Increasing Minority Participation and Awareness in Clinical Trials (IMPACT) for Lupus

Navigator Training Manual
Training Manual Overview

The following set of modules were developed as part of a training to prepare Navigators to raise lupus clinical trial awareness and education within the IMPACT for Lupus model. Topic area experts - from doctors to clinical trial specialists and health educators - facilitated these presentations to provide Navigators with a general education on lupus and lupus clinical trials. Anyone implementing the IMPACT for Lupus model can draw upon these presentations as part of their Navigator training:

- IMPACT for Lupus Model
- Lupus: for Navigators
- Lupus Nephritis and Ancestry (Presentation by Dr. Brad Rovin)
- Understanding Clinical Research: for Navigators
- Introduction to SLE Clinical Trials (Presentation by Dr. Richard Furie)
Help Us Solve The Cruel Mystery

LUPUS™
FOUNDATION OF AMERICA

Increasing Minority Participation and Awareness in Clinical Trials (IMPACT) for Lupus

Thursday, December 14, 2017
Overview

PART 1

▪ IMPACT for Lupus Background
  – Project Approach
  – Common Barriers to Clinical Trial Participation
  – Pathway to Clinical Trial Participation

▪ IMPACT for Lupus Model

▪ Navigator Role
  – Overview
  – Navigator Steps

PART 2

▪ Material Review
Part 1

BACKGROUND
IMPACT for Lupus

Background: Project Approach

- Grant from the Office of Minority Health
  - Target population: African Americans, piloted through the church

- Community-Based Participatory Research Approach & Collective Impact Model

- IMPACT for Lupus Action Partnership (AP)
  - Lupus Experts
  - Clinical Trial Education Experts
  - Family Physician
  - Community & Church Leaders
  - Industry Representatives
  - Lupus Patient Perspective
IMPACT for Lupus
Background: Pathway to Clinical Trial Participation

- **Awareness**
  - Patient and HCP knowledge, belief and attitudes about CTs
  - Culturally/linguistically appropriate materials about clinical trials (modified by health literacy levels)
  - Knowledge about lupus, treatments and CT as appropriate treatment option
  - Knowledge about where to find clinical trial availability/information

- **Opportunity**
  - Study design: recruitment method, inclusion/exclusion criteria
  - Concerns: cost to patient (i.e., time, transportation, childcare)
  - Provider communication competency and comfort about clinical trials

- **Acceptance**
  - Trust in HCP/system
  - Family decision making
  - Cultural or religious beliefs
  - Perceived benefit

Adapted from Ford et al. 2008
IMPACT for Lupus Model
Development of the Model

PART I: Primary Research Phase
- Systematic Literature Review
- Interviews with Key Opinion Leaders
- Surveyed Physicians and Patients

PART 2: Model Development & Testing
- Model Development
- Material Creation & Testing
- Model Testing (Pilot)
Part 1 cont.

IMPACT FOR LUPUS MODEL
IMPACT for Lupus Model

IMPACT for Lupus Action Partnership Advisory Board

CHURCH ← Navigator (Volunteer Ambassador will support the work of Navigator) → LFA

PATIENT ← HEALTHCARE PROVIDER ← CLINICAL TRIAL (Study Coordinator)
Part 1 cont.

NAVIGATOR ROLE
Navigator Role

Overview

- Navigator Training Video
Navigator Role

Overview

- Educate and raise awareness
  - Provide resources and education on lupus and lupus clinical trials to people with lupus

- Connector
  - Navigator is a trusted resource in and from the community that connects people with lupus to available resources for lupus and on lupus clinical trials

- Encourages patient-physician communication
  - Encourages patients to ask their physician whether a lupus clinical trial is right for them
  - Helps identify the questions patients need to ask their physician
The Navigator is not:

- a medical expert
- a therapist or an alternate for mental health expert
- a financial advisor
- a decision maker or enforcer of care
- a the only resource
Navigator Role
Steps

1. Pray
2. Connect with church leadership
3. Organize a health sermon
4. Organize health workshops or other events
5. Identify potential congregants/families who may be interested in lupus clinical trials and consider direct outreach
6. Connect with patients and primary care physicians with options/availability
7. Counsel on the benefits/opportunities/safeguards/risks of clinical trials
8. Be a resource for patients and clinical trial providers/centers
9. Follow up
10. Pray
Part 2

