



# Systemic Lupus Erythematosus Treatment

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# Objectives

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- Describe outcome measures of SLE disease activity
- Learn about the non-pharmacological treatments
- Review the medications used to treat SLE, including
  - mechanisms of action
  - doses
  - contraindications
  - potential toxicities
  - monitoring requirements

# A Case Study

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- The patient is a 23 year old married woman with 3 children under the age of 5. She presents with vague complaints of intermittent fatigue, joint pain, alopecia and low-grade fevers.
- Physical examination revealed:
  - Scaly erythematous rash across the nose, cheeks, back & chest
  - Swelling/ tenderness of the bilateral wrist MCP, PIP joints & knees
- Laboratory results:
  - Positive antinuclear antibody titer 1:320
  - Hgb 10 g/dL
  - Low C3 and C4 complements
- Joint X-rays: joint swelling without joint erosions

# ACR (Revised) Criteria for Classification of SLE

4/11 = 95% Specificity; 85% Sensitivity

1. Malar Rash
2. Discoid Rash
3. Photosensitivity
4. Oral Ulcers
5. Arthritis
6. Serositis
7. Renal Disorder
8. Neurologic Disorder
9. Hematologic Disorder
10. Antinuclear Antibody
11. Immunologic Disorder

# What is the patient's diagnosis?

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- Systemic lupus erythematosus:
  - The malar rash
  - Polyarthrititis
  - Anemia
  - Positive ANA titer
  
- What is the disease activity?

# SLE Disease Activity Index

## SELENA-SLEDAI Score

Check box: If descriptor is present at the time of visit or in the proceeding 10 days.

Wt	Present	Descriptor
8	<input type="checkbox"/>	Seizure
8	<input type="checkbox"/>	Psychosis
8	<input type="checkbox"/>	Organic Brain Syndrome
8	<input type="checkbox"/>	Visual Disturbance
8	<input type="checkbox"/>	Cranial Nerve Disorder
8	<input type="checkbox"/>	Lupus Headache
8	<input type="checkbox"/>	CVA
8	<input type="checkbox"/>	Vasculitis
4	<input type="checkbox"/>	Arthritis
4	<input type="checkbox"/>	Myositis
4	<input type="checkbox"/>	Urinary Casts

# SLE Disease Activity Index

## SELENA-SLEDAI Score

Check box: If descriptor is present at the time of visit or in the proceeding 10 days.

Wt	Present	Descriptor
4	<input type="checkbox"/>	Proteinuria
4	<input type="checkbox"/>	Pyuria
2	<input type="checkbox"/>	New Rash
2	<input type="checkbox"/>	Alopecia
2	<input type="checkbox"/>	Mucosal Ulcers
2	<input type="checkbox"/>	Pleurisy
2	<input type="checkbox"/>	Pericarditis
2	<input type="checkbox"/>	Low Complement
2	<input type="checkbox"/>	Increased DNA binding
1	<input type="checkbox"/>	Fever
1	<input type="checkbox"/>	Thrombocytopenia

# What is the patient's SELENA-SLEDAI Score?

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- The malar rash - 2
- Polyarthritits - 4
- Anemia - 0
- Positive ANA titer – 0
- Alopecia - 2
- Low Complement – 2
- Fever – 1
- **Total Score: 11**



# Medications Approved by FDA for Treatment of SLE

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- Aspirin
- Corticosteroids: prednisone, methylprednisolone, dexamethasone
- Hydroxychloroquine (Plaquenil)
- **Belimumab**

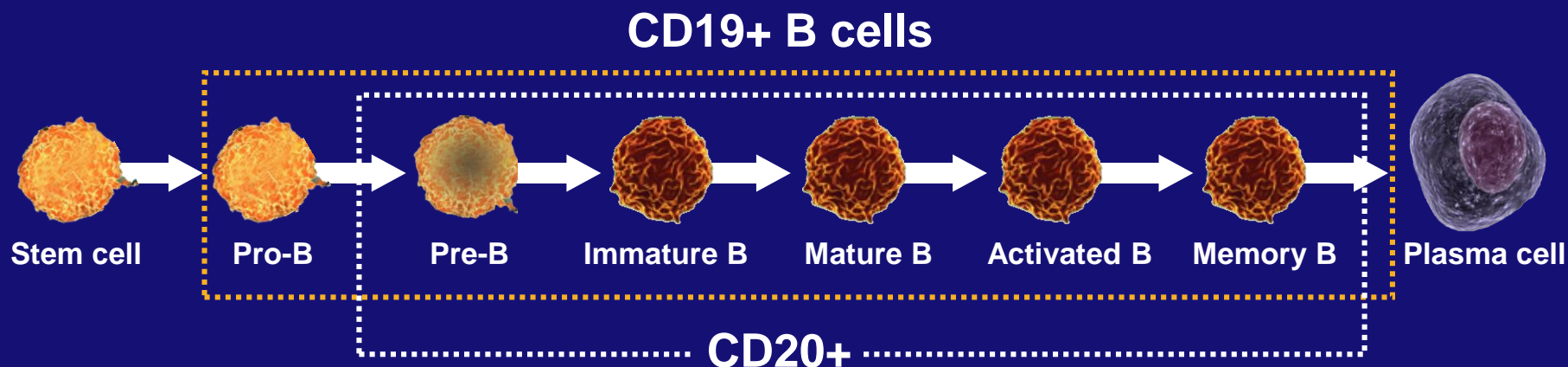
# Immunomodulating Drugs Used Off Label in Patients with SLE

