RHEUMATOID ARTHRITIS

OPTIMIZING DISEASE CONTROL AND PATIENT OUTCOMES IN RHEUMATOID ARTHRITIS

Dr. Cameil Wilson-Clarke
Clinical Pharmacist/ Lecturer
School of Pharmacy
College of Health Sciences
University of Technology, Jamaica
OBJECTIVES

• To outline proposed pathophysiologic mechanisms that result in the inflammation and pathology of Rheumatoid Arthritis (RA).

• To recognize the clinical features of RA.

• To understand the principles behind current and future therapy of RA.

• To identify the pharmacist's role in providing adequate pharmaceutical care for patients living with RA.
RHEUMATOID ARTHRITIS

• A chronic systemic inflammatory condition characterized by potentially deforming polyarthritis and a wide spectrum of extra-articular manifestations.

• It affects the joints and sometimes other organs and tissues throughout the body.

• Extra-articular involvement including:
  • rheumatoid nodules
  • Vasculitis
  • eye inflammation
  • neurologic dysfunction
  • cardiopulmonary disease
  • lymphadenopathy
  • splenomegaly
• Disease course is usually chronic, some patients will enter a remission spontaneously

• It is an auto-immune disease of unknown etiology

• It is a systemic inflammatory disease that is both chronic and progressive in nature.
EPIDEMIOLOGY OF RHEUMATOID ARTHRITIS

- Rheumatoid Arthritis affects 1-2% adult population
- Ratio of women to men = 3:1
- Peak incidence = 30-40 years of age
- >9 million doctor’s visit per year.
- >250,000 hospitalizations per year
• Immunological reaction maybe set off by infectious agent such as virus or bacteria.

• RA induced joint destruction begins with inflammation of the synovial lining.

• Disease process begins in joint where there is edema, vascular congestion, and fibrin exudates.
PATHOPHYSIOLOGY

• Synovial fluid becomes turbid with decreasing viscosity, it becomes swollen and moves into joint space.

• Pannus (highly erosive enzyme-laden inflammatory exudates) invades cartilage and bone surfaces.

• This then cause erosions of bone and cartilage → joint destruction.
Diagram illustrating the comparison between a normal joint and a joint with Rheumatoid Arthritis.

- **Synovial membrane with synovial lining cells**
- **Inflamed thickened synovial membrane**
- **Macrophage (type A synoviocyte)**
- **Fibroblast-like synoviocyte (type B synoviocyte)**
- **Polymorphonuclear leucocyte**
- **Invading pannus**
- **Cartilage**
- **Chondrocyte**
- **Joint capsule**
- **Plasma cell**
- **Dendritic cell**

**Normal** vs **Rheumatoid arthritis**
PATHOPHYSIOLOGY

• **Trigger of Auto immune reactions**
  
  • Occasionally immune cells (T or B lymphocytes) may react to a self-protein while developing in the thymus or bone marrow.

  • These cells are usually killed or inactivated.

  • However a self-targeted immune cell can escape destruction and become activated years later, initiating an autoimmune response.
1. Breakdown of tolerance

2. Deposit of auto Ab complexes in joints

3. Complement activation
   Recruitment/activation of PMNs, macrophages and mast cells through C5aR

4. Pannus formation
   Production of MMPs, cytokines and angiogenic factors
RISK FACTORS

• Many cases are believed to result from an interaction between genetic factors and environmental exposures.

Genetics:

• Evidence that specific HLA class II genotypes are associated with increased risk.

• Most attention has been given to the DR4 and DRB1 molecules of the major histocompatibility complex HLA class II genes.

• More recent investigations indicate that of the more than 30 genes studied, the strongest candidate gene is PTPN22, a gene that has been linked to several autoimmune conditions.
MODIFIABLE RISK FACTORS

- Modifiable:
  - including reproductive hormonal exposures, tobacco use, dietary factors, and microbial exposures.

- Smoking

  - A history of smoking is associated with a modest to moderate (1.3 to 2.4 times) increased risk of RA onset.

  - This relationship between smoking and RA is strongest among people who are ACPA-positive (anti-citrullinated protein/peptide antibodies), a marker of auto-immune activity.

