CONGRESS REPORTER

2010 Annual Meeting of the Canadian Rheumatology Association

February 3 to 6, Quebec City, Quebec

In February 2010, Quebec City hosted the annual meeting of the Canadian Rheumatology Association (CRA). This report highlights some of the major themes covered during the four-day event, summarizing for rheumatologists the key messages they can incorporate into the management of their patients with rheumatic disease.

Rheumatoid Arthritis in the Real World: Key Messages from Databases and Registries

Rheumatoid arthritis (RA) remains somewhat undertreated throughout Canada, but strides are being made towards optimizing management and understanding the importance of proper and early intervention.

These were among the general conclusions that participants at the 2010 annual CRA meeting could draw after seeing reports from several large database and registry programs being conducted across the country to examine the current real-world landscape of RA management.

Key Message 1: RA Remains Undertreated

Within an administrative database of more than 37,000 cases of RA in British Columbia, only 43% of patients had ever received a disease-modifying antirheumatic drug (DMARD) over a five-year period, and only 31% over a one-year period (Figure 1). Furthermore, less than half of the patients were seen by a rheumatologist over a five-year period, and only 10% of patients managed by primary-care physicians received DMARD therapy.

An Ontario population-based database, compiled by researchers of the Ontario Biologics Research Initiative (OBRI) including data from the Institute for Clinical Evaluative Sciences (ICES), has similarly shown that DMARD use is low among RA patients treated in primary care (20% in one study during the first year of diagnosis).[1]

Key Message 2: RA Can be Effectively Treated

On a more positive note, Canadian registry data have also shown that RA can be effectively treated when patients are managed appropriately. A study based on the national CATCH database, for example, found that DMARD use is associated with improved quality of life.[2]

The OBRI data, meanwhile, showed that RA treatment with DMARDs or with biologic agents confers significant improvement, with the largest changes observed with biologics.[3] The Alberta Biologics Registry[4] further confirmed that use of biologics (specifically anti-TNF therapies) is associated with decreased resource use, improved quality of life, and increased work productivity.

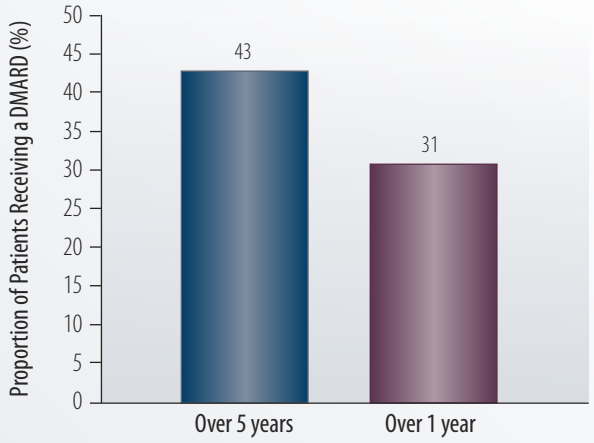
Key Message 3: Earlier Intervention May be Best for RA

A common theme within much of the database/registry data presented was that of the role for earlier intervention in RA, particularly regarding the use of biologics. One CATCH database analysis, for example, showed the excellent effi-

cacy of early, optimally dosed parenteral methotrexate.[5] This is particularly noteworthy in the context of another CATCH analysis, which showed that work disability is low in early arthritis, offering an opportunity for optimal interventions to prevent work disability from occurring.[6]

Another Canadian registry presented at the 2010 CRA meeting, RemiTRAC, has shown that RA patients are being prescribed infliximab slightly earlier in the disease process, at lower levels of disease activity and with less DMARD use before infliximab initiation, than in early years when the registry started.[7] Data from this registry also show that infliximab is significantly effective in managing RA, and that earlier initiation of treatment may increase the beneficial effect (for example, Figure 2 shows response rates for ACR 20, 50 and 70 within this registry).[8]

Figure 1. **Proportion of RA Patients in the B.C. Database Who Had Taken a DMARD**



