Appendix B: Study protocol.

Hematologist identifies potential participant based on age, chelation therapy and offers informed consent/assent form.

Patient signs informed consent/assent form

Complete Eligibility Form

Patient is eligible

Complete Enrollment Form and Perform Randomization

Patient is not eligible

Primed group: Ambiodipine and Chelation Therapy

1. Schedule baseline visit for cardiac MRI
2. Schedule visit to CTU for drug dispensing
3. Schedule 6 and 12 month visits for cardiac MRI, echocardiography and blood test for serum ferritin

Control group: Chelation Therapy only

1. Schedule baseline visit for cardiac MRI, echocardiography and blood test for serum ferritin
2. Schedule 6 and 12 month visits for cardiac MRI, echocardiography and blood test for serum ferritin

Patient refuses to participate

Thank patient. Take no further action.

Thank patient. Explain that he/she is not eligible. Take no further action.

Baseline Serum Ferritin*

- **<2500 ng/dl**
  - 1. Deferasirox (Asunra) 20 mg/kg/day
  - 2. DFO 30 mg/kg/day s/c

- **>2500 ng/dl**
  - 1. Deferasirox (Asunra) 30 mg/kg/day
  - 2. DFO 35 mg/kg/day s/c

*Serum Ferritin:
- Do not do if there is any fever, acute infection of respiratory or GI tract, hepatitis or any other infections
- Follow-up ferritin levels should not be done earlier than 6 months


Age: 2 – 3 years

At 6 Months follow-up Serum Ferritin*

- **Increased by >500 ng/dl**
  - 1. Deferasirox (Asunra) 40 mg/kg/day
  - 2. DFO 45 mg/kg/day s/c

- **If rise is <500 ng/dl or maintained at baseline**
  - Repeat Serum Ferritin at 6 months

Ferritin, if less than baseline; Continue Treatment
Ferritin, if maintained or increased

‡ This is the maximum recommended dose for the given scenario, to achieve this dosage please refer to dosage chart

*Serum Ferritin:
- Do not do if there is any fever, acute infection of respiratory or GI tract, hepatitis or any other infections
- Follow-up ferritin levels should not be done earlier than 6 months

- Deferasirox (Asunra)
  - Always Start at 20 mg / kg / day and escalate according to dosage chart
- Desferal / DFO
  - Always Start at 30 mg / kg / day and escalate according to dosage chart
- Deferiprone
  - Always Start at 75 mg / kg / day and escalate according to dosage chart

<table>
<thead>
<tr>
<th>Escalation Chart</th>
<th>Deferasirox (Asunra) (in mg / kg / day)</th>
<th>Desferal / DFO (in mg / kg / day s/c)</th>
<th>Deferiprone (in mg / kg / day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start</td>
<td>20 (start)</td>
<td>30</td>
<td>75 (start)</td>
</tr>
<tr>
<td>Weeks</td>
<td>For 2 weeks</td>
<td>For 2 weeks</td>
<td>For 2 weeks</td>
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<td>25</td>
<td>35</td>
<td>100</td>
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<td>For 2 weeks</td>
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<td>30</td>
<td>40</td>
<td>Continue</td>
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<td>35</td>
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