POST-TRANSPLANT IRON DEPLETION

ANTONIO PIGA

CENTRE FOR HEMOGLOBINOPATHIES
S. LUIGI GONZAGA UNIVERSITY HOSPITAL AND SCHOOL OF MEDICINE
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DISCLOSURE

Research grants and speaker honoraria from Novartis, Apopharma, Ferrokin
("Stem Cell Transplantation"[Mesh] OR "Bone Marrow Transplantation"[Mesh] OR "Cord Blood Stem Cell Transplantation"[Mesh])
AND "humans"[MeSH Terms]
("Stem Cell Transplantation"[Mesh] OR "Bone Marrow Transplantation"[Mesh] OR "Cord Blood Stem Cell Transplantation"[Mesh])
AND "humans"[MeSH Terms]
Management of iron overload

Is iron overload clinically relevant?

- YES
- NO
Management of iron overload

Is iron overload clinically relevant?

Any chance to worsen?

Follow-up

Reassure the pt
Serum ferritin decreases slowly after HSCT in β-thalassaemia patients

How Should Be Determined Iron Body Status in Transplant Recipients?

- Transfusion history
- Serum ferritin > 1000 μg/L
- Transferrin saturation > 50%
- Liver Iron > 7 mg/g dry weight
- Cardiac MRI T2* <20 msec
- Any sign of iron-related dysfunction (liver, heart, hypophysis, thyroid, pancreas)
Management of iron overload

Is iron overload clinically relevant?

- YES
  - Is phlebotomy feasible?

- NO
  - Any chance to worsen?
    - YES
      - Follow-up
    - NO
      - Reassure the pt

Is phlebotomy feasible?

Any chance to worsen?

Follow-up

Reassure the pt
CONTRAINDICATIONS

• Bone marrow failure
• Anemia
• Hypotension
• Recent infection
• Unstable angina
Management of iron overload

Is iron overload clinically relevant?

- **YES**
  - Is phlebotomy feasible?
    - **YES**
      - 6 ml/kg every 2w
    - **NO**
      - Follow-up

- **NO**
  - Any chance to worsen?
    - **YES**
      - Follow-up
    - **NO**
      - Reassure the pt

Follow-up

Thalassemia Centre
University of Torino
THERAPEUTIC PHLEBOTOMY

MODALITIES

• Treatment
  Amount ➔ 200-500 ml; 5-7 ml/kg
  Interval ➔ 1-2 weeks
  Duration ➔ up to iron depletion
  ( plus EPO )

• Monitoring of iron overload
  Serum ferritin
  Liver Iron Concentration
  Transferrin saturation
<table>
<thead>
<tr>
<th>Reference</th>
<th>Design</th>
<th>Disease</th>
<th>Pt</th>
<th>SC T</th>
<th>Treatment</th>
<th>Whe n</th>
<th>Efficacy</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Busca A, 2010</td>
<td>Retrospective</td>
<td>Leukemia, MDS</td>
<td>19</td>
<td>Allo</td>
<td>Phlebotomy</td>
<td>Post</td>
<td>↓Ferritin, ↓LIC</td>
<td>OK</td>
</tr>
<tr>
<td>Majhail NS, 2010</td>
<td>Controlled</td>
<td>AML, NHL</td>
<td>5</td>
<td>Allo</td>
<td>Observation, Phlebotomy, DFX 20 mg/kg</td>
<td>Post</td>
<td>↓Ferritin, ↓LIC</td>
<td>OK, OK, Rash, ↑creat</td>
</tr>
<tr>
<td>Rose C, 2007</td>
<td>Prospective</td>
<td>Leukemia, MDS, NHL</td>
<td>29</td>
<td>Allo</td>
<td>Phlebotomy</td>
<td>Post</td>
<td>↓Ferritin, ↓LIC</td>
<td>OK</td>
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<td>Kamble , 2006</td>
<td>Controlled</td>
<td>AML, CML, MDS</td>
<td>6</td>
<td>Allo</td>
<td>Phlebotomy+ EPO</td>
<td>Post</td>
<td>↓Ferritin, ↓LIC, ↓hepatic GVHD</td>
<td>OK</td>
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<tr>
<td>Cho SJ, 2005</td>
<td>Case report</td>
<td>AML→MDS</td>
<td>1</td>
<td>Allo</td>
<td>Phlebotomy+ EPO</td>
<td>Post</td>
<td>↓Ferritin, ↓LIC</td>
<td>OK</td>
</tr>
<tr>
<td>Meo A, 2005</td>
<td>Case report</td>
<td>Sideroblastic anemia</td>
<td>1</td>
<td>Allo</td>
<td>Phlebotomy+ s.c. DFO-DFP</td>
<td>Post</td>
<td>↓Ferritin, ↓LIC, ↑Hb</td>
<td>OK</td>
</tr>
<tr>
<td>Shinjo K, 2001</td>
<td>Case report</td>
<td>MDS</td>
<td>1</td>
<td>Allo</td>
<td>Phlebotomy</td>
<td>Post</td>
<td>↓Ferritin, ↑glucose tolerance</td>
<td>OK</td>
</tr>
<tr>
<td>Li CK, 2000</td>
<td>Controlled</td>
<td>Thalassemia</td>
<td>21</td>
<td>Allo</td>
<td>i.v. or s.c. DFO 50 Phlebotomy</td>
<td>Early post</td>
<td>↓Ferritin, ↓ALT</td>
<td>OK</td>
</tr>
<tr>
<td>Angelucci E, 1997</td>
<td>Retrospective</td>
<td>Thalassemia</td>
<td>41</td>
<td>Allo</td>
<td>Phlebotomy</td>
<td>Post</td>
<td>↓Ferritin, ↓LIC</td>
<td>OK</td>
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<tr>
<td>Schettini F, 1994</td>
<td>Retrospective</td>
<td>Thalassemia</td>
<td>4</td>
<td>Allo</td>
<td>Phlebotomy</td>
<td>Post</td>
<td>↓Ferritin</td>
<td>OK</td>
</tr>
</tbody>
</table>

