# Can a Stem Cell Transplant Cure an Autoimmune Disease?

## Celebrating a Second Chance at Life Survivorship Symposium

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# Can a Stem Cell Transplant Cure an Autoimmune Disease?

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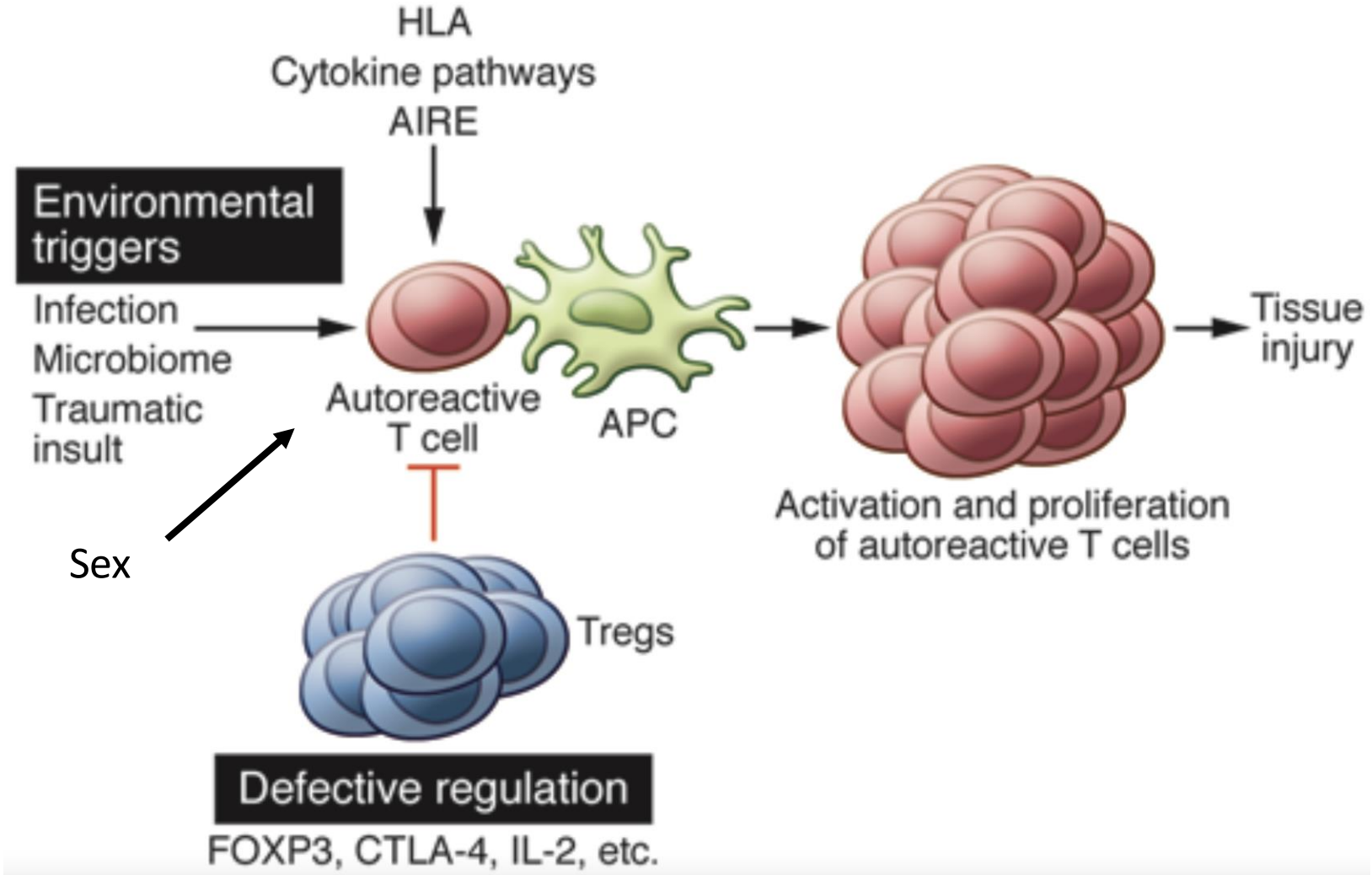
# Disclosures

- Nothing to disclose.

# Outline

- The origin of autoimmune disease (AD)
- Treatment of AD
- Autologous or allogeneic transplantation for AD?
- How does an autologous hematopoietic cell transplant (AutoHCT) work in AD?
- What ADs can be treated with autoHCT?
- What factors determine if a patient with an AD is a candidate for autoHCT?
- Short and long-term effects of autoHCT for AD

# Autoimmune disease (why it happens?)



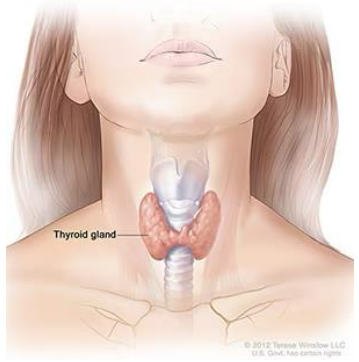

Rosemblum et al. Journal of clinical investigation 2015; 125: 2228-2233

# Autoimmune Disease – Clinical Characteristics

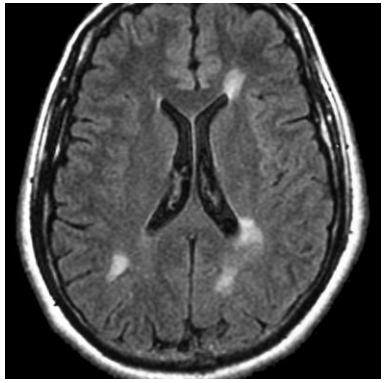
- Predominantly in women
- Young to middle age
- Cell and antibody-mediated damage to different tissues
- Affects any system:
  - Neurological
  - Gastrointestinal
  - Rheumatological
  - Endocrine