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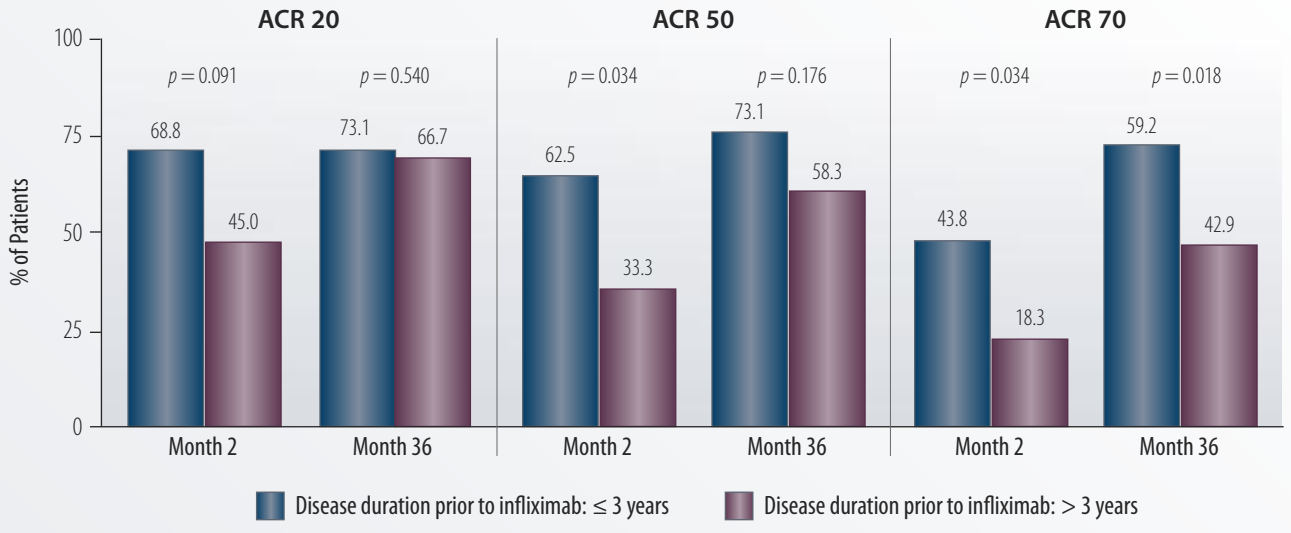
7. Bensen WG, Choquette D, Imhoff H, et al. Changing Profile of Patients with Rheumatoid Arthritis Treated with Infliximab in Canada Between 2002 and 2008—RemiTRAC Rheumatology. Presented at the 2010 Annual Meeting of the CRA, Quebec City. Poster 119.
8. Choquette D, Bensen WG, Khalil H, et al. Impact of Disease Duration on the Outcome of RA Patients Treated with Infliximab in Canada—RemiTRAC Rheumatology. Presented at the 2010 Annual Meeting of the CRA, Quebec City. Poster 150.

Figure 2. **RemiTRAC Registry: Proportions of RA Patients with Therapeutic Response (ACR Criteria) at Months 2 and 36[8]**



A Matter of Perspective: Surveys Highlight Need for Better Communication Between Patients and Rheumatologists

Patients' needs can be better met if their perspectives and expectations are aligned with those of their physicians. Furthermore, better patient-physician communication can impact patient perception and thus enhance RA medication adherence.

According to results of the Rheumatoid Arthritis in Canada: Insights, Strategies and Expectations (RAISE) survey,[1] rheumatologists need to be more aware of the importance of fatigue in their patients' lives and need to do a better job at helping patients understand key information about their disease management.

The survey, designed to determine similarities and differences between the perspectives of patients and their physicians regarding the burden of RA and treatment success, stratified by whether or not patients were receiving biologic therapy, was completed by 221 patients and 34 rheumatologists in the fall of 2009. Its results—presented during the 2010 annual CRA meeting—identified several key areas in which rheumatologists and their patients have different perceptions, highlighting opportunities for rheumatologists to improve upon their management of RA.