- Reproductive and breastfeeding history

  Hormones related to reproduction have been studied extensively as potential risk factors for RA:
MODIFIABLE RISK FACTORS

• Oral contraceptives (OC):
  • The estrogen concentration of contemporary OCs is typically 80-90% less than the first OCs introduced in the 1960s (15), which may account for the lack of association in recent studies.

• Hormone replacement therapy (HRT):
  • There is mixed evidence of an association between HRT and RA onset
MODIFIABLE RISK FACTORS

• **Live birth history**: Most studies have found that women who have never had a live birth have a slight to moderately increased risk of RA.

• **Breastfeeding**: Recent population based studies have found that RA is less common among women who breastfeed.

• **Menstrual history**: At least two studies have observed that women with irregular menses or a truncated menstrual history (e.g., early menopause) have an increased risk of RA.

• Because women with polycystic ovarian syndrome (PCOS) have an increased risk of RA, the association with an aberrant menstrual history may result from PCOS.
CLINICAL PRESENTATIONS OF ARTHRITIS

• Insidious onset of fatigue, weakness, joint stiffness, vague arthralgias and myalgias in 60-70%.

• Persistent bilaterally symmetrical, early morning joint swelling which occurs often in hand and feet.

• Swelling may be accompanied by pain, redness, warmth and tenderness.
AFFECTED AREAS
PRESENTATIONS OF VARIOUS DEFORMITIES

Swan-neck and Boutonniere deformity
PRESENTATIONS OF VARIOUS DEFORMITIES

Ulnar deviation deformity

[Diagram of MP Ulnar Deviation with labels for Radius and Ulna, and an illustration of two hands showing Ulnar deviation]
Stages of RA

Early

Intermediate

Late
RHEUMATOID NODULES
FIRM, NON-TENDER, AND ROUND TO OVAL; IN THE SKIN, THEY ARISE IN THE SUBCUTANEOUS TISSUE
### Classification Criteria for RA.

**Target population:**
Patients who (i) have at least one joint with clinical synovitis, and (ii) the synovitis not better explained by another disease

Add score of categories A-D, score of ≥6/10 needed to classify patient as having definite RA

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Joint involvement (tender/swollen)</td>
<td>Morning stiffness in and around the joints, lasting at least an hour before maximal improvement</td>
</tr>
<tr>
<td>1 large joint</td>
<td>0</td>
</tr>
<tr>
<td>2-10 large joints</td>
<td>1</td>
</tr>
<tr>
<td>1-3 small joints (with or without involvement of large joints)</td>
<td>2</td>
</tr>
<tr>
<td>4-10 small joints (with or without involvement of large joints)</td>
<td>3</td>
</tr>
<tr>
<td>&gt;10 joints (at least 1 small joint)</td>
<td>5</td>
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</table>

<table>
<thead>
<tr>
<th>B. Serology</th>
<th></th>
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<tbody>
<tr>
<td>Negative RF/ACPA</td>
<td>0</td>
</tr>
<tr>
<td>Low-positive RF/low positive ACPA</td>
<td>2</td>
</tr>
<tr>
<td>High positive RF/high-positive ACPA</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. Acute phase reactants</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Normal CRP &amp; ESR</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal CRP &amp; ESR</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>D. Duration of symptoms</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 weeks</td>
<td>0</td>
</tr>
<tr>
<td>≥6 weeks</td>
<td>1</td>
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</tbody>
</table>

1987 ACR Classification criteria for RA[3]

2010 ACR/EULAR Classification criteria for RA[5]

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DIAGNOSTIC CRITERIA BY AMERICAN COLLEGE OF RHEUMATOLOGY (ACR)

- Requires confirmation of at least 4 criteria
  - Morning stiffness lasting for more than 1 hour
  - Simultaneous arthritis of 3 or more joints
  - Arthritis of hand joints
  - Symmetrical arthritis
  - Rheumatoid nodules
  - Abnormal serum rheumatoid factor
  - Radiographic changes typical of RA on posterior/anterior hand and wrist radiographs
LABORATORY TEST

