LONG TERM FOLLOW-UP OF PATIENTS WITH FANCONI ANEMIA AFTER ALLOGENEIC T-CELL DEPLETED HEMATOPOITEIC STEM CELL TRANSPLANTATION FROM ALTERNATIVE DONORS

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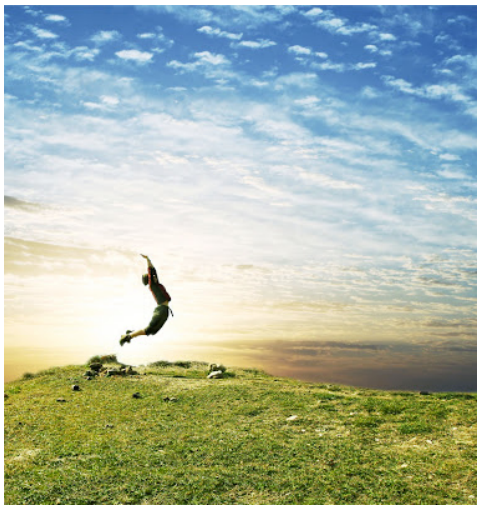
YAY!
Done with Transplant



…. But not quite yet …

Still need to cross a small river

Post-BMT Long Term Follow-Up

The etiology of late effects can be attributed to

1. the underlying diagnosis of FA,
2. the hematologic complication of FA (AA, MDS/ AML)
3. the treatment the individual patient has received prior to transplant and
4. the transplant cytoreduction (radiation – chemotherapy) and the allogeneic transplant itself.

The goal of long-term follow-up is three fold:

1. to identify problems already present in patients and treat them accordingly and efficiently so they do not lead to greater complications (e.g.: hemochromatosis)
2. to screen patients for late effects before they develop, such that, in case they do develop, they are diagnosed early and treated accordingly (e.g.: primary or secondary cancers)
3. to prevent harmful late effects that may give rise to more late complications (e.g.: avoiding sun exposure)

