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MD Anderson Cancer Center
Making Cancer History®

Allogeneic Stem Cell Transplantation for Cutaneous T-cell Lymphoma: Updated results from a single center

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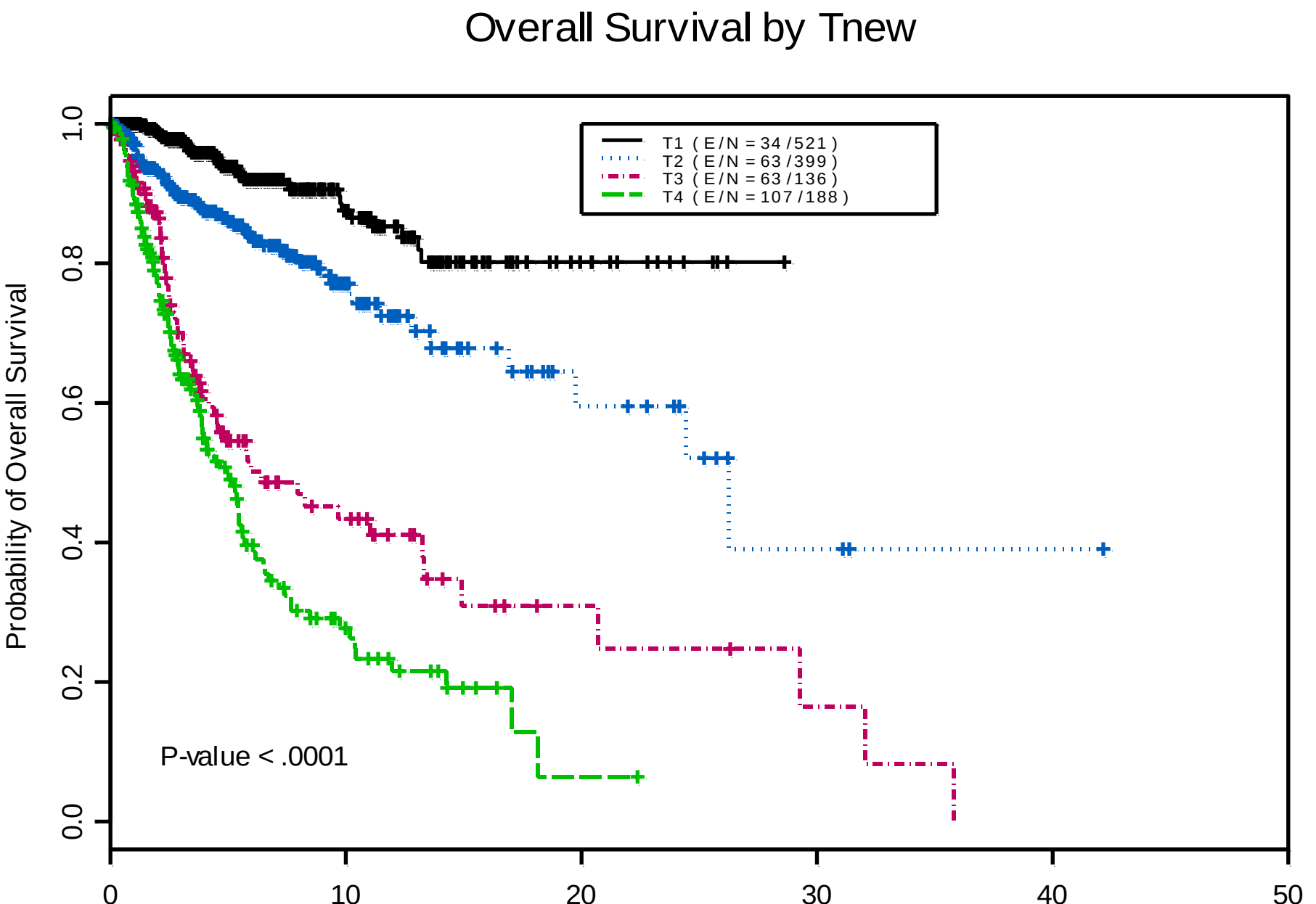
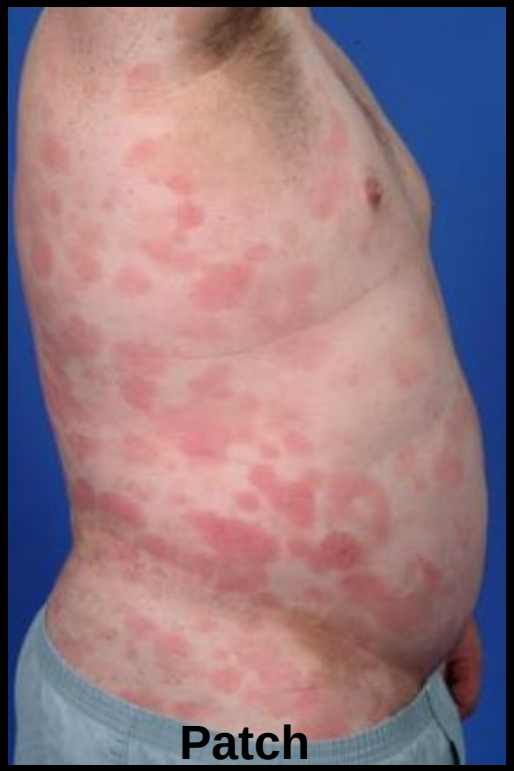
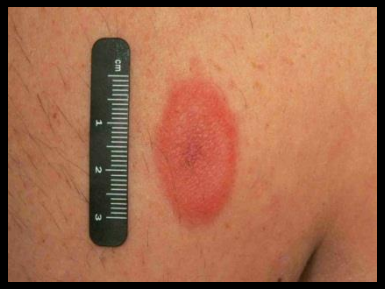
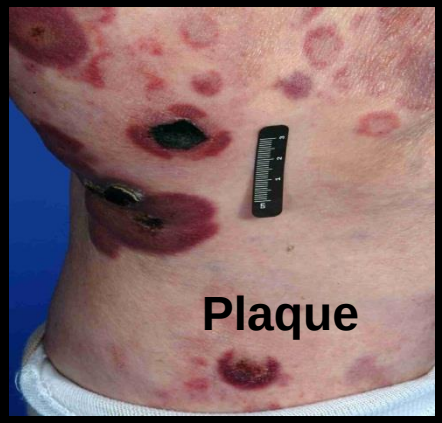
Duvic & Talpur et al. *Clin Cancer Res.* 2012;18:5051-5060 – 1423 patients