- Erythrocyte sedimentation rate (ESR)
- Rheumatoid factor (RF)
- Antinuclear antibody (ANA)
- Lupus erythematosus (LE) cell test
- C-reactive protein (CRP) use +ve
- Mild-moderate normocytic, hypochromic, or normochromic anemia
- Synovial fluid
TREATMENT OPTIONS

• NSAIDs, Salicylates, or COX-2 inhibitors

• Glucocorticoids

• Disease Modifying Anti-rheumatic Drug (DMARDs)
  • Biologics
  • Immunosuppressants
GOAL OF THERAPY

• To induce a complete remission
• To reduce joint swelling stiffness and pain
• Preserve range of motion and joint function
• Improve quality of life
• Prevent systemic complications
• Slow destructive joint change
TREATMENTS IN 2008

• The American College of Rheumatology recommendations for initiating or resuming DMARDs and biologic agents:
  • DMARDs
    1. Hydroxychloroquine
    2. Leflunomide
    3. Methotrexate
    4. Minocycline
    5. Sulfasalazine

And, when appropriate, combination DMARDs therapy.
TREATMENTS IN 2008

• Biologic agents
  • Non-TNF
    1. Abatacept
    2. Rituximab
  • Anti-TNF
    3. Adalimumab
    4. Eteanercept
    5. Infliximab
DMARDS: BIOLOGICS

Immunogenicity

Nomenclature

-ximab  Chimeric antibody
-zumab  Humanised antibody
-umab  Human antibody
-cept  Fusion protein
CURRENT TREATMENTS

• The American College of Rheumatology recommends for initiating or resuming DMARDs and biologic agents:

  • DMARDs
    1. Hydroxychloroquine
    2. Leflunomide
    3. Methotrexate
    4. Minocycline
    5. Sulfasalazine

And, when appropriate, combination DMARDs therapy
CURRENT TREATMENTS

• Biologic agents
  • Non-TNF
    1. Abatacept
    2. Rituximab
    3. Tocilizumab

• Anti-TNF
  4. Adalimumab
  5. Etanercept
  6. Infliximab
  7. Certolizumab pegol
  8. Golimumab
INITIATING THERAPY FOR EARLY RHEUMATOID ARTHRITIS

- Patient to be initiated with DMARDs as early as possible to control symptoms and delay disease progression.

- Use of NSAIDs to provide rapid anti-inflammatory and analgesic effects.

- Glucocorticoids are generally reserved for brief period of active disease (low dose oral therapy).
The ACR guideline recommend that patients with early rheumatoid arthritis, low disease activity, and good prognostic factors should be treated with DMARD mono-therapy, such as methotrexate.
TREATMENT:
SIDE EFFECTS THAT MAY OCCUR

- Methotrexate- GI effects such as NVD, pulmonary effects and liver damages. Contraindicated in pregnancy and nursing mothers
- Leflunomide- Liver toxicities. CI in persons with existing liver diseases
- Hydroxychloroquine- GI, blurred vision, night blindness etc, rash, skin pigmentation, hair loss and headache, insomnia
- Corticosteroids- Weight gain, steroid induce Diabetes
- Biologics- Rash, Pain at injection site, leukaemia, possible psoriasis, risk for infections from bacteria, viruses and fungi
• Patients with poor prognostic factors and higher degrees of disease activity should be treated with combination therapy that includes Methotrexate and other drugs such as sulfasalazine and hydroxychloroquine
SWITCHING AMONG BIOLOGIC DUE TO LACK OF RESPONSE OF LOSS OF BENEFIT

• **Scenario 1:** After 3 months of anti-TNF biologic therapy, the patient still has moderate or high disease activity.

• **Treatment recommendation:** Switch to another anti-TNF biologic agent or a non-TNF biologic agent.
SWITCHING AMONG BIOLOGIC DUE TO LACK OF RESPONSE OF LOSS OF BENEFIT

• **Scenario 2:** After 6 months of non-TNF biologic therapy, the patient still has moderate or high disease activity.