MATERIAL REVIEW
Material Review

**MAIN**
- What is Lupus?
- What is a Clinical Trial?
- Patient Video

**SUPPLEMENTARY**
- Clinical Trials FAQs
- Lupus FAQs
- Co-Branded Materials (CISCRP, NMA)

**RESOURCES**
- Church Bulletin
- Resource Sheet
- Scriptures
- Current Clinical Trials

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Lupus for Navigators
Topics for Discussion

- Lupus Foundation of America
- What is lupus?
- What are the different types of lupus?
- Who is at risk?
- What are the common symptoms of lupus?
- How is lupus diagnosed?
- How is lupus treated?
- What resources are available for Navigators?
About the Lupus Foundation of America

- National Organization Founded in 1977
- Vision:
  A world without lupus. The organization will advance the science and medicine of lupus to find a cure and improve the quality of life for all people affected by this disease.
- Mission:
  The Lupus Foundation of America is dedicated to improving the quality of life for all people affected by lupus through programs of research, education and advocacy.
73% of the public know little or nothing about lupus

Most at risk are least familiar with lupus

Low awareness results in late diagnosis, increased morbidity, and increased costs

Average several years to get a correct lupus diagnosis

Lupus Awareness
What is Lupus?

- Lupus is a chronic autoimmune disease that can damage any organ or tissue.

- With autoimmune diseases, the body cannot tell the difference between “invaders” (i.e., bacteria and viruses) and the body’s own healthy tissues.

- Attacks the normal tissue causing inflammation, pain and damage.
Lupus is…

▪ Different for each person
▪ Currently not curable
▪ A disease that ranges from mild to life-threatening
▪ Symptoms of the disease may increase (flare), decrease, or stop when the disease becomes inactive (remission)
▪ Lupus is NOT contagious or transmissible nor related to HIV or cancer
Types of Lupus

- Systemic Lupus Erythematosus (SLE)
- Cutaneous Lupus Erythematosus
- Drug-Induced Lupus
- Neonatal Lupus
Systemic Lupus Erythematosus (SLE)

- Commonly referred to as “lupus”
- Most common form of lupus
  - 70% of those with lupus have SLE
- Immune system is said to be overactive
- Can be mild or severe
- Active (flares) and inactive (remission)
- Multi-systemic disease
Central and Peripheral Nervous System
- Seizures, Psychosis, Headaches, Cognitive Dysfunction, Neuropathies, Depression, Low Grade Fever

Heart, Lungs
- Pericarditis, Myocarditis, Endocarditis, Pleuritis, Pneumonitis

Liver, Kidneys
- Edema, Hypertension, Proteinuria, Cell Casts, Renal Failure

Reproductive System
- Pregnancy Complications, Miscarriages, Menstrual Cycle Irregularities

Blood
- Anemia, Thrombocytopenia, Leukopenia, Thrombosis, Circulating Autoantibodies and Immune Complexes

Eyes and Mucous Membranes
- Ulcers in the Eyes, Nose, Mouth or Vagina, Sjögren’s Syndrome

Gastrointestinal
- Nausea, Vomiting, Diarrhea, Weight Changes

Musculoskeletal
- Extreme Fatigue, Arthralgia, Myalgia, Arthritis, Myositis

Skin
- Butterfly Rash, Cutaneous Lesions, Photosensitivity, Alopecia, Vasculitis, Raynaud’s Phenomenon
Cutaneous Lupus Erythematosus

- Accounts for 10% of all lupus cases
- Symptoms may include rashes/lesions, hair loss, vasculitis, ulcers, photosensitivity
- Three major subsets of cutaneous lupus
  - Chronic cutaneous (discoid) lupus
  - Subacute cutaneous lupus
  - Acute cutaneous lupus
- 10% of cutaneous lupus will become systemic lupus
Examples of Cutaneous Lupus

Malar Rash
or
“butterfly rash”

Subacute Cutaneous Lupus

Discoid Lupus Erythematosus
Neonatal Lupus

- A rare condition
- Affects infants of women who have lupus
- Caused by antibodies from the mother acting upon the infant in the womb
- Most infants of mothers with lupus are entirely healthy
Drug Induced Lupus