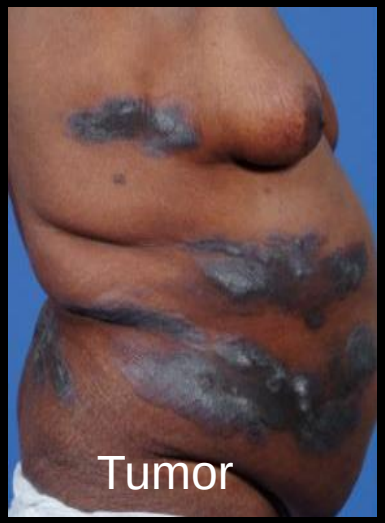


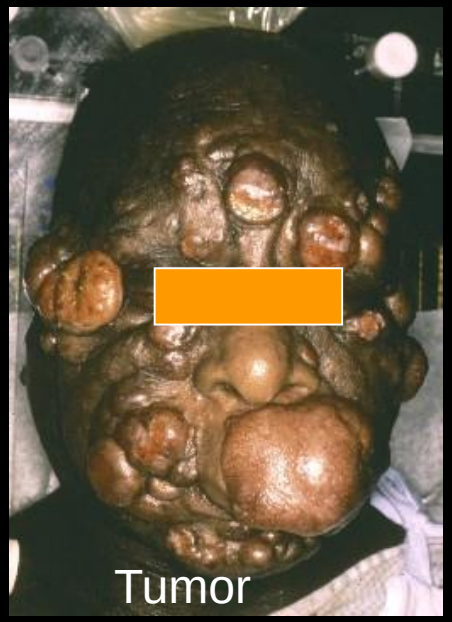
Mycosis fungoides & Sezary Syndrome

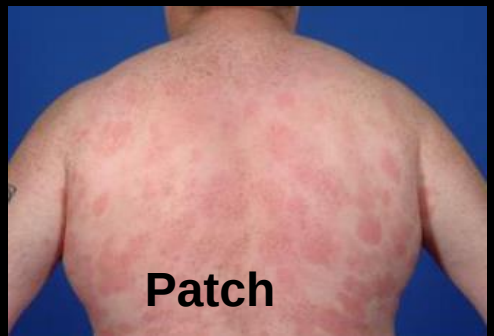


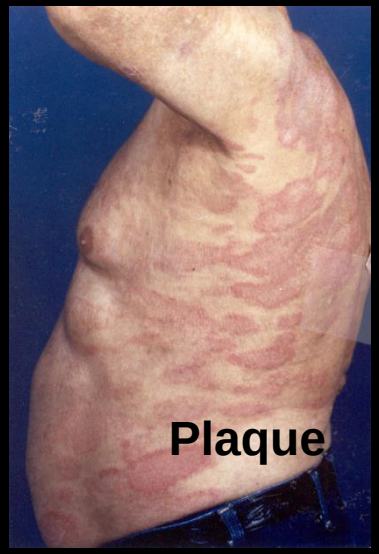


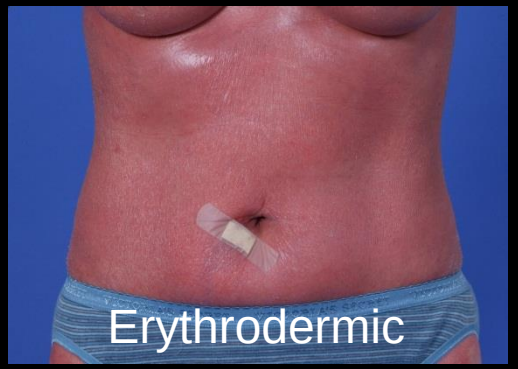













Cancer®

Methods

- Prospective analysis of 48 MF/SS patients
- Allogeneic HSCT at MDACC 7/2001 - 9/2013 TNMB staging, biopsy MF/SS $\geq$ IIB
- Good health, Age < 65, $\leq$ 2 yr OS
- Failed skin directed or systemic therapy
- Visceral disease treated, no opened skin sores
- HLA 10/10 or 9/10 matched donor
- 42 had 36 Gy TBSEB prior to HSCT
- 89% fludara/melphalan reduced intensity
- GVHD tacrolimus/methotrexate, steroids, ECP

Duvic et al. JCO 28 (14) MAY 10 2010

Statistical Methods

- Kaplan-Meier analysis to estimate distribution of following from transplant
  - Median overall survival (OS)
  - Progression-free survival (PFS)
- Cox proportional hazards regression analysis- survival to demographics
- Method of Fine and Gray to fit regression models to same covariants.

Demographics of 48 patients

Age (y), median (range)	**51.5 years (19-72 years)**	
Sex	Male	22 (46%)
	Female	26 (54%)
Ethnicity	Caucasians	33 (69%)
	African American	11 (23%)
	Hispanics	4 (8%)
Clinical and Pathologic Diagnosis	Sezary Syndrome	17
	MF with LCT	24
	SS + LCT	7
	Stage IVA LN+ or IIB	4 nodal; 1 tumor
	Folliculotropic MF	4

TNMB Stage at Diagnosis

Stage	**N = 48**
IB - IIA Refractory IB	2
IIB Tumors (includes Tumors w LCT)	12
IIIA Erythrodermic MF (< B2)	1
IVA – SS blood (B2) and/or LN	18
IVB – also BM+, liver (n=2)	15

TNMB Maximum Stage Pre-Transplant

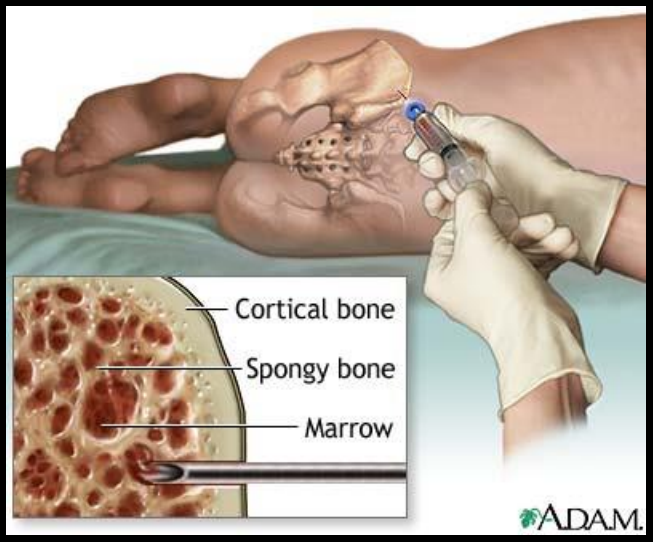
Stage	**N = 48**
IB - IIA Refractory IB	4
IIB Tumors & LCT Tumors	8
IIIA Erythrodermic MF (< B2)	3
IVA – includes SS blood (B2) and/or nodes	11
IVB – BM+ or liver (n=2)	21

Prior Therapies

Parameter	**Patients (N=48)**
Median Therapies	6 (range 2-11)
Bexarotene	31 (65%)
Interferon	24 (50%)
ECP	20 (42%)
Chemotherapy	32 (67%)
TBSEB	43 (90%)

Collection stem cells for transplant

- Bone Marrow Aspiration
- Apheresis
- Cord Blood Collection



Disease and HSCT

Time from Diagnosis to SCT	27 months (11-672 months)	
Stem cell source	HPC-A	35 (74)
	HPC-BM	12 (26)
Disease status prior to SCT	CR/CRU	7 (15)
	PR	28 (60)
	SD/PD	12 (26)
Donor type	Matched sibling	21 (45)
	Matched Unrelated	24 (51)
	1 antigen mismatch related	2 (4)
Median Cells infused x 10^6	CD34+ x 10^6	5.3 (0.99-33.5)
GVHD prophylaxis	Tacro/MTX	48 (100)

Conditioning Regimens

Regimen	Patients
Total Body Skin Electron Beam 36 Gy CR	42 (89%) 25 (59%)
Fludarabine/melphalan +/- thymoglobulin	42 (89%)
Fludarabine/busulfan	3 (6%)
Fludarabine/cyclosporin/ Rituximab	2 (4%)

TBSEB prior to SCT in 42/48 pts

- Among 42 patients who received TBSEB prior to SCT, 58% achieved a CR

- 5 patients without TBSEB - 3/5 (60%) CR

- Pt # 3- Limited facial erythema
- Pt#10- scalp tumors- Local XRT
- Pts # 15 & 26 had CR with campath
- PT# 30- CR with EPOCH

Overall Complete Response 58% (28 of 48)
Relapse rate 33% (16 of 48)
Mortality rate 44% (21/48)

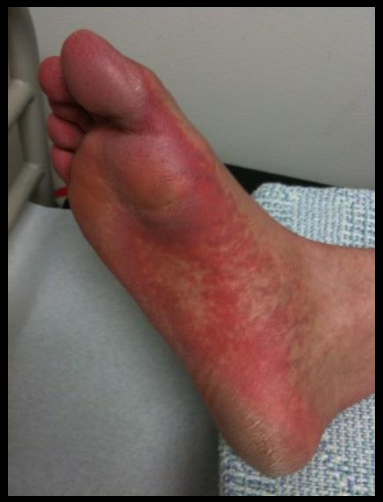
Clinical Variant	**N**	**Responders 58% (28/48)**		**Relapsed 33% (16/48)**		**Non-engraftment 8% (4/48)**		**Dead/Alive 44% (21/48)**
SS	**14**	**11**	**79%**	3	21%			3/11
LCT	16	9	56%	4	25%	3	19%	6/10
SS + LCT	9	4	44%	5	56%			4/9
IVA (LN+) IIB	4 1	2	40%	2	40%	1	20%	1/4
Fol -MF	4	2	50%	2	50%			2/2

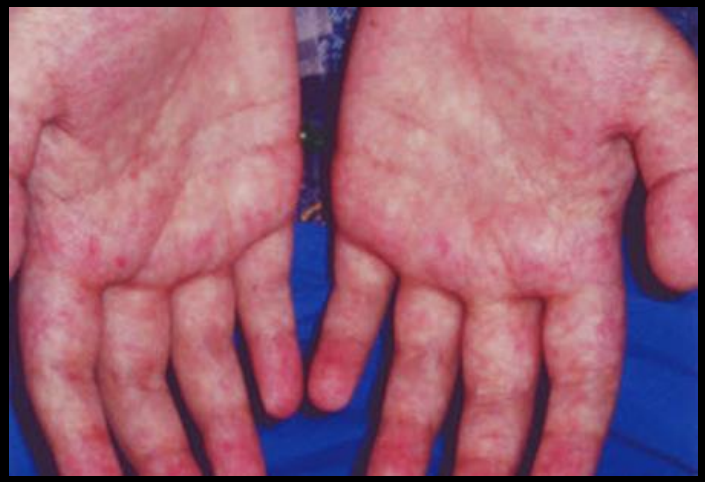
Results

- 3 patients died before engraftment
- 44 pts - neutrophils and platelets recovered in median of 12 days (9-23) and (0-88)
- Complete chimerism in 36 (76.5%) and
- 6 with mixed
- 8 of 22 w relapse/progression had CR after DLI or second SCT(2)
- Median Pruritus: 44 pts - baseline 8, post radiation 3, and 0 one year post TP

Acute and/or Chronic GVHD 29/48 (60%)