# Autoimmune Disease – Clinical Characteristics

- Can affect one organ:

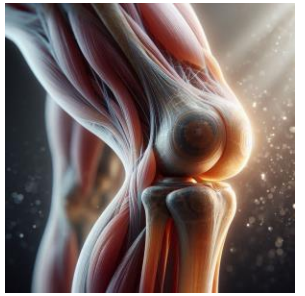


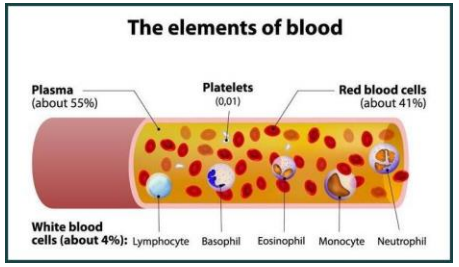

Thyroiditis

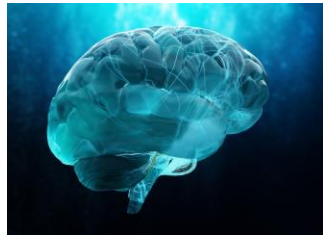


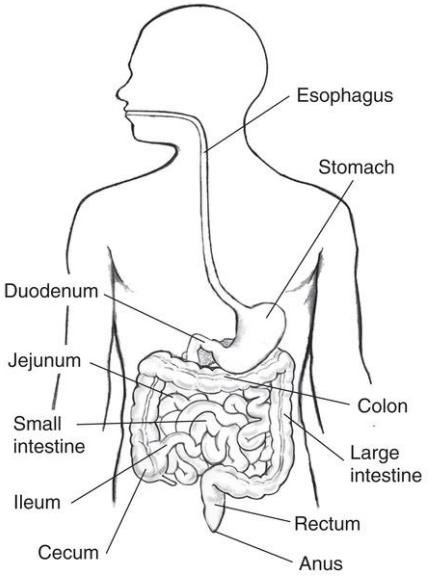
Multiple Sclerosis (MS)

- Or multiple organs:








Scleroderma, Lupus, Crohn's disease, Rheumatoid arthritis

# Autoimmune Disease - Treatment

Steroids

Immunosuppressive medications

Disease modifiers: Antibodies that target immune response

*Treatment must be done for many years, frequently lifelong*

*Risk of breakthrough*

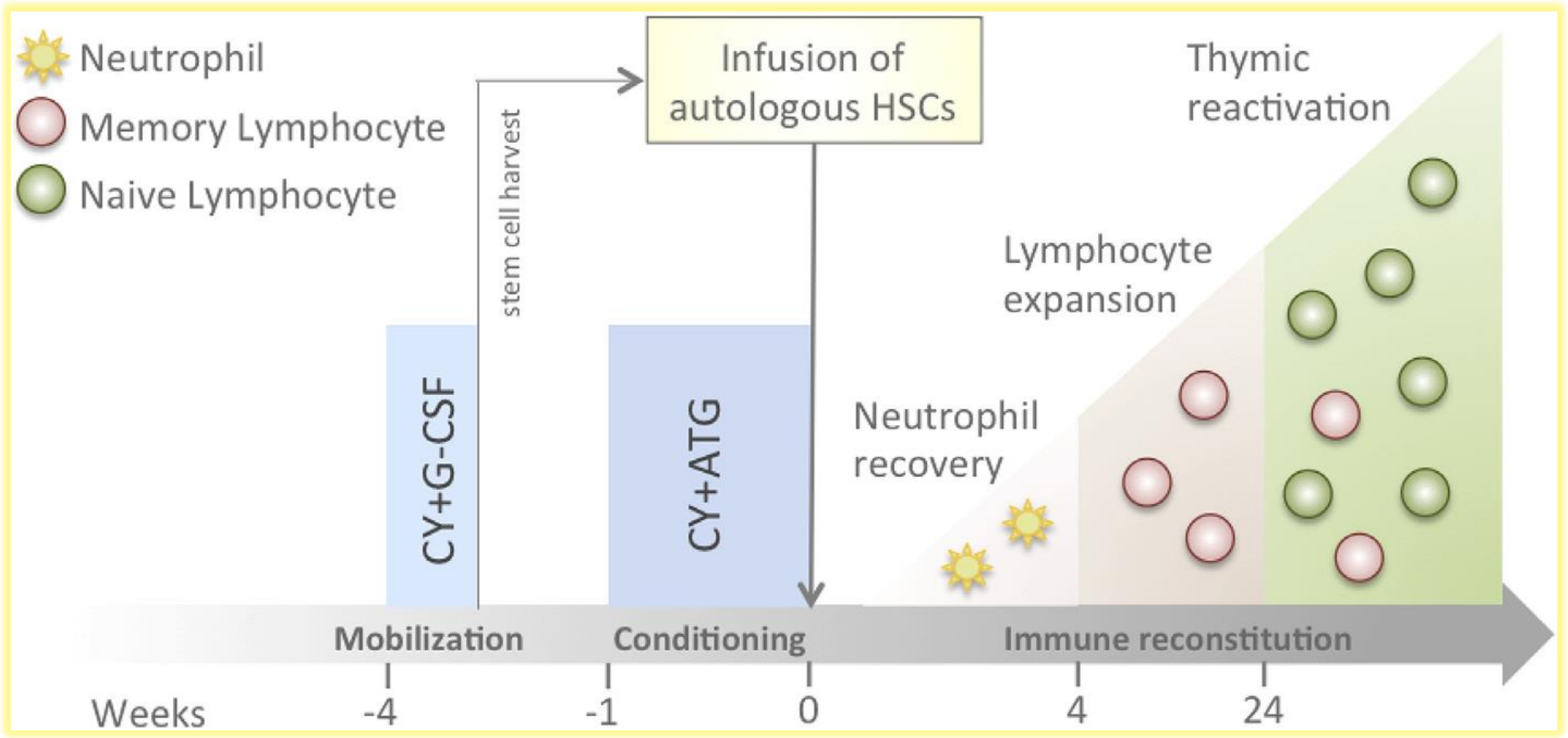
# Autologous vs. Allogeneic Transplantation

