Use of Biologics Cuts Stroke, Heart Attack Risk

BY BRUCE JANCIN
Denver Bureau

Amsterdam — Rheumatoid arthritis patients on tumor necrosis factor inhibitors appear to have a twofold reduction in stroke incidence, compared with similarly ill patients being treated with methotrexate or other traditional disease-modifying antirheumatic drugs. Dr. Will G. Dixon reported at the annual European Congress of Rheumatology.

There is evidence to suggest that rheumatoid arthritis (RA) patients on tumor necrosis factor (TNF) inhibitors may also have a reduced MI rate. This benefit appears to be confined to patients whose joint disease responds well to the mediation, said Dr. Dixon of the University of Manchester (England).

He presented the first report from the British Society of Rheumatology Biologics Register, an ongoing observational database that in 2001 began prospectively enrolling all RA patients in the United Kingdom who were prescribed etanercept, infliximab, or adalimumab. RA patients are known to have an overall mortality twice that of the general population, with most of the excess attributed to a steep increase in cardiovascular deaths, explained Dr. Dixon at the meeting, which was sponsored by the European League Against Rheumatism. Inflammation is known to play a central role both in RA and in atherosclerotic cardiovascular disease.

The study hypothesis was that inhibition of joint inflammation using powerful anti-TNF agents might produce a parallel reduction in the inflammation that triggers atherosclerotic plaque rupture and acute coronary and cerebrovascular events, he continued.

This first analysis of the British national registry database included 10,999 patients on a TNF antagonist for at least 6 months and a comparison arm that consisted of 2,097 RA patients treated with traditional disease-modifying antirheumatic drugs (DMARDs).

There were 42 strokes in the TNF blocker group and 12 in the DMARD group, translating into an incidence of 3.9 strokes per 1,000 person-years in RA patients on TNF inhibitors, compared with 5.7 strokes per 1,000 person-years in the DMARD group. After statistical adjustment for baseline differences between the two populations in terms of age, gender, smoking status, body mass index, being on a TNF inhibitor was independently associated with a 49% stroke risk reduction.

The MI analysis was done earlier, at a point when the TNF inhibitor group was smaller by roughly 2,000 patients. No difference in the MI rate between the two groups was found.

However, by restricting the analysis to patients whose RA responded well to anti-TNF therapy, a favorable trend was found. And upon further restricting the analysis to the first 6 months of follow-up—a prospectively secondary study end point on the grounds that marked inhibition of atherosclerotic inflammation might be expected to rapidly quell coronary plaque rupture—being on a TNF inhibitor was associated with a 72% reduction in MI. This difference didn’t achieve statistical significance, however, because of small numbers, said Dr. Dixon.

“The clinical implication of these findings is that if we’re able with the anti-TNF drugs to reduce rates of heart attacks and strokes in our patients, which are their leading cause of death, then it may be that in addition to improving their joint symptoms we may be reducing their mortality,” he concluded.

MADRID — Aliskiren, the novel renin-blocker drug, improved 24-hour blood pressure control and showed greater systolic and diastolic blood pressure reductions, compared with ramipril, in diabetics with uncontrolled hypertension, according to data presented at the annual meeting of the European Society of Hypertension.

Aliskiren also can be safely combined with the ACE inhibitor in this population, the combination giving the greatest degree of pressure reduction. Aliskiren works by blocking the renin-regulated conversion of circulating angiotensinogen to angiotensin I. The new drug, also known by the brand name Rasilez, is the first of what may soon be a burgeoning class of renin blockers. It is being considered for approval by regulatory authorities in Europe and the United States.

Dr. Yagiz Uresin, professor of clinical pharmacology at Istanbul (Turkey) University, presented a multicenter international study of 837 patients with diabetes and hypertension. At baseline, the patients had blood pressures of over 155 mm Hg systolic and 98 mm Hg diastolic.

After a washout period and a placebo run-in of 2.4 weeks, the patients were randomly assigned to aliskiren monotherapy, 150 mg/day; ramipril monotherapy, 5 mg/day; or a combination of 150 mg aliskiren plus 5 mg ramipril per day.

After 4 weeks, the investigators doubled the doses in all study groups.

After 8 weeks, aliskiren gave mean pressure reductions of 14.7 mm Hg systolic and 11.3 mm Hg diastolic. This was significantly better than the 12.0- and 10.7- mm Hg reductions with ramipril alone. In combination, the two drugs gave mean pressure reductions of 16.6 mm Hg systolic and 15.8 mm Hg diastolic.

With a target pressure of 130/80 mm Hg, slightly over 8% of the patients in the monotherapy arms could be considered well controlled by the end of the study. Combination therapy bumped this up to 13%.

The low number of patients who were able to reach target pressures reflects the difficulty of treating long-standing hypertension in diabetic patients, said Dr. Uresin.

Crude Incidence of Strokes in RA Patients, by Medication (per 1,000 person-years)

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<thead>
<tr>
<th>Medication</th>
<th>Incidence (per 1,000 person-years)</th>
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<tbody>
<tr>
<td>DMARD group</td>
<td>3.9</td>
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<td>TNF blocker group</td>
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B Y E R I K G O L D M A N
Contributing Writer

WASHINGTON — Diabetic patients who had myocardial infarctions and had not resumed their antihyperglycemic medications by discharge were 24% more likely to die within 1 year than were similar patients who had resumed their medications at discharge, according to a report during a poster presentation at the annual scientific sessions of the American Diabetes Association.

The increased risk of death was especially telling in the first 30 days after discharge, said Dr. Silvio Inzucchi, principal investigator and professor of medicine at Yale University, New Haven, Conn. He and his associates, Dr. Barry Goldenman, and Dr. Arthur Reiner, found that the charts of Medicare patients aged 65 years and older in the National Heart Care Project. All of the patients had a confirmed acute MI and previously documented diabetes treated with antihyperglycemic agents. The study excluded those who died before discharge, were transferred to another facility, or needed long-term hemodialysis.

Of the 8,751 patient charts, 1,170 (13%) indicated patients had not resumed their diabetes medications by discharge. Within 1 year of discharge, 38% of these patients died, compared with the 31% in the 7,581 who were taking their diabetes medications at discharge.

Notably, 36% of the deaths occurred within the first 30 days after hospital discharge in patients who had not resumed their medications, compared with 23% of the deaths in those discharged on diabetes medications.

The difference was statistically significant after multivariate Cox analysis for 78 clinical variables, including diabetes medications at discharge and the outcome of primary care physicians who need to address diabetes during discharge planning, if only to have patients follow up with their primary doctors.

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