MEETING HIGHLIGHTS

American Heart Association 2008 Scientific Sessions

United European Gastroenterology Week

American College of Rheumatology Scientific Meeting

Walter Alexander

American Heart Association 2008 Scientific Sessions

At the most recent AHA meeting, from November 8 to 12, 2008, in New Orleans, 1,600 presenters offered roughly 4,000 abstracts. Among the topics discussed were pharmacological agents designed to help prevent cardiovascular events and the optimal use of other agents when such events occur. This article reviews one late-breaking clinical trial on statin use in individuals with normal low-density lipoprotein-cholesterol (LDL-C) levels, two trials seeking to identify optimal therapy for acute coronary syndromes (ACS), and another session on early treatment in children with familial hypercholesterolemia.

AHA Studies Show Benefits of Statins, Optimal Dosing for Acute Coronary Syndromes

The TMACS Trial

• Shamir R. Mehta, MD, McMaster University, Hamilton, Ontario, Canada

“Most patients with ACS can be managed safely with either an early or a delayed invasive strategy,” suggested Dr. Mehta. An early invasive strategy, however, is best for those at high risk, he added.

He presented results of TMACS (TIMing of intervention in patients with Acute Coronary Syndromes), a clinical trial that included patients with unstable angina or non–ST-elevation myocardial infarction (NSTEMI) who met two of three criteria: age older than 60 years, ischemic electrocardiographic (ECG) changes or increased biomarkers, and suitability for revascularization.

Patients received aspirin, clopidogrel (Plavix, Bristol-Myers Squibb/Sanoﬁ-Aventis), and glycoprotein (GP IIb/IIIa) antagonists as per routine practice. They were randomly assigned to undergo an early invasive procedure (coronary angiography) as soon as possible and percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) at or before 24 hours, or a delayed invasive procedure (angiography) at 36 hours or later, followed by PCI or CABG.

Death, new MI, or stroke at six months was the primary outcome, occurring at rates of 9.7% for the early strategy and 11.4% for the delayed strategy (P = 0.15). The difference between strategies for the secondary outcome, adding refractory ischemia to the primary outcome combination, however, significantly favored the early strategy (9.6% vs. 13.1%; P = 0.002). Looking separately at patients with low-risk or inter-

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The ATLAS TIMI 46 Trial: Rivaroxaban

- C. Michael Gibson, MD, Director, TIMI Data Coordinating Center, Harvard Medical School, Boston, Mass.

Despite the use of aspirin and clopidogrel, rates of cardiovascular events remain at about 10% at one year in ACS patients, noted Dr. Gibson. "So there is still an unmet need," he said.

The goal of ATLAS TIMI 46 (Aspirin with or without thienopyridine in Subjects with Acute Coronary Syndromes-Thrombolysis in Myocardial Infarction) was to identify tolerable doses of rivaroxaban (BAY 59-7939, Bayer), a potent, selective, direct factor Xa inhibitor, to be carried forward to a phase 3 trial. The atypically large phase 2 trial included nearly 3,500 patients who were given placebo for six months or various rivaroxaban doses (total, 5–20 mg once or twice daily) after being selected by their physicians to receive aspirin (N = 761) or aspirin plus clopidogrel (N = 2,730). The researchers required a large patient population in order to have a sufficient number of bleeding events to evaluate for safety.

Bleeding was assessed in three categories: standard TIMI, major and TIMI minor bleeding, and as a less severe category of bleeding requiring medical attention.

The primary efficacy endpoint, characterized by Dr. Gibson as exploratory because of an insufficient sample size, was combined death/MI/stroke and severe ischemia requiring revascularization. Analysis revealed a trend favoring the rivaroxaban groups (7% receiving placebo, 5.6% receiving rivaroxaban; P = 0.10) at six months. The secondary efficacy endpoint, described as adequately powered, significantly favored rivaroxaban (5.5% for placebo, 3.9% for rivaroxaban; P = 0.028).

As a result of reduced event rates and increased bleeding rates with rivaroxaban, the investigators are proceeding with a phase 3 trial of rivaroxaban 2.5-mg and 5-mg twice-daily doses. Assessing results in the current trial for those doses in the aspirin-alone group showed the rates of events with placebo (cardiovascular death/MI/stroke) to be 11.9% with a 0% TIMI major bleeding rate. With rivaroxaban added, the event rate dropped to 6.6%, with an increase to 1.2% for the TIMI major bleeding rate.