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- Methotrexate
- Leflunomide (Arava)
- Azathioprine (Imuran)
- Mycophenolate mofetil (Cellcept)
- Cyclophosphamide (Cytosan)
- Cyclosporine
- IV Immunoglobulin
- Plasma exchange
- Rituximab
- Thalidomide

# Potential Targets in B-Cell Lineage

Expression of CD20 During B-Cell Maturation<sup>1</sup>

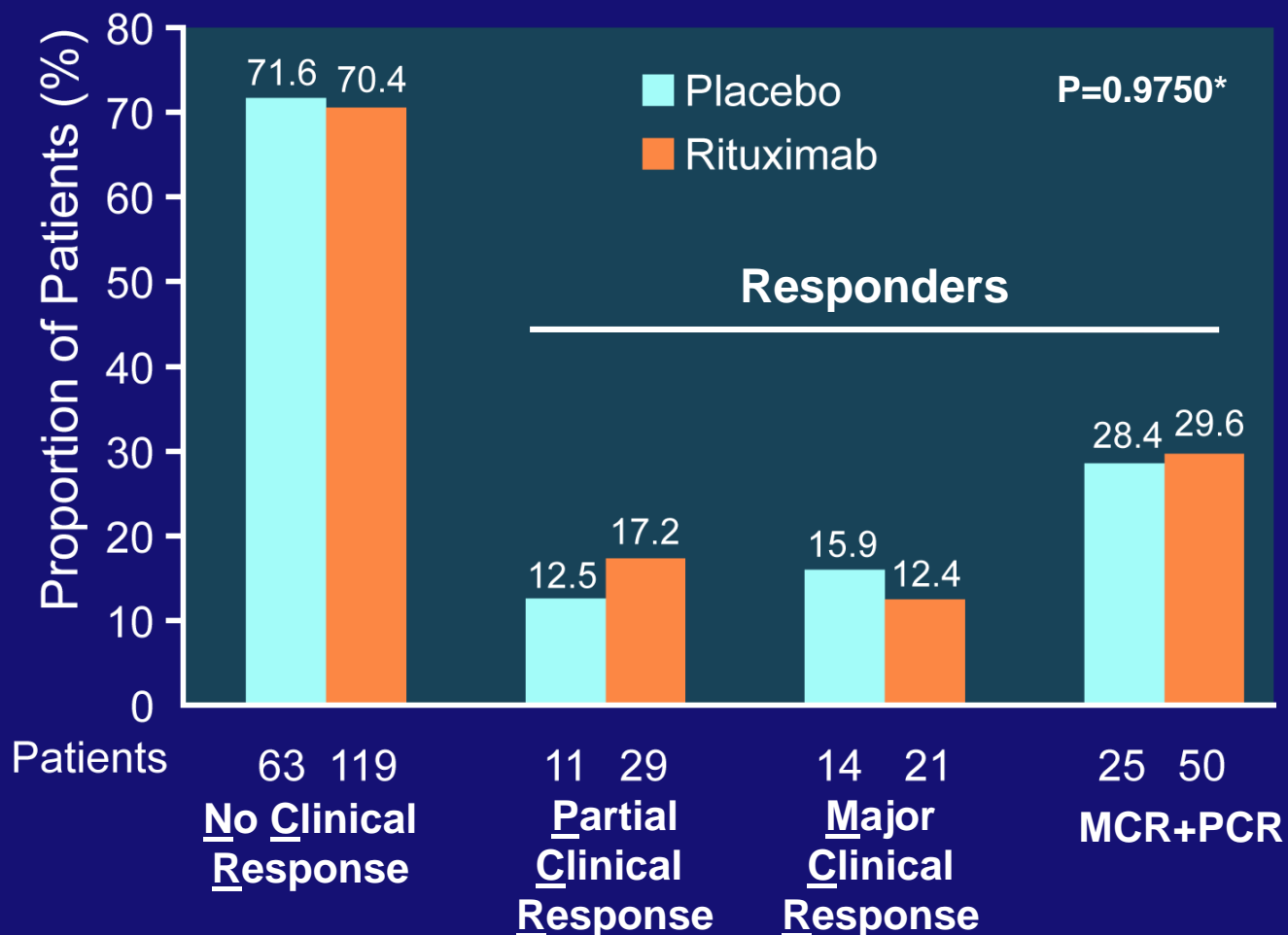


- Rituxan binds specifically to the CD20 antigen located on pre-B and mature B lymphocytes
