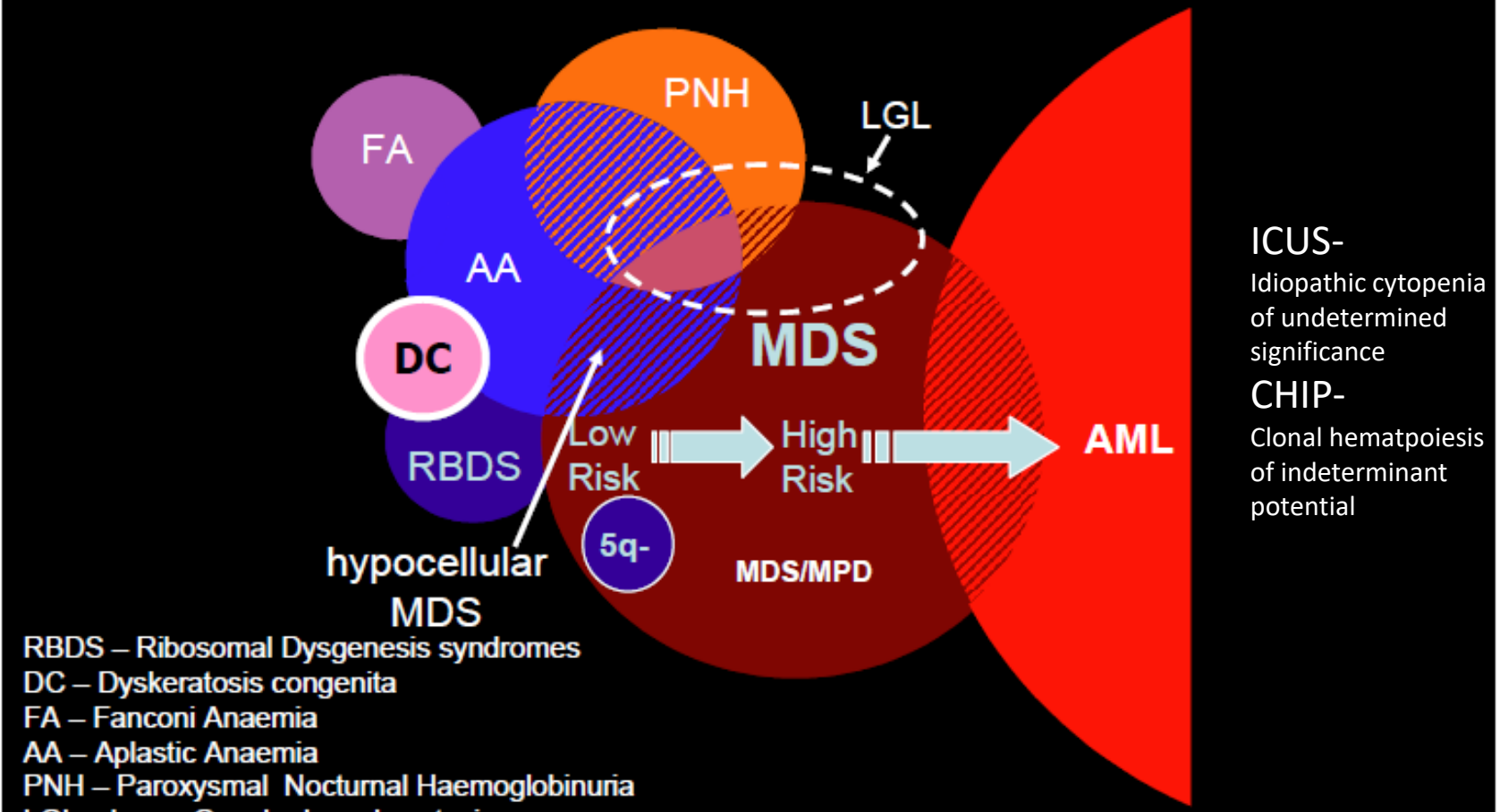
Allogen stamcelletransplantasjon ved aplastisk anemi

Hematologisk vintermøte, Solastrand, 2022

The Bone Marrow Failure Syndromes



RBDS – Ribosomal Dysgenesis syndromes
DC – Dyskeratosis congenita
FA – Fanconi Anaemia
AA – Aplastic Anaemia
PNH – Paroxysmal Nocturnal Haemoglobinuria
LGL – Large Ganular Lymphocytosis