For aspirin plus clopidogrel, the event rate for placebo was 3.8%, with an 0.2% TIMI major bleeding rate. With rivaroxaban added, the event rate was 2% with a 1.2% TIMI major bleeding rate. Event rate reductions with rivaroxaban in both groups (aspirin alone [P = 0.08] and aspirin plus clopidogrel [P = 0.09]) approached, but did not achieve, statistical significance.

- Elaine M. Hylek, MD, MPH, Associate Professor of Medicine, Boston University School of Medicine, Boston, Mass.

Although adding rivaroxaban to antiplatelet therapy caused an increase in dose-dependent bleeding, stated Dr. Hylek, an AHA discussant, it “exhibited a trend toward improved efficacy in reducing recurrent ischemic events.”

- Paul Gurbel, MD, Director, Cardiovascular Research, Sinai Hospital, Baltimore, Md.

Most bleeding episodes in ATLAS TIMI 46 required medical attention, noted Dr. Gurbel. His research is credited with bringing the problem of clopidogrel resistance to the attention of the cardiology community. In an interview, he added that the greatest bleeding increase was seen in the patients receiving aspirin plus clopidogrel, with the rate in the 5-mg rivaroxaban arm of 10% being quintuple the 2% rate with aspirin alone. Thrombosis risk goes up, he emphasized, when these bleeding episodes lead to discontinuation of therapy.

Dr. Gurbel is currently evaluating an investigational oral antiplatelet agent, a thrombin receptor antagonist (TRA/SCH 530348, Schering-Plough) to which there is no known resistance. The hope, he said, would be to reduce adverse cardiovascular events without increasing bleeding rates. He says: “A thrombin receptor antagonist that specifically blocks platelet-thrombin interactions has less potential for bleeding.”

JUPITER: C-reactive Protein and Rosuvastatin (Crestor)

- Paul Ridker, MD, Department of Epidemiology, Harvard School of Public Health, Boston, Mass.

The item generally acknowledged as the biggest news story at the AHA meeting was JUPITER (Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin). Individuals who, according to current guidelines, had not then qualified for statin therapy, were enrolled. JUPITER was investigator-initiated and funded by AstraZeneca. The trial included 17,802 apparently healthy men and women with elevated levels of high-sensitivity C-reactive protein (hsCRP), stated Professor Ridker. He noted that hsCRP is an inflammatory biomarker that reproducibly and independently predicts future vascular events, even when cholesterol levels are low.

In Dr. Ridker’s 2001 *post hoc* analysis of AFCAPS/TexCAPS (Air Force/Texas Coronary Atherosclerosis Prevention Study) individuals with low levels of both LDL-C and hsCRP had extremely low rates of vascular events, which statin therapy did not improve. Among patients with low LDL-C but high hsCRP levels, however, vascular event rates were just as high as rates among those with overt hyperlipidemia. Statin therapy significantly reduced events in this group.

In JUPITER, men older than 50 years of age and women older than 60 years of age (N = 17,802), with no prior cardiovascular disease or diabetes, were randomly assigned to receive rosuvastatin (Crestor, AstraZeneca) 20 mg (n = 8,901) or placebo (n = 8,901). Each participant had LDL-C levels of below 130 mg/dL and hsCRP levels of 2 mg/L or higher. The actual median hsCRP levels were 4.2 in the rosuvastatin group and 4.3 in the placebo group. The median LDL-C level was 108 mg/dL for both groups.

The primary endpoint in the prospective, multinational, randomized, double-blind, placebo-controlled trial was combined MI/stroke/unstable angina/revascularization and cardiovascular death. Although the follow-up period had initially been planned to last for five years, the trial was stopped prematurely at 1.9 years after a review by an independent data safety monitoring board.

The primary endpoint was met by 251 of 8,901 patients (2.82%) in the placebo group and by 142 of 8,901 patients (1.6%) in the rosuvastatin group (a 44% risk reduction; P < 0.00001), with a number needed to treat (NNT) of 25. Risk
reductions of 47% were found for rosuvastatin in combined MI/stroke/cardiovascular death and for arterial revascularization or hospitalization for unstable angina \( (P < 0.00001 \text{ for both groups}) \). A subgroup analysis showed consistent benefits for age, smoking status, race, and region (U.S., Canada, and the rest of the world), or hsCRP above the subgroups receiving 2 mg/L only. Rates of serious adverse events were similar: 15.2% with rosuvastatin and 15.5% with placebo.

