

Biomarker Helped Predict CV Risk From NSAIDs

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ROME – N-terminal prohormone brain natriuretic peptide level provides a simple, previously untapped, and powerful predictor of cardiovascular risk in arthritis patients on long-term NSAID therapy, according to a large prospective study.

“Risk stratification based on NT-proBNP may offer a handle to cope with the risk of cardiovascular side effects of nonsteroidal anti-inflammatory drugs in our aging population,” Dr. Kay Brune said while presenting the cardiac biomarker analysis from the Multinational Etoricoxib and Diclofenac Long-term (MEDAL) study at the meeting.

MEDAL involved more than 34,000 patients with rheumatoid arthritis or osteoarthritis who were randomized to receive treatment with either the cy-

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cloxygenase-2 (COX-2) selective inhibitor etoricoxib or diclofenac. The primary outcomes have previously been reported (Lancet 2006;368:1771-81).

Dr. Brune presented a secondary cardiac biomarker analysis involving the 6,273 MEDAL participants for whom baseline plasma NT-proBNP and high-sensitivity C-reactive protein measurements were available.

The two treatment arms were combined for this analysis because the 2-year thrombotic cardiovascular event rates were virtually identical in the etoricoxib- and diclofenac-treated subjects, she explained.

The key new finding was that baseline NT-proBNP showed a strong, graded relationship with 2-year rates of myocardial infarction, stroke, heart failure, and cardiovascular death, said Dr. Brune, professor of clinical pharmacology at the University of Erlangen (Germany).

Patients with a baseline NT-proBNP level below the median of 78 pg/mL had zero incidence of heart failure at 2 years of follow-up.

Their combined thrombotic cardiovascular event rate – consisting of myocardial infarction, stroke, and cardiovascular death – was less than 1% after 2 years of NSAID therapy.

In contrast, the patients who were in the third quartile for NT-proBNP, with a value of 78-148 pg/mL, had a 2.3% incidence of the combined end point of myocardial infarction, stroke, cardiovascular death, and heart failure, while those in the top quartile had an incidence of 4.4%.

After adjustment for patient demographics, type of arthritis, and standard cardiovascular risk factors including hypertension, NT-proBNP remained strongly predictive of cardiovascular outcomes, Dr. Brune said.

The implication of these results is that if an arthritis patient has an NT-proBNP value above the median, NSAID therapy may not be a good option from the standpoint of cardiovascular risk,

which is already increased in rheumatoid arthritis patients above what would be predicted by the standard cardiovascular risk factors.

And when an arthritis patient who is already on long-term NSAID therapy develops a high NT-proBNP, it is time to consider alternative strategies for pain management, the physician said at the meeting.

NT-proBNP is a marker of cardiac

function widely used in clinical practice for screening, diagnosing, and monitoring patients with heart failure.

Baseline C-reactive protein level was not associated with cardiovascular event rates in the MEDAL analysis.

Dr. Brune disclosed having received research grant support from Merck & Co. and Roche Diagnostics, which funded the study. MEDAL was funded by Merck. ■

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