

# HSCT in Crohn's Disease

Long-Term Results

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# Remission Rates

- Corticosteroids acute induction, 40 % long term
- Azathioprine 30 %
- Infliximab 30 % 40-50 % clinical response
- Infliximab plus azathioprine 57 %

# Remission in IBD

- Unclear on a molecular level what remission is
- Conversely, unclear precisely what re-activation is
- Is therapy simply suppression of inflammation allowing for spontaneous remission?

# Therapeutic challenges

- All therapies ineffective for many patients
- Need for surgery, especially stricturing and fistulizing disease
- Disease morbidity
  - Fistulae, obstruction, bleeding, pain
  - Short bowel, malnutrition
  - Narcotic addiction
  - Necessity of parenteral nutrition

# Bottom line

- Dysregulation of immune response underlying pathophysiology
- Removal of offending immunologic makeup should effect improvement or cure

# Theoretical basis

- Immune ablation
- Replacement with immature stem cells not programmed to induce intestinal damage

# Theoretical objections

- Persistent antigens (bacteria, virus, etc.)  
with reexposure to trigger
- Leaky intestinal epithelium (defective  
innate immunity)
  - Increased access to noxious antigens

# Background HSCT

- Immune ablation vs. hemato ablation
- Allogeneic vs. autologous
- Some centers 5 % mortality rate for autologous
- NUMS mortality for autologous 1 %
  - Extensive experience
  - Immune ablation

# Crohn's mortality

- Mortality data limited
- Most longitudinal studies show excess mortality
- Recent study (Gut 2006) showed nearly double expected mortality

# Methods

- Subjects 16-40 years
- Failure standard therapy including Anti-TNF
- CDAI 250-400 or severity index  $> 16$

# Mobilization phase

- Cyclophosphamide plus G-CSF
- Peripheral blood leukapheresis
- CD34+ Immunoselection
- 2,000,000 cells per kg

# Conditioning phase

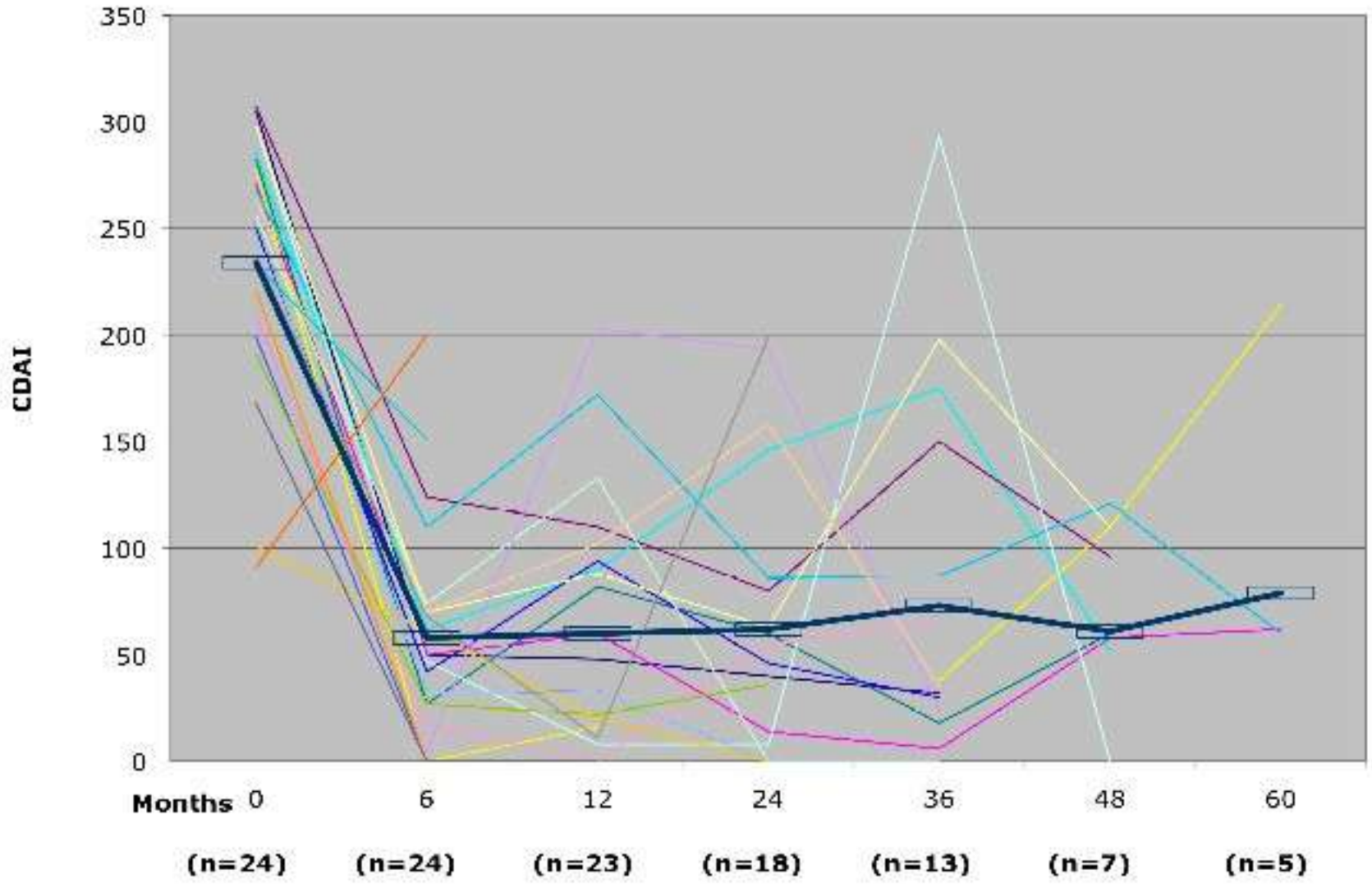
- 1 month later
- Cyclophosphamide higher dose
- ATG, methylprednisolone, G-CSF
- Reinfusion of stem cells