- Allogeneic Transplant (uses donor stem cells)
  - Replaces the immune system with a new one from a donor
  - It is a definitive therapy
  - But increased risk and mortality
- Autologous Transplant (uses the patient's own stem cells)
  - Resets the immune system
  - Has lower risk
  - Effective in most patients

# Mechanism of Action in AutoHCT in AD

- Goal:
  - Re-establish self-tolerance
- Destroy pathogenic autoreactive immune cells
- Immunological renewal
  - Generate new naïve T- and B- lymphocytes
  - Reactivate  thymic function
  - Re-establish regulatory T-cells
- “Re-set the immune system”

# AutoHCT for AD – How it works



# Autologous HCT for AD

## Pre-transplant assessment

- Heart
- Kidney
- Liver
- Lung
- Fertility
- Psychosocial
- Disease specific assessments

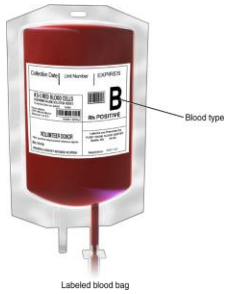
## Mobilization and harvest of peripheral blood stem cells

GIFT OF LIFE

# Autologous Stem Cell transplantation for AD Timetable

Cyclophosphamide
Rabbit ATG

*Conditioning regimen:*
Chemotherapy, total body irradiation, antibodies




PBSC
Infusion

<u>Acute problems:</u>
Low blood counts, fever, risk of infection, need for transfusions, mucositis, diarrhea

Discharge

-5 0 +5 +10 +15

# Autoimmune diseases treated with autoHCT

- Neurological:
  - *Multiple Sclerosis*
  - Myasthenia Gravis
  - Stiff person syndrome
  - Neuromyelitis optica
  - Other
- Gastroenterologic:
  - *Crohn's disease*

Rheumatological:

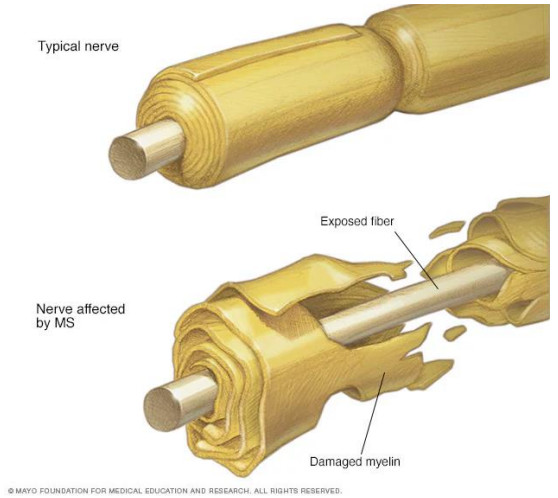
- *Scleroderma*
- Lupus
- Inflammatory myositis
- Rheumatoid Arthritis
- Behcet's disease
- Vasculitis

- Other

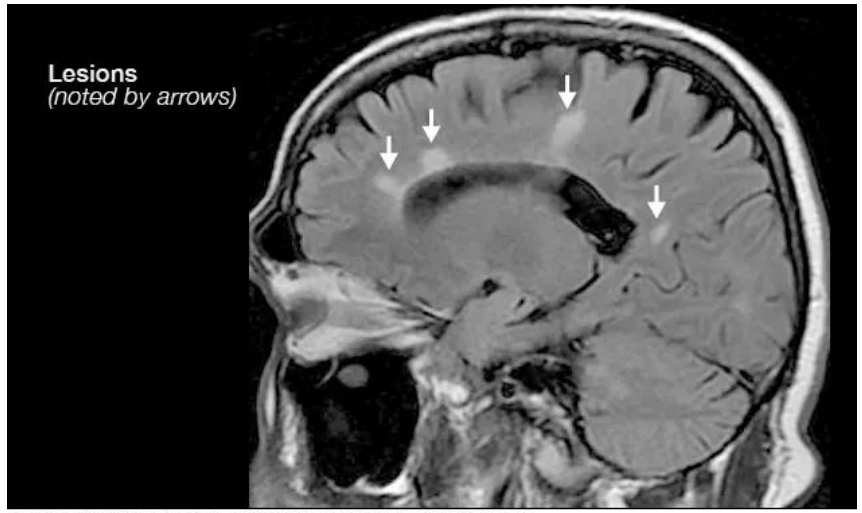
# Multiple Sclerosis (MS)