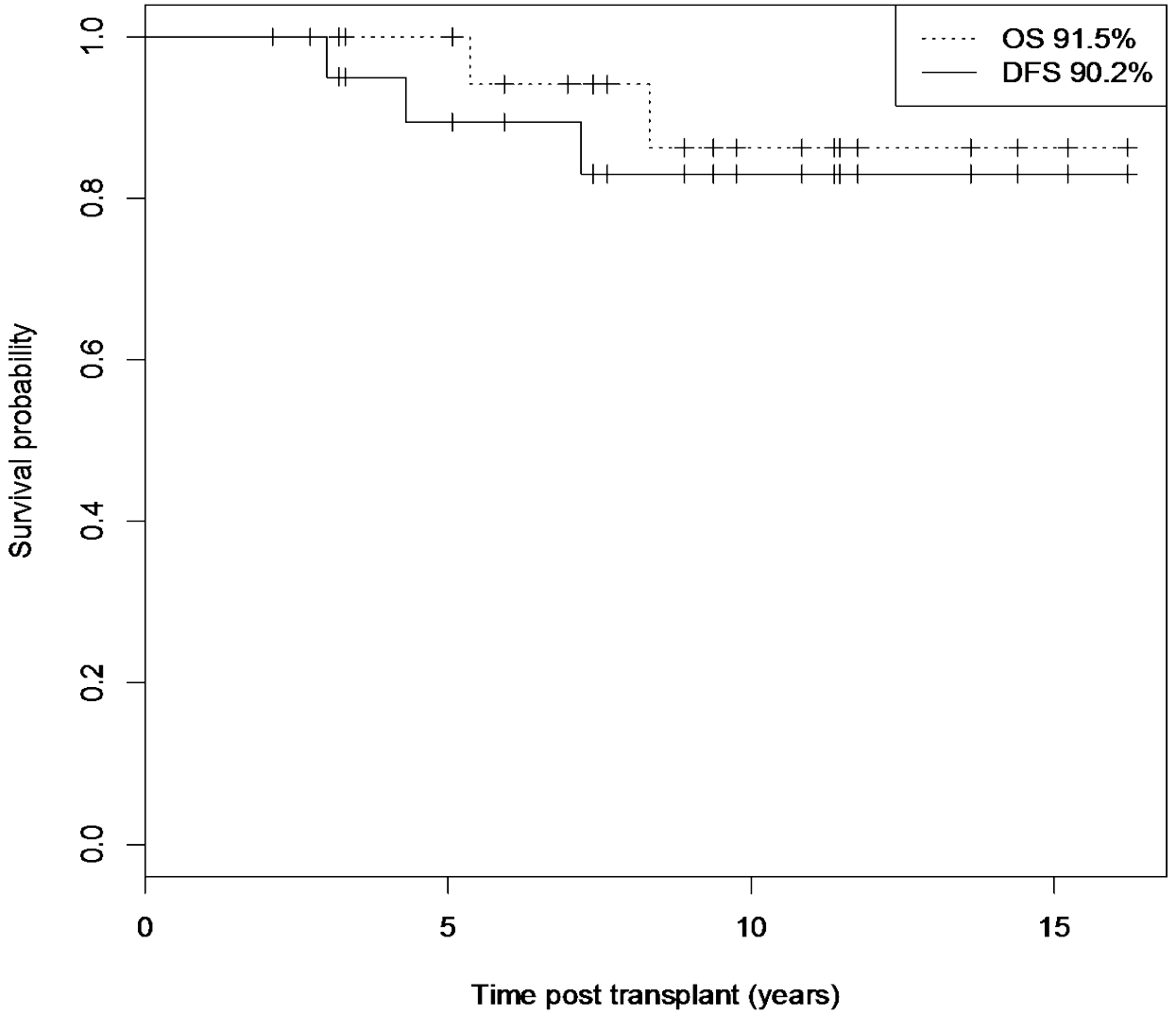
FANCONI ANEMIA – LFTU post SCT

- We reviewed the medical records of patients with FA who underwent an allogeneic HSCT from alternative donors for the treatment of AA, MDS or AML, at MSKCC, and survived at least one year post transplant.

N	**22**
Years BMT	March 1999 – December 2012
Gender	Male 14 – Female 8
Age at BMT	11.9 years (range 4.4 – 34 years) SCT at age < 10: (N=6)
Median Follow-Up	8.3 years (range 2.1 – 16.0)
Diagnosis at BMT	SAA (N=11) – MDS (N=6) – AML (N=5)
SCT Regimen	TBI FLU CY (N=18) - BU FLU CY (N=4)
Donors	Matched or Mismatched Unrelated N=14) Mismatched Related (N=8)

Good news:

For patients who pass the 1 year post BMT mark
The chances of doing well are very good



FANCONI ANEMIA – LFTU post SCT

Chronic GVHD

Other Good News:

None of the 22 patients
had any evidence of
chronic GvHD

(14 unrelated donors - 13 HLA-mismatched donors)

FANCONI ANEMIA – LFTU post SCT
Secondary Neoplasms

- **MDS – AML (N=1)**
  - One patient s/p HSCT for MDS in RA had a relapse of primary MDS three years post HSCT

- **Squamous Cell CA (N=2)**
  - One patient s/p HSCT for AML – in CR of AML developed SCC of the vulvo-vaginal area 3.7 years post HSCT at age 27 – Died of disease
  - One patient s/p HSCT also for AML – in CR of AML developed SCC of the tongue 7.2 years post HSCT at age 28 – Died of disease

FANCONI ANEMIA – LFTU post SCT
Hematologic and Immunologic function

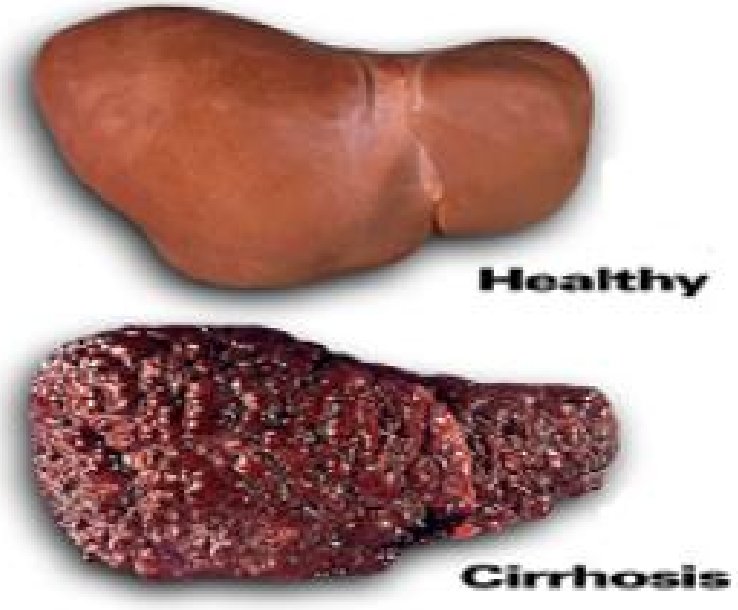
- Normal Counts – All patients

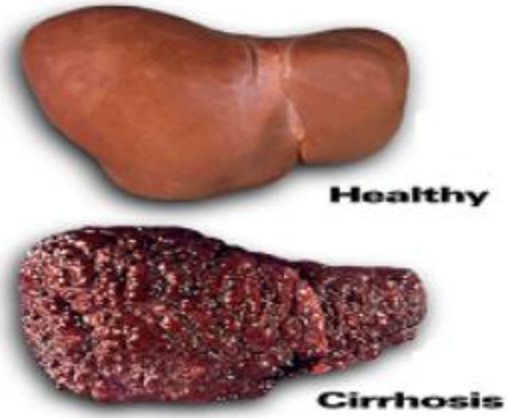
- Normal Immune Function
  All but 1 patient – IgG deficient
  Low B cells – Post rituximab
  on monthly IGIG