- CD20 not on hematopoietic stem cells, pro-B cells, normal plasma cells, or other normal tissues

1. Roitt et al, eds. *Immunology*. 6th ed. 2001.

Rituxan® (rituximab) Full Prescribing Information. Genentech USA, Inc., and Biogen Idec Inc. September 2008.

# Phase II Explorer Study did not Meet its Primary Endpoints: No Differences in Patients Achieving Clinical Response (ITT Population)

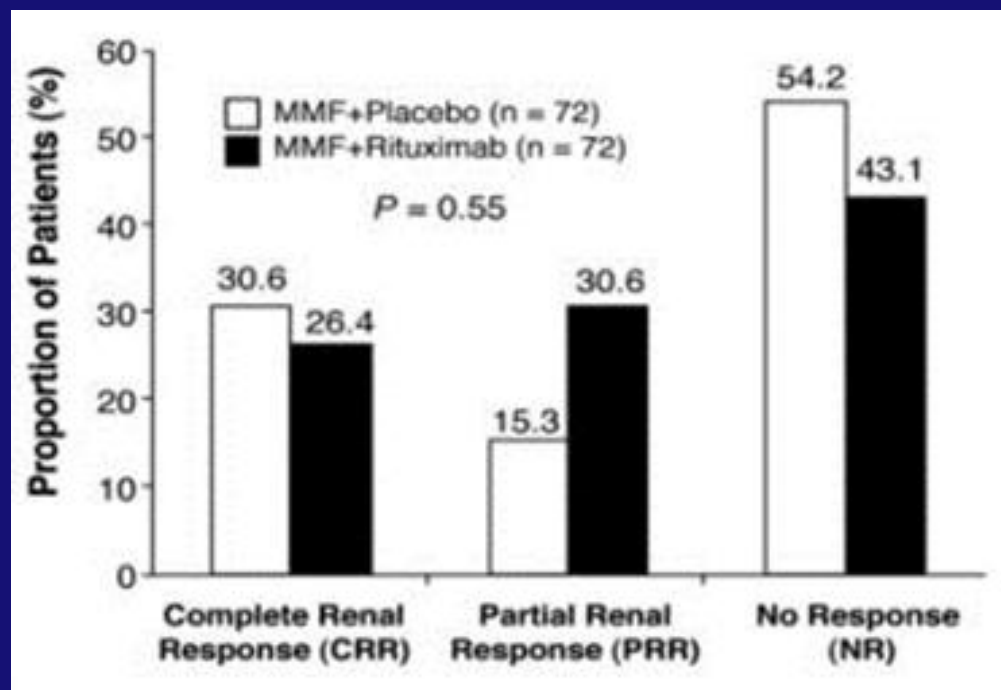


All early terminations treated as NCR.

\*p value is based on Wilcoxon Rank sum test stratified by race and baseline assigned prednisone dose.