LIC= Liver Iron Concentration
DFO= deferoxamine
DFP= deferiprone
DFX= deferasirox
Time to serum ferritin normalization in 4 patients who completed a phlebotomy program: 350-500 mL every 1-2 weeks (+EPO if Hb<11g%)
The impact of phlebotomy on serum ferritin (A→B) and LIC (C→D) in 19 pts after HSCT

Busca A, Biol Bone Marrow Transplant, 2010
Phlebotomy for management of iron overload post-HSCT in β-thalassaemia: serum ferritin

Values are expressed as medians with a range (25–75 percentile)

Phlebotomy for management of iron overload post-HSCT in β-thalassemia: LIC

Values are expressed as medians with a range (25–75 percentile)

LIC = liver iron concentration.

Iron depletion reduces liver fibrosis

Before BMT: serum ferritin 4,044 μg/L; LIC 24.74 mg Fe/g dry wt; Ishak histological score 3

6 years after BMT: patient started on iron-reductive treatment with regular phlebotomies

10 years after BMT, after 54 phlebotomies: serum ferritin 128 μg/L; LIC 1.43 mg Fe/g dry wt)
Management of iron overload

Is iron overload clinically relevant?

- YES
  - Is phlebotomy feasible?
    - YES
      - 6 ml/kg every 2w
        - Follow-up
    - NO
      - Set iron chelation
        - Follow-up
        - Is intensive chelation needed?
          - YES
          - Follow-up
          - Reassure the pt
          - NO
          - Follow-up
          - Yes
          - NO

- NO
  - Any chance to worsen?
    - YES
      - Follow-up
    - NO
      - Reassure the pt
Successful Allogeneic Bone Marrow Transplantation for Diamond-Blackfan Anemia Complicated by Severe Cardiac Dysfunction due to Transfusion-Induced Hemochromatosis

Sumie Tabata¹, Minako Mori¹, Yuya Nagai¹, Hisako Hashimoto², Hiroshi Arima¹, Seiji Nagano¹, Yoko Takiuchi¹, Daichi Inoue¹, Takaharu Kimura¹, Sonoko Shimoji¹, Soshi Yanagita¹, Kiminari Ito², Akiko Matsushita¹, Kenichi Nagai² and Takayuki Takahashi¹

(DOI: 10.2169/internalmedicine.49.2991)
Management of iron overload

Is iron overload clinically relevant?