- Accounts for 10% of lupus cases
- A side effect of long-term use of certain medications
- At least 46 drugs can cause drug-induced lupus.
- Drugs most commonly connected with drug-induced lupus are:
  - Hydralazine (Apresoline®)
  - Quinidine (Quiniglute®)
  - Procainamide (Pronestyl®)
  - Isoniazid®
- Symptoms include joint and muscle pain, arthritis, flu-like symptoms, and inflammation of the heart & lungs, which resolve when drug is discontinued (usually within six months)
What Causes Lupus?

- Exact cause(s) are unknown
- Most scientists believe
  - Genetic predisposition (increases chances)
  - Environmental trigger (can trigger the disease)
    - Exposure to ultraviolet radiation (UVB, UVA)
    - Female hormones
    - Exposure to infections
    - Physical and emotional stress
    - Medications
Who Gets Lupus?

- **Gender**
  - Women are approximately 10 times more likely than men to have lupus.

- **Age**
  - Disease strikes mostly women in childbearing years (15-44).

- **Race and Ethnicity**
  - Hispanic and Black women are 2-3 times more likely to develop lupus.

- **Genes**
  - Relatives of people with lupus have a 20 percent chance of developing lupus but 5 percent of children will develop lupus if their mother has lupus.
Common Symptoms

- Extreme fatigue (tiredness)
- Headaches
- Painful or swollen joints
- Fever
- Anemia
- Swelling in feet, legs, hands, and/or around eyes
- Pain in chest on deep breathing
- Butterfly-shaped rash across cheeks and nose
- Sun or light sensitivity (photosensitivity)
- Hair loss
- Abnormal blood clotting
- Raynaud’s phenomenon
- Mouth or nose ulcers
How is Lupus Diagnosed?

- Review of current symptoms
- Physical examinations by Health Care Provider
  - May need to see specialists
  - This can include blood work and urine tests
- Medical history of close family members
  - Family members with autoimmune diseases
How is Lupus Diagnosed?

- Review of your medical history
- Laboratory tests
  - No single test is used to diagnose lupus
  - An array of different laboratory tests can help arrive at a diagnosis. These tests may include:
    - Urine tests
    - ANA test
    - Anti-dsDNA
    - Anti-Sm
- Tissue biopsies
  - Skin or kidney
Facts About Diagnosing Lupus

- It can be difficult to diagnose because
  - Disease is heterogeneous
  - Symptoms vary greatly and change over time
  - Symptoms can mimic other diseases
  - There is no single diagnostic test

- May require time and multiple medical visits
  - Depending on symptoms may need to see specialists
  - May require seeking specialists more familiar with lupus
  - May need referral to a rheumatologist
How is Lupus Treated?

- Treatments vary for each person depending upon symptoms and organs involved with disease.

- FDA Approved Therapies for Lupus:
  - Antimalarials: Plaquenil®, Chloroquine (Aralen®), Quinacrine
  - Corticosteroids: prednisone, prednisolone, methylprednisolone, and hydrocortisone
  - Monoclonal antibodies: BENLYSTA® (Belimumab)
  - Aspirin
How is Lupus Treated?

- Commonly prescribed therapies
  - NSAID (Non-Steroidal Anti-inflammatory Drugs)
  - Acetaminophen (an analgesic, antipyretic)
  - Immunosuppressive (immune modulators)
    - Cyclophosphamide (Cytoxan®)
    - Methotrexate (Rheumatrex™)
    - Azathioprine (Imuran®)
  - Anticoagulants
    - Heparin (Calciparine®, Liquaemin®)
    - Warfarin (Coumadin®)
Treatment Goals

- The goals of any treatment plan are to:
  - Reduce inflammation caused by lupus
  - Suppress the overactive immune system
  - Prevent flares, and treat them when they occur
  - Control symptoms like joint pain and fatigue
  - Minimize damage to organs
Fatigue may trigger flares, so people with lupus are encouraged to get plenty of rest.

Physical activity is important to do within each person’s ability.