• **Treatment Recommendation:** Switch to another non-TNF agent or an anti-TNF biologic agent.
### DMARD prescribing and monitoring information

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Dosage</th>
<th>Monitoring parameters</th>
<th>Adverse events</th>
<th>Cost*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate</td>
<td>Inhibits cytokine production</td>
<td>7.5-25 mg PO/IM/SC weekly</td>
<td>LFTs, CBC, BMP at baseline and every 2-3 mo</td>
<td>Stomatitis, GI, bone marrow suppression, hepatotoxicity, pneumonitis</td>
<td>Solution</td>
</tr>
<tr>
<td></td>
<td>(give in combination with folic acid)</td>
<td></td>
<td></td>
<td></td>
<td>25 mg/mL</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(2 mL) 14.99</td>
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<td></td>
<td>Tablets</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.5 mg</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(30) 33.99</td>
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<tr>
<td>Leflunomide</td>
<td>Inhibits pyrimidine synthesis</td>
<td>100 mg PO daily x 3 days, then 10-20 mg PO daily</td>
<td>LFTs, CBC, BMP at baseline and every 2-3 mo</td>
<td>Diarrhea, alopecia, rash, hepatotoxicity</td>
<td>Tablets</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(30) 39.99</td>
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<tr>
<td>Sulfasalazine</td>
<td>Unknown</td>
<td>500-2,000 mg PO daily</td>
<td>LFTs, CBC, BMP at baseline, then every week x 1 mo, then every 1-2 mo</td>
<td>GI, anorexia, rash, bone marrow suppression, hepatotoxicity</td>
<td>Tablets</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>500 mg</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(100) 18.99</td>
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<tr>
<td>Hydroxychloroquine</td>
<td>Impairs complement-dependent antigen-antibody reactions</td>
<td>200-400 mg PO daily</td>
<td>BMP and ophthalmic exam at baseline and annually</td>
<td>GI, ocular toxicity, rash, alopecia</td>
<td>Tablets</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>200 mg</td>
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<td></td>
<td></td>
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<td>(60) 35.99</td>
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</tbody>
</table>

*Pricing information from www.drugstore.com

Abbreviations: DMARD, disease-modifying antirheumatic drugs; BMP, basic metabolic panel; CBC, complete cell count; GI, gastrointestinal; IM, intramuscular; LFT, liver function tests; PO, by mouth; SC, subcutaneous.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Dosage</th>
<th>Monitoring parameters</th>
<th>Adverse events</th>
<th>Cost*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etanercept</td>
<td>TNF inhibitor</td>
<td>50 mg SC weekly or 25 mg SC twice weekly</td>
<td>Baseline TB skin test, hepatitis B &amp; C screening, CBC</td>
<td>Injection-site reactions, infusion reactions, serious bacterial and fungal infections, TB reactivation, new or worsening CHF, possible increased risk of malignancy</td>
<td>Solution 50 mg/mL (4 mL) $1,903.07 SureClick pen 50 mg/mL (4 pens) $2,030.98</td>
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<tr>
<td>Infliximab</td>
<td></td>
<td>3 mg/kg IV at 0, 2, and 6 weeks, then every 8 weeks (in combination with MTX)</td>
<td></td>
<td></td>
<td>Solution 100 mg, $790.96</td>
</tr>
<tr>
<td>Adalimumab</td>
<td></td>
<td>40 mg SC every 2 weeks</td>
<td></td>
<td></td>
<td>Kit 40 mg/0.8 mL (2) $2,040.01 Kit (pen) 40 mg/0.8 mL (2) $2,055.07</td>
</tr>
<tr>
<td>Golimumab</td>
<td></td>
<td>50 mg SC monthly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Certolizumab pegol</td>
<td></td>
<td>400 mg SC at 0, 2, and 4 weeks, then 200 mg every 2 weeks or 400 mg every 4 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rituximab</td>
<td>B-cell modulator</td>
<td>1,000 mg IV on days 1 and 15</td>
<td></td>
<td>Infusion reaction, reactivation of hepatitis B</td>
<td>Concentrate 10 mg/mL (10) $704.97</td>
</tr>
<tr>
<td>Abatacept</td>
<td>T-cell modulator</td>
<td>500-1,000 mg IV at 0, 2, and 4 weeks, then every 4 weeks 125 mg SC weekly after 1 IV loading dose</td>
<td></td>
<td>Infusion reactions, serious infections</td>
<td>Solution 250 mg (1) $606.98</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>IL-6 inhibitor</td>
<td>4-8 mg/kg IV every 4 weeks</td>
<td>Baseline TB skin test, hepatitis B &amp; C screening, CBC, LFTs, then CBC and LFTs monthly</td>
<td>Infusion reactions, hypertension, neutropenia, elevated LFTs, serious infections</td>
<td></td>
</tr>
</tbody>
</table>