Importance of Fatigue Underestimated by Rheumatologists

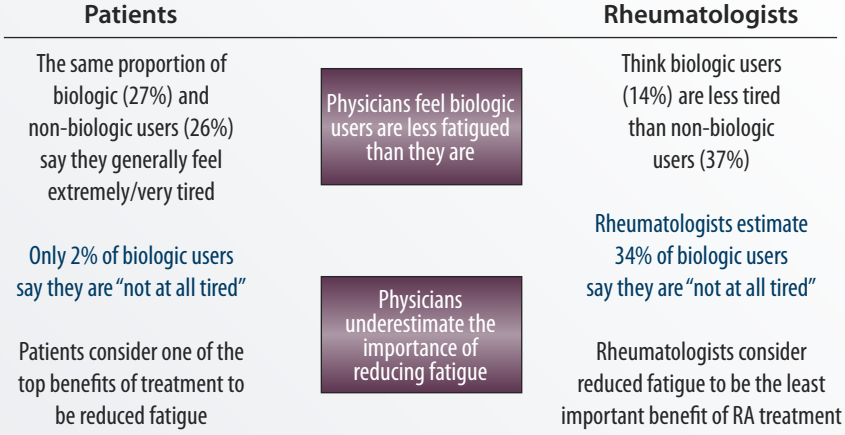
While a similar proportion of patients reported being fatigued regardless of whether or not they were taking a biologic, rheumatologists surveyed indicated that they think biologic-treated patients are less fatigued than those not treated with these agents (Figure 1). More important, patients reported that reduced fatigue is one of the top benefits of treatment, while rheumatologists consider this to be the least important benefit of RA treatment.

Based on these findings, rheumatologists should consider evaluating fatigue (and its importance to patients) during office assessments, and discussing measures that may help alleviate fatigue (including non-pharmacologic approaches).

Differing Perspectives on RA Treatment

Patients reported similar rates of satisfaction with their RA treatment whether they were taking biologics (75% satisfied) or non-biologic therapy (71% satisfied). However, rheumatologists estimated that patients taking biologics were more likely to be satisfied than those not taking biologics (81% vs. 58%). Of note, more patients taking biologics (93%) reported that their symptoms were greatly or somewhat improved with treatment than those not taking biologics (83%).

Figure 1. **RAISE Survey: Differences in Perception About Fatigue Between Patients and Rheumatologists**[1]



Almost all rheumatologists surveyed (94%) said they explained different treatment options to their RA patients, but about half of patients in each group reported that their doctor had provided them with only one treatment option (while about half reported that different treatment options had been presented to them).

Patient preferences regarding administration of biologic therapy were also not aligned with physicians' perceptions. While 69% of patients treated with biologics said they prefer self-administered injection and 31% indicated a preference for intravenous (IV) infusion (with no patients responding that they did not have a preference), rheumatologists thought that 66% of patients would prefer self-injection and 23% IV infusion while 11% would have no preference.

In general, these findings, along with other key results of the RAISE survey presented, indicate that rheumatologists may need to do a better job of ensuring their patients understand key information about their RA management, including treatment options or changes made to their treatment, potential side effects, and options for occupational therapy. This could include in-office discussions as well as providing guidance regarding where to get further information, such as trusted web sites and other resources.

The Importance of Patient Perception: A Focus on Adherence to RA Therapy

The important role of patient perceptions in overall RA management—and specifically in terms of patient adherence to RA medications—was the subject of further study by Olszynski et al as part of the PROGRESS patient support program.[2] Through this program, 250 Canadian RA patients receiving adalimumab completed questionnaires covering such topics as demographics, disease characteristics/status, current/past RA management, medication adherence, and their experiences in terms of patient-physician interaction.

The findings of this research show that rheumatologists can have a postive impact on adherence to RA medications through their interactions with patients. For example, approximately 92% of patients reported that being involved in decisions regarding their treatment would cause them to take their medication as prescribed, and having the physician explain ways to prevent illness or injury was significantly associated with greater adherence to RA medications.

Patients indicated that they preferred less complex RA therapies and less frequent dosing. As well, patient belief that RA medications would not work optimally unless always taken as prescribed was significantly associated with better adherence, highlighting the importance of taking the time to explain the link between RA medication benefits and adherence to patients.