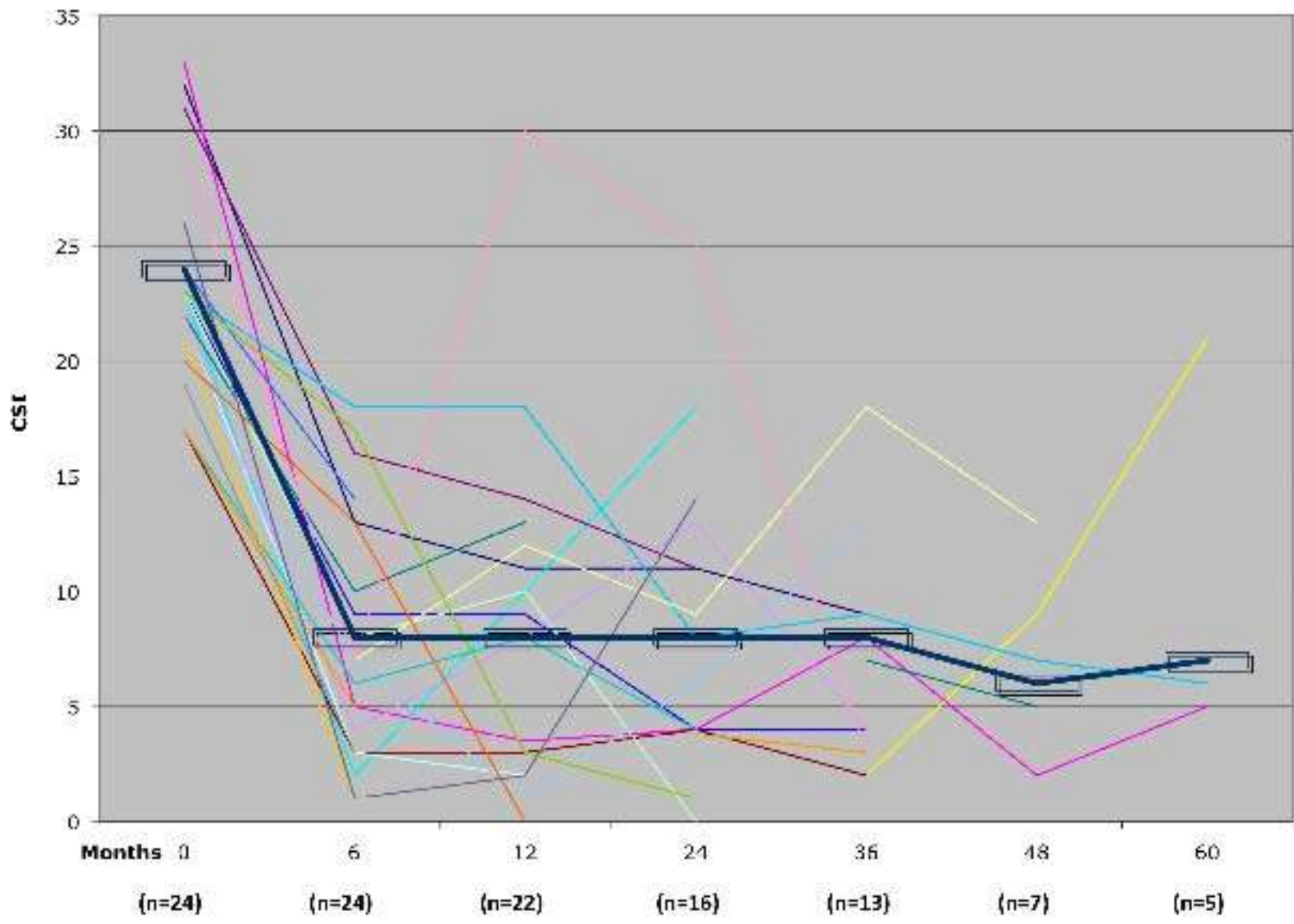
# HSCT course

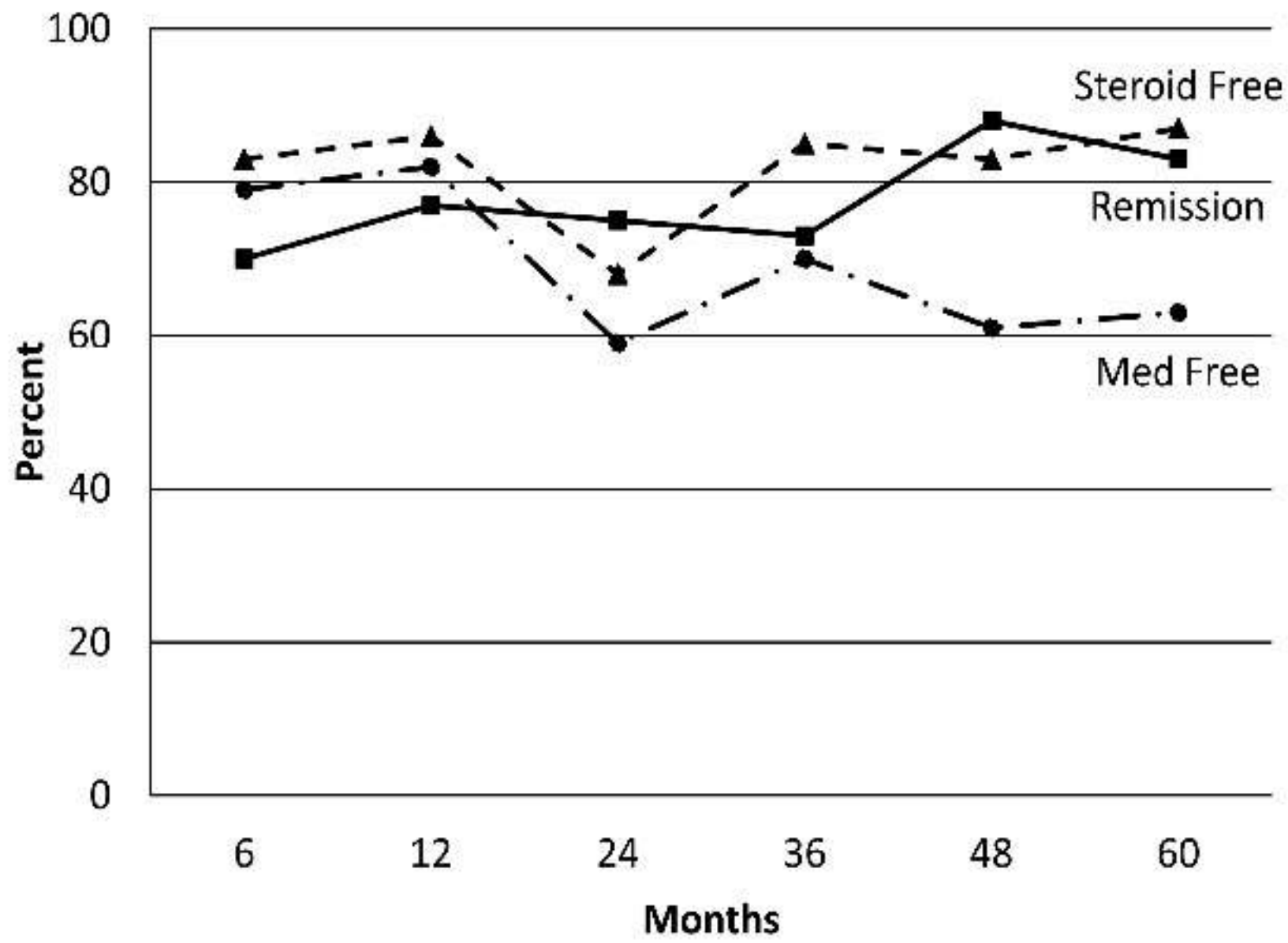
- Most immediate improvement
- All significant improvement/remission
- CD therapy discontinued
- Relapses occur in about 1/3

# Relapses

- When occur, more easily treated
- Different phenotypic expression







# Conclusion

- Immune ablation, HSCT can be performed safely in appropriate medical center
- Long term remissions occur
- Relapses occur in about 1/3, but are more easily treated.