Biologic Therapies- The Changing Landscape of the Management of Rheumatoid Arthritis

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Established in 1959, 321 Canada Gairdner International Awards have been given to scientists from 15 countries; of these recipients, 82 have subsequently won the Nobel Prize.

- Great research has no borders. The Gairdners ...Canada’s only major international scientific prize, inspire medical research, present and future. They are ours, but they belong to the world.

Globe and Mail, Editorial October 2009
"For the discovery of anti-TNF therapy for the treatment of rheumatoid arthritis and other inflammatory diseases"

Sir Ravinder Maini
"For the discovery of anti-TNF therapy for the treatment of rheumatoid arthritis and other inflammatory diseases"

• Sir Marc Feldman
The Impact

They discovered the first treatment for RA, using monoclonal antibodies which are genetically engineered natural defense molecules. Not only was this a novel treatment, but it was the first demonstration of the efficacy of a biological therapy for a chronic autoimmune disease and led to the recognition by the pharmaceutical industry that biological drugs are a viable class of therapeutic agents that can compete with traditional chemical drugs. The effective results have not only transformed the treatment for patients, but have led to other successful anti-TNF treatments, and encouraged much further work using antibodies for treatment.
The Past
• 1000 RA patients treated at the Royal Devonshire Rehab Hospital in Buxton, England from 1953-1958
• Most patients substantially disabled bed bound, 84% moderately to severely disabled
• 60% between the ages of 40-60 years
• Admitted for “relatively short” stay- 3 months
• Work resettlement issues- patients systemically unwell, relapse rate high, effects small and large joints
• Upon discharge 33% fit for work, and at follow up > 50% disabled
• Conclusion: “Having returned to work in a single year would cover the cost of treatment of all RA patients treated in our rehab unit”
What has changed? What is the present

• Early recognition and early treatment of RA
• Treat to target
• Use of combination DMARDs
• Effective new therapies- biologics!
Traditional Treatment Pyramid for RA

Self-management: education, rest, exercise

NSAIDs and analgesics

Immunosuppressants, gold-based drugs, and antibiotics

Experimental drugs and procedures

Intra-articular corticosteroid injections

Mechanical: orthopedic and surgical
Disease Duration Predicts Response to Treatment in RA

N=1435

Proportion of Patients Improving 20%

Disease Duration (Years)

Joint Erosions Occur Early in RA

- Up to 93% of patients with <2 years of RA may have radiographic abnormalities
- Erosions can be detected by MRI within 4 months of RA onset
- Rate of progression is significantly more rapid in the first year than in the second and third years

Course of RA Over 30 Years: Schematic Representation

Severity (Arbitrary Units)

- Inflammation
- Disability
- Radiographs

Duration of Disease (Years)

Treatment

• Therapies for Active RA after Methotrexate Failure- N Engl J Med 2013; 369:307-318- 48 week double blind non inferiority trial of 253 patients demonstrating the non inferiority of triple therapy vs etanercept and MTX

• 27% at week 24 required a switch of therapy

• Swefot and TEAR trials also demonstrated efficacy of DMARDs in early disease
CATCH- Canadian Early Arthritis Cohort

- 19 sites in Canada, 1450 patients
- <50% clinical remission despite methotrexate, jrheum 2010
- Results of disease activity different at different sites with best results from sites using combination therapy and sc MTX: jrheum 2013
Treat to Target

The Results

• 8 biologic therapies on the market in Canada with various mechanisms of action
• 60/40/20 rule, about 30% in clinical remission
• Few in patient beds in the country for patients with rheumatic diseases
• Orthopedic surgery almost eradicated in this population
• Decrease in cardiac disease and other co-morbidities
Evolution of cost structures in rheumatoid arthritis over the past decade

• BMJ January 2014
• Cost increase of €4914 to €8206 in patients aged 18–64, and from €4100 to €6221 in those aged ≥65, attributable to increasing prescription of biologic agents (18–64 years from 5.6% to 31.2%, ≥65 years from 2.8% to 19.2%).
• Decrease in hospitalization, disability and sick leave
“Given the trend to earlier treatment initiation, improved treatment strategies with conventional DMARDs, including triple therapy and overall better outcomes, we do not expect further large cost increases for the treatment of RA in Germany in the next few years.”
Inflammatory Arthritis MOC: Six Key Elements

1. Identification
2. Access
3. Medical Management
4. Shared Care

5. PATIENT SELF-MANAGEMENT

6. PATIENT AND SYSTEM PERFORMANCE MEASUREMENTS TO INFORM QUALITY IMPROVEMENT
The Future

• Subsequent entry biologics
• Small molecules
• New disease indications
• Personalized medicine
If we don’t measure it, we don’t know what we are doing!!

Central Intake

Secure Central Data Repository

Demographic Data
Clinical Data
Administrative Data

Measurement and Longitudinal Follow-up of All Patients

Patient and System Outcomes
Thank You!
Emerging Themes in RA Management

- Early diagnosis
- Early treatment

- Biologics
  - Preserve function
  - AND
  - quality of life

- Damage prevention
  - Maintain structural integrity

Disease control of signs and symptoms

Remission