- YES
  - Is phlebotomy feasible?
    - YES
      - 6 ml/kg every 2w
      - Follow-up
    - NO
      - Set iron chelation
      - Follow-up
  - NO
    - Any chance to worsen?
      - YES
        - Follow-up
        - Is intensive chelation needed?
          - YES
            - Combination i.v. DFO + DFP
          - NO
            - Reassure the pt

- NO
  - Follow-up
  - Is intensive chelation needed?
    - YES
      - Combination i.v. DFO + DFP
    - NO
      - Reassure the pt

DFO=deferoxamine  DFP=deferiprone  DFX=deferasirox
Management of iron overload

Is iron overload clinically relevant?

YES

Is phlebotomy feasible?

6 ml/kg every 2w

Follow-up

Set iron chelation

Follow-up

Is intensive chelation needed?

YES

Combination i.v. DFO + DFP

NO

s.c. DFO

DFP

DFX

NO

Any chance to worsen?

YES

Follow-up

Reassure the pt

NO
defereroxamine (DFO) Desferal®
STANDARD TREATMENT

- Deferoxamine (Desferal®)
- 20-50 mg/kg/day
- 10% solution
- 8-12 hours s.c. slow infusion
- Portable pump
- 7 days a week

MANAGEMENT OF IRON CHELATION

Thalassemia Centre
University of Torino
deferiprone (DFP) Ferriprox®
Ferriprox®
100 mg/ml
Solution buvable
Orale oplossing
Lösung zum Einnehmen
Déféripone/Deferipron
500 ml, solution buvable
500 ml orale oplossing
500 ml Lösung zum Einnehmen

Ferriprox®
100 mg/ml
Deferiprone (DFP)

- 50-100 mg/kg/day orally
- Thrice a day
- At meals
Deferiprone: Metabolism

Deferiprone Glucuronidation by Human Tissues and Recombinant UDP Glucuronosyltransferase 1A6: An in Vitro Investigation of Genetic and Splice Variants

Benoit-Biancamano MO, Drug Metabolism and Disposition, 2009
Changes in Myocardial T2* during iron chelation

RCT of DFP vs DFO

Pennell DJ, Blood, 2006
Changes in LVEF during iron chelation
RCT of DFP vs DFO

Pennell DJ, Blood, 2006
## Comparison of Iron Chelators

<table>
<thead>
<tr>
<th>PROPERTY</th>
<th>DFO</th>
<th>DFP</th>
<th>DFX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chelator:iron binding</td>
<td>1:1</td>
<td>3:1</td>
<td>2:1</td>
</tr>
<tr>
<td>Mol. Weight Chelator</td>
<td>560</td>
<td>139</td>
<td>373</td>
</tr>
<tr>
<td>Mol. Weight Chelator:Iron Complex</td>
<td>619</td>
<td>470</td>
<td>798</td>
</tr>
<tr>
<td>Lipophylicity (PC) Chelator</td>
<td>0.02</td>
<td>0.18</td>
<td>6.3</td>
</tr>
<tr>
<td>Binding to plasma proteins</td>
<td>&lt;10%</td>
<td>&lt;10%</td>
<td>99%</td>
</tr>
<tr>
<td>Charge of Chelator</td>
<td>positive</td>
<td>neutral</td>
<td>negative</td>
</tr>
<tr>
<td>Charge of Chelator:Iron Complex</td>
<td>positive</td>
<td>neutral</td>
<td>negative</td>
</tr>
<tr>
<td>Elimination half-life</td>
<td>5-10 min</td>
<td>1.5-2-5 h</td>
<td>12 -18 h</td>
</tr>
</tbody>
</table>
# Side Effects From Iron Chelators

<table>
<thead>
<tr>
<th>Type</th>
<th>DFO</th>
<th>DFP</th>
<th>DFX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local side effects</td>
<td>YES</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Growth arrest</td>
<td>YES</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Bone changes</td>
<td>YES</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>YES?</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Arthropathy</td>
<td>Rare</td>
<td>YES</td>
<td>No</td>
</tr>
<tr>
<td>Yersinia infections</td>
<td>YES</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>G.I. symptoms</td>
<td>Rare</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Liver enzymes changes</td>
<td>No</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Renal changes</td>
<td>High doses</td>
<td>No</td>
<td>YES</td>
</tr>
<tr>
<td>Retinal toxicity</td>
<td>YES</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Lens opacity</td>
<td>Rare</td>
<td>No</td>
<td>Rare</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>YES</td>
<td>No</td>
<td>Rare</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Rare</td>
<td>YES</td>
<td>Rare</td>
</tr>
<tr>
<td>Agranulocytosis</td>
<td>No</td>
<td>YES</td>
<td>No</td>
</tr>
<tr>
<td>Weight gain</td>
<td>No</td>
<td>YES</td>
<td>No</td>
</tr>
<tr>
<td>Skin rashes</td>
<td>No</td>
<td>No</td>
<td>YES</td>
</tr>
</tbody>
</table>