Location	Acute GVHD (n=17)	Chronic GVHD (n=15)
Grade 1-2	8	3
Grade 3-4	9	12

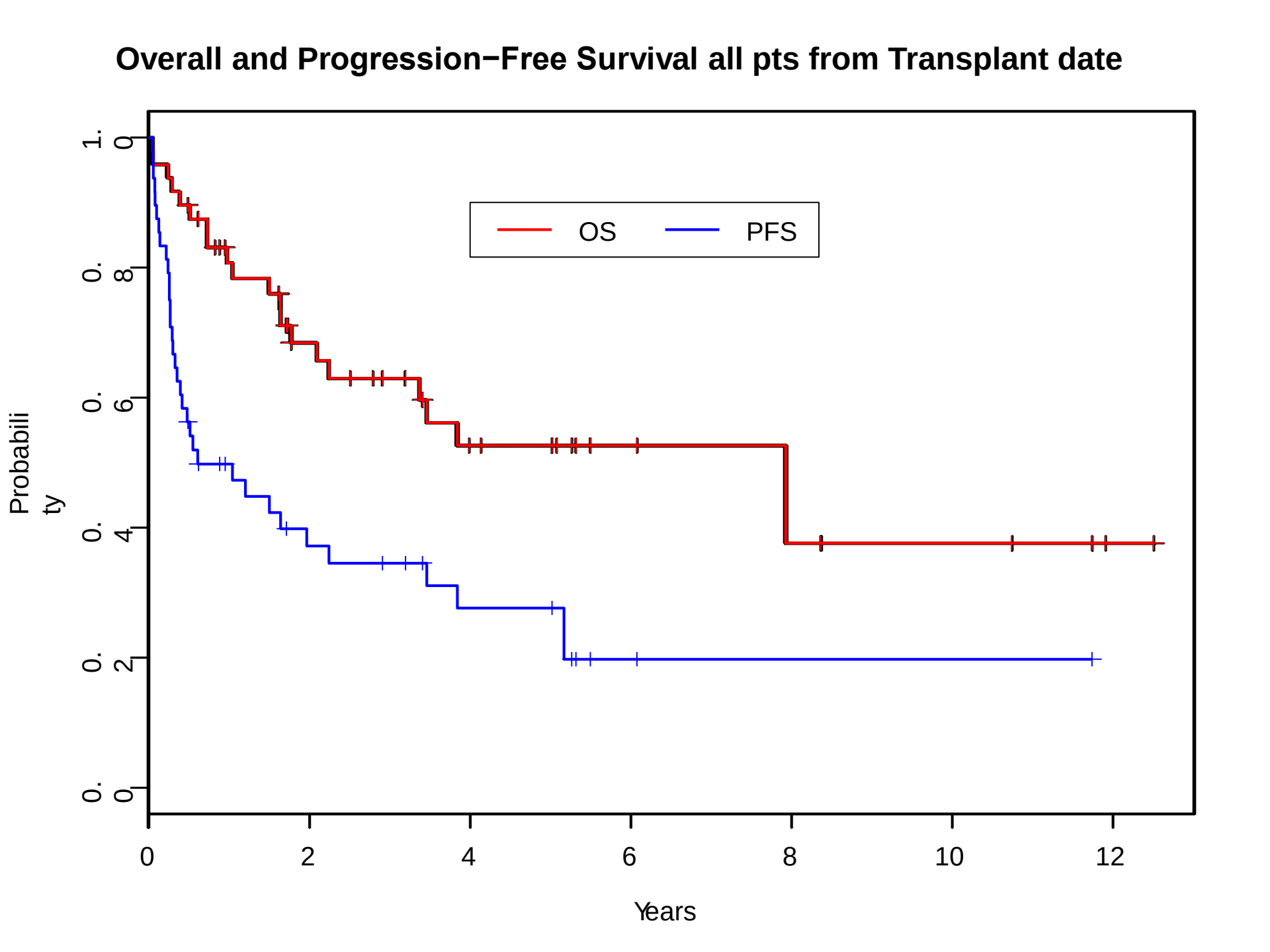




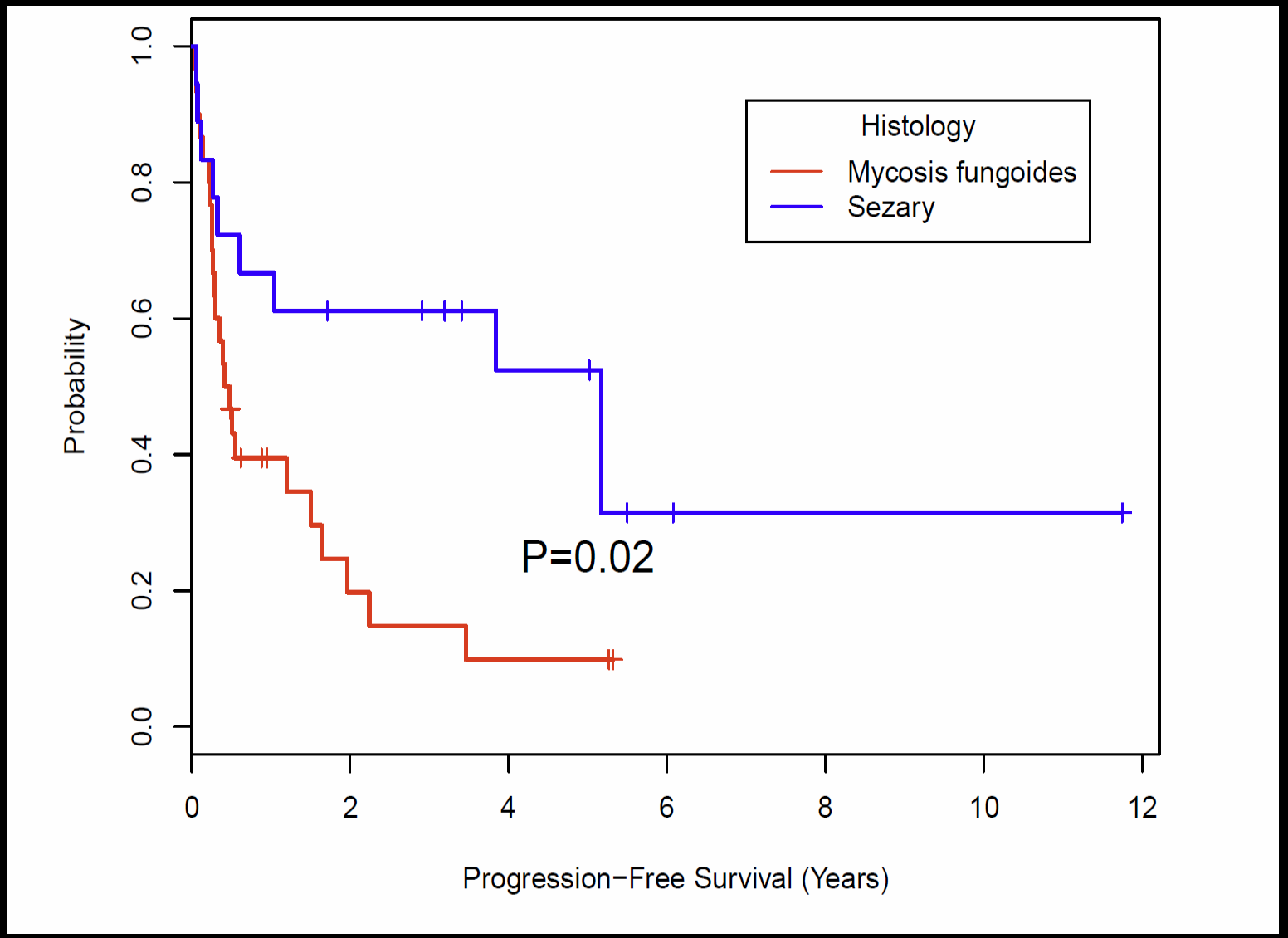
Acute GVHD SKIN
Death from 3 chronic, 1 acute GVHD