*Pricing information from www.drugstore.com

Abbreviations: CBC, complete blood count; CHF, congestive heart failure; IL, interleukin; IV, intravenous; LFT, liver function test; MTX, methotrexate; SC, subcutaneous; TB, tuberculosis; TNF, tumor necrosis factor
Many emerging biologic treatments are aimed at:
- simplifying dosing
- decreasing adverse events
- improving efficacy in the treatment of Rheumatoid Arthritis.

Pro-inflammatory cytokines such as:
- interleukins (IL)-1
- beta, IL-6,
- IL-17

Look the most promising as target for new monoclonal antibody.
FUTURE AGENTS IN LATE-STAGE DEVELOPMENT FOR RHEUMATOID ARTHRITIS

• These agents work by:
  
  • neutralizing a cytokines or its receptor
  
  • blocking costimulation molecules signaling
  
  • inducing osmotic cell lysis, apoptosis, or depletion of target-cell molecules.
<table>
<thead>
<tr>
<th>Pipeline agent</th>
<th>Therapeutic target</th>
<th>Phase of development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canakinumab</td>
<td>Human anti-IL-1 beta monoclonal antibody</td>
<td>FDA approved for CAPS Phase 2/3</td>
</tr>
<tr>
<td>Gevokizumab</td>
<td>Humanized anti-IL-1 beta monoclonal antibody</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Sirukumab</td>
<td>Human anti-IL-6 monoclonal antibody</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>Human anti-IL-17A monoclonal antibody</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Ofatumumab</td>
<td>Human anti-CD20 monoclonal antibody</td>
<td>FDA approved for CLL Phase 3</td>
</tr>
<tr>
<td>Veltuzumab</td>
<td>Humanized anti-CD20 monoclonal antibody</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Belimumab</td>
<td>Human monoclonal anti-BLyS antibody</td>
<td>FDA approved for SLE Phase 2</td>
</tr>
<tr>
<td>Atacicept</td>
<td>Recombinant fusion protein targeting BLyS and APRIL</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Denosumab</td>
<td>Monoclonal antibody that targets RANKL</td>
<td>FDA approved for osteoporosis Phase 2</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>JAK Inhibitor</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Fostamatinib</td>
<td>Syk Inhibitor</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Apremilast</td>
<td>PDE4 Inhibitor</td>
<td>Phase 2</td>
</tr>
</tbody>
</table>

Abbreviations: APRIL, proliferation-inducing ligand; BLyS, B-lymphocyte stimulator; CAPS, cryopyrin-associated periodic syndromes; CLL, chronic lymphocytic leukemia; JAK, janus kinase; IL, interleukin; PDE4, phosphodiesterase type 4 Inhibitor; RANKL, receptor activator for nuclear factor kappa-B ligand; SLE, systemic lupus erythematosus; Syk, spleen tyrosine kinase
FUTURE AGENTS IN LATE-STAGE DEVELOPMENT FOR RHEUMATOID ARTHRITIS

- **Canakinumab**
  - A fully human anti-IL-1 beta monoclonal antibody currently FDA approved for treatment of cryopyrin-associated periodic syndrome (CAPS).
  - It is now being investigated for Rheumatoid Arthritis in phase 2 and phase 3 trials.
  - It is hoped that canakinumab will be found to be more effective than anakinra due to greater affinity to IL-1.
FUTURE AGENTS IN LATE-STAGE DEVELOPMENT FOR RHEUMATOID ARTHRITIS

• **Gavokizumab**

  • Humanized anti-IL-1 beta monoclonal being investigated for many auto-inflammatory conditions including Rheumatoid Arthritis.