Also of note, 90% of PROGRESS patients reported that they preferred subcutaneous administration of their RA treatment rather than intravenous injection. Still, even within the PROGRESS population, which was receiving exclusively subcutaneous administration of their RA treatment, 10% indicated that they would prefer to have intravenous injections.

PROGRESS Survey: Factors Associated with Better RA Medication Adherence[2]

- **Patient perception of less difficulty/complexity in taking their RA medications**
  - adalimumab: $r = 0.22$, $p < 0.01$
  - all RA medications: $r = 0.20$, $p < 0.01$
- **Patient belief that RA medications would not work optimally unless always taken as prescribed**
  - adalimumab: $r = 0.17$, $p < 0.05$
  - all RA medications: $r = 0.28$, $p < 0.01$
- **Having physician explain ways to prevent illness or injury**
  - adalimumab: $r = 0.12$, $p < 0.05$
  - all RA medications: $r = 0.17$, $p < 0.01$

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Updates on the Diagnosis and Management of Spondyloarthropathies

Diagnostic criteria, prognostic indicators, and treatment approaches for SpA continue to evolve. Some of these advances were reviewed within sessions at the 2010 CRA meeting.

New ASAS Diagnostic Criteria for SpA

As diagnostic tools, criteria sets should be sensitive, specific, and easily applicable in routine clinical practice. Part of a session focused on SpA at the CRA meeting was aimed at reviewing the new diagnostic criteria developed by the Assessment of Spondyloarthritis International Society (ASAS) and published in the *Annals of the Rheumatic Diseases*.[1] Under this diagnostic model, for patients with back pain for at least three months and aged less than 45 years at onset, a diagnosis can be made in the presence of sacroiliitis on imaging plus at least one additional SpA feature. Alternatively, a diagnosis can also be made if the patient is HLA-B27 positive and has at least two additional SpA features. An evaluation of these criteria[2] showed that the ASAS criteria for axial SpA are more sensitive and specific than a diagnostic algorithm or the likelihood ratio (LR) product approach.

Predictors of Structural Damage in AS

During this same session, data was presented from a variety of sources showing that males and those with hip disease, elevated CRP, MMP3, sclerostin or the ERAP variant were at elevated risk of structural damage in ankylosing spondylitis (AS).

Treatments for AS: Roles for DMARDs and Biologics

The session went on to examine the role of new treatments in AS management. As presented, traditional DMARDs have not been shown to be effective against the axial manifestations of AS.[3-8] However, research has shown that some biologic therapies are associated with significant benefit. Infliximab, etanercept, and adalimumab, for example, have been associated with a significantly higher proportion of patients reaching ASAS 40 compared to placebo (Figure 1).[6-8] More recently, golimumab has also demonstrated a significant beneficial effect (ASAS responses shown in Figure 2).[9,10] An open-label study[11] has also identified rituximab as a potentially beneficial agent in AS.

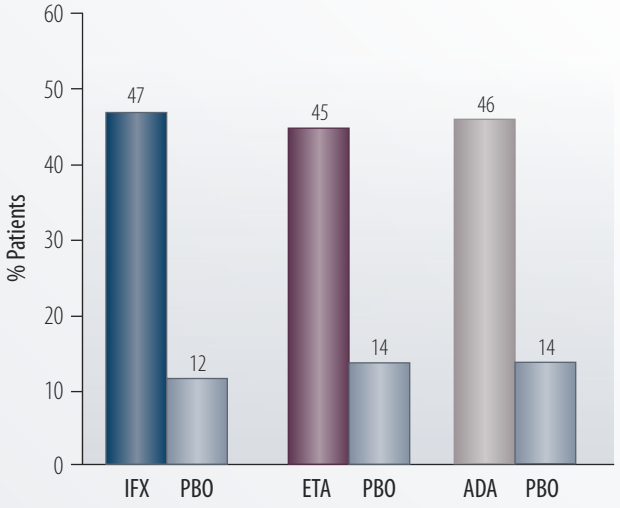
Finally, for cases in which the index biologic does not lead to adequate response in AS, there is evidence suggesting that a switch to another biologic is a viable approach. For example, one study[12] showed that response rates to a second TNF inhibitor were generally similar to responses of the first TNF inhibitor within the same patient group (and similar to responses in patients who did not switch).