4 yrs : OS 53% & PFS 28%

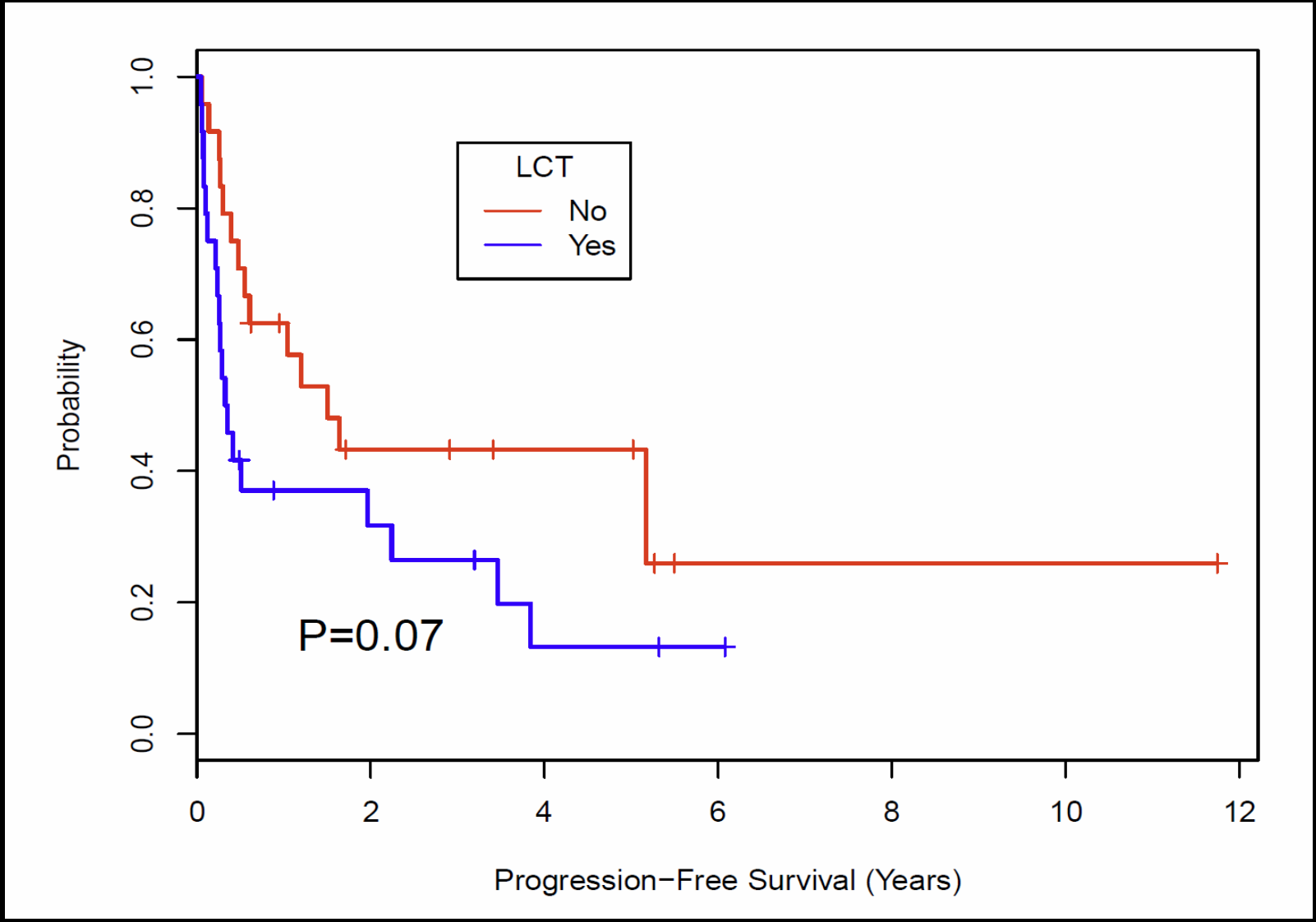
Clinical	Overall Survival (OS)	Progression Free Survival
All patients	53%	28%
Mycosis fungoides	65%	9.9%
Sezary Syndrome	72%	52%
MF/SS/LCT	57%	
MF/LCT	27%	13%


Overall and Progression−Free Survival all pts from Transplant date
OS
PFS
Probabili
ty
1.0
0.8
0.6
0.4
0.2
0.0
0
2
4
6
8
10
12
Years

Progression Free Survival
MF (red) versus Sezary Syndrome

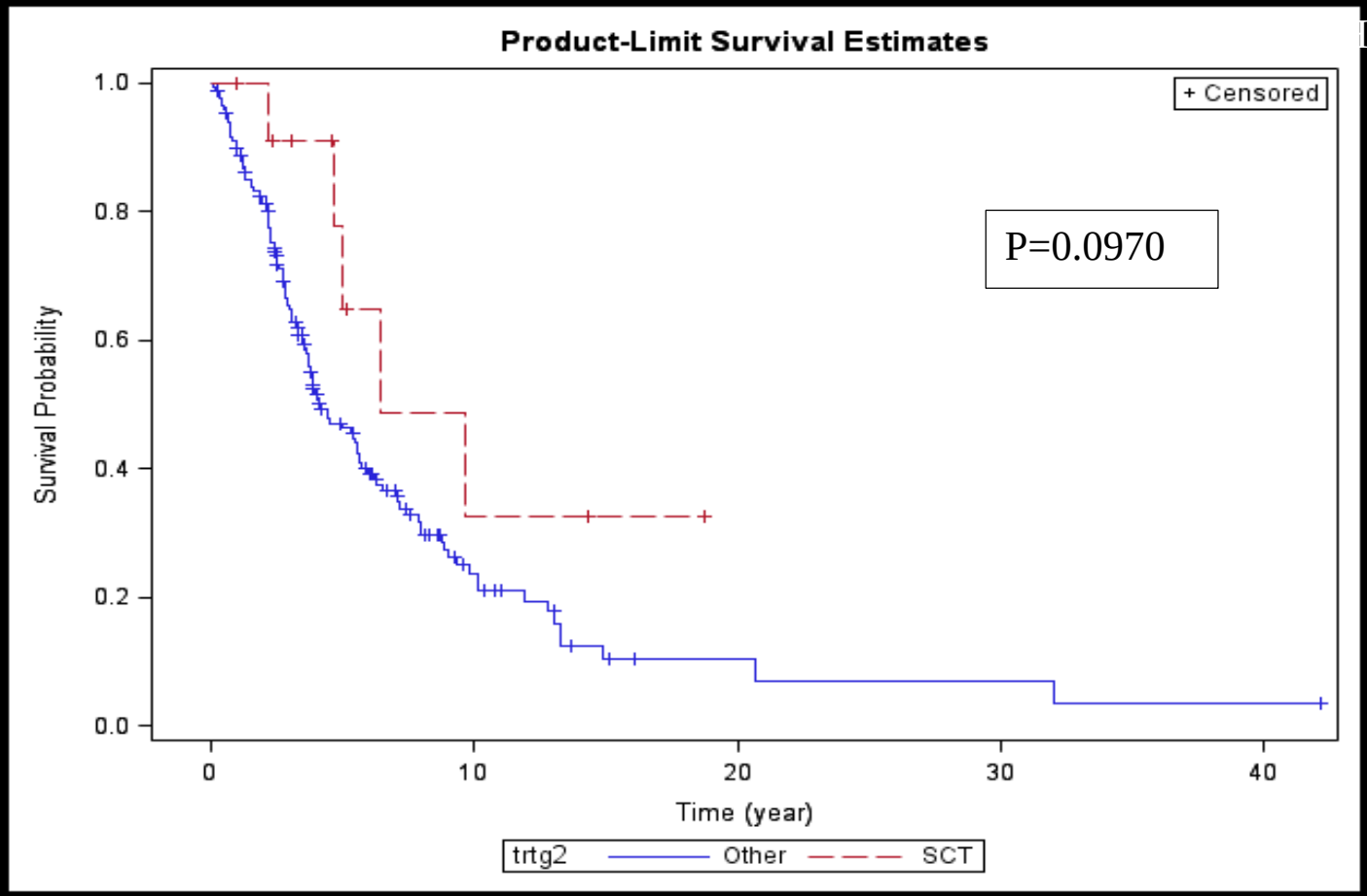


Progression free survival
all patients with/without LCT



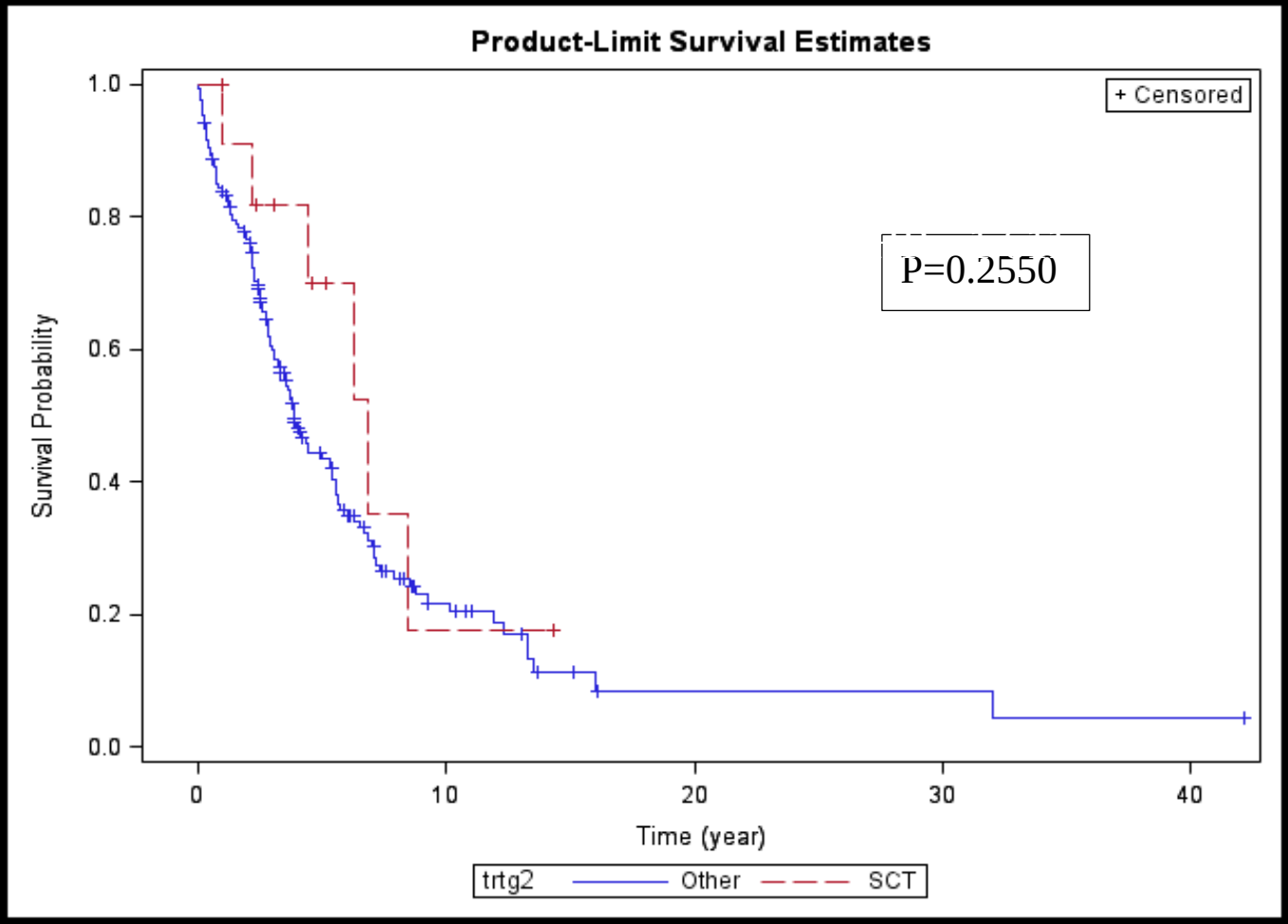
Overall survival of patients with LCT
All other systemic treatments vs
patients w LCT and SCT

