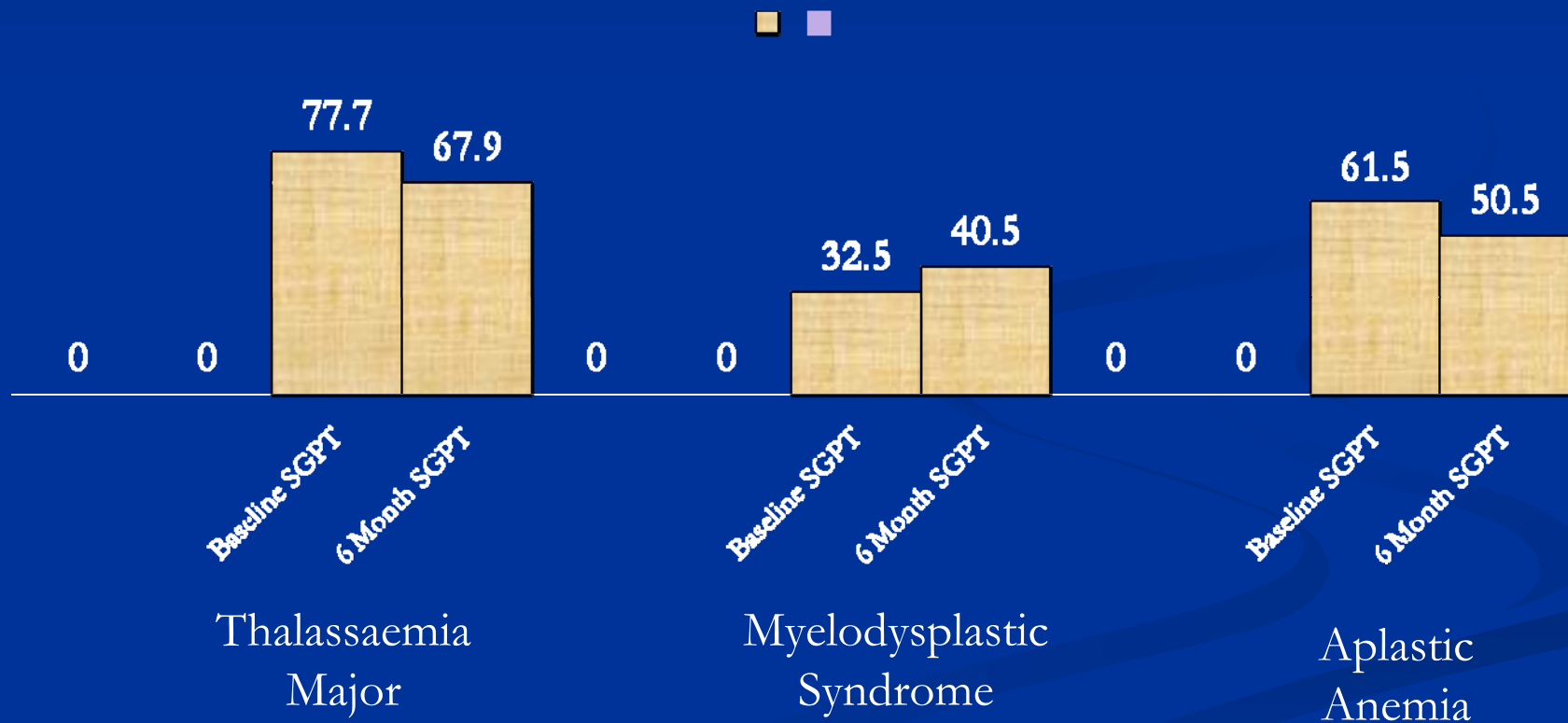
■ Males ■ Females



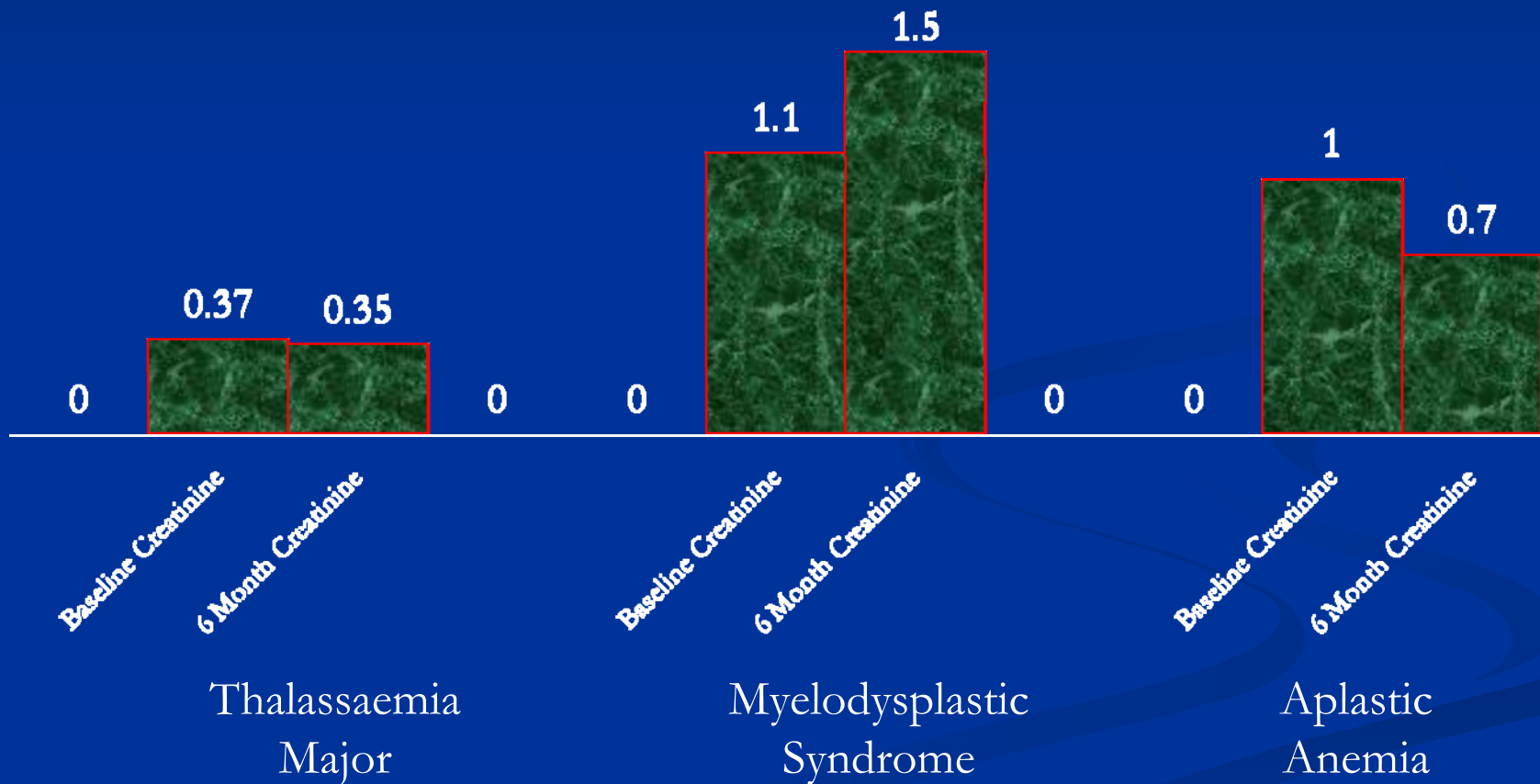
Mean Ferritin Levels



Mean SGPT Levels



Mean Creatinine Levels



Comparative Data

(Thalassaemia Major)

Study	Year	Sample Size	Change in Ferritin Mean (SD)
Capellini et al	2006	84	↑ 36(817)
Porter et al	2008	17	↓ 385(876)
Nisbet et al	2003	6	↓ 119 (1054)
Our Study	2009	40	↓ 153(1129)

Comparative Data

(Myelodysplastic Syndrome)

Study	Year	Sample Size	Change in Ferritin Mean (SD)
List AF et al	2006	93	↓896(1467)
Porter et al	2008	17	↓410(1632)
Our Study	2009	5	↓187(281)

Conclusion

- This is an ongoing study. (Interim results)
- No significant change in serum ferritin levels was observed after 6 months of therapy with deferasirox at 20mg/kg/daily.
- No significant elevation in serum creatinine and SGPT levels were noted as an indicator of renal and hepatic toxicity respectively at 20mg/kg/daily.

Recommendation

- Longterm prospective studies at increased dose are required to clarify the efficacy of this agent in our settings.

■ Thank You