Remission Becoming a Reachable Goal in RA

Strategies now include intensive management, treatment to target, and combined DMARDs.

BY SHARON WORCESTER

EXPERT ANALYSIS FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF RHEUMATOLOGY

ATLANTA – Getting to the place in rheumatoid arthritis therapy where remission is a possibility has been much like the process of conquering a treacherous mountain, according to Dr. Duncan Porter.

Early climbers struggled and failed, but lessons were learned, better equipment was developed, and those who followed in the footsteps of the pioneers achieved what was once thought to be impossible.

"In rheumatology, we have had our own mountain to climb: Twenty years ago we were still puttering around in the foothills with symptom control, through the '80s and '90s we were developing increasing evidence that confirmed that conventional disease-modifying drugs … truly did modify disease activity, but it's been only recently that we've come to focus on the possibility of achieving remission," he said at the meeting.

Now the top of the mountain is being reached "a good deal more often and a good deal more quickly," he said, citing findings from the Dutch Rheumatoid Arthritis Monitoring (DREAM) cohort study, which were also presented at the meeting, showing that in 64% of 534 patients with newly diagnosed RA, remission was rapidly achieved with a tight control treatment strategy (Arthritis Rheum. 2010;62[suppl.]:abstract 662).

"I think the reason we're getting there is because we've got better equipment, so we've got more drugs to employ," Dr. Porter said, adding that although the "better equipment" includes biologics, the improvements are primarily due to the new strategies of care.

"It's how we attack the mountain, it's how we deploy the drugs that we have that has yielded the greatest improvements in outcome," said Dr. Porter of the University of Glasgow (Scotland).

The treatment strategies he discussed included intensive management, treatment to target, combination disease-modifying anti-rheumatic drug (DMARD) strategies, and remission induction.

Although intensive management and treatment to target often overlap, they are not the same, he stressed.

Intensive management, using monthly patient visits, liberal intramuscular and intra-articular steroid injections, escalation of therapy for persistent disease, and step-up dosing, has been shown to be highly effective for inducing remission. In the TICORA (Tight Control for Rheumatoid Arthritis) study (Lancet 2004;364:263-9), for example, 65% of patients achieved remission, compared with 16% of patients who did not receive intensive management.

Treatment to target was a component of that study, but treatment to target doesn't necessarily include intensive management components, Dr. Porter explained, adding, "I think that may be significant."

Nonetheless, a recent literature review concluded that although few studies have used a randomized approach to test the value of treatment to target strategies, there is "unanimous" and "compelling" evidence that targeted approaches have value (Ann. Rheum. Dis. 2010;69:638-43).

With a treatment to target strategy, it is important to measure progress toward the target and to adjust therapy accordingly based on clinical judgment. Targets can be based on disease activity scores, or they can be based on remission, ultrasound findings, or biomarkers.

"If nothing else, using [the] disease activity score and applying it to treat to target and intensive management strategies has simply been proven to work," Dr. Porter said, adding that "starting [patients] on methotrexate and sending them away for 6 months is no longer acceptable."

Because most studies use a constant dose of the study drug, interpretation in terms of treatment to target strategies can be difficult, as that's not the way treatment to target works, and it's not the way most physicians practice, he said.

"Keeping that in mind is critical if we're to … come to the best strategy," he added.

One area where it is important to make a distinction between intensive management and treatment to target is with the third strategy Dr. Porter discussed: the combined use of DMARDs. These can include step-up, step-down, and parallel therapy.

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In the Bone Estrogen Strength Training (BEST) study, for example, treatment to target, but not intensive management, was used. Four strategies were evaluated, including sequential monotherapy, step-up combination therapy, initial combination therapy plus steroids, and initial biologic therapy.

At 2 years, the groups were identical, and importantly, 39% of patients had sustained low disease activity on monotherapy (Arthritis Rheum. 2005;52:3381-90).