IR=2.137



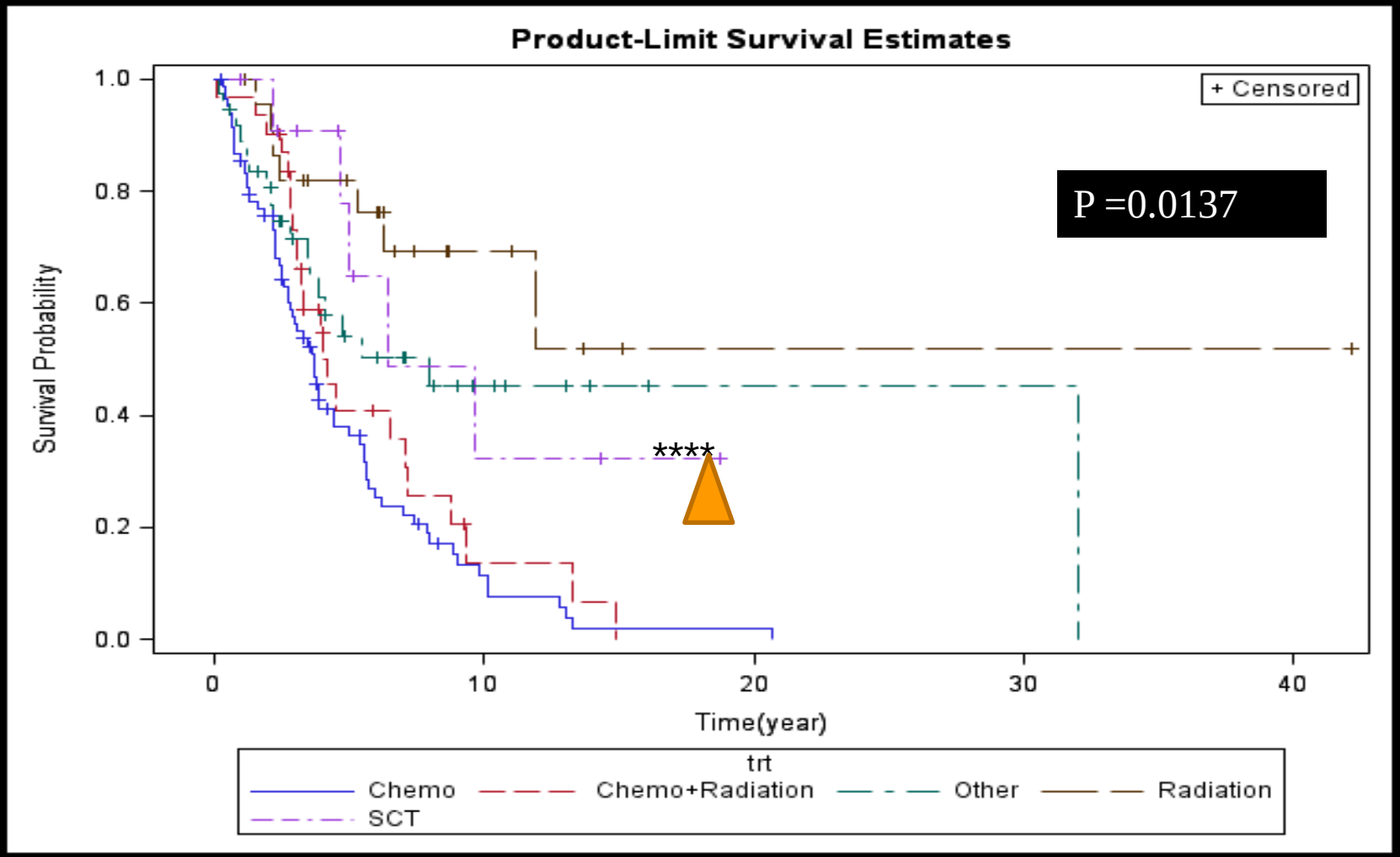
Talpur Unpublished data

Progression free survival
All treatments vs SCT

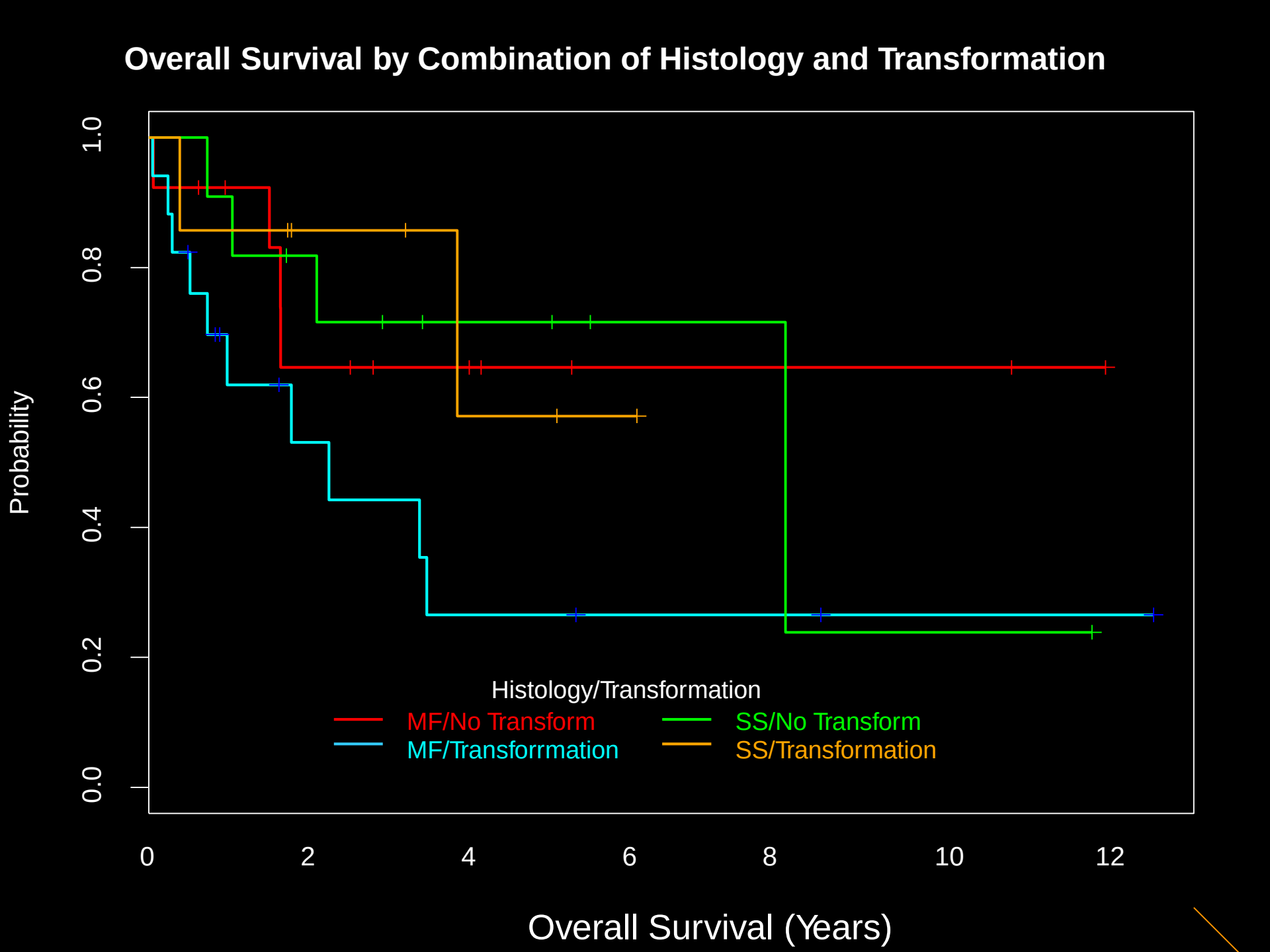


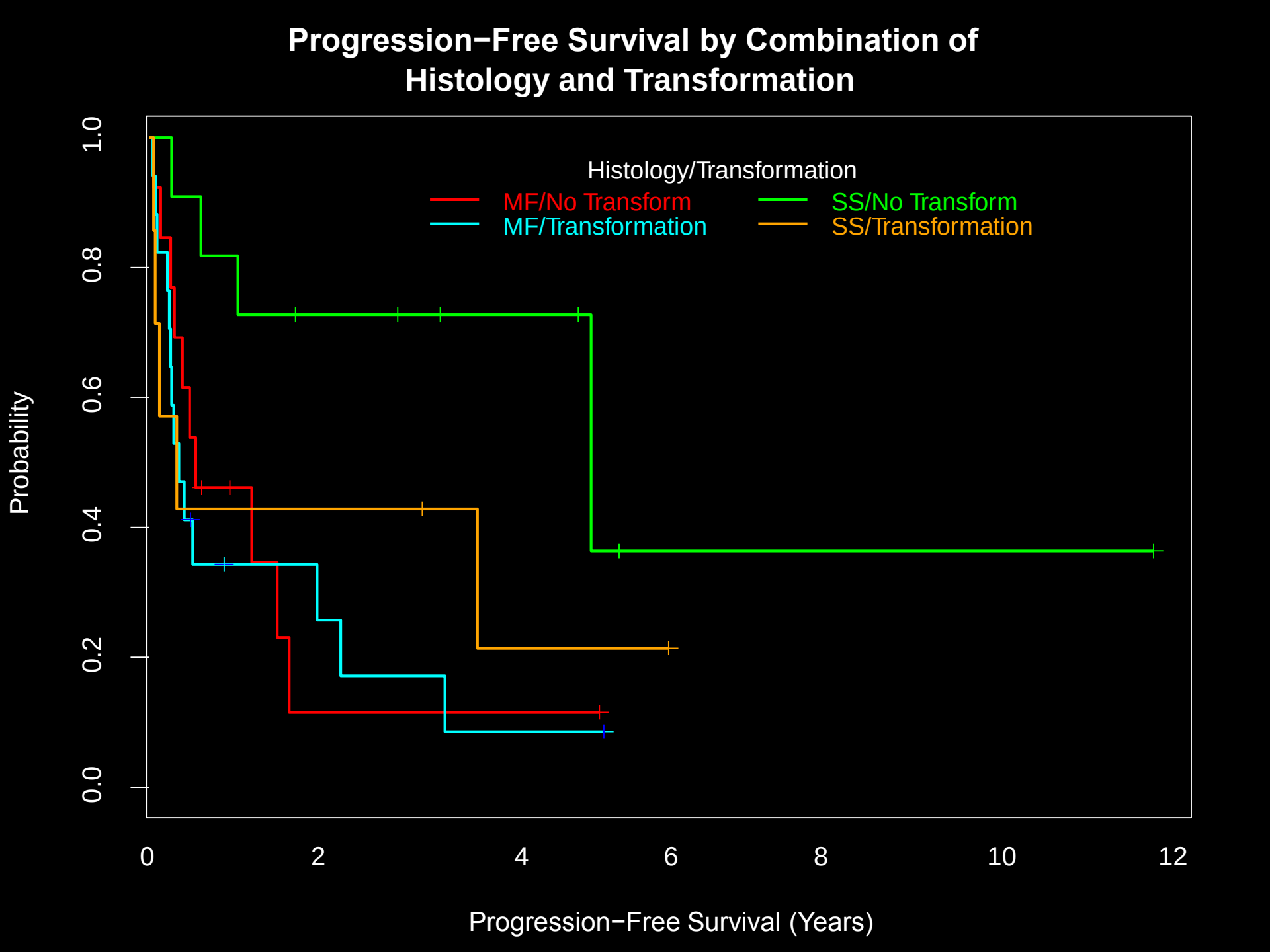
Unpublished data

Treatment of LCT
Impact on Overall survival



Duvic & Talpur -Unpublished data


Overall Survival by Combination of Histology and Transformation
Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
2
4
6
8
10
12
Overall Survival (Years)
Histology/Transformation
MF/No Transform
MF/Transforrmation
SS/No Transform
SS/Transformation


Progression−Free Survival by Combination of Histology and Transformation
Histology/Transformation
MF/No Transform
MF/Transformation
SS/No Transform
SS/Transformation
Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
2
4
6
8
10
12
Progression−Free Survival (Years)

Conclusions