Adapted from N. Young, G. Mufti

ICUS-
Idiopathic cytopenia of undetermined significance

CHIP-
Clonal hematpoiesis of indeterminant potential

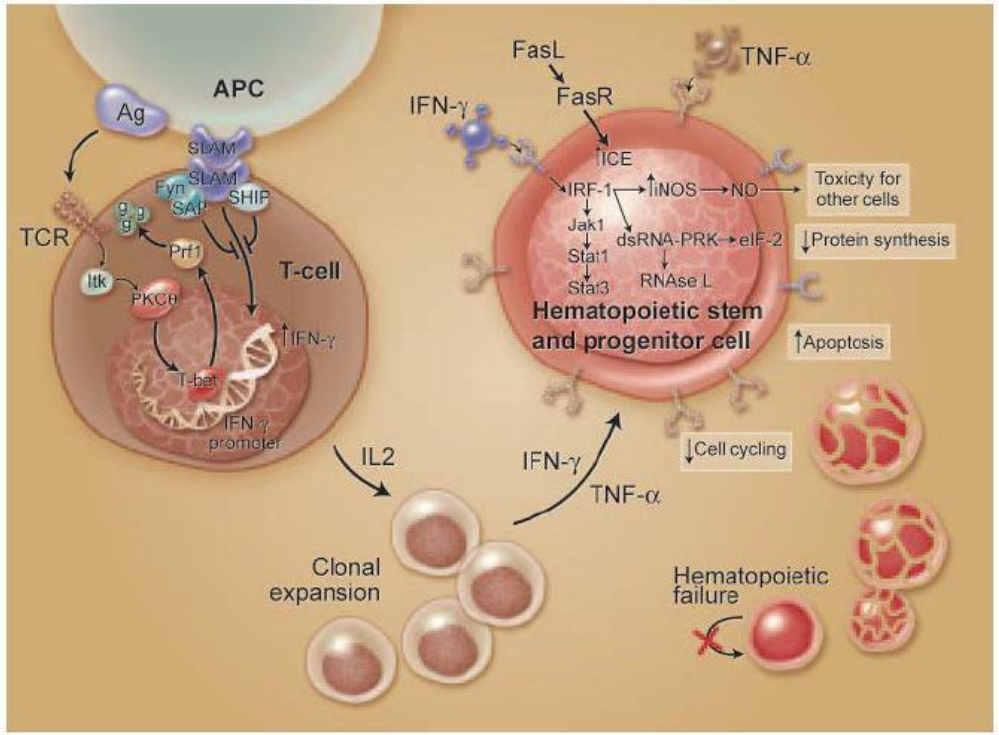
Aplastisk anemi; pancytopeni i PB,
< 30% cellularitet i BM uten reticulinøkning
Eller abnorm celleinfiltrasjon.

Sjeldent; Insidens ca 2/mill i Scandinavia
Bifasisk alder: 15-20 år og > 60 år

Sekundær AA < 5%
Idiopatisk AA 70-80%
Kongenital AA 15-20%- konsekvenser for tx

5 års overlevelse >90% for <30 år,
28% for > 70 år (Vaht K et al Hematologica 2017)

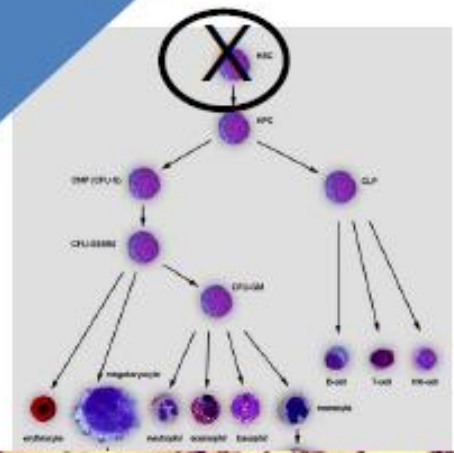
Aplastic anemia is an immune-mediated T-cell destruction of the marrow