All-cause mortality, the secondary endpoint, was reduced by 20% in the rosuvastatin group (247 of 8,901 placebo patients, 198 of 8,901 rosuvastatin patients; \( P = 0.02 \)).

Dr. Ridker concluded, “Despite evaluating a population with lipid levels widely considered to be ‘optimal’ in almost all current prevention algorithms, the relative benefit observed in JUPITER was greater than in almost all prior statin trials.”

- **Marvin Lipman, MD, Chief Medical Adviser for Consumer Reports, and Professor Emeritus of Clinical Medicine, New York Medical College, Valhalla, N.Y.**

Among infrequent, less than enthusiastic responses to the JUPITER conclusions, Dr. Lipman commented in an interview:

“You have to look at the minutiae. About half the population had significant risk factors. About 15% were smokers, and about 41% had metabolic syndrome. So this is not exactly a low risk population that he [Dr. Ridker] was studying—as was implied by the low LDL levels.”

Dr. Lipman also pointed out that the calculation of an NNT of 25 was based on extrapolations to five years. At 1.9 years, when the study was stopped, the NNT was 125.

He added, “I don’t think this study will change my way of using a CRP in the treatment of patients. I find it handy where the LDL-C is borderline—between 125 and 140 mg/dL—where you hem and haw about putting someone on a statin for the rest of his or her life.”

**Familial Hypercholesterolemia and Colesevelam (Welchol)**

- Evan Stein, MD, PhD, Professor of Pathology and Laboratory Medicine, University of Cincinnati, Ohio

Colesevelam (Welchol, Daiichi Sankyo) safely and effectively lowered LDL-C levels in children with heterozygous familial hypercholesterolemia (heFH), according to preliminary data on treatment with the bile acid sequestrant in this population. Investigator Stein said that untreated individuals with heFH die of cardiovascular disease (CVD), on average, between 40 and 50 years of age. In an interview, he said that children with FH at age 13 have carotid intimal thickening equivalent to that of a middle-aged man. Earlier research in adults had shown that colesevelam alone reduced LDL-C levels by up to 15% and in combination with statins, it reduced LDL-C levels by up to 48%.

Dr. Stein’s 32-week, randomized, double-blind, parallel-group study (in 41 sites and 12 countries) enrolled 194 children with heFH between 10 and 17 years of age. LDL-C levels in these children were above 160 mg/dL or above 130 mg/dL if they were using statins. After a stabilization period, the children received placebo or one of two doses of colesevelam (1.875 g/day or 3.75 g/day) for eight weeks. During a subsequent open-label period, all patients received colesevelam 3.75 g/day with or without a statin for 16 weeks.

LDL-C reductions were greatest with the higher dose of 3.75 mg/day, with the percent change in LDL-C from baseline (the primary endpoint) at −10.0 after eight weeks and −14.0 at 26 weeks \( (P \leq 0.0001) \). Triglyceride levels increased significantly \( (P \leq 0.0001) \) but not in a dose-dependent manner, and the increase was not significantly greater than with placebo. Gastrointestinal (GI) disorders, the most common adverse events likely to be drug-related, were similar in all groups. Similarly, compliance was approximately 85% in all groups.

In an interview, Dr. Stein described his own recent unpublished longitudinal study, which compared heart attacks in 1,200 children with heFH before 1977 and after 1983 when treatment with statins became widespread. That study showed almost a 50% reduction in heart attacks and an extension of time between cardiovascular events from about five years to 8.5 and nine years.

He concluded, “The use of colesevelam may improve the management of LDL-C abnormalities in pediatric patients with heFH.”

**References**


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**United European Gastroenterology Week**

The meeting in Vienna hosted a record total number of almost 12,000 participants from October 18 to 22, 2008.

**Decade-Long Trend Shows Increasing NSAID-Related Lower GI Complication Rates**

- Angel Lanas, MD, Professor of Medicine, University Hospital, Zaragoza, Spain
- Ingvar Bjarnason, MD, Professor of Digestive Diseases; Guy’s, King’s, and St. Thomas’ School of Medicine; London, U.K.

The puzzle pieces coming together to suggest increasing rates of lower GI risk may also point to effective therapeutic strategies. But more clinical study pieces need to be assem... continued on page 35
ble, according to Dr. Lanas, who studied long-term patterns of GI complications in 10 Spanish hospitals, before clear conclusions can be stated.