- TBSEB with non-ablative allogenic stem cell transplant can induce complete durable remissions, especially in Sézary Syndrome.
  - ORR was 58% (28/48) for all patients)
  - 79% Sézary Syndrome (n=17) plus 7 w LCT
  - 56% for MF with LCT (n=24)
- Incidence of relapse/progression was 50%
  - SS 21%, LCT 25%, SS+LCT 56%
- 44% (21/48) died: 10 relapsed MF, 5 GVHD, 4 infection, 2 second malignancy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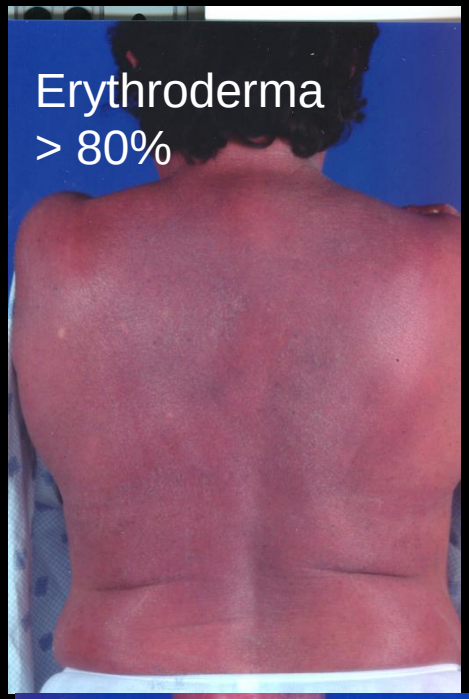
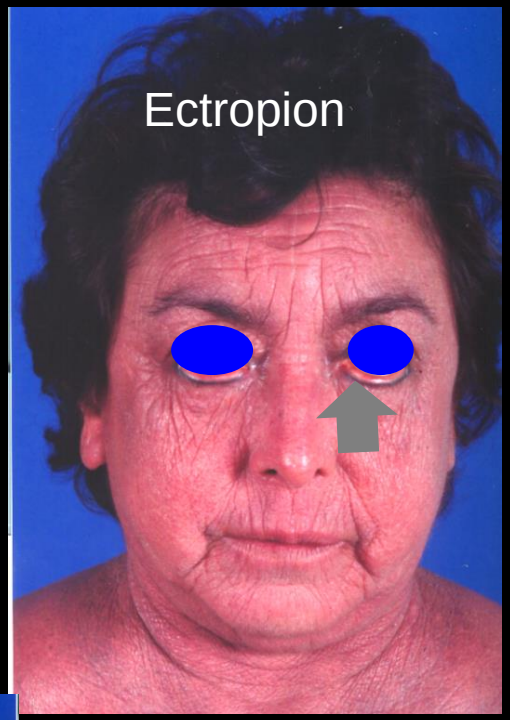
Introduction

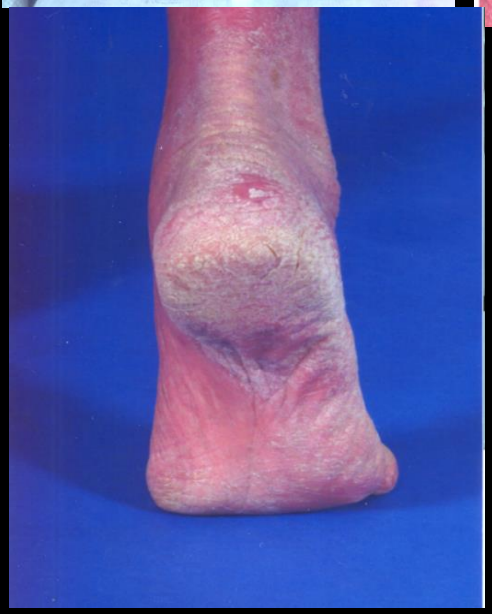
- Advanced (T3,T4) cutaneous T-cell lymphomas (CTCL), Mycosis fungoides (MF) with LCT and Folliculotrophism and Sézary Syndrome (SS) have poor prognosis and are incurable with traditional chemotherapy

- Experience with allogeneic hematopoietic stem cell transplantation (HSCT) is limited in CTCL because it is a rare disease occurring more frequently in the elderly

