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ARTICLES

Adalimumab Induction Therapy for Crohn Disease Previously Treated with Infliximab. A Randomized Trial 829

W.J. Sandborn, P. Rutgeerts, R. Enns, S.B. Hanauer, J.-F. Colombel, R. Panaccione, G. D'Haens, J. Li, M.R. Rosenfeld, J.D. Kent, and P.F. Pollack

Patients with Crohn disease often respond to infliximab initially but then become intolerant or unresponsive to it. Sandborn and colleagues randomly assigned 325 patients with Crohn disease who were intolerant of or unresponsive to infliximab to receive adalimumab (another tumor necrosis factor antagonist) or placebo. After 4 weeks, adalimumab induced more remissions than did placebo (21% vs. 7%). The study did not address long-term maintenance of response or the immunogenicity of adalimumab.

Summary for Patients 1-20

Effects of the Phytoestrogen Genistein on Bone Metabolism in Osteopenic Postmenopausal Women. A Randomized Trial 839

H. Marini, L. Minutoli, F. Polito, A. Bitto, D. Altavilla, M. Atteritano, A. Gaudio, S. Mazzaferro, A. Frisina, N. Frisina, C. Lubrano, M. Bonaiuto, R. D'Anna, M.L. Cannata, F. Corrado, E.B. Adamo, S. Wilson, and F. Squadrito

Studies suggest that isoflavone phytoestrogens, which are found in soy products, reduce bone loss in women, but the evidence is not definitive. Marini and colleagues compared the phytoestrogen genistein with placebo in 389 osteopenic postmenopausal women. At 24 months, women who took genistein had a greater increase in bone mineral density than did those who took placebo. Genistein improved markers of bone metabolism. It did not increase endometrial thickness, but it did cause gastrointestinal side effects.

Summary for Patients 1-34

Different Ways to Describe the Benefits of Risk-Reducing Treatments. A Randomized Trial 848

P.A. Halvorsen, R. Selmer, and I.S. Kristiansen

Patients respond differently when given equivalent but different descriptions of the outcomes of a treatment. Halvorsen and colleagues randomly assigned 1754 healthy people to receive 1 of 3 surveys with equal but different descriptions of the outcome of a hypothetical drug to prevent either myocardial infarction (MI) or hip fracture. Respondents consented to treatment more frequently when the outcome was described as the number of people who needed to take the drug for 5 years to prevent 1 MI or hip

fracture. They consented less frequently when the description said that the treatment delayed the outcome.

Summary for Patients 1-50

REVIEWS

Meta-analysis: Antithrombotic Therapy to Prevent Stroke in Patients Who Have Nonvalvular Atrial Fibrillation 857

R.G. Hart, L.A. Pearce, and M.I. Aguilar

Hart and colleagues provide an update of a previous meta-analysis of antithrombotic agents for stroke prevention in patients with atrial fibrillation. The updated meta-analysis shows that, compared with placebo, adjusted-dose warfarin reduces stroke risk by 64% (6 trials) and antiplatelet agents reduce stroke risk by 22% (8 trials). Adjusted-dose warfarin is more effective than antiplatelet therapy, but it doubles the risk for major extracranial hemorrhage and intracranial hemorrhage (12 trials). However, the rates of these serious adverse events were only 0.2% per year.

Meta-analysis: Acupuncture for Osteoarthritis of the Knee 868

E. Manheimer, K. Linde, L. Lao, L.M. Bouter, and B.M. Berman

Randomized trials of the effectiveness of acupuncture for treating knee osteoarthritis have yielded inconsistent results. Manheimer and colleagues' meta-analysis included 8 medium-duration randomized trials that compared acupuncture with a sham, usual care, or waiting list control group. Sham acupuncture and active acupuncture were equivalent. In trials that did not use a sham control, the acupuncture group gave better results than the control group.

PERSPECTIVES

Ethical Issues in Stopping Randomized Trials Early Because of Apparent Benefit 878

P.S. Mueller, V.M. Montori, D. Bassler, B.A. Koenig, and G.H. Guyatt

Historically, investigators have felt ethically obliged to stop a trial before completion if the results show a large effect, in order to protect the interests of trial participants assigned to the less effective treatments. Mueller and colleagues argue a contrary position: Stopping a randomized trial early because of apparent benefit is often unethical and can be justified only under restricted circumstances.

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Stopping at Nothing? Some Dilemmas of Data Monitoring in Clinical Trials 882

S.N. Goodman

In contrast to Mueller and colleagues' position, Goodman argues that the goal of a trial is to decide whether a treatment is better and that precisely estimating the benefit is less important if it is large. He also states that trials should not continue in the face of large efficacy differences if offsetting harms do not occur. Society allows researchers to perform controlled trials that could harm participants assigned to the inferior treatment, with the proviso that they avoid unnecessary harm. Society must therefore participate in the discussion of policies that would shift this ethical balance.

EDITORIALS

GAIN for Loss: Adalimumab for Infliximab-Refractory Crohn Disease 888

P. Mannon

In this issue, Sandborn and colleagues evaluated whether treatment with adalimumab would reduce disease activity in patients with Crohn disease who had symptoms despite infliximab treatment or who had become infliximab-intolerant. Their trial suggests that adalimumab can be used in these patients, but fewer patients will respond to adalimumab treatment than to the initial infliximab treatment, and fewer will achieve remission. Treatment with 1 tumor necrosis factor antagonist may alter Crohn disease so that other members in this class of drugs are less effective.

Straight Talk about Disease Prevention 891

H.C. Sox

In this issue, Halvorsen and colleagues remind us about framing effects. They report that the way in which an outcome is described strongly influences whether a patient will consent to an intervention. But how should physicians

use this knowledge? It is hoped that this study will remind researchers, medical students, and practicing physicians that talking time is more than a pleasurable exercise of clinical skills—it can change people's lives.

ON BEING A DOCTOR

When My Father Died 893

H.G.C. Van Spall

I had never known failure, sorrow, loss, or despair, until all of them descended upon me when my father died. This is how it came to be that I, the object of my father's affection and praise, began to believe that I had a hand in his death.

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W.L. Rich III; T. Bodenheimer, R.A. Berenson, and P. Rudolf

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J. Fisher Wilson

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