# Multiple Sclerosis

- Most common cause of neurological disability in young adults
- Median age: 30 years
- Women 3:1
- Immune attack of the myelin, the protective cover of the neuron axons in the brain
- Progressive neurological disability, loss of function







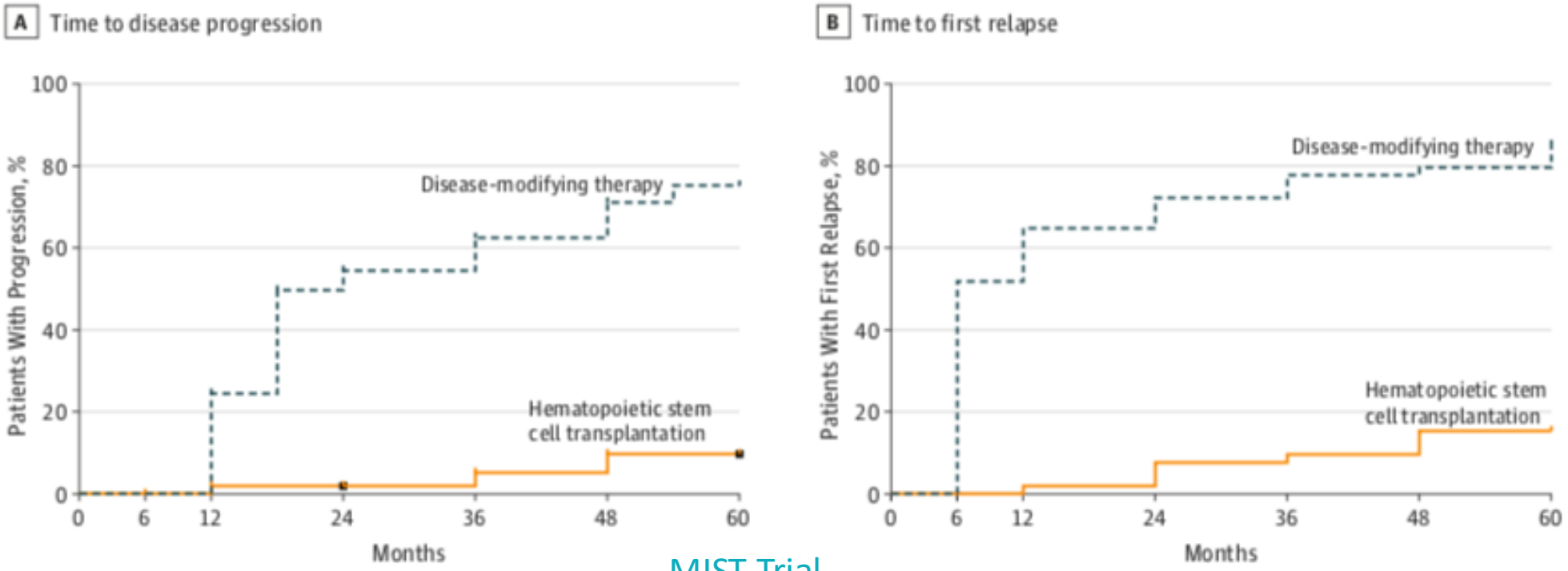
# AutoHCT for Multiple Sclerosis

- MS is the most common AD indication for AutoHCT
- AutoHCT has been used in MS for 20 to 25 years, many published series, one comparative trial
- More commonly used in Europe
- The American Society for Transplantation and Cellular Therapy endorses autoHCT as “an efficacious and safe treatment for active relapsing forms of MS, to prevent clinical relapse, MRI detectable lesion activity, and worsening disability.”

Cohen et al. Biol Blood Marrow Transplant, 2019

# AutoHCT stopped the progression of disease in the vast majority of patients, and was more effective than any other therapy

**Figure 2. Time to Disease Progression and First Relapse Among Patients Receiving Hematopoietic Stem Cell Transplantation vs Disease-Modifying Therapy**