A nutritious, well-balanced, and varied diet that contains plenty of fresh fruits and vegetables, whole grains and moderate amounts of meats, poultry, and fish is recommended.
Lifestyle Considerations

- Smoking increases risk of cardiovascular and pulmonary disease and blood clots, finding a smoking cessation program may help.
- To prevent infections, consider vaccinations
  - No live vaccines (nasal spray vaccine for flu, MMR, shingles vaccines, yellow fever vaccine)
- Stress may trigger flares, management programs or counseling may help.
- If sensitive to UV rays, sun protective strategies can help minimize exposure.
Complimentary Therapies

- It’s important that healthcare providers are aware of complimentary therapies.
- Some people find it beneficial to participate:
  - Tai chi
  - Aerobics
  - Water fitness
  - Meditation
  - Yoga
  - Therapy
  - Pet therapy
  - Light massage
  - Stress management
  - Reiki
  - Acupuncture
  - Talk therapy
The prognosis of lupus is better today than ever before. With close follow-up and treatment, 80-90% of people with lupus can expect to live a normal life span.

Causes of death among people with lupus

- Heart attacks and cardiovascular diseases
- Serious infections, often related to the immunosuppressive drugs, may occasionally be fatal.
If Someone Suspects Lupus

- Refer to health care provider or a rheumatologist if individual has one or several symptoms. Refer to symptoms checklist.

- Advise individuals to
  - Keep track of symptoms.
  - Educate themselves about the disease.
  - Go to their doctor’s appointment prepared to ask questions.

- Emphasize that early diagnosis and proper medical treatment are the best way to manage the disease.
If Someone is Living With Lupus

- Encourage them to
  - Get regular medical care.
  - Take medications as prescribed.
  - Track their symptoms and side effects.
  - Know when to call their doctor.
  - Learn and avoid their triggers.
  - Practice healthy lifestyle behaviors.
  - Keep all medical records.
If Someone Cares For or Loves a Person with Lupus

- Encourage them to
  - Inform themselves about the disease and its symptoms
  - Be understanding
  - Offer help
Resources available to you

- National Resource Center for Lupus, www.resources.lupus.org
  - Online resources
  - Download and print materials
- National Health Educator, #1-800-558-0121
Lupus Nephritis and Ancestry

Brad H. Rovin, MD
Professor of Medicine
Director, Division of Nephrology
Ohio State University
Lupus Nephritis is…

- The most common form of kidney involvement in SLE
- It occurs when immune complexes deposit in the glomeruli (the filtering units) of the kidney and initiate an inflammatory response
- The inflammation in the kidney damages the kidney and results in the loss of protein and blood in the urine
- If untreated the damage can be extensive and permanent and result in chronic kidney disease or kidney failure
The Scope of Lupus Nephritis

- LN may be present in up to 90% of patients with SLE
- This is mainly low-grade, clinically silent disease, but may represent the earliest changes in the natural history of LN
- Clinically important kidney disease in 38% of patients, however there are considerable ethnic differences in LN incidence

<table>
<thead>
<tr>
<th>Population</th>
<th>LN (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>12-33</td>
</tr>
<tr>
<td>Black</td>
<td>40-69</td>
</tr>
<tr>
<td>Asian</td>
<td>47-53</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>48</td>
</tr>
<tr>
<td>Hispanic</td>
<td>35-61</td>
</tr>
<tr>
<td>Overall (n=2290)</td>
<td>37.8</td>
</tr>
</tbody>
</table>
Risk for Developing LN

- **Hierarchy of Risk**
  - Asian (Chinese)
  - Afro-Caribbean; African-American
  - Hispanic
  - Indo-Asian
  - Indigenous (African, Maori, Aborigines, Indian)
  - Caucasian
Ancestry and LN

Developing LN after diagnosis of SLE

- Ancestry Category
  - African-American
  - Hispanic
  - Caucasian


Slides courtesy of Dr. Richard Glassock, 2012
ESRD and CKD in LN

- Based on the United States Renal Data Service Database:
  - 4.4-4.9 cases of ESRD due to LN/million general population
  - 17-20 cases/million Blacks
  - 6 cases/million Hispanics
  - 2.5 cases/million Caucasians