Dr. Lanas’ study, which included more than 30,000 patients admitted for upper and lower GI complications between 1996 and 2005, identified a distinct trend showing declining rates of upper GI events and increasing rates of lower GI events (e.g., colitis, colonic angiodysplasia, anemia caused by occult GI bleeding, small-bowel perforation). Dr. Lanas reviewed data from the study, presented also at this year’s Digestive Disease Week meeting, at a Pfizer-sponsored media roundtable entitled “The Importance of Evaluating the Entire GI Tract: Emerging Data” at the current meeting. He also discussed data confirming the link between upper GI adverse drug events such as dyspepsia and abdominal pain and endoscopically detected ulcers. Such events are leading factors for discontinuation of therapy with nonsteroidal anti-inflammatory agents (NSAIDs).

Presenting a background on NSAID-associated GI toxicity, Dr. Bjarnason, the previous roundtable speaker, had stated that 1% to 4% of patients taking nonselective NSAIDS experience ulcer complications each year. Multiple and high-dose nonselective NSAID use, among the major risk factors for complications, are common in the aging population; 70% of patients 65 years of age and older take an NSAID at least once weekly. Unfortunately, ulcer complications warranting hospitalization occur most often (81%) without prior symptoms.

Although attention has been paid predominantly to upper GI events, NSAID trials have shown lower GI events as accounting for about 40% of all GI events. Dr. Bjarnason found that NSAID enteropathy frequently included small-bowel bleeding (70%) and protein loss (70%), with an occasional incidence of perforations, bleeding ulcers, strictures, and sudden death.

“The importance and clinical relevance of lower GI events are becoming increasingly acknowledged,” he said.

However, even though the incidence, mortality, and costs associated with upper GI complications have been established, less is known about the lower GI tract and its related complications. Difficulties in diagnosing lower GI complications is part of the reason, he pointed out.

Major recent therapeutic advances may account for the prevention of either Helicobacter pylori–induced or NSAID-induced gastroduodenal complications, Dr. Lanas noted. Reducing acid with proton pump inhibitors (PPIs), however, does not protect the lower GI tract.

He added: “While excess acid penetrates the mucosa in the stomach and does damage, we believe that bacteria are more important in small-bowel damage. You can’t just give antibiotics, though.”

Dr. Lanas’ earlier research showed that GI perforation is associated with NSAID use as often in the lower GI tract as in the upper GI tract (75% lower GI, 70% upper GI). His later study showed that 18,191 among 50,114 GI complications reported in 2001 were attributable to NSAID and aspirin use. Among 2,800 deaths reported in the overall group, more than 1,000 were attributed to NSAID use with aspirin. Upper GI bleeding and lower GI bleeding were given as the cause in 5.7% and 5.3% of cases, respectively, and upper and lower GI perforations were the cause in 30.1% of cases.

Dr. Lanas noted that more than 80% of the Spanish population of about 40 million uses the 10 general hospitals included in the study. The clear trend from 1996 to 2005 was of a declining estimated upper GI complication rate per 100,000 (reduced from approximately from 87 to 48 and an increasing lower GI complication rate (increased from approximately 20 to 32).

Lower GI complications incurred a significantly longer hospital stay (10 or more days) than did upper GI complications (8 days) \( (P < 0.001) \). In 2005, the mortality rate per 100,000 per year for GI complications was 0.688 for upper GI complications and 0.728 for lower GI complications. Complication rates in the presence of PPI use were significantly higher in the group with complications of the lower GI tract than in those with upper GI complications (16.5% vs. 11.3%; \( P < 0.001 \)).

Looking at differences in risk factors for upper and lower GI complications, Dr. Lanas explained that upper GI complications are more likely to occur in younger males with fewer comorbidities and that lower GI complications are more common in older women with more comorbidities. Summarizing the trends identified by the study, he said that the ratio of upper GI versus lower GI events fell from 7.1 in 1996 to about 1.4:1 in 2005:

“The clinical impact and severity of hospitalizations due to lower GI events were greater than those of upper GI events. Given these results, the evaluation of safety throughout the entire GI tract is important and has the potential to improve patient care by focusing on all GI events, rather than just some of them.”

Dr. Lanas urged further study of NSAID-related risks throughout the entire GI tract and identification of the most appropriate risk-reduction strategies. In an interview, he said that for high-risk patients, the combination of a PPI to protect the upper GI tract and a coxib to protect the lower GI tract might prove to be the best strategy. Limited preliminary data have suggested a superior safety profile for coxibs, such as celecoxib (Celebrex, Pfizer) than for NSAIDs, he commented. Other puzzle pieces needing definition, he suggested, include confirmation of the identified trends in non-Spanish populations.