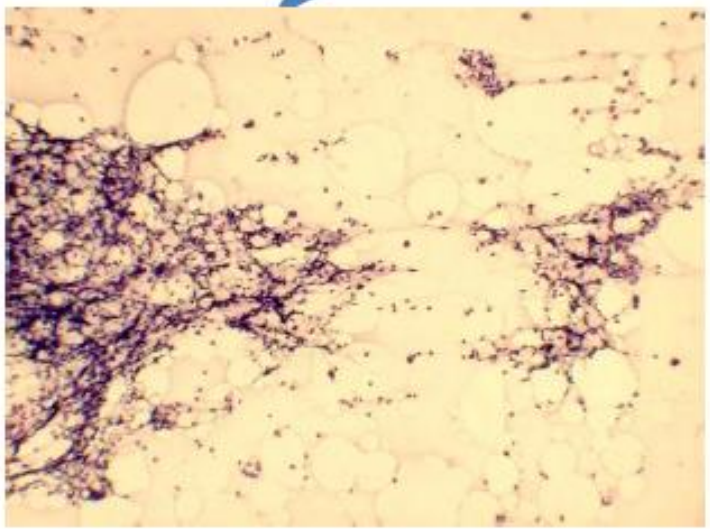


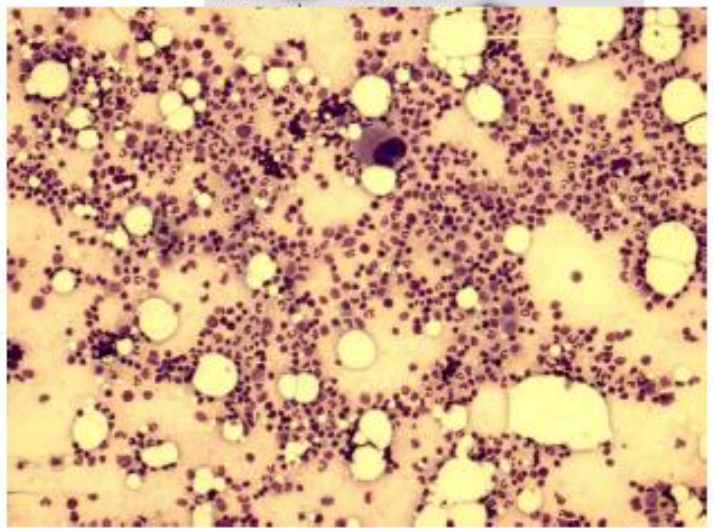
- Cytotoxic T cell expansion
- Expressing cytokines (g-INF)
- Oligoclonal expansion (immunodominant clonotypes)
- Decrease of the hematopoietic stem cell pool
- Trigger of the T cell proliferation?