Management of Psoriatic Arthritis

A separate workshop at the CRA meeting examined the topic of psoriatic arthritis (PsA), beginning with the message that, while the majority of recent PsA research being published and presented deals with biologic therapies, traditional DMARDs should still be considered, as they can be very effective (and cost-effective) for some patients. Although sulfasalazine, leflunomide and methotrexate have each demonstrated similar efficacy,[13] methotrexate is preferred due to its profile of effects on joints and skin.

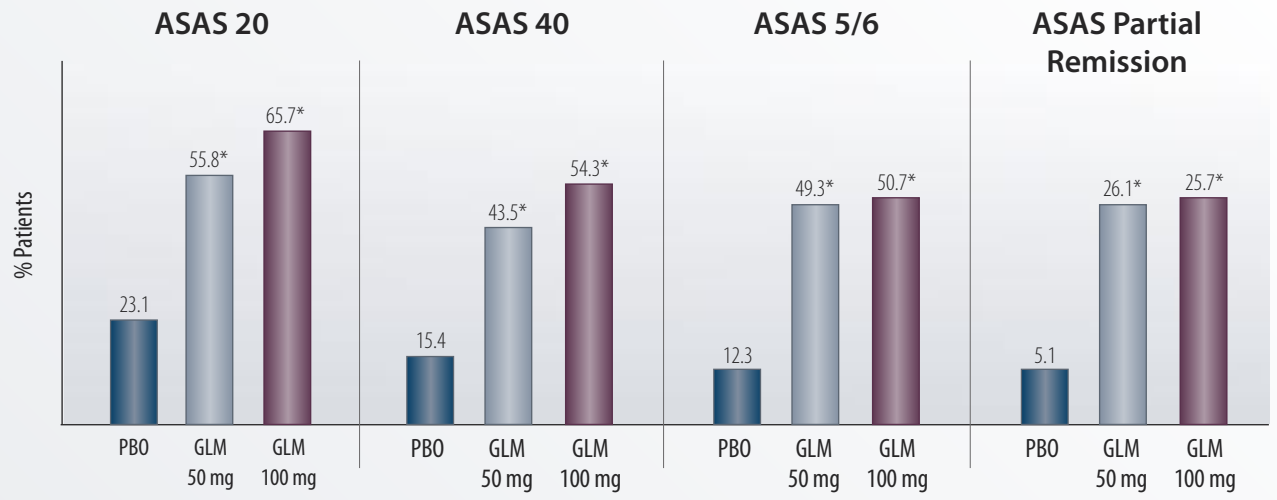
TNF inhibitors are also effective in treating PsA. In the RESPOND trial,[14] for example, infliximab + methrotrexate was compared to methotrexate alone in methotrexate-naive patients with active PsA. Compared to methotrexate alone, a greater number of infliximab + methotrexate patients achieved

Figure 1. **ASAS 40 Response After 24 Weeks of Treatment with Anti-TNF Therapies in AS[6-8]**



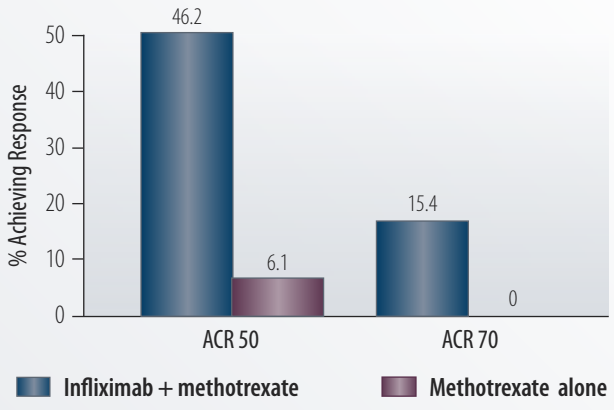
Note: Different studies, not head-to-head comparisons of anti-TNF agents.
IFX = infliximab; ETA = etanercept; ADA = adalimumab; PBO = placebo.