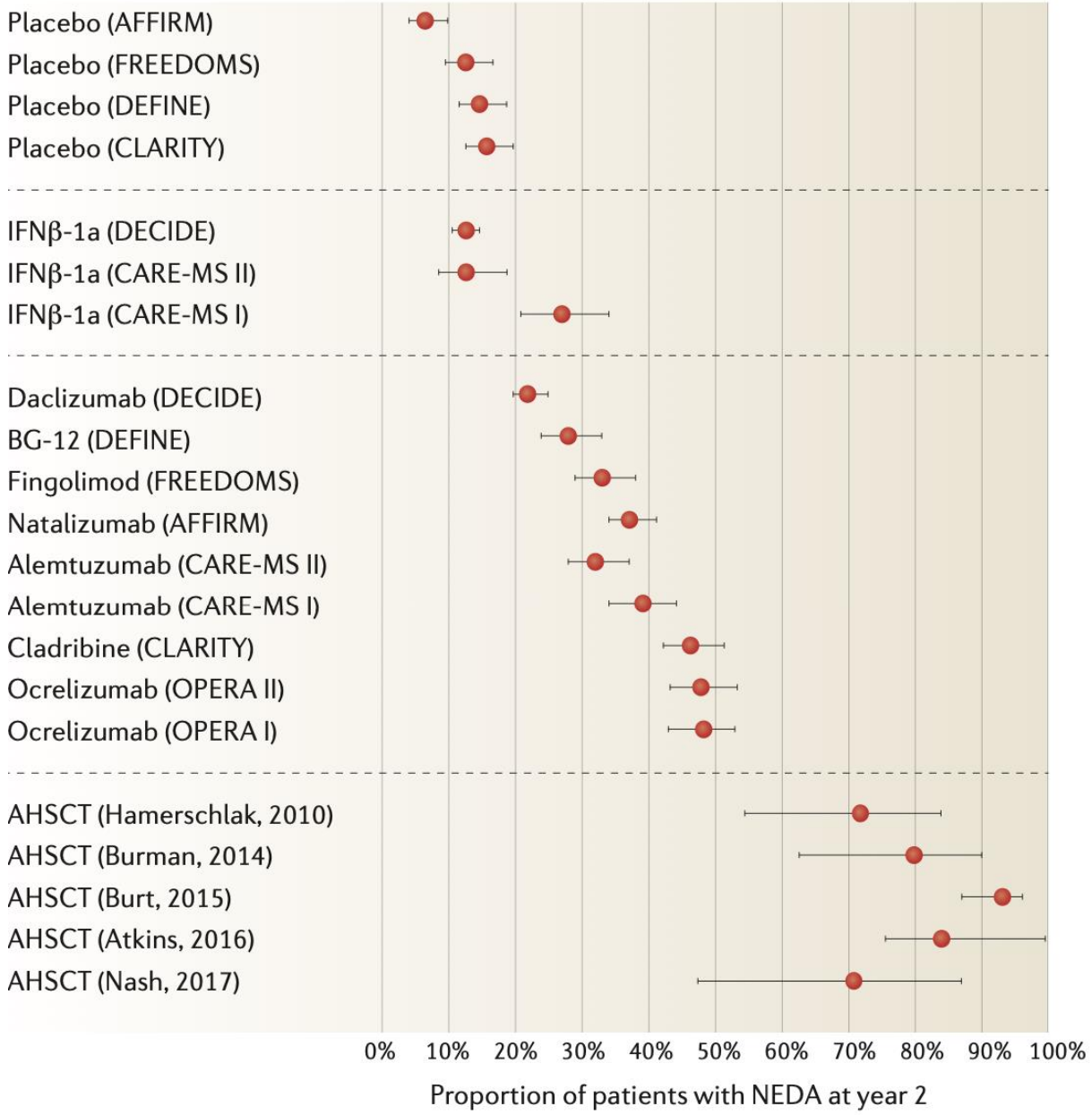



MIST Trial

Burt et al. JAMA 2019

# The efficacy of autoHCT compared with other therapies

NEDA: No evidence of disease activity, by clinical assessment and MRI imaging




Muraro et al. Nature Reviews Neurology 2017

# AutoHCT in Multiple Sclerosis

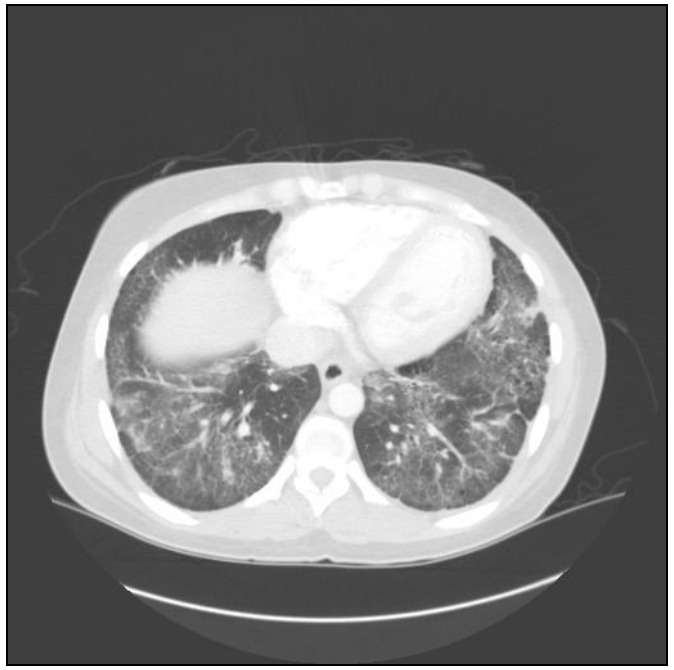
- Effective in the majority of patients
- More effective than standard disease-modifying therapy
- Most useful in the early stages of the disease (relapsing-remitting), before a patient has accumulated neurological damage or progressed to the degenerative phase
- Remission may last decades
- One-off treatment
- Risk of relapse 10 to 20%

# Scleroderma

# Scleroderma (Systemic Sclerosis)

Severe progressive rheumatologic disorder characterized by:

- Vascular damage
- Extensive organ fibrosis (deposition of scar tissue)
- Progressive organ injury



# Scleroderma

- Progressive lung and heart fibrosis
- Renal dysfunction
- Gastrointestinal involvement with poor absorption and weight loss
- Patient is “trapped”
- Mortality is 30% by 10 years