"I think that's quite important if we're to avoid overtreating patients with multiple drugs when they will just do fine on one drug alone," he said.

Other studies have compared various combinations, and showed that nothing is lost in waiting to see whether combination therapy versus monotherapy is needed. As for the use of biologics, the decision must be based on the complex synthesis of knowledge about efficacy, toxicity, and cost.

A key factor – and a challenge – is knowing the clinical significance of small numbers of Sharp score changes, particularly when you recognize that there is no evidence at all of a window of opportunity when it comes to biologic therapy and halting radiographic progression, Dr. Porter said.

The final strategy – remission induction – remains largely uncharacterized, he said, noting that there are few good studies, and more definitive research is needed to clarify its role.

"By and large we need to maintain the therapies we've started that get our patients into remission, and by and large we cannot plan to withdraw therapies large scale. … There's little compelling evidence, as far as I can see, of early aggressive therapy of any form that can substantially and permanently modify disease processes such that therapy can be withdrawn," Dr. Porter said.

That suggests rheumatologists are doing much better than 20 years ago in terms of climbing the RA therapy mountain but that the summit has not been reached. And if the RA therapy goals of drug-free remission, cure, and prevention are added to that mountain – which currently has symptom control at its base, followed by disease modification and remission, then half of the mountain remains to be conquered.

In conclusion, Dr. Porter quoted a recent editorial that accompanied another DMARD combination trial (Lancet 2009;374:430-2):

"The most important information to be gathered from clinical trials in RA is not necessarily comparison of agents, but rather the strategy of tight control aiming for remission."

Dr. Porter said that he has received research funding, served as a consultant, and/or served on the speakers bureau for Abbott, Pfizer, Roche, Schering Plough, and UCB. ■

TNF Inhibitors Appear to Reduce Diabetes Risk in RA

BY HEIDI SPLETE

FROM THE ANNUAL SCIENTIFIC MEETING OF THE AMERICAN ACADEMY OF RHEUMATOLOGY

ATLANTA – Use of tumor necrosis factor inhibitors reduced the risk of developing type 2 diabetes by 60%, based on data from 1,287 nondiabetic adults with rheumatoid arthritis.

"Interventions that treat RA and improve insulin resistance are highly desirable," said Dr. Jana Antohe of Geisinger Health System in Danville, Penn.

To examine the impact of TNF inhibitor use in RA patients, Dr. Antohe and her colleagues followed 1,287 incident RA patients who were identified during January 2001–March 2008 at a rural tertiary health center.

Of the 1,539 RA patients identified, 252 with preexisting diabetes were excluded.

The researchers compared the 884 patients who had never used TNF inhibitors with the 403 patients who had ever used them.

VITALS

Major Finding: TNF inhibitor use was associated with a 60% reduction in the risk of developing diabetes.

Data Source: Data from 1,287 adults with nonincident RA.

Disclosures: Dr. Antohe said that she had no financial conflicts to disclose. Several of her co-investigators have received research grants from pharmaceutical companies including Wyeth, Amgen, and Centocor.

Patients in the ever-use group had a higher median body mass index and C-reactive protein (CRP) level than did the never-use group, but these differences were not significant.

After a median follow-up time of 35 months for the ever users and 23 months for the never users, the researchers identified 13 new cases of diabetes in the ever-use group and 43 in the never-use group, for incidence rates of 11/1,000 person-years and 22/1,000 person-years, respectively, according to the researcher.

The median age of the patients was 61 years, the median BMI was 28.6 kg/m^2, 63% were women, and 97% were white.

The findings were adjusted for gender, age, race, hypertension, BMI, positive rheumatoid factor and anti–cyclic citrullinated peptide (anti-CCP) levels, erythrocyte sedimentation rate, CRP levels, and the use of NSAIDs, glucocorticoids, hydroxychloroquine, and methotrexate.

Additional research is needed to confirm the findings in patients at increased risk for cardiovascular disease, Dr. Antohe said. ■