*Piga A, Disorders of Iron Homeostasis, Erythrocytes, Erythropoiesis, 2006*
D.F., thal. major, 34 yrs old, splenectomized

ANC

28/03/2000 - 21/11/2000

G - CSF 10 mcg/Kg/9d

DEFERIPRONE

Thalassemia Centre
University of Torino
Deferasirox (DFX)

- 20-40 mg/kg/day orally
- Once a day
- Accurate dispersion
24 hours coverage with a single dose

Mean ± SEM deferasirox concentration (µmol/L)

Degree of constant chelation coverage

Multiple dosing with deferasirox 20 mg/kg/day

Piga A et al Haematologica 2006; 91:873-880
Hepatic glucuronidation by UGT1A1 (UGT1A3) is the main metabolic path for deferasirox in humans.
A new HPLC UV validated method for therapeutic monitoring of deferasirox in thalassaemic patients

Silvia De Francia\textsuperscript{a,}\textsuperscript{*}, Davide Massano\textsuperscript{b}, Francesca Maria Piccione\textsuperscript{a}, Elisa Pirro\textsuperscript{a}, Silvia Racca\textsuperscript{a}, Francesco Di Carlo\textsuperscript{a}, Antonio Piga\textsuperscript{b}

\textsuperscript{a} Clinical Pharmacology, Department of Clinical and Biological Sciences, University of Turin, S. Luigi Gonzaga Hospital, Regione Gonzole 10, 10043 Orbassano (TO), Italy
\textsuperscript{b} Microcythemia Center, Department of Clinical and Biological Sciences, University of Turin, S. Luigi Gonzaga Hospital, Regione Gonzole 10, 10043 Orbassano (TO), Italy
Non-progressive Change in Creatinine Clearance Over 2.6 Years of Deferasirox

Deferasirox 20 mg/kg/day (n = 84)
Deferasirox 30 mg/kg/day (n = 118)

Core Extension

Data on file by Novartis (Studies 107 and 107E)
Acquired Proximal Renal Tubular Dysfunction in β-Thalassemia Patients Treated With Deferasirox

Joanne Yacobovich, MD,* Pinhas Stark, MD,† Shlomit Barzilai-Birenbaum, MD,* Irit Krause, MD,‡ Idit Pazgal, MD,† Isaac Yaniv, MD,* and Hannah Tamary, MD*

TABLE 1. Summary of Patient Clinical Data

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (y)</th>
<th>Length of Therapy (mo)</th>
<th>6 mo Average Ferritin ± SD (ng/dL)</th>
<th>Deferasirox Dose (mg/kg/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.5</td>
<td>8</td>
<td>1360 ± 129</td>
<td>33</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>24</td>
<td>575 ± 153</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>36</td>
<td>480 ± 166</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>32</td>
<td>33</td>
<td>1335 ± 190</td>
<td>38</td>
</tr>
</tbody>
</table>

deferasirox. Although subclinical proximal tubulopathy was described in β-thalassemia homozygotes, overt Fanconi kidney is not an established disease complication. We describe 4 cases out of 50 children and adults with transfusion-dependent β-thalassemia, treated with deferasirox for iron overload, who developed clinically significant Fanconi syndrome. Three had concomitant infectious events; the fourth case was entirely spontaneous. In addition, all 4 patients were moderately to well chelated. Cessation of deferasirox resulted in prompt recovery. We propose the necessity for diligent monitoring for proximal tubule nephropathy, possibly related to infectious events, during treatment with deferasirox.
deferoxoxamine (DFO) Desferal® + deferiprone (DFP) Ferriprox®
MANAGEMENT OF IRON CHELATION

COMBINATION

DFO + DFP

CONCOMITANT OR SIMULTANEOUS

MONDAY

TUESDAY

WEDNESDAY

THURSDAY

FRIDAY

SATURDAY

SUNDAY

DFO

DFP

I.V. or S.C.