Figure 2. **GO-RAISE Study: ASAS Responses to Golimumab in AS[9,10]**



*$p < 0.001$; PBO = placebo; GLM = golimumab.

Figure 3. **RESPOND Trial: ACR 50 and ACR 70 Responses to Infliximab + Methotrexate vs. Methotrexate Alone in Methotrexate-naive Patients with Active PsA[14]**



ACR 50 and ACR 70 responses by week six (Figure 3). Separate data have shown that persistence rates are high in PsA patients taking TNF inhibitors, with at least 75% of patients still taking their first prescribed TNF inhibitor at one year.[15]

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Examining Risks of Malignancy Related to Rheumatoid Arthritis and its Treatment

Patients with RA probably are not at higher risk for cancer than the overall population, but may exhibit a different pattern of specific malignancies. It is too early to draw conclusions about the effects of biologics on cancer risk.

The relative risk of malignancy among patients with rheumatoid arthritis (RA), and the related risks associated specifically with the use of biologic agents for the treatment of RA, were addresed in a workshop session at the 2010 annual CRA meeting.

Cancer Risk Among RA Patients Similar to Overall Population

Analysis has shown that the incidence of cancer in patients with newly diagnosed RA is not significantly different from that in the overall population,[1] and that overall, patients with RA are not any different in terms of malignancy risk compared to the overall population.[2] However, the pattern of particular malignancies in RA sufferers is different, with a higher risk of lymphoma and lung cancer, and possibly decreased risk for colorectal and breast cancer, compared with the general population.

Cancer Risk and Biologics: Too Early to Tell

It is probably too early to make a definitive assessment regarding the effects of biologic agents on cancer risk. Cancer development is a multi-step process, taking many years between initial phases and overt disease. Biologic therapies for RA have not been in use long enough for reliable observations about cancer risk. As well, clinical trials are not of sufficient duration to detect differences between treatment agents and placebo in this regard, and there is a shortage of data for comparisons between active treatments.

There are also discrepancies in terms of reported overall cancer risk in biologic-treated vs. biologic-naive patients. Some research has found no overall difference between these groups in total cancer risk,[3] while an observational study[4] detected a potential increased risk for skin cancers (but not for solid tumors or lymphoproliferative malignancies) with biologic therapies. Of note, the duration of biologic therapy does not seem to influence the risk of malignancy (Table 1).[5]

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Table 1. **Relative Risk of a First, Primary Cancer in RA Patients Receiving Anti-TNF Therapy Compared with a National Swedish Cohort of Unselected, Biologics-naive Contemporary Patients with RA[5]**

	RR (95% CI); number of events				
	First etanercept (n = 2,216)	*First infliximab (n = 3,249)*	*First adalimumab (n = 899)*	*p†*	*All first anti-TNF therapy as a single class (n = 6,364)*
Overall	0.78 (0.61-1.00); 70	1.09 (0.91-1.30); 144	1.32 (0.87-1.98); 26	0.034	1.00 (0.86-1.15); 240
Time since start of anti-TNF					
< 1 year	0.43 (0.22-0.84); 10	1.23 (0.85-1.77); 31	1.91 (1.11-3.31); 15	0.0027	1.03 (0.78-1.36); 56
≥ 1-2 years	0.80 (0.46-1.40); 13	0.83 (0.53-1.28); 21	0.84 (0.37-1.92); 6	0.99	0.82 (0.59-1.13); 40
≥ 2 years	0.92 (0.68-1.24); 47	1.13 (0.91-1.41); 92	1.08 (0.43-2.67); 5	0.53	1.05 (0.88-1.25); 144

Relative risks (RRs) and 95% confidence intervals (95% CIs) were determined by Cox regression analysis of data stratified by sex, age, and country of residence and adjusted for four comorbid conditions. RA = rheumatoid arthritis. †For difference between the anti-TNF drugs.