- In the UK, 19% of Caucasians and 62% of Blacks progressed to ESRD

- CKD is also an important outcome of LN. CKD is a non-traditional risk factor for cardiovascular disease. SLE also predisposes to premature cardiovascular disease. Incidence of CKD in LN difficult to estimate
## Response Rates in LN

<table>
<thead>
<tr>
<th>Study</th>
<th>% CRR at 12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUNAR</td>
<td>26-31</td>
</tr>
<tr>
<td>ELNT (Euro-lupus cyc)</td>
<td>30-50</td>
</tr>
<tr>
<td>Dutch Working Party on SLE</td>
<td>30-35</td>
</tr>
<tr>
<td>BMS (CTLA4Ig); LUNAR criteria</td>
<td>6-24</td>
</tr>
</tbody>
</table>
# Enrollment in Recent Trials

<table>
<thead>
<tr>
<th>Race n (%)</th>
<th>Control (n=88)</th>
<th>Low-Dose Voclo (n=89)</th>
<th>High-Dose Voclo (n=88)</th>
<th>Total (n=265)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>42 (47.7)</td>
<td>30 (33.7)</td>
<td>36 (40.9)</td>
<td>108 (40.8)</td>
</tr>
<tr>
<td>Black</td>
<td>5 (5.7)</td>
<td>3 (3.4)</td>
<td>6 (6.8)</td>
<td>14 (5.3)</td>
</tr>
<tr>
<td>Asian (South)</td>
<td>18 (20.5)</td>
<td>22 (24.7)</td>
<td>20 (22.7)</td>
<td>60 (22.6)</td>
</tr>
<tr>
<td>Asian (Other)</td>
<td>18 (20.5)</td>
<td>30 (33.7)</td>
<td>24 (27.3)</td>
<td>72 (27.2)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (5.7)</td>
<td>4 (4.5)</td>
<td>2 (2.3)</td>
<td>11 (4.2)</td>
</tr>
<tr>
<td>Hispanic n (%)</td>
<td>13 (14.8)</td>
<td>9 (10.1)</td>
<td>13 (14.8)</td>
<td>35 (13.2)</td>
</tr>
</tbody>
</table>

## The ACCESS Trial

<table>
<thead>
<tr>
<th>Placebo (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/Male</td>
</tr>
<tr>
<td>Asian</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Hispanics</td>
</tr>
<tr>
<td>Non-Hispanics</td>
</tr>
</tbody>
</table>
Summary

- African Americans with lupus are particularly vulnerable to lupus nephritis
- The consequences of lupus nephritis are severe in African Americans
- The rate of remission of LN is very modest, so new drugs are needed
- African American participation in clinical trials of novel drugs is essential to insure that these drugs are effective in this population
Understanding Clinical Research: for Navigators

Thursday, December 14, 2017
Clinical Research is...

- Research on a particular method, tool, procedure or medicine used to treat individual with specific needs or expand clinical knowledge

- Two main types of clinical studies:
  - Clinical Trials (interventional studies)
  - Observational Studies
How does clinical research work?

Research can be sponsored by:
- Government
- Universities
- Medical Centers
- Patient advocacy organizations
- Physician group

Lab research and pre-clinical research

Interested participants connect with researchers for eligibility requirements

- After U.S. Food and Drug Administration approval (FDA)
- Clinical trial is held on a continuum of 4 phases
4 Phases of Clinical Trials

Phase I
- Experimental intervention in a small group of healthy volunteers (20-80 people)
- Evaluates safety and identifies side effects
- Can take months-years

Phase II
- Intervention is given to a larger group of volunteer (100-500), this time patients with focused disease
- Determines effectiveness and further evaluates its safety within the focused group of patients
- Takes up to 2 years

Phase III
- The intervention is given to larger and more diverse group of patients with focused disease (1,000-3,000 or more), multi-institution, multi-country
- Confirms effectiveness, monitors side effects, and compares it with standard or equivalent treatments
- Longest Phase before FDA approval, 6 months - 2 years

Phase IV
- The intervention is approved by the FDA and made available to the public
- Tracks safety and seeks more information about the intervention's benefits and optimal use
- Ongoing for many years

FDA APPROVAL
So... are there FDA approved treatments for lupus?