He concluded, “A need exists for standardized measures of safety that reflect adverse events in the entire GI tract. That would provide a comprehensive picture for the clinician.”

References

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GO-REVEAL: Golimumab (CNTO 148) For Psoriatic Arthritis

• Arthur Kavanaugh, MD, Professor of Medicine, University of California, San Diego

One-year data show sustained improvements in signs and symptoms of active psoriatic arthritis with subcutaneous (SQ) injections every four weeks of either 50 mg or 100 mg of golimumab (Centocor/Schering-Plough). The finding, according to GO-REVEAL (Golimumab, A Randomized Evaluation of Safety and Efficacy in Subjects with Psoriatic Arthritis Using a Human Anti-TNF Monoclonal Antibody), said Dr. Kavanaugh, the lead investigator, “demonstrate the long-term efficacy of this golimumab dosing in improving physical symptoms, functional ability, and quality of life.”

Golimumab, a human anti-tumor necrosis factor–alpha (TNF-α) monoclonal antibody, is being evaluated also in phase 3 trials for treating rheumatoid arthritis and ankylosing spondylitis. It targets and neutralizes both the soluble and membrane-bound forms of TNF-α.

The original 24-week phase of GO-REVEAL enrolled 405 patients who had at least three swollen and at least three tender joints. They received the same golimumab SQ dose of 50 or 100 mg every four weeks and were evaluated according to three endpoints, defined by the American College of Radiology criteria in the percentage of improvement in signs and symptoms (ACR20, ACR50, and ACR70). Patients with more than 3% body surface area (BSA) skin involvement at baseline were evaluated for Psoriatic Area and Severity Index (PASI) responses.

At week 24, 52.1% of patients receiving golimumab 50 mg and 61% of those receiving golimumab 100 mg had achieved ACR20, compared with 12% of those receiving placebo ($P < 0.001$) (Table 1). By week 52, among 237 evaluable subjects, 78.4% of patients in the 50-mg group and 74.1% of those in the 100-mg group achieved ACR20.

All subjects still receiving placebo at week 20 were switched to golimumab 50 mg from weeks 24 through 52 (Table 2).

In patients with more than 3% of their BSA affected by psoriatic skin involvement at baseline, 55.9% of those in the 50-mg group and 66% of those in the 100-mg group achieved at least 75% PASI improvement (PASI 75) at 24 weeks, compared with 1.4% of those receiving placebo ($P < 0.001$). At 52 weeks, the rates were 62% and 69.3% of treated patients, respectively.

Of the golimumab patients, 2.4% reported serious adverse events through week 24, compared with 6.2% of the placebo patients. Up to week 52, golimumab was generally well tolerated, with a safety profile similar to that observed in the first 24 weeks of treatment.

Dr. Kavanaugh concluded, “The sustained effects of golimumab here are encouraging for physicians and for the many patients living with this potentially debilitating disease.”

RADIATE: Tocilizumab for Rheumatic Arthritis

• Paul Emery, MD, University of Leeds, Leeds, U.K.

For rheumatoid arthritis (RA) that has been refractory to one or more anti-TNF agents, tocilizumab plus methotrexate (MTX) provides rapid and significant improvement in signs and symptoms. The improvements, stated Dr. Emery, are experienced irrespective of multiple, previous anti-TNF treatments.

Interleukin 6 (IL-6) is a key pleiotropic pro-inflammatory cytokine that plays a pivotal role in the pathogenesis of RA. Tocilizumab is a humanized anti–IL-6 receptor monoclonal antibody that inhibits pro-inflammatory effects of IL-6. It has been efficacious in patients whose response to MTX or disease-modifying anti-rheumatic drugs (DMARDs) is inadequate. Patients in RADIATE (Research on Actemra Determining efficacy after Anti-TNF failureS), said Dr. Emery, had moderate-to-severe RA for at least six months and had responded inadequately to etanercept (Enbrel, Amgen, Wyeth), adalimumab (Humira, Abbott) or infliximab (Remicade, Centocor).

Patients were predominantly female (82%) (mean age, 53 years). They were randomly assigned to receive placebo plus MTX (n = 160), tocilizumab 4 mg/kg plus MTX (n = 163), or tocilizumab 8 mg/kg plus MTX (n = 175). The primary endpoint was the proportion of patients achieving ACR20. Secondary endpoints included ACR50 and ACR70 responses.