  • Data from preclinical trials showed that it may be effective and well tolerated; however, the only phase 2 study for Rheumatoid Arthritis was suspended at the end of May 2011.
FUTURE AGENTS IN LATE-STAGE DEVELOPMENT FOR RHEUMATOID ARTHRITIS

- **Sirukumab**
  - Human anti-IL-6 monoclonal antibody; phase 2 studies are planned for patients with Rheumatoid Arthritis.
  
  - So far in studies, a 20% improvement in ACR 20 was seen in 75% of patients taking sirukumab compared to 21% of patients taking placebo and treatment was well tolerated.
FUTURE AGENTS IN LATE-STAGE DEVELOPMENT FOR RHEUMATOID ARTHRITIS

• **Secukinumab**
  
  • Human anti-17A monoclonal antibody currently under phase 3 development for multiple diseases, including Rheumatoid Arthritis.

  • The first study completed in 2010 included patients with psoriasis, Rheumatoid Arthritis, and chronic non-infectious uveitis.

  • Response rate was good, with 50% patients responding to treatment by 4 weeks.
FUTURE AGENTS IN LATE-STAGE DEVELOPMENT FOR RHEUMATOID ARTHRITIS

• **Ofatumumab and Ocrelizumab**
  - Both anti-CD20 molecules, that are similar to rituximab in their basic mechanism of action.
  - Both have fewer mouse-protein sequences in molecular content than rituximab the expectation is that allergic reactions will occur less frequently
FUTURE AGENTS IN LATE-STAGE DEVELOPMENT FOR RHEUMATOID ARTHRITIS

• **Tasocitinib**

  • Is an inhibitor of the protein kinase JAK-3, a key molecule in the intracellular activation cascade that occurs when various cytokines bind to leucocytes.

  • The first large scale trials with tasocitinib have indeed suggested excellent efficacy compared to placebo, well in line with anti-TNFs
• Tasocitinib

• The side-effect profile that has emerged from the trials may in part be related to the fact that tasocitinib is not 100% specific for JAK-3 and it could also block JAK-2, which could lead to neutropenia, thrombocytopenia, and anemia (mild and manageable in trials)
FUTURE AGENTS IN LATE-STAGE DEVELOPMENT FOR RHEUMATOID ARTHRITIS

- **Fostamatinib**

  - Small molecule inhibitor of the protein kinase Syk, which plays a role similar to that of JAK-3.

  - Phase II clinical trials have supported an acceptable safety similar to Tasocitinib, and efficacy was encouraging in some trials but not all trials.
The drugs under investigation for the treatment for rheumatoid arthritis are geared to:

- target specific receptors, cytokines and other inflammatory mediators that are actively involved in the disease process.

- This is to increase the efficacy of treatments and decrease the side effects.
FUTURE AGENTS IN LATE-STAGE DEVELOPMENT FOR RHEUMATOID ARTHRITIS

• DMARDs and biologic will continue to be the standards of care until newer agents can prove superiority in terms of efficacy, safety, and ease of use.

• Unknown how these agents compare to the current biologics as no head-to-head trial to date.
  • Adalimumab and rituximab in Europe (2012) awaiting results

• Most studies are on patients who have already failed current therapy, likely niche for these newer pipeline agents may be for RA that is more severe.
ROLES OF THE PHARMACIST

• Counsel patients on how to take their Rheumatoid Arthritis medications.

• Stress the importance of compliance to medication regimen.

• Assist physician to individualized Rheumatoid Arthritis therapy.
ROLES OF THE PHARMACIST

- Monitor for adverse events that are associated with Rheumatoid Arthritis medications.
- Recommends over-the-counter anti-inflammatory/analgesics for rapid pain relieve.
- Educate patients about disease condition and how to identify adverse events.
EVALUATION OF THERAPEUTIC OUTCOMES

- Based primarily on improvements of clinical signs and symptoms of RA.

- Clinical signs of improvement include:
  - a reduction in joint swelling
  - decreased warmth over actively involved joints
  - decreased tenderness to joint palpation.