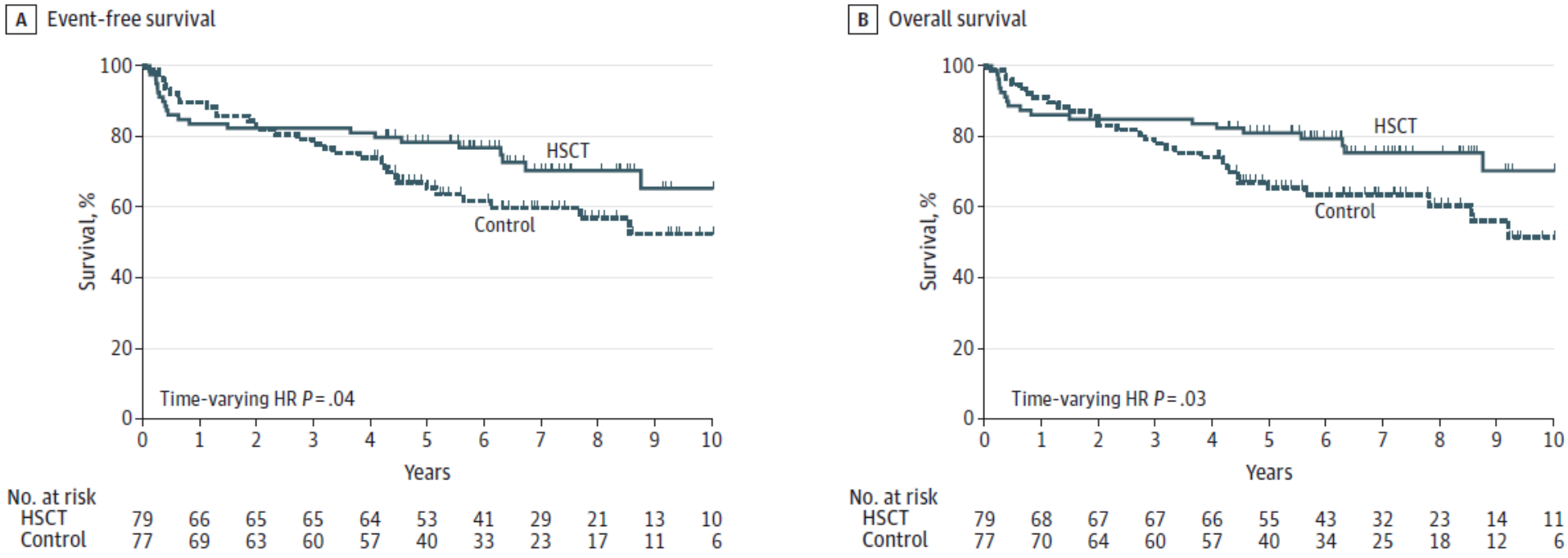
# AutoHCT in Scleroderma

- Three prospective comparative studies (SCOT, ASTIS, ASSIST) proved that autoHCT is superior to best available therapy
- AutoHCT is endorsed as the “standard of care” for patients with scleroderma that fails standard therapy
- AutoHCT:
  - Stops the progression of the disease
  - Allows organ healing
  - Improves quality of life
  - Induces long-lasting remissions

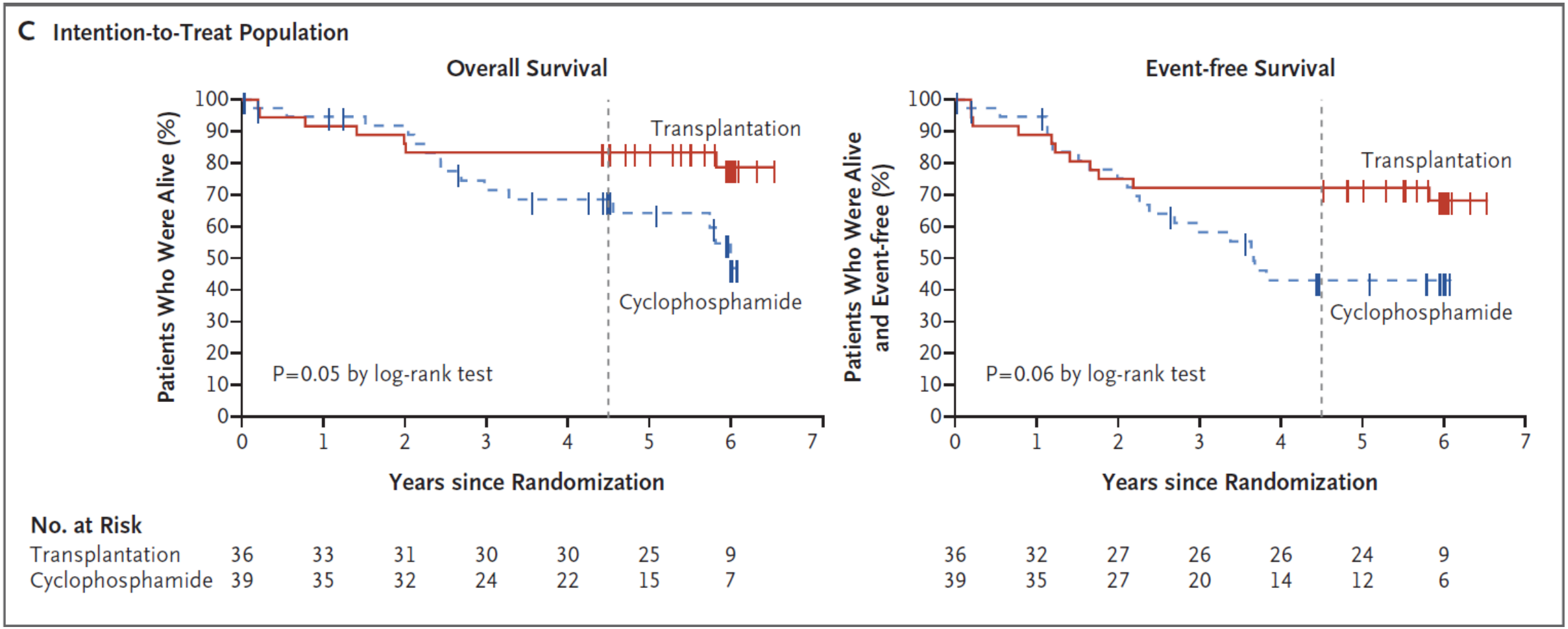
Sullivan et al. Biol Blood Marrow Transplant, 2019