N. Young et al. Blood. 2006. 108; 2509-2519

Aplastic Anemia



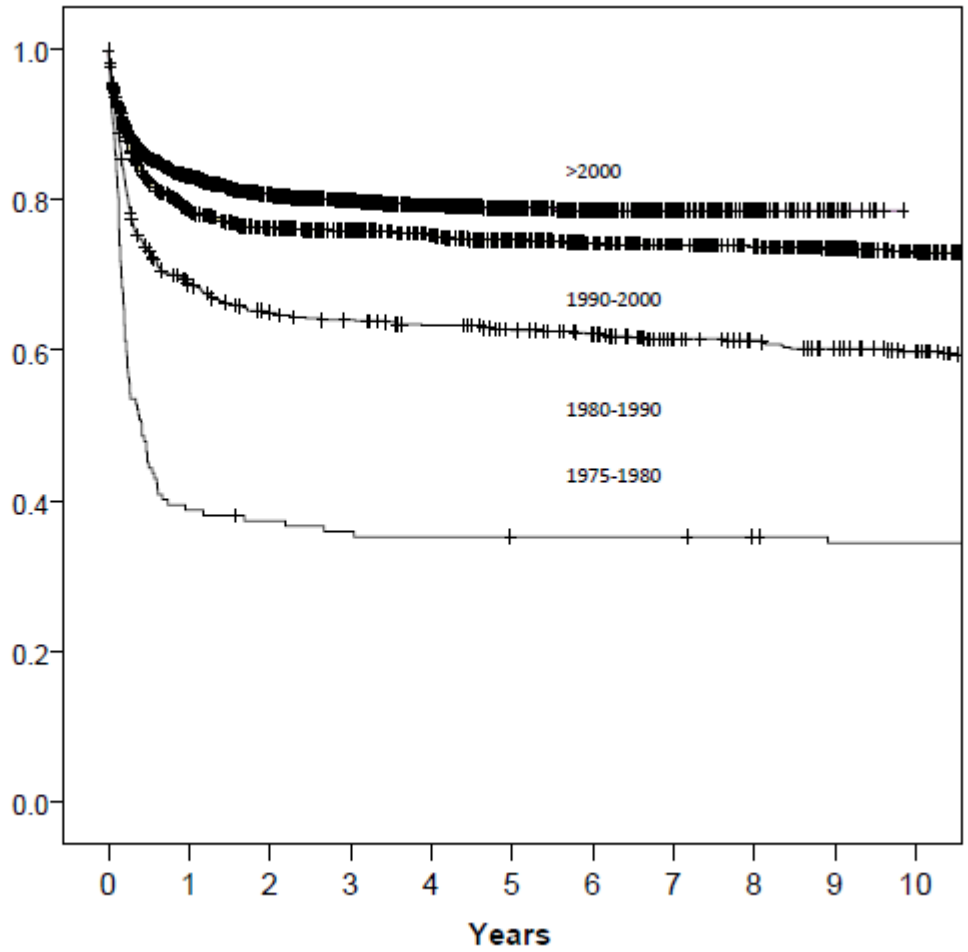




Acquired SAA

Transplants
From
HLA identical
Sibling Donors

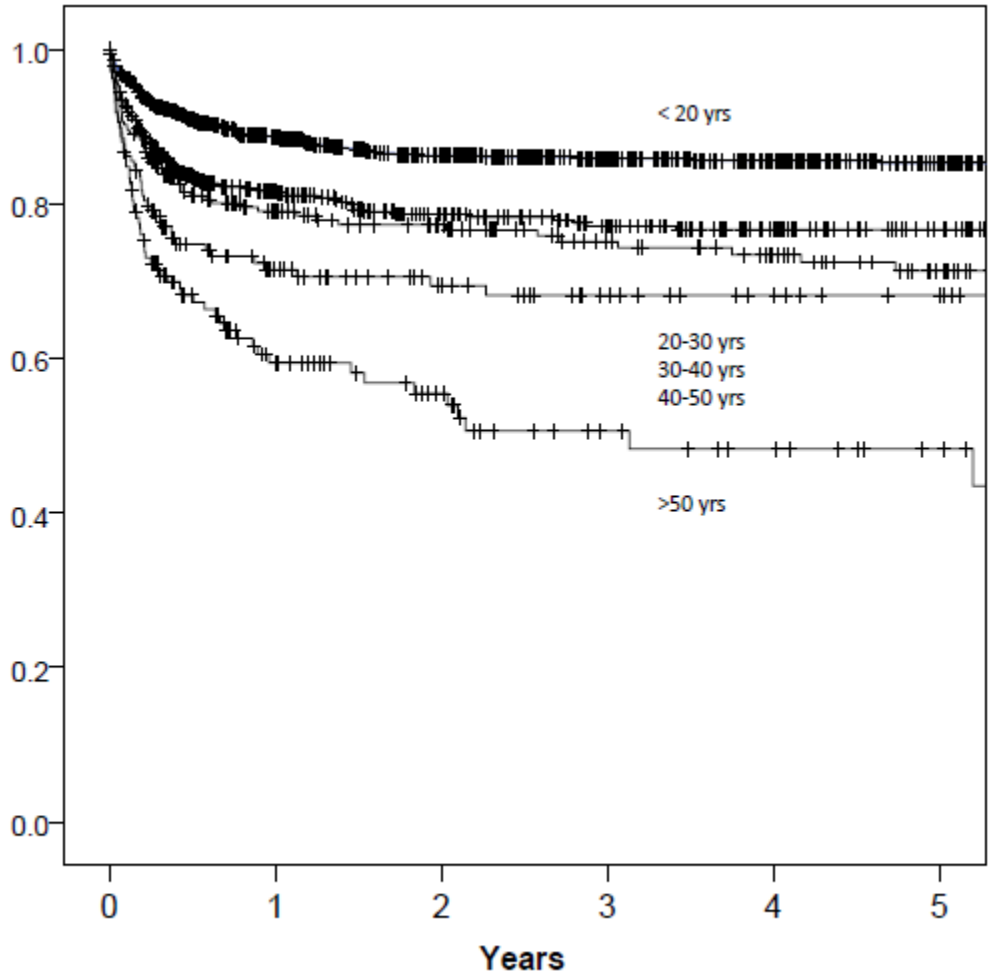
Effect of
Year of Transplant



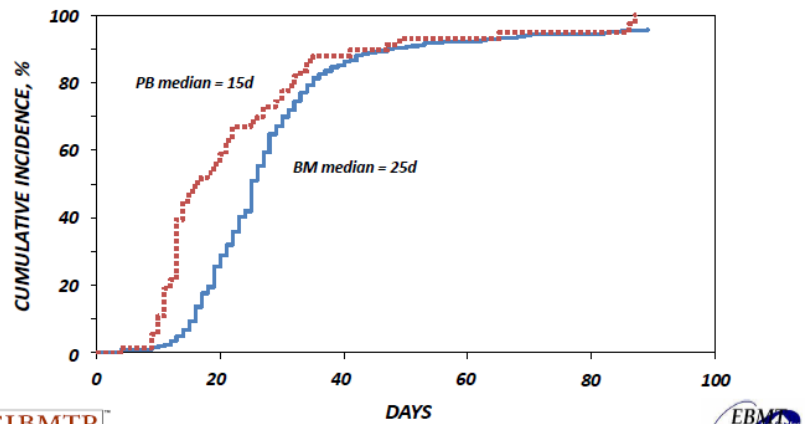
Acquired SAA

Transplants From HLA identical Sibling Donors

Effect of Patient Age



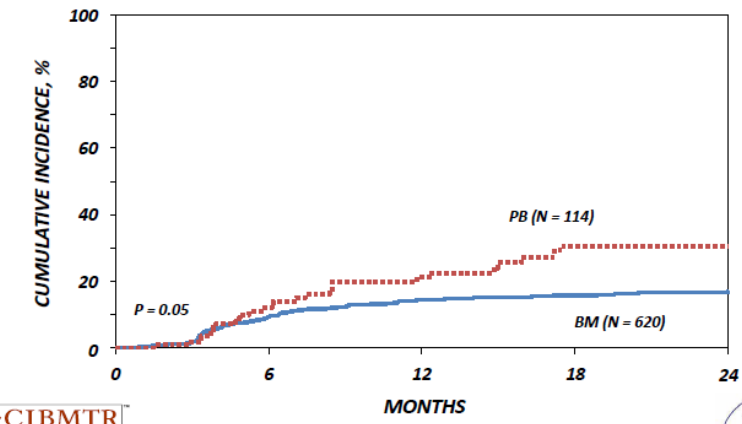
Stem Cell Source
PLATELET RECOVERY



CIBMTR

EBMT

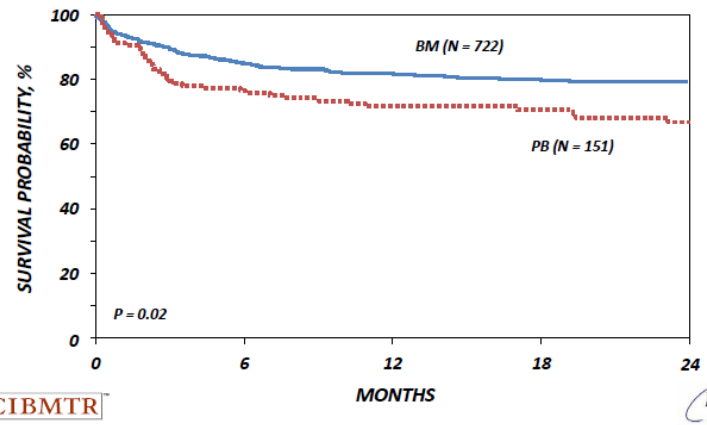
Stem Cell Source
CHRONIC GVHD



CIBMTR

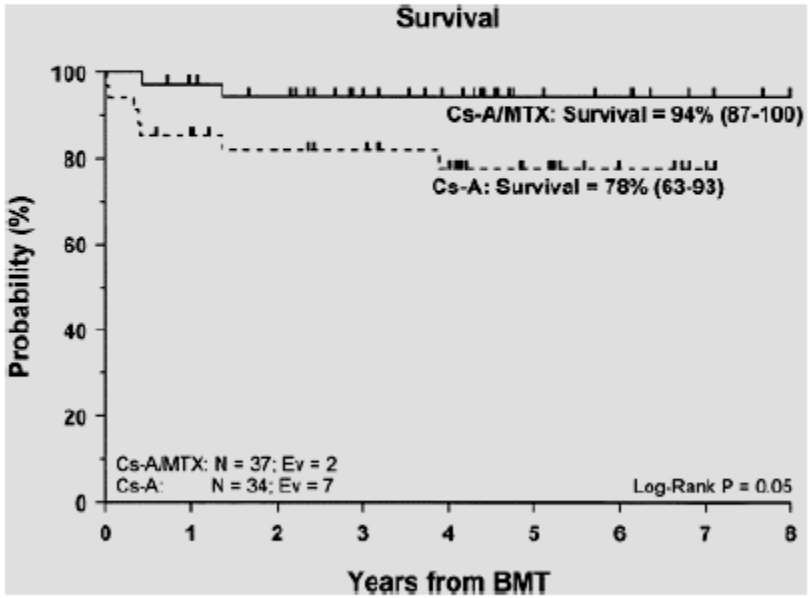
EBMT

Stem Cell Source
SURVIVAL



CIBMTR

GvHD Prophylaxis