- Improvement in RA symptoms includes:
  - reduction in perceived joint pain and morning stiffness
  - longer time to onset of afternoon fatigue
  - improvement in ability to perform activities of daily living
EVALUATION OF THERAPEUTIC OUTCOMES

- Improvement of activities of daily living may be assessed objectively using a Health Assessment Questionnaire score.

- Joint radiographs may be of some benefit in assessing the progression of the disease and should show little or no evidence of disease progression if treatment is effective.

- Laboratory monitoring is of little value in monitoring individual patient response to therapy.
The order of DMARD or biologic agent choice is not clearly defined. No direct comparative studies exist for biologics to guide in the determination of optimal treatment order.

Should combination DMARD be tried before biologic agents?

Even the best therapy available today does not completely eliminate all signs and symptoms of disease for most patients. How much treatment is enough?

Some patients show evidence of disease progression in spite of apparent control of clinical symptoms. How can these patients be identified and treatment course changed before progression occurs?
CONCLUSIONS

• Rheumatoid arthritis is the most common inflammatory arthritis, affecting approximately 1% of the population.

• The disease is characterized by symmetrical swelling and stiffness of the involved joints. The stiffness is usually more prominent in the morning.

• Extraarticular features of RA include rheumatoid nodules, vasculitis, and ocular, cardiac, and pulmonary complications. The course of the disease is highly variable.

• Treatment is aimed at relieving pain and inflammation and maintaining and preserving joint function.

• Nondrug therapy, including exercise and adequate rest periods, should also be used early in the course of treatment.
CONCLUSIONS

- Early use of a DMARD or biologic agent results in better patient outcomes. Methotrexate, sulfasalazine, and hydroxychloroquine are often considered for initial therapy.

- Biologics have shown to be effective in these patients but may be considered 2nd choice because of cost considerations.

  - They are effective in patients who fail to achieve adequate response from nonbiologic DMARDs.
CONCLUSIONS

• Combination DMARDs or biologics may be considered in those who fail adequate trials of single-agent therapy.
  • Corticosteroids and NSAIDs may be useful adjuncts for treatment, but because of adverse effects and limited impact on long-term outcomes, they should not be considered as sole treatment for most patients.

• Early use of a DMARD or biologic agent results in better patient outcomes.
  • Methotrexate, sulfasalazine, and hydroxychloroquine are often considered for initial therapy.
REFERENCES

• FDA. Drugs@FDA. FDA Approved Drug Products. Canakinumab (Ilaris).

REFERENCES


REFERENCES

• 2012 update of the 2008 America College of Rheumatology Recommendations for the Use of Disease-Modifying Anti-rheumatic Drugs and Biologic Agents in the Treatment of Rheumatoid Arthritis.

A Phoenix Represents My Life With Rheumatoid Autoimmune Disease

THANK YOU
Five years ago I was diagnosed with rheumatoid arthritis (RA). The jury is still out as to whether I really have it since after various tests, here and abroad, I have never tested positive. I was diagnosed based on symptoms. Although I like to tell myself that I do not have RA (optimistic bias on my part), I have taken some steps to treat it—lifestyle strategies and prescription medication.

Many of these are grossly expensive, but help is here—the National Health Fund subsidises the cost of RA treatment.

Dahlia McDaniel is a pharmacist and final-year doctoral candidate in public health at the University of London; email: yourhealth@gleanerjm.com.
Do you or a loved one have rheumatoid arthritis (RA)? If so, painful and crippling symptoms may make you feel like a prisoner in your own body. Consider a research option if you have tried treatment with no success.

Don’t delay — it’s time to start exploring potential research options for RA. If you meet the study criteria, you’ll receive at no cost:

- Investigational drug being studied for RA
- Study-related visits and lab tests
- Compensation up to $500 for your time and travel

Please visit RAStudy.com or call toll-free 1-877-232-2126 anytime — 24 hours a day, seven days a week.

- Location: Puerto Rico, Throughout USA
- Post ID: 2744282 Jamaica
• Meeting: Rheumatoid Arthritis Support Group

• Thursday, June 27, 2013

• Contact:
  • Mrs. Hermine Metcalf
  • Email: hermine.metcalf@gmail.com
  • Cell: 361-9206 or 406-2031