# AutoHCT in Scleroderma – ASTIS trial

Figure 2. Event-Free and Overall Survival During 10-Year Follow-up



# AutoHCT in Scleroderma – SCOT trial



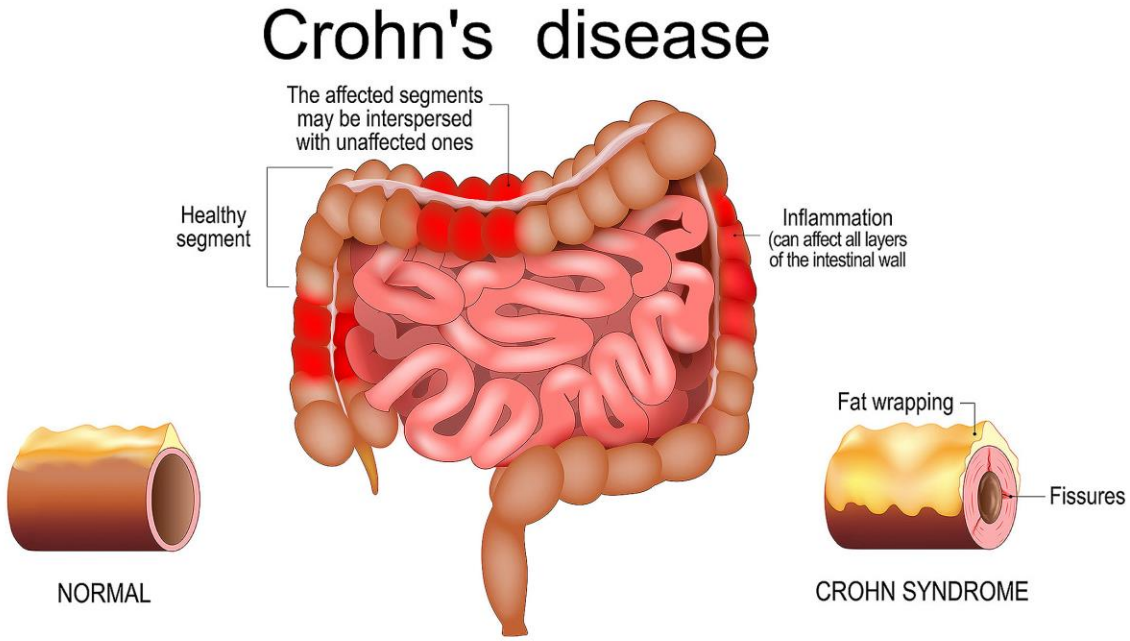
# AutoHCT in Scleroderma – Summary

- More scleroderma patients who receive an autoHCT survive than those on other therapies
- More patients recover their quality of life after autoHCT
- Patients can return to a productive life