Sézary Syndrome Adenopathy, pruritus, Staph aureus



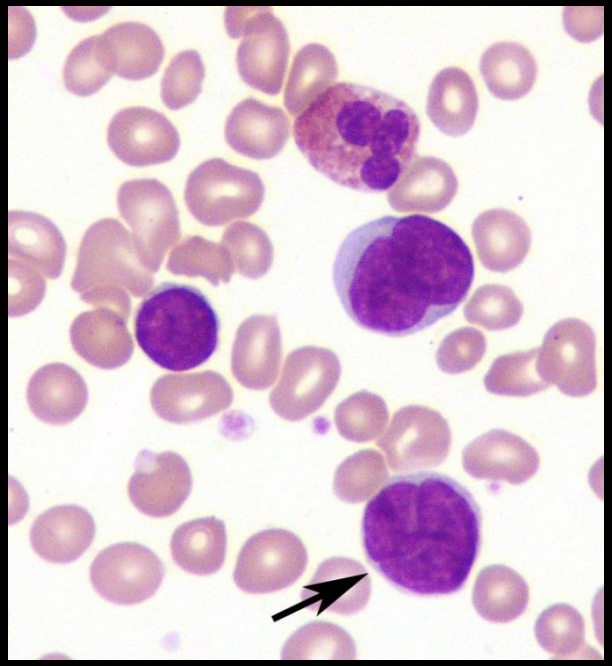




Keratoderma
With tinea

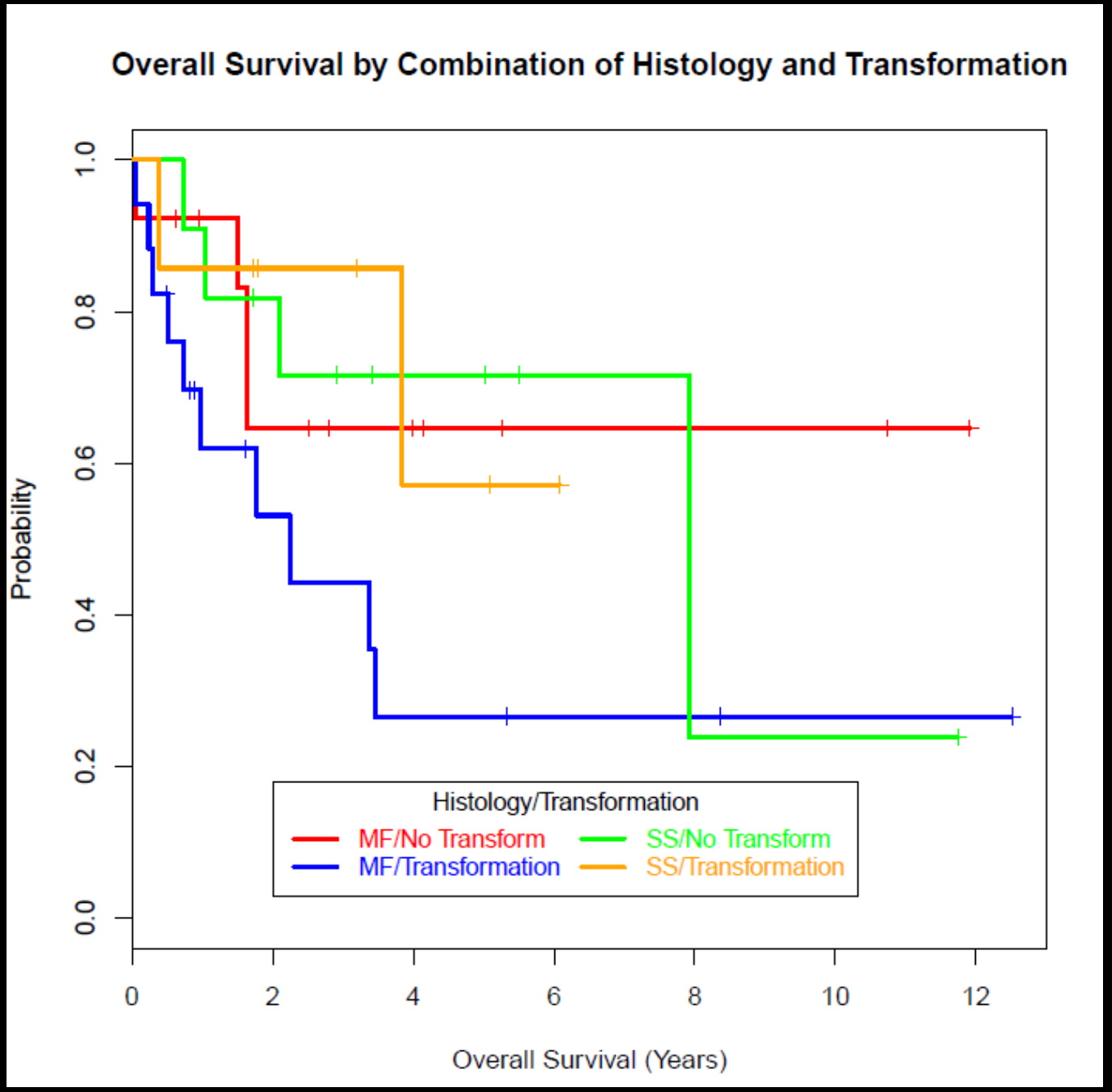
Vidulich et al. *Int J Dermatol.* 2009 Mar;48(3):243-52

Sézary cells / ul in blood
Predicts overall survival
7.6 years: < 1000/ul
5.4 years: 1000 -10,000
2.4 years: ≥10,000



Large cell transformation

- LCT has been reported to have a more aggressive disease course and shorter overall survival than untransformed MF
- Median overall survival was 4.79 years patients with LCT in all MDACC patients cohort (unpublished data)
- OS is similar to published results of non-LCT in T3 (tumor) MF patients (6.24 yrs) and significantly worse than all MF patients (26.26 years) (p=.001)
- Overall survival examined with or without SCT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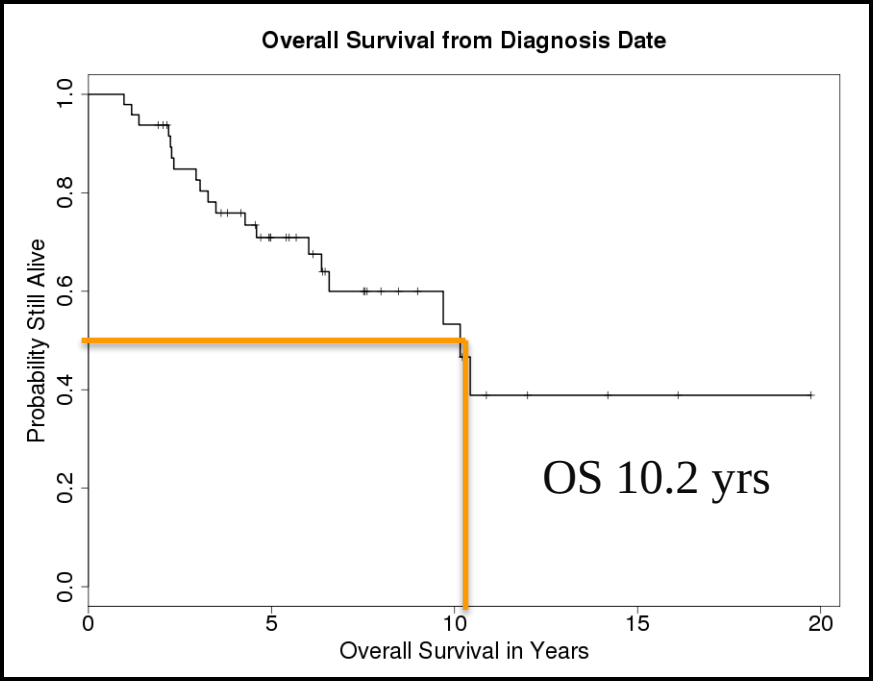
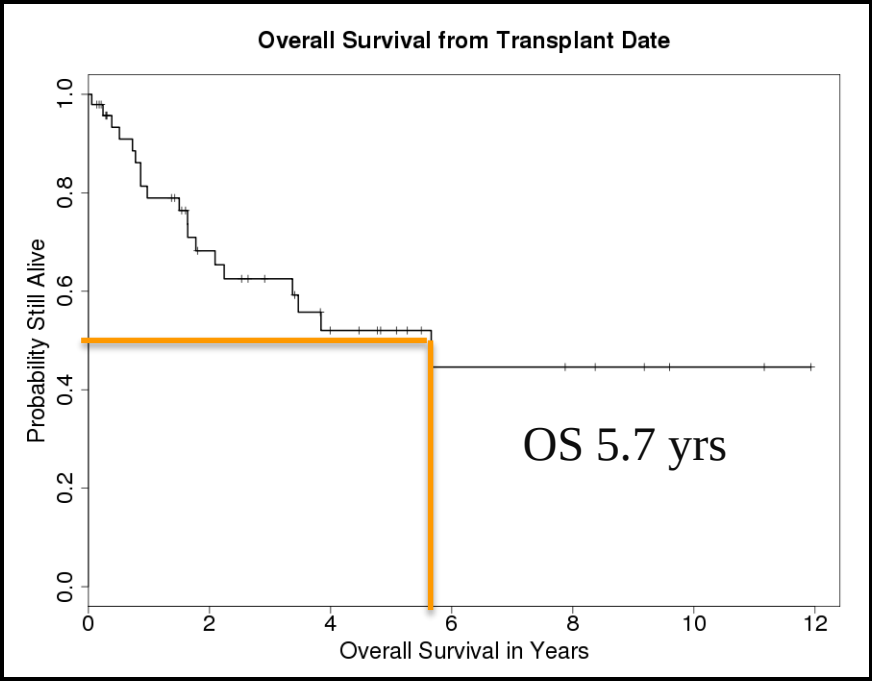
12
Overall Survival (Years)
Histology/Transformation
MF/No Transform
MF/Transformation
SS/No Transform
SS/Transformation