# Rituximab (anti-CD20) in SLE: Worth another look?

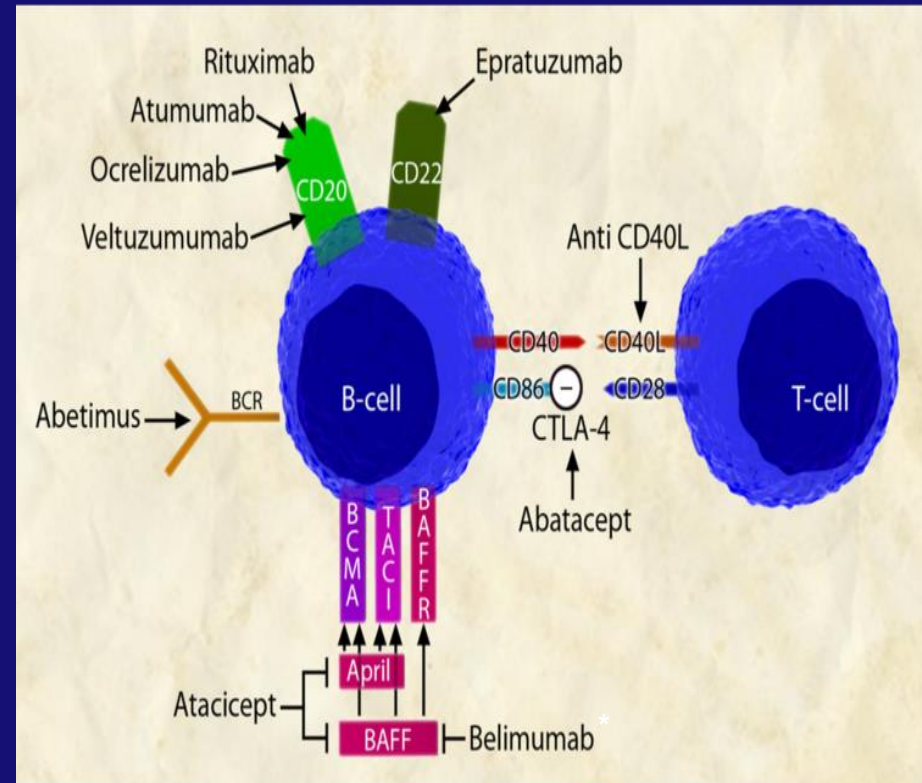
'LUpus Nephritis Assessment with Rituximab' (LUNAR) compared MMF + steroids + placebo with MMF + steroids + rituximab in 144 patients with class III or IV LN.



Failed to achieve primary end point in CR or PR at 52 wks in RTX group. At 1 year there was no difference in the proportion achieving CR but a 15% increase in those achieving a PR in the rituximab group. LUNAR was underpowered

# New Therapeutic Strategies— Targeted Immunotherapy

- Immune targeted therapy
  - B-cell directed
    - anti-CD22 (Epratuzumab)
    - anti-CD20 (Rituximab)
    - anti-BLyS/ BAFF receptors, BLyS & APRIL (Atacicept)
  - Cytokine inhibitors (IL-6)
  - Costimulation blockade
  - Small molecules
  - T regulatory cells
  - Anti-IFN- $\alpha$  and IFN- $\gamma$
- Stem cell transplant



\*Recently FDA approved for lupus

# Case Study cont.

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- The patient was started on Plaquenil 200 mg po BID
- Six month later, she reports tolerating it well. She noticed improvement in her symptoms.
- She denies alopecia and fevers, but still c/o joint pain and fatigue
- Physical examination revealed:
  - No rashes
  - Only mild swelling/ tenderness of the bilateral wrist and knee
- Laboratory results:
  - Hgb 10.3 g/dL
  - C3 and C4 complements still low

# What is the patient's SELENA-SLEDAI Score?

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- The malar rash - 0
- Polyarthritits - 4
- Anemia - 0
- Positive ANA titer – 0
- Alopecia - 0
- Low Complement – 2
- Fever – 0
- **Total Score: 6**



# Case Study cont.

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- The patient was instructed to continue the Plaquenil
- Ten months later, she comes back c/o flare: worse arthralgias, myalgias, fevers, rash and severe LE edema
- Labs revealed:
  - Positive DsDNA antibody
  - C3 and C4 complements have decreased
  - Hgb 9.1 and lymphopenia
  - UA: +3 protein, RBC and WBC, with casts
- Renal biopsy: class IV diffuse proliferative nephritis

# Case Study cont.

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- Methylprednisolone 1000 mg IV x 3 days
- Prednisone 60 mg p.o. daily with taper
- Mycophenolate mofetil 1500 mg po BID
- Hydroxychloroquine 200 mg po BID

# Case Study cont.

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- The patient responded to the therapy
- After 1 year, she was asymptomatic & off the steroids
- Physical exam – normal
- Labs:
  - DsDNA antibody - negative
  - C3 and C4 complements - normal
  - Hgb 11.1, normal differential
  - UA: trace protein, no RBC, WBC, or casts
- Mycophenolate mofetil dose decreased to 1000 mg BID
- Instructed to continue the Plaquenil

# Guiding Therapeutic Strategies

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- Therapeutic combinations aimed at **induction of remission**, **maintenance therapy**, and **supportive therapy**
- Titrate dose to treat effectively with focus on involved organs, and to minimize toxicity
- Strategic use of preventive therapies, antibiotics, and vaccinations
- Cardiovascular screening
- Cancer screening
- Osteoporosis screening

# Summary

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- There are several SLE activity outcome measures:
  - SELENA-SLEDAI, BILAG, SLE Responder Index
- Most of the therapeutic agents for lupus are off label
- Treatment is targeted to
  - Clinical manifestations
  - Severity of organ system involvement
- All immunomodulating agents used to treat lupus carry increased risk of infections and other potential side effects
- Patients require close monitoring