- Several medicines have been approved for use in lupus patients:
  - Corticosteroids: Prednisone
  - Aspirin
  - Antimalarials: Plaquenil

- There is only 1 FDA approved medication specifically for lupus... Benlysta
Benlysta

- BENLYSTA is a human monoclonal antibody approved for the treatment of lupus by the FDA on March 9, 2011
- It recognizes & blocks the biological activity of B-lymphocyte stimulator
- First drug approved to treat lupus in 50 years AND is the first drug specifically for lupus
- BENLYSTA targets specific immune cells, rather than the blanket approach of other therapies which suppress the entire immune system
Benlysta limitations

- Not evaluated in patients with severe active lupus nephritis nor severe active CNS lupus
- Has not been studied in combination with other biologics or intravenous cyclophosphamide and therefore not recommended in these situations
- The population size of African Americans in the study was not large enough to determine the effectiveness of BENLYSTA in that population Additional research is needed
- Not approved for use in children
Why do we need more studies?

- Inclusion/Exclusion criteria may eliminate some participants
- Research participant shift: some participants may choose to leave the study
- Specificity: research focuses treatment on one aspect of disease, one trial can’t serve all symptoms
- Lupus is a heterogeneous disease: meaning symptoms are widely variable, thus a variety of treatment options are needed
- We need participants from all people groups; we need more therapy options for all lupus patients
Is Clinical Research a good fit?

Help patient consider Risk/Benefit

**Risk**
- May take time for extra appointments
- May need to leave study
- Trials can be lengthy
- May not receive treatment

**Benefit**
- Be a part of breakthrough for lupus
- Possible free or discounted treatment
- Close supervision
- May receive new treatment

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Who qualifies?

- Interested parties can find clinical trials through:
  - Lupus Foundation of America site:
    www.lupus.org/northeast/pages/clinical-trials
  - Primary Care Provider’s office

- Trials are specific in their selection groups if patient is not eligible for one study, they should ask if another one is available
Before enrolling in trial, ask...

- Physical implications
  - How do the possible risks, side effects, and benefits in the study compare with my current treatment?
  - Will I be allowed to keep taking my other medicines?
  - Will this affect my ability to have children some day?
  - Will I be allowed to keep seeing my regular doctors?
  - Who will be in charge of my care?
  - How often will I have to visit the hospital or clinic?
  - Will hospitalization be required?
  - How will I know that the treatment is working?
Before enrolling in trial, ask...

- Nature of the study
  - What is the purpose of the study?
  - What kinds of tests and treatments are involved?
  - How long will the study last?
  - Will results from the trial be shared with me?

- What kind of study
  - Blind
  - Double blind
  - Double blind randomized
  - Placebo
Are Clinical Trials safe?

- Acute **supervision** by your Clinician
- **Institutional Review Board (IRB)**, an independent ethics committee that monitors clinical trials
- **Informed consent** required by all participants and should outline protocol synopsis of the study
- Patient **confidentiality**
- **Can stop at any point** (just notify your provider)
- Only **FDA approved** trials proceed
Who is the Clinical Trials Team?

- Doctor, Nurses, Social Workers
- Researchers
- Navigators, LFA, Family support
- You
Introduction to SLE
Clinical Trials

Richard Furie, MD
Chief, Division of Rheumatology
Northwell Health
Professor of Medicine
Hofstra Northwell School of Medicine
New York
Current SLE Therapies

- NSAIDs
- Steroids (low dose to “pulse”)
- Antimalarials (hydroxychloroquine; quinicrine)
- Immunosuppressives
  - (MMF; AZA, MTX; calcineurin inh)
- Chemotherapy (cyclophosphamide)
- Biologics (belimumab; rituximab; abatacept)
- Miscellaneous (thalidomide)
- Adjunctive therapies (ACEi; bisphosphonates)
## How Are We Performing Now? (SLE)