Overall survival in 48 SCT patients

53% OS at 4 years

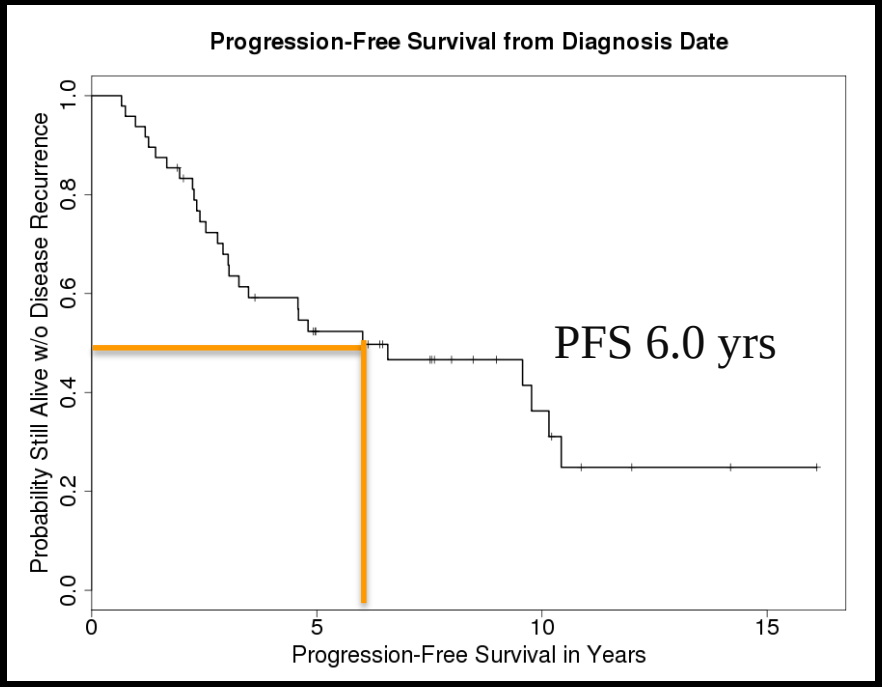


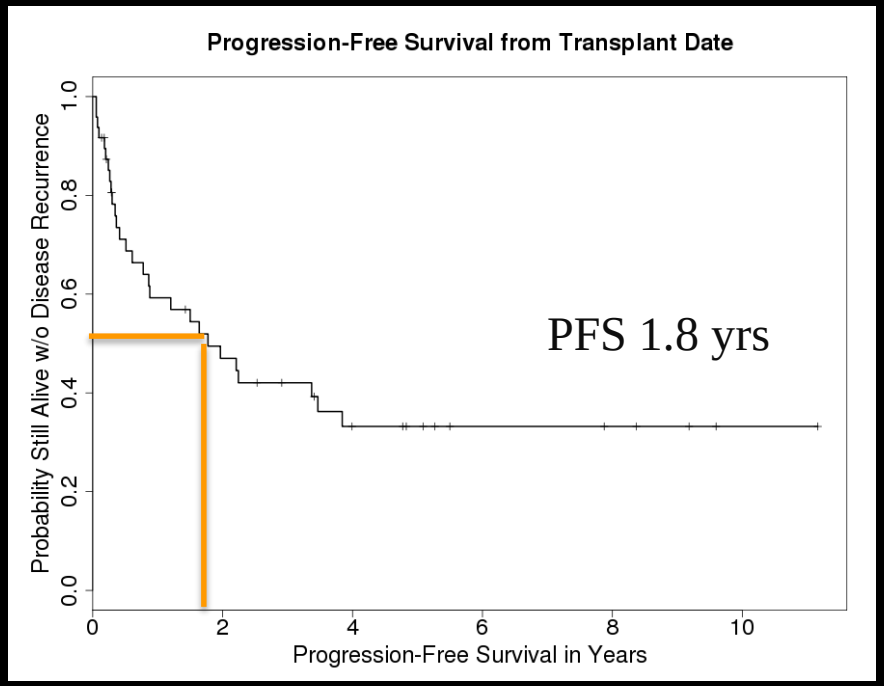


Overall survival from diagnosis
Range 1-19.8 years

Overall survival from transplant date
First transplant July 2001
Range 1 mos – 11.5 years

Progression Free Survival (PFS)

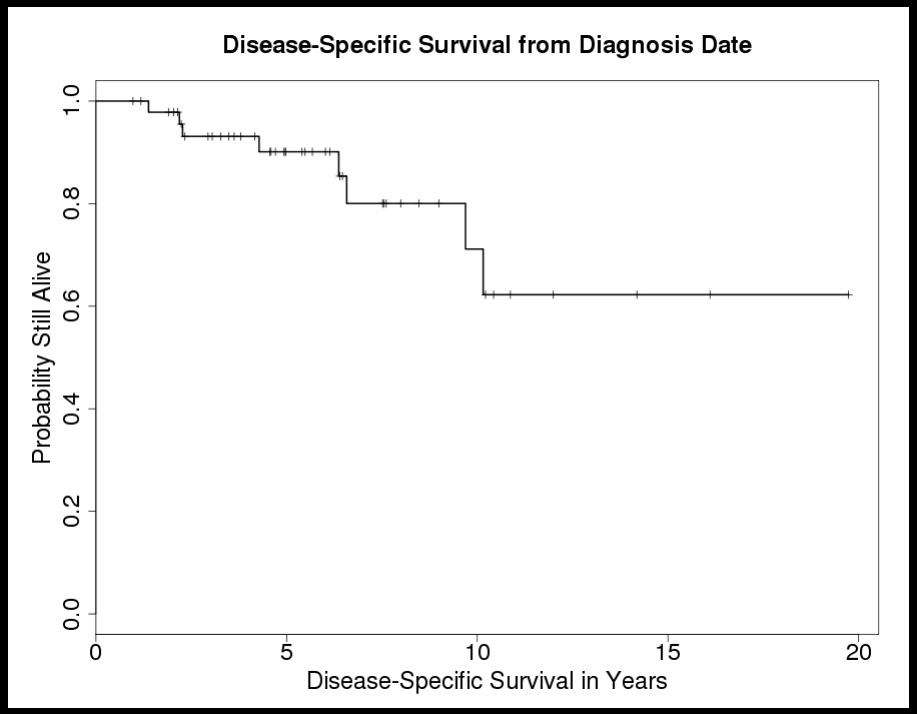


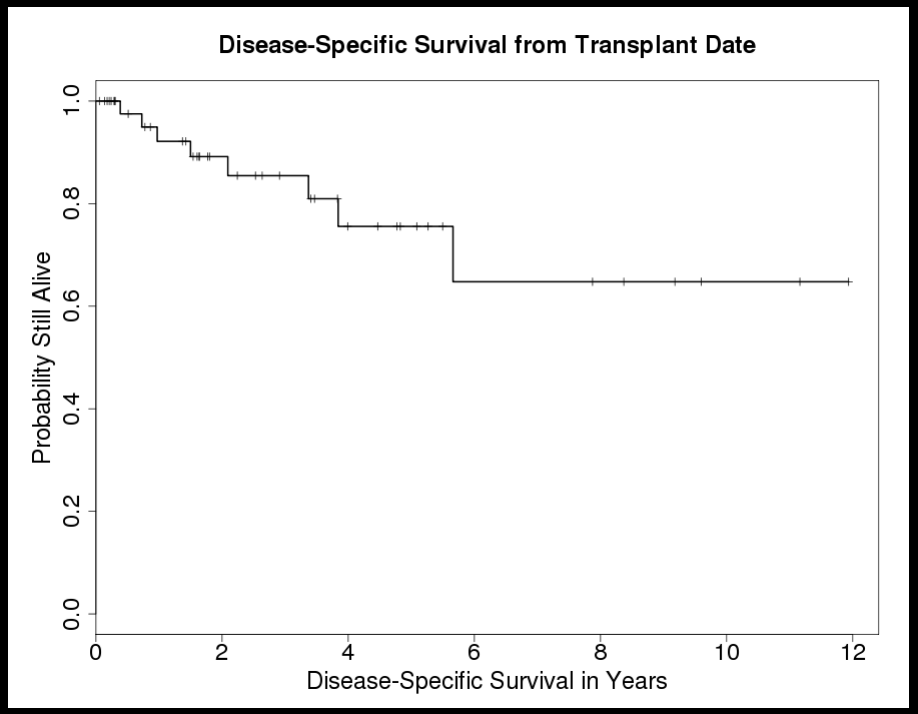


From Diagnosis 6 yrs

From Transplant date 1.8 yrs
PFS at 4 yr 28% all patients
SS 52.4% vs no SS 9.9%

Disease Specific Survival
48 SCT patients





Disease specific survival from
Date of diagnosis (not reached)

Disease Specific Survival from
Transplant date (not reached)

Overall Survival: All Patients