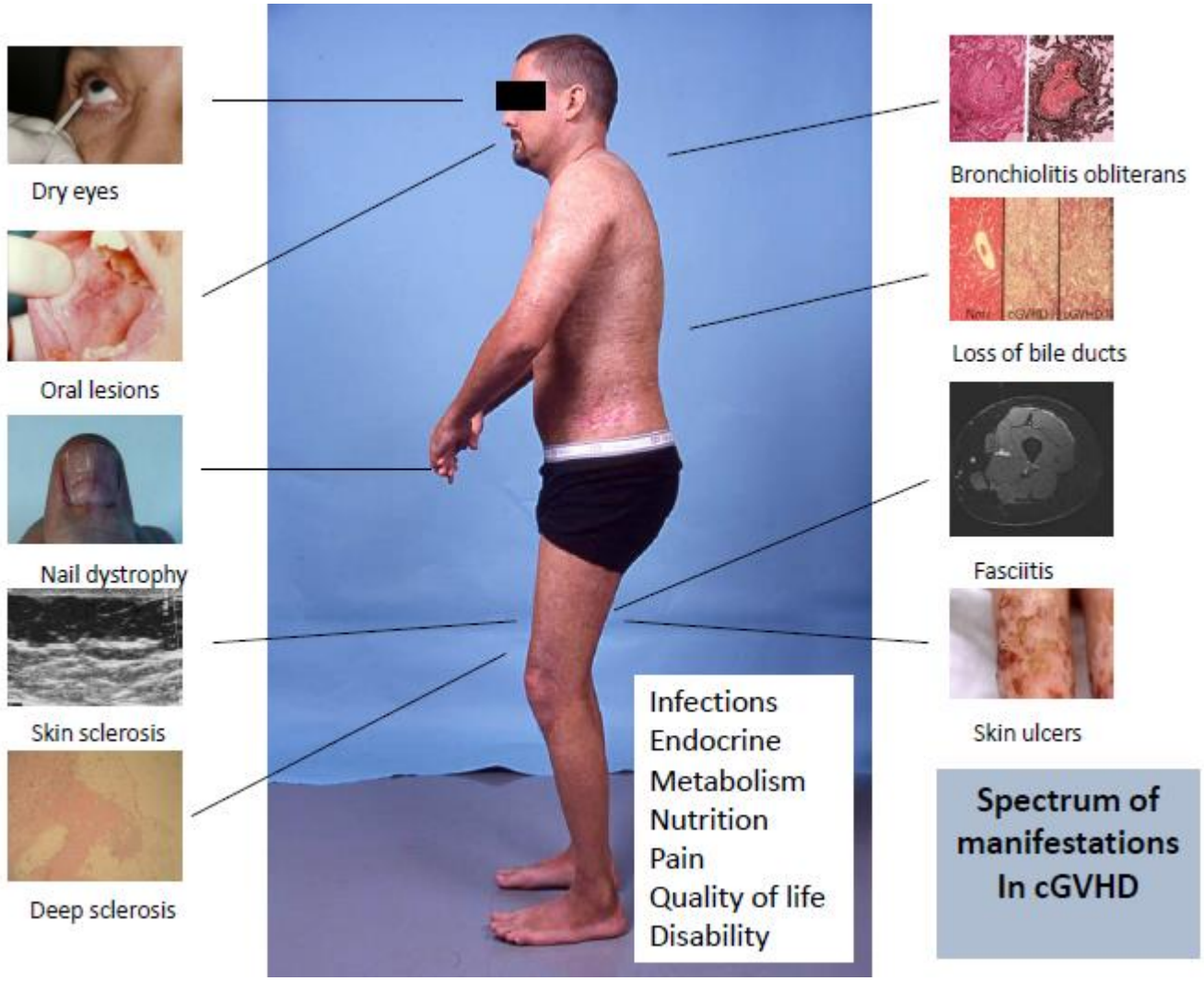


GITMO
GRUPPO ITALIANO TRAPIANTO MIDOLLO OSSEO

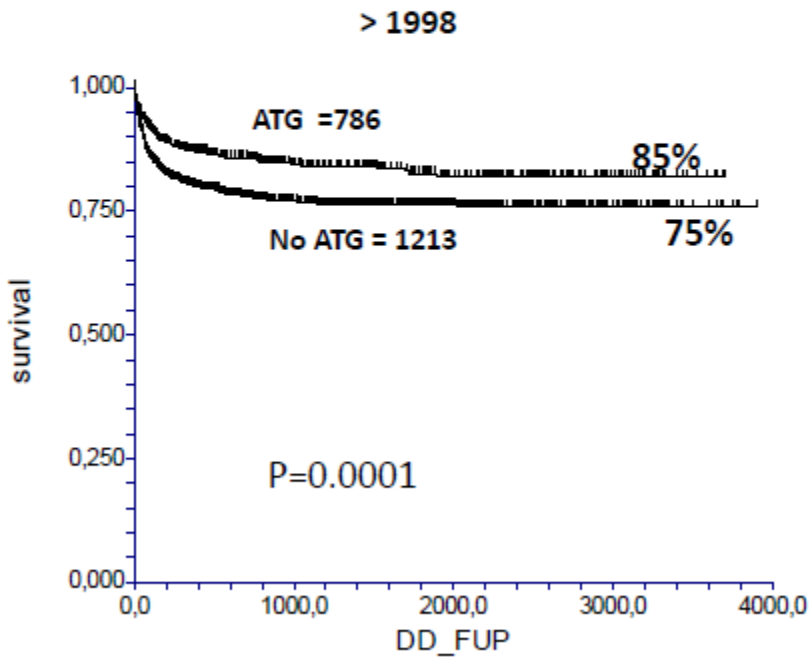
EBMT

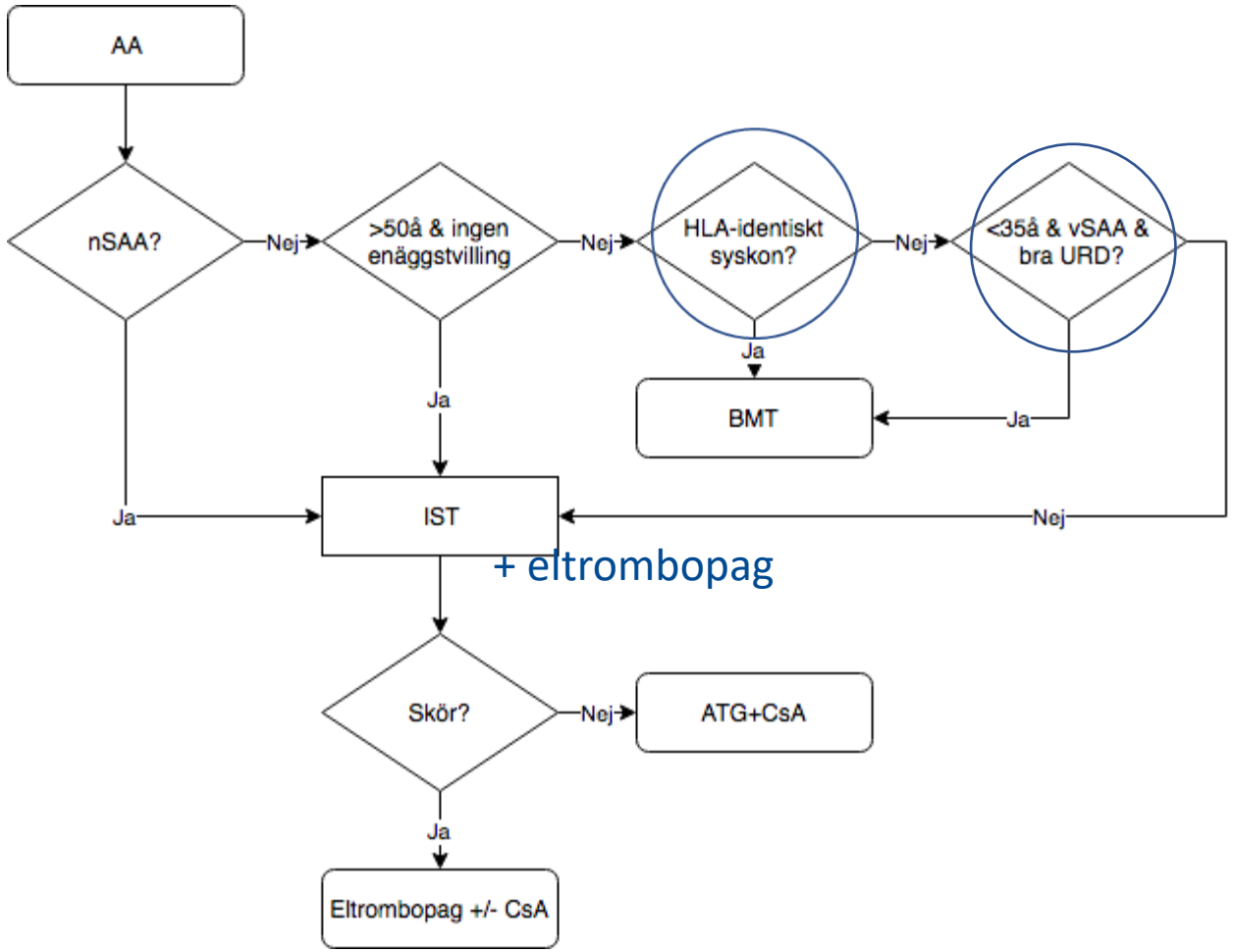
Oslo University Hospital

UiO : University of Oslo

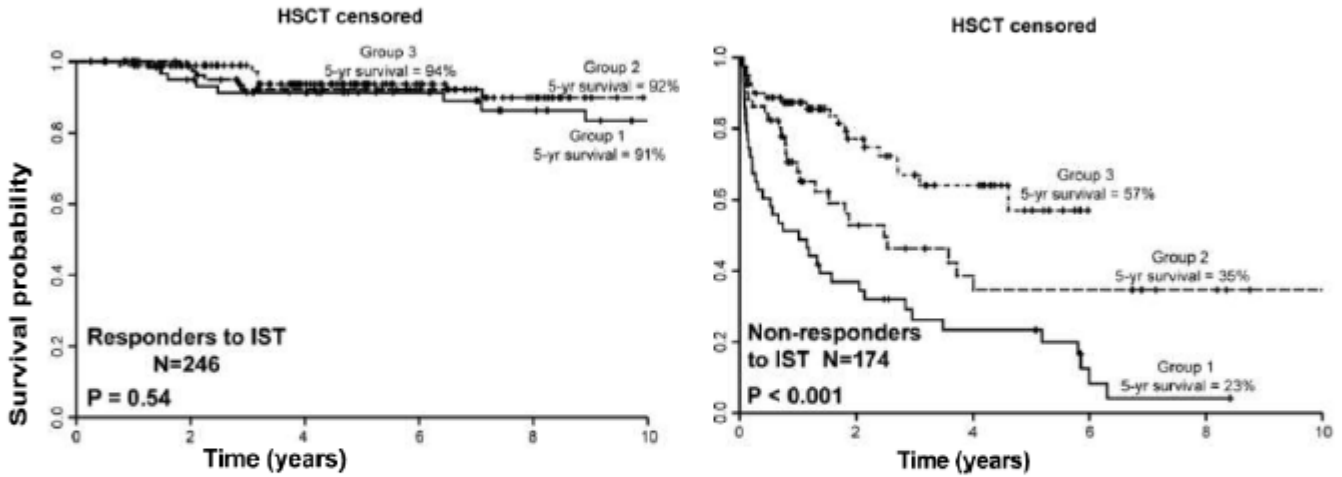

Dry eyes
Oral lesions
Nail dystrophy
Skin sclerosis
Deep sclerosis
Bronchiolitis obliterans
Loss of bile ducts
Fasciitis
Skin ulcers
Infections
Endocrine
Metabolism
Nutrition
Pain
Quality of life
Disability
Spectrum of manifestations In cGVHD

HLA id sibling transplantation
10 yr OS by use of ATG in the conditioning regimen




AA
nSAA?
Nej
>50å & ingen enäggstvilling