About 50% of the patients had received one prior anti-TNF agent and approximately 15% had tried three. Analysis revealed that all outcomes with 8 mg/kg and most outcomes with 3 mg/kg were significantly better than those in the control group. Withdrawal from treatment or the need for rescue therapy occurred in 25% and 34% of the tocilizumab groups, respectively, and in 60% of controls.
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Table 3 Responses to Tocilizumab at 24 Weeks In Patients with Rheumatoid Arthritis

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Patients receiving the 8-mg/kg dose were nine times more likely than controls to achieve a 20% improvement in signs and symptoms of disease according to ACR criteria (ACR20) at week 24, and patients receiving 4 mg/kg were four times more likely than controls to achieve ACR20 \((P<0.0001)\) (Table 3).

The investigators reported a clear separation between tocilizumab 8 mg/kg and placebo in ACR response rates by week 4 as well as between ACR50 and ACR70 responses by week eight.

Remission rates, defined by the Disease Activity Score using 28 joint counts (DAS 28), increased continually through the study among patients receiving tocilizumab 8 mg/kg. The DAS 28 remission rate reached 30% at week 24.

Common adverse events included diarrhea, upper abdominal pain, rash, and dizziness. Serious adverse events were reported at rates of 6.3%, 7.4%, and 11.3% of the three groups, respectively. Serious infections rates were 4.6%, 1.8%, and 3.1% in the three groups, respectively. The overall response rates were 84% with 8 mg/kg and 87.1% with 4 mg/kg. Discontinuations were attributed to adverse events in approximately 6% of patients in the tocilizumab groups and in 9% of the placebo plus MTX group.

Dr. Emery concluded that treatment with the combination of tocilizumab and MTX was associated with rapid and significant clinical improvement in this population with inadequate response to previous anti-TNF therapy. Examining the effect of prior anti-TNF therapy on outcomes, he said:

“Tocilizumab is efficacious irrespective of the number of prior anti-TNFs, although the level of efficacy tends to be lower after failure with three prior anti-TNFs.”

ASPIRE: Infliximab (Remicade) plus Methotrexate For Rheumatoid Arthritis

- Chenglong Han, MD, Johnson & Johnson, Malvern, Pa.

Treating early RA with infliximab plus MTX, compared with MTX alone, increases a patient’s chances of becoming or staying employed, according to an analysis of ASPIRE (Active Controlled Study of Patients Receiving Infliximab for Treatment of RA of Early Onset). Dr. Han noted that with RA occurring most frequently at the productive ages of 40 to 50 years, loss of employment is a major economic consequence.

“Treatments that prevent disease progression may delay the time to loss of employability due to disability,” he said.

ASPIRE compared the efficacy and safety of the two strategies in infliximab and MTX-naive patients with disease history of less than three years. Clinical efficacy and employment data were collected from the baseline appointment through 54 weeks.

The researchers used a Markov model to estimate the one-year transition probability from employable to unemployable or from unemployable to employable, calculating employable life-years from age 45 to 55 years.

For patients 45 years of age in ASPIRE, 31.4% of women and 29.7% of men were unemployable according to a regression model at baseline.

For patients beginning at age 45 and employable at baseline, the probability of continuing to be employable after one year of treatment was 0.928 in men and 0.905 in women in the infliximab group, and 0.899 in men and 0.867 in women receiving MTX, respectively.

For patients who were unemployable at baseline, the probability of being employable after one year of treatment was 0.481 for men and 0.405 for women in the infliximab groups and 0.390 in men and 0.319 in women in the MTX groups, respectively.

With the Markov model, it was predicted that after 10 years at age 55, 18.5% of women and 14.1% of men in the infliximab groups and 30.7% of women and 24.2% of men in the MTX groups would be unemployable. The model also predicted that 0.99 employable life-years would be expected to be retained per patient over 10 years in the infliximab patients compared with the MTX patients. The analysis, Dr. Chan concluded, demonstrated that patients treated with infliximab could gain economic benefit by retaining employability over time.

- Jon Giles, MD, Assistant Professor of Medicine, Johns Hopkins University, Division of Rheumatology, Baltimore, Md.

Dr. Giles commented in an interview:

I think the bottom line is that patients who are very disabled and have a lot of active swelling and joint inflammation with the potential to have fairly rapid destruction of their joints are the ones you want to be very aggressive with and use the combination. If you can keep them working, then some of the enormous societal expenditures for RA can be averted.

As for avoiding the much higher cost of infliximab, compared with that of generic MTX, he said: “In those with milder disease, you may not need a biologic combination. You still have a good chance of getting them under control with MTX by itself.”