# Crohn’s Disease

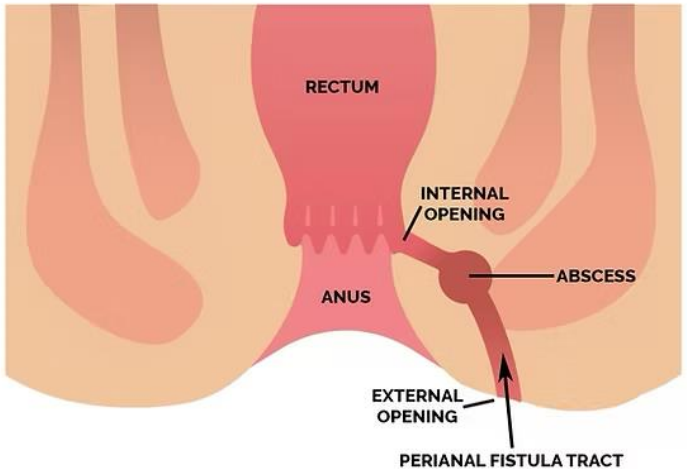
# AutoHCT in Crohn’s Disease

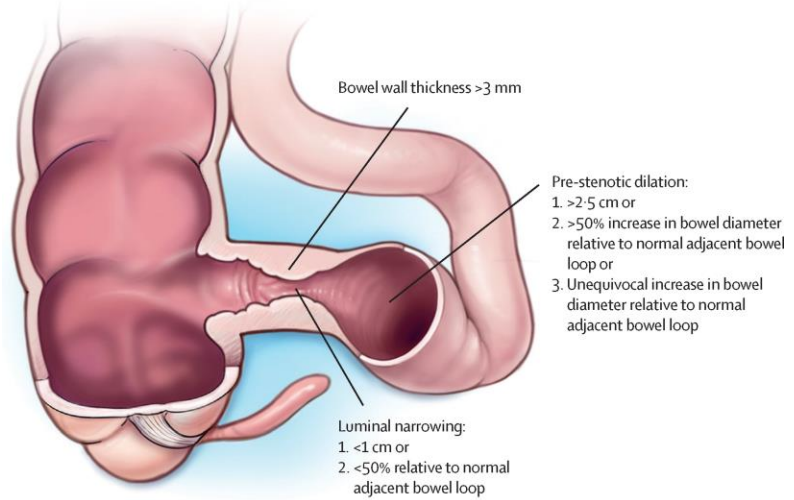
- Crohn’s disease is a severe autoimmune inflammatory disease of the gastrointestinal tract
- Most commonly affects the ileum and colon
- Causes extensive ulceration, with diarrhea, malaise, weight loss



# AutoHCT in Crohn's disease

- It is complicated by the formation of abscesses, fistulas (abnormal communications between bowel and other organs or exterior), strictures (closing of the lumen)
- Frequently requires surgery with progressive loss of bowel



# AutoHCT in Crohn's disease

- AutoHCT can induce long-lasting remissions, free of therapy in a large proportion of patients
- Risk of relapse is higher than in scleroderma or multiple sclerosis
- However, patients who relapse respond to many therapies they have failed in the past, contributing to adequate control of the disease
- Most effective early on

# Can AutoHCT Cure Autoimmune Diseases?

- It is not entirely clear yet
- Many patients have remained in remission for more than 10 years, free of therapy
- Are they cured?

# Who is a good candidate for an AutoHCT for AD?

- Most patients are sent to the transplant doctor as a “last resort.”
  - Many have accumulated irreversible damage
- Should do autoHCT in the first 5 years of the disease after the patient has failed at least two lines of standard therapy.
  - Even sooner in Scleroderma
- The patient should be free of major medical problems that would increase the risk of the transplant
- Early consultation with a transplant physician with experience in AD to establish if the patient is a good candidate

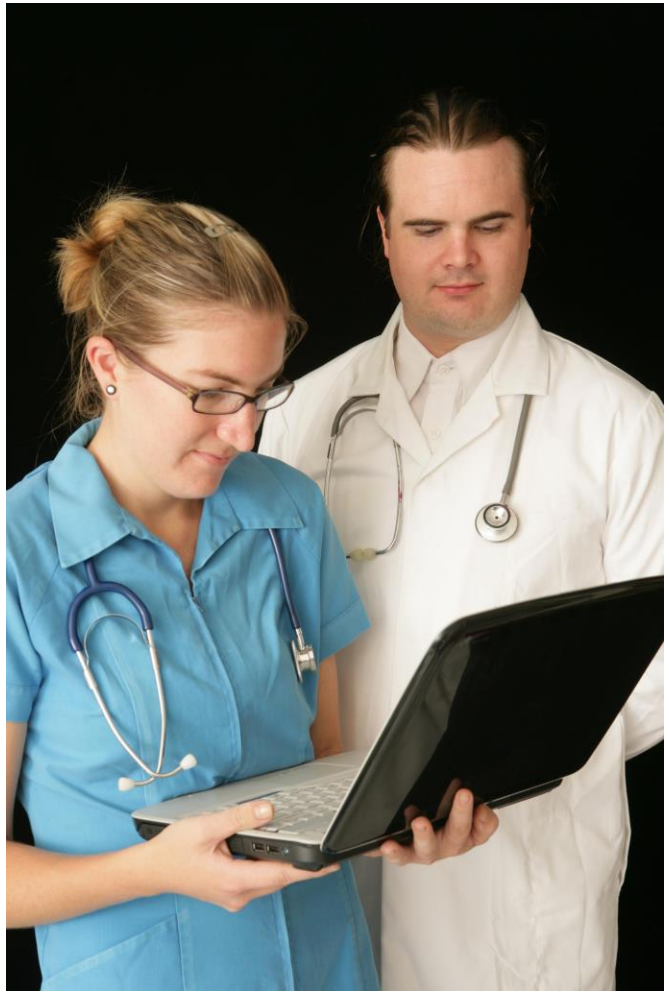
# Teamwork in patients with AD

Close collaboration between the referring specialist and the BMT specialist is critical

Decide who is the right patient and when is the right time is for the transplant

Decide what therapy the patient needs before transplant

Decide adequate follow up after transplant



# Short-term effects of autoHCT in Autoimmune Disease

**They mostly occur in the hospital:**

- Infection
- Organ injury
- Mucositis/enteritis

**After discharge:**

- Infection
- AD symptoms (rare)

# Long-term effects of autoHCT in Autoimmune Disease

Recurrence of AD

Secondary malignancy

Slow recovery and need for intensive support

# Summary

- AutoHCT induces long-term remissions in many patients with AD
- The proportion and duration of remission depends on the primary disease and the number of previous therapies
- AutoHCT leads to a major improvement in quality of life
- Careful patient selection is critical
- It works much better in the early phase of the AD
- Close collaboration between the BMT specialist and the referring specialist is critical

# Questions?

**Ernesto Ayala, MD**
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# Let Us Know How We Can Help You


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