Nej
HLA-identiskt syskon?
Nej
<35å & vSAA & bra URD?
Ja
BMT
Ja
Ja
Ja
IST
Nej
+ eltrombopag
Skör?
Nej
ATG+CsA
Ja
Eltrombopag +/- CsA

Supportive Care –the underestimated treatment



	Treatment between	Patient number	5 yr-survival responder	5-yr-survival non-responder (NR)	6 mo survival NR
Group 1	12/1989 -10/1996	43	91%	23%	61%
Group 2	11/1996 – 10/2002	51	92%	35%	82%
Group 3	11/2002 – 04/2008	80	94%	57%	89%

Valdez J. et al Clinical Infection Diseases 2011

Haploidentical BMT for severe aplastic anemia with intensive GVHD prophylaxis including posttransplant cyclophosphamide

Amy E. DeZern,1,2 Marianna L. Zahurak,1,3 Heather J. Symons,1,4 Kenneth R. Cooke,1,4 Gary L. Rosner,3 Douglas E. Gladstone,1 Carol Ann Huff,1 Lode J. Swinnen,1 Philip Imus,1 Ivan Borrello,1 Nina Wagner-Johnston,1 Richard F. Ambinder,1 Leo Luznik,1

Blood Advances 2020

Allo-HSCT SAA#, OUS ,,fom 2012 tom 2021 **n = 15, 1 «lost to follow up» & 1 mors etter 2 år**

DONOR	3 HLA-id sibl.	12 10/10 MUD
Kondisjonering.	3 ATG/Cy.	12 Flu/Cy/ATG/2GyTBI
GvHD profylakse	3 Mtx/Cia.	12 Mtx/Cia

FA, DC, MDS, IBMFS ekskludert

Anbefalinger Allo-HSCT for AA 2022:

Som førstelinjebehandling: For vsAA og sAA pasienter < ca 50 år uten komorbiditet og HLA-id søskendonor.
Syngen tvillingdonor -> allo-SCT også ved høyere alder
Vurder for pasienter < ca 35 år **(eldre ??)** m vsAA om minst 10/10 MUD

Øvrige bør ha IST + som førstelinjebehandling (skjøre pasienter; Eltrombopag + Ciklosporin, ev Eltrombopag alene)

Som andrelinjebehandling: (ikke respons på IST + Eltrombopag etter 4 mnd ?)
Ved svikt på 1 x IST: Individuell vurdering; alder, komobiditet, donoralternativer

Generelt:
Histiokompatibilitet spesielt viktig ! BMSC > PBSC. Donor alder!

Kondisjonering: Yngre pasienter m HLA-id sibl donor: Cyklofosfamid + ATG, GVHD profylakse: Mtx+Sandimmun ≥ 1 år
Pasienter > 40 år Flu/Cy/+ATG
MUD: Flu/Cy/ATG/2Gy TBI
(Flu/Cy/alemtuzumab)