<table>
<thead>
<tr>
<th>Drug study</th>
<th>Study type</th>
<th>Year</th>
<th>Endpoint</th>
<th>Placebo response standard of care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belimumab</td>
<td>SLE</td>
<td>2011</td>
<td>SRI</td>
<td>43.6% (B-52); 33.5% (B-76)</td>
</tr>
<tr>
<td>Tabalumab</td>
<td>SLE</td>
<td>2015</td>
<td>mSRI(5)</td>
<td>28%</td>
</tr>
<tr>
<td>Sifalimumab</td>
<td>SLE</td>
<td>2016</td>
<td>SRI</td>
<td>45%</td>
</tr>
<tr>
<td>Rituximab</td>
<td>SLE</td>
<td>2010</td>
<td>Major Clinical</td>
<td>16%</td>
</tr>
<tr>
<td>Epratuzumab</td>
<td>SLE</td>
<td>2016</td>
<td>BICLA</td>
<td>34%</td>
</tr>
<tr>
<td>Blisibimod</td>
<td>SLE</td>
<td>2016</td>
<td>mSRI(6)</td>
<td>42%</td>
</tr>
</tbody>
</table>

## How Are We Performing Now? (LN)

<table>
<thead>
<tr>
<th>Drug study</th>
<th>Study type</th>
<th>Year</th>
<th>Endpoint</th>
<th>Placebo response standard of care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab⁷</td>
<td>LN</td>
<td>2012</td>
<td>CR</td>
<td>31%</td>
</tr>
<tr>
<td>MMF⁸</td>
<td>LN</td>
<td>2009</td>
<td>CR</td>
<td>9%</td>
</tr>
<tr>
<td>Abatacept⁹</td>
<td>LN</td>
<td>2014</td>
<td>CR</td>
<td>3%; 12% (CRrev)</td>
</tr>
<tr>
<td>Abatacept¹⁰</td>
<td>LN</td>
<td>2014</td>
<td>CR</td>
<td>30%</td>
</tr>
<tr>
<td>Sirukumab¹¹</td>
<td>LN</td>
<td>2016</td>
<td>CR (modified)</td>
<td>0%</td>
</tr>
<tr>
<td>BIIB023¹²</td>
<td>LN</td>
<td>2016</td>
<td>CR + &gt; 50% prot red</td>
<td>6% (+ 14% CR 3m run-in)</td>
</tr>
<tr>
<td>Voclosporin¹³</td>
<td>LN</td>
<td>2016</td>
<td>CR (+ pred &lt; 10 mg/d)</td>
<td>19% (6 m); 24% (12 m)</td>
</tr>
</tbody>
</table>

Do We Need New Lupus Treatments?

Absolutely!!!

- Safer therapies
- More effective therapies
- Replace steroids
- Replace immunosuppressives and chemotherapy
- Improve quality of life
- Prevent flares
- Cure!!!
Survival in SLE by Treatment Era

- Cytotoxic Agents
- Glucocorticoids
- Pre-Glucocorticoids

Years After Diagnosis

Probability of Survival

0 1 5 10

0 20 40 60 80 100
What are the Different Types of Research?

• Basic science research
  – “Test tube” research using biologic samples

• Translational research
  – Applied research that bridges basic science research and patient care

• Clinical research
  – Research involving patients
What are the Different Types of Clinical Research?

• Observational studies
  – “Non-invasive” collection of information
  – Questionnaires
  – Epidemiology
  – Registries

• Tissue acquisition studies
  – Provide materials for basic science research

• Clinical trials
  – Interventions with experimental therapies performed with the goal of improving clinical outcomes
What is a Clinical Trial?

• A study designed to yield information about an experimental therapy in development
• Generally sponsored by pharmaceutical or biotechnology companies
• Highly regulated with oversight by FDA and local authorities (IRB: Institutional Review Board) to assure patient protection and safety
• Necessary for new drug development
• Different phases (I-IV)
• Most always placebo controlled and double-blinded
• Successful completion generally means a drug approval
Drug Development Process

- Laboratory discovery
- Preclinical animal studies
  - Efficacy
  - Toxicity
- Human studies
  - Phase I
  - Phase II
  - Phase III
  - Phase IV
Drug Development Process

Goals

• Phase I (~50 patients)
  - Drug metabolism and safety
• Phase II (~100-300 patients)
  - Safety and efficacy
• Phase III (~500-800 patients)
  - Safety and efficacy
  - Two successes required for approval
• Phase IV (after drug approval)
  - Post-marketing surveillance
Why Participate?