DFO

DFP

DFO

DFP

DFO

DFP

DFO

DFP

DFO

DFP

DFO

DFP

Thalassemia Centre
University of Torino
deferoxamine (DFO) Desferal® + deferasirox (DFX) Exjade®
deferiprone (DFP)
Ferriprox®

+ 

deferasirox (DFX)
Exjade®
Iron chelators

- Deferoxamine (DFO)
- Deferiprone (DFP)
- Deferasirox (DFX)

- Monotherapy
- Combination of DFO + DFP
- Potential use of any combination of any 2 or 3 chelators
DEVELOPMENT OF NEW IRON CHELATORS

FBS0701
C18H25MgNO8S
A phase 2 study of the safety, tolerability and pharmacodynamics of FBS0701, a novel oral iron chelator, in transfusional iron overload


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**Post-transplant iron depletion by iron chelation**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Design</th>
<th>Disease</th>
<th>Pt s</th>
<th>SC T</th>
<th>Treatment</th>
<th>When</th>
<th>Efficacy</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yesilipek MA, 2010</td>
<td>Prospective</td>
<td>Thalassemia</td>
<td>6</td>
<td>Allo</td>
<td>DFX 30 mg/kg</td>
<td>Post</td>
<td>Ferritin</td>
<td>creat</td>
</tr>
<tr>
<td>Unal S, 2010</td>
<td>Controlled</td>
<td>Thalassemia</td>
<td>2</td>
<td>Allo</td>
<td>DFX 20 mg/kg</td>
<td>Post</td>
<td>Partial</td>
<td>OK</td>
</tr>
<tr>
<td>Kaloyannidis P, 2010</td>
<td>Retrospective</td>
<td>Leukemia, MDS, NHL</td>
<td>36</td>
<td>Allo</td>
<td>s.c. DFO 50 mg/kg</td>
<td>Early post</td>
<td>Relapse, DFS</td>
<td>OK</td>
</tr>
<tr>
<td>Majhail NS, 2010</td>
<td>Controlled</td>
<td>AML, NHL</td>
<td>5</td>
<td>Allo</td>
<td>Observation Phlebotomy, DFX 20 mg/kg</td>
<td>Post</td>
<td>Ferritin, LIC</td>
<td>OK</td>
</tr>
<tr>
<td>Meo A, 2005</td>
<td>Case report</td>
<td>Sideroblastic anemia</td>
<td>1</td>
<td>Allo</td>
<td>Phlebotomy+ s.c. DFO-DFP</td>
<td>Post</td>
<td>Ferritin, LIC, Hb</td>
<td>OK</td>
</tr>
<tr>
<td>Li CK, 2000</td>
<td>Controlled</td>
<td>Thalassemia</td>
<td>21</td>
<td>Allo</td>
<td>i.v. or s.c. DFO 50 Phlebotomy</td>
<td>Early post</td>
<td>Ferritin, ALT</td>
<td>OK</td>
</tr>
</tbody>
</table>

LIC= Liver Iron Concentration  
DFO=deferoxamine  
DFP=deferiprone  
DFX=deferasirox
Post-transplant iron removal in 7 ex-thalassemic patients by iron chelation with deferasirox 30 mg/kg/d
Management of iron overload

Is iron overload clinically relevant?

- YES
  - Is phlebotomy feasible?
    - YES
      - 6 ml/kg every 2w
    - NO
      - Set iron chelation
        - Follow-up
  - NO
    - Any chance to worsen?
      - YES
        - Follow-up
      - NO
        - Reassure the pt

Is intensive chelation needed?

- YES
  - Combination i.v. DFO + DFP
- NO
  - s.c. DFO
  - DFP
  - DFX

DFO=deferoxamine  DFP=deferiprone  DFX=deferasirox
# Pre-transplant iron depletion

<table>
<thead>
<tr>
<th>Paper</th>
<th>Design</th>
<th>Disease</th>
<th>Pts</th>
<th>SCT</th>
<th>Treatment</th>
<th>When</th>
<th>Efficacy</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chueh HW, 2012</td>
<td>Open</td>
<td>Solid tumors</td>
<td>18</td>
<td>Auto</td>
<td>DFX 25 mg/kg</td>
<td>Pre</td>
<td>↓VODs</td>
<td>Renal AEs, Fanconi S.</td>
</tr>
<tr>
<td>Lee JW, 2009</td>
<td>Retrospective</td>
<td>ALL, AML</td>
<td>25</td>
<td>Allo</td>
<td>s.c. DFO 43 mg/kg</td>
<td>Pre</td>
<td>↓TRM, ↑DFS</td>
<td>-</td>
</tr>
<tr>
<td>De la Serna J, 1999</td>
<td>Case report</td>
<td>Leukemia</td>
<td>1</td>
<td>Allo</td>
<td>Phlebotomy</td>
<td>Pre</td>
<td>↓Ferritin, ↓ALT</td>
<td>OK</td>
</tr>
</tbody>
</table>
Iron chelation prior to HSCT improves survival