FANCONI ANEMIA – LFTU post SCT

Hemochromatosis

- Patients who receive a lot of transfusions may have iron accumulation in different organs (liver, heart, pancreas)
- Iron is an irritant - causes scarring of the liver
  The sooner you get rid of it, the less chances of scarring





Fe →

To get iron out of the liver:

1. The easiest is to remove RBCs which contain Fe
   is (1) to remove RBCs (**phlebotomy** – removal of blood)
   then have the body make new RBCs by using more Fe
2. The other way is to use a medication called
   Iron Chelator – **deferasirox** – used by mouth
   Deferasirox binds to Fe and gets it out of the body
   But it may have some side-effects (liver – kidneys)
   and is therefore plan B

FANCONI ANEMIA – LFTU post SCT

Hemochromatosis

- **Ferritin**
  - 9 patients who had < 20 transfusions pre-SCT had low ferritin post-SCT – All 9 pts are doing well
  - 12 pts had high ferritin post-SCT
    - 6 pts had < 20 transfusions and low ferritin pre-SCT
    - 7 pts had > 20 transfusions and high ferritin pre-SCT
  - 1 pt had > 20 transfusions and low ferritin post SCT

- **T2*MRI**
  - Performed in 4 patients – good correlation with ferritin

- **Treatment**
  - Phlebotomy – whenever possible – Poor compliance
  - Deferasirox (Exjade) (N=1) secondary transaminitis – D/C

FANCONI ANEMIA – LFTU post SCT

Endocrinopathies – Metabolic disorders

- **Hypothyroidism**
  - Of 22 pts
    - 5 pts had hypothyroidism pre-SCT and post SCT
    - 5 pts had hypothyroidism post SCT (4 TBI – 1 Bu)
    - 12 pts had normal thyroidism
- **Hyperglycemia**
  - Insulin resistance: N = 10 - All post TBI
  - IDDM: N =4 (19%) – One pt pre SCT – All post TBI
- **Hypertriglyceridemia**
  - N=5 - All post TBI
  - Often associated with insulin resistance

FANCONI ANEMIA – LFTU post SCT

Gonadal Dysfunction

- **Males N=14 – 12 pts evaluable post pubertal**
  - Affected N=8 – 7 post TBI and 1 post BU
  - Leydig cell dysfunction – On testosterone N=1

- **Females N=8 – 5 pts evaluable post pubertal**
  - Affected N = 4 - All post TBI
  - On hormonal replacement: all 4 patients
  - ONE successful pregnancy

Patient ID	Cytoreduction	Age at BMT(yrs)	Disease	Ferritin	Hypothyroid	Insulin Resistance	Triglycerides	Gonadal Dysfunction
1	TBI/Flu/Cy	5.7	AA	Y	N	N	N	N
2		7.0	AA	Y	N	N	N	N
3		8.5	AA	Y	N	N	N	N
4		10.0	AA	N	N	Y	Y	Y
5		10.0	AA	Y	N	N	N	N
6		10.7	MDS	Y	Y	Y	Y	Y
7		11.5	MDS	N	Y	IDDM	N	Y
8		11.5	AA	N	N	N	N	Y
9		12.3	AML	Y	Y	Y	N	Y
10		12.8	MDS	Y	Y	Y	N	N
11		14.0	AA	Y	N	N	N	N
12		15.2	AA	Y	N	IDDM	Y	Y
13		16.5	MDS	N	Y	Y	Y	Y
14		19.5	MDS	N	N	N	N	Y
15		21.5	AML	Y	Y	Y	Y	Y
16		24.0	AML	N	N	N	N	NE
17		24.0	AML	Y	Y	N	N	Y
18		35.0	AML	N	N	Y	Y	NE
19	Bu/Cy/Flu	4.5	MDS	N	Y	N	N	NE
20		7.4	AA	N	Y	N	N	NE
21		7.8	AA	Y	Y	N	N	NE
22		31.5	AA	N	N	N	N	N

FANCONI ANEMIA – LFTU post SCT
SUMMARY (1)

- Patients with Fanconi anemia can be cured of their hematologic disorders with allogeneic HSCT
- However, they remain at risk for long term complications from (1) their primary disease and (2) its treatment.
- There is a tendency for poor compliance of post transplant care of late complications, and we need to be more vigilant in following FA patients post HSCT

FANCONI ANEMIA – LFTU post SCT

SUMMARY (2)

- Multi-disciplinary follow-up clinics are important to follow: (1) Iron overload, (2) endocrinopathies and metabolic disorders, (3) ENT and (4) Gynecologic function. For screening, prevention and treatment of potential complications

- It will be very important to follow patients transplanted at a younger age, after HPV vaccine, without TBI and without chronic GvHD for (1) overall late complications and (2) particularly secondary neoplasms.

- It would be VERY important to have a **multi-center protocol** for the management of FA patients with squamous cell carcinoma post transplant with surgery, radiation, chemotherapy and targeted therapy.

THANKS

- Our long term follow-up teams with Dr Charles Sklar for pediatric patients and Dr Kevin Oeffinger for adult patients

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