1. To advance the search for better and safer therapies
2. To receive state-of-the-art medical care
3. To benefit one’s self, family members, or friends
4. To receive medical care and treatment that might not be affordable
What Are the Risks and Benefits?

• Risks:
  – Time commitment
  – Treatment might not work
  – There may be side effects
  – You might get placebo (not always a bad thing)

• Benefits:
  – Access to state-of-the-art therapy and care
  – The investigational drug might be beneficial
  – Possible modest financial rewards
What Can a Clinical Trial Participant Expect?

• Informed consent process
• Screening
• Randomization (placebo vs. investigational drug)
• Study visits (physical exam, blood tests, surveys, etc.)
• Careful medical attention
How is Safety Ensured?

• Approval by FDA
• Approval by IRB
• Frequent visits monitored by a physician and research coordinator
• Sites are monitored by the sponsor
• Safety data are reviewed by external review boards (DSMB: Data Safety Monitoring Board)
• Safety updates provided to sites
What is the Cost of Participating in a Clinical Trial?

- Generally covered by the study sponsor
- Travel expenses are often reimbursed
- Costs incurred as a result of a drug side effect are generally covered by the sponsor
What Happens After the Clinical Trial Ends?

• Data will be analyzed for safety and efficacy
• Investigational treatment may end or study medication is sometimes provided to all in what is called an open-label extension
• You will be eventually notified of the treatment you received during the study
• If the data are good, the drug advances to the next phase; if in phase III, probable drug approval!
Types of Lupus Clinical Trials

- Extra-renal SLE
- Lupus Nephritis
Design of Extra-Renal Lupus Clinical Trials

• What aspect of SLE is being studied?
  • Global
  • Organ-specific
    • Musculoskeletal
    • Mucocutaneous
Design of Extra-Renal Lupus Clinical Trials

• How does one qualify?
  • Entry criteria
    • Inclusion criteria
      • Disease activity
      • Serologies
    • Exclusion criteria
      • Medications
      • Lab values (safety)
Design of Extra-Renal Lupus Clinical Trials

• How is efficacy measured?
  • Disease activity instruments
    • SLEDAI (several versions)
    • BILAG
  • Composite endpoints
    • SRI
    • BICLA
• Organ-specific
  • Joint scores
  • Skin activity and damage (CLASI)
Design of Extra-Renal Lupus Clinical Trials

• Other measures
  • Ability to taper prednisone
  • Flares
  • Quality of life
  • Fatigue
What to Expect During a Trial

• Screening
  • ICF, history, PE, lab tests, EKG, CXR

• Randomization
  • Surveys, PE, lab tests, drug (oral or parenteral)

• Study visits
  • Interval history, surveys, PE, lab tests
Drugs in Development for SLE

- 1986
- 1996
- 2006
- 2016

Benlysta approved 2011
Lupus Clinical Trials
Won – Loss Record

• Phase 3 or 4:
  • Extra-renal trials: 4 wins
    • Belimumab: BLISS 52; BLISS 76; BLISS-SC; BLISS Northeast Asia)
  • Lupus nephritis: 0 wins
    • None (maintenance phase of ALMS successful)

• Phase 2:
  • Extra-renal trials: 2 wins
    • Anifrolumab (currently in phase 3)
    • Epratuzumab (later failed in phase 3)
  • Lupus nephritis: 1 wins
    • Voclosporin

Lots of losses
Number of Patients Required for SLE Clinical Trials
Why Should Patients Participate?

- The lupus community needs to support the lupus community!
- “Let the other person do it” doesn’t work
- Narrow opportunity for success (companies might get frustrated and divert resources to other diseases)
How Can the Navigator Help?

- Educate patients about SLE
- Direct patients to specialized centers
- Introduce the concept of a clinical trial
- Interact with the trial site and learn more about SLE, medications and clinical trials
Let’s Make this Era the Golden Era of SLE Drug Development

Rheumatoid Arthritis, Psoriatic Arthritis, Psoriasis, Crohn’s Disease, Ulcerative Colitis, Multiple Sclerosis collectively have had over 2 dozen drugs approved since the late 1990’s.

SLE has had just one!!

If interested in participation, ask your lupus doctor or contact the LFA