IC = patients with serum ferritin decreased to < 1,000 µg/L with ICT before HSCT;
ICT = iron chelation therapy;
SF > 1,000 = patients with serum ferritin ≥ 1,000 µg/L at the time of HSCT;
SF < 1,000 = patients with serum ferritin < 1,000 µg/L at the time of HSCT, without ICT.

NTBI during allogeneic HSCT

C = onset of conditioning regimen.

Early and late complications from iron overload in HSCT

Majhail NS, Bone Marrow Transplantation, 2008
The Deferasirox–AmBisome Therapy for Mucormycosis (DEFEAT Mucor) study: a randomized, double-blind, placebo-controlled trial

Spellberg B, Am. J. Hematology, 2012
Iron overload and iron chelation therapy in patients with myelodysplastic syndrome treated by allogeneic stem-cell transplantation: Report from the working conference on iron chelation of the Gruppo Italiano Trapianto di Midollo Osseo

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Many myelodysplastic syndrome (MDS) patients have a long history of transfusion before eventually undergoing transplantation and therefore are at high risk of developing parenchymal iron overload. Recently, retrospective studies suggested that iron overload has some prognostic impact in MDS patients treated by allogeneic stem-cell transplantation (allo-SCT) as previously observed in thalassemia. However, the optimal strategy to assess iron overload and to reduce iron burden during and after transplant procedure remains to be determined. The Gruppo Italiano Trapianto di Midollo Osseo (GITMO) promoted a consensus process aimed at providing clinical practice recommendations that can support the appropriate choice for iron overload assessment and for iron chelation therapy (SCT, and MDS patients management/treatment). The Panel met three times in Pavia at the Department of Hematology and Oncology, Fondazione IRCCS Polidinico S. Matteo, University of Pavia. A systematic review of the literature was performed including indexed original papers, indexed reviews, and educational, abstracts of conference proceedings (ASH, EHA, and EBMT). Indexed papers and reviews were searched in PubMed and limited to English language publications edited between 1990 and 2010. Full papers were ranked according to the Scottish Intercollegiate Guideline Network criteria [22]. During the first Panel meeting, the Expert Panel agreed on the goal of the project to provide clinical practice recommendations that can support the appropriate choice for iron overload assessment and for iron...
Recommended Screening and Preventive Practices for Long-Term Survivors after Hematopoietic Cell Transplantation

Navneet S. Majhail, J. Douglas Rizzo, Stephanie J. Lee, Mahmoud Aljurf, Yoshiko Atsuta, Carmem Bonfim, Linda J. Burns, Naeem Chaudhri, Stella Davies, Shinichiro Okamoto, Adriana Seber, Gerard Socie, Jeff Szer, Maria Teresa Van Lint, John R. Wingard, Andre Tichelli for the Center for International Blood and Marrow Transplant Research (CIBMTR), American Society for Blood and Marrow Transplantation (ASBMT), European Group for Blood and Marrow Transplantation (EBMT), Asia-Pacific Blood and Marrow Transplantation Group (APBMT), Bone Marrow Transplant Society of Australia and New Zealand (BMTSANZ), East Mediterranean Blood and Marrow Transplantation Group (EMBMT), and Sociedade Brasileira de Transplante de Medula Ossea (SBTMO)

Advances in hematopoietic cell transplantation (HCT) technology and supportive care techniques have led to improvements in long-term survival after HCT. Emerging indications for transplantation, introduction of
Survivors with mild iron overload may not require any therapy, as there are reports of iron load decreasing with time, but they should be counseled to avoid iron supplements and alcohol ingestion.

Patients with significant iron overload (eg, 7 mg/g dry weight liver iron) and liver dysfunction are candidates for phlebotomy or iron-chelation therapy.

Iron-chelation therapy before or early post-transplantation is being investigated in patients with pre-transplantation iron overload.

*mod. from Majhail NS, Biol Bone Marrow Transplant, 2012*