

Two Procedures Can Be Done at Once, Safely

BY SHARON WORCESTER
Southeast Bureau

TUCSON, ARIZ. — Proximal aortic replacement performed at the time of aortic valve surgery adds no additional risk to the patient, Dr. T. Brett Reece said at the annual meeting of the Southern Thoracic Surgical Association.

A retrospective study of 430 cases involving aortic valve intervention alone and 146 cases involving aortic valve inter-

vention with proximal aortic replacement showed that complication mortality and in-hospital mortality were similar in the two groups, said Dr. Reece of the University of Virginia, Charlottesville.

The 30-day mortality was 4% in the valve intervention-only group, and 3% in the proximal aortic replacement group. The operative complication rate was 7% vs. 9%, respectively. The differences were not statistically significant.

Neurologic, pulmonary, and renal com-

plications, however, were significantly more common in the valve intervention-only group, compared with the proximal aortic replacement group (21% vs. 8%, 23% vs. 12%, and 8% vs. 3%, respectively), Dr. Reece noted, adding that hospital and intensive care unit stays were also significantly longer in the valve intervention-only group.

Patients included in the study were treated electively at the University of Virginia between 1996 and 2004. The mean

age was significantly higher in the valve intervention-only group (68 vs. 60 years), but the groups were similar with regard to comorbidities, including rates of diabetes, pulmonary disease, hemodialysis, cerebrovascular disease, coronary artery disease, and heart failure.

Numerous studies suggest proximal aortic replacement is indicated at the time of valve intervention in patients with proximal aorta diameter greater than 5 cm, but in practice this often doesn't occur because of concern that the replacement adds risk for patients who might never need the second procedure.

But many of these patients will indeed develop a problem with their proximal aorta. These patients are at risk for aortic catastrophe and require a second operative procedure.

Recent studies have shown that proximal aortic replacement can be done with acceptable risk in patients with previous surgery, but the perioperative risk is consistently higher than with the original procedure, said Dr. Reece. When considering the risks associated with a second procedure, risks associated with both the first and second procedure should be considered, he said.

The actual numbers in terms of risk related to a single procedure vs. separated procedures are not clear in the literature, but they are high enough that there's secondary literature on revisions in patients who need proximal aortic replacement after prior intervention, he noted.

Thus, although it may be true that not all patients with an enlarged proximal aorta will require later replacement, a large population will, and therefore the findings of the current study show that concomitant replacement at the time of valve intervention is warranted, he said.

"We advocate replacement of the proximal aorta in patients undergoing an aortic valve procedure with a [proximal aorta] diameter of 5 cm," he said. ■

OMACOR® (omega-3-acid ethyl esters) Capsules

Brief Summary of Prescribing Information

CONTRAINDICATIONS

Omacor is contraindicated in patients who exhibit hypersensitivity to any component of this medication.

PRECAUTIONS

General:

Initial Therapy: Laboratory studies should be performed to ascertain that the patient's TG levels are consistently abnormal before instituting Omacor therapy. Every attempt should be made to control serum TG levels with appropriate diet, exercise, weight loss in overweight patients, and control of any medical problems (such as diabetes mellitus and hypothyroidism) that may be contributing to the patient's TG abnormalities. Medications known to exacerbate HTG (such as beta blockers, thiazides, and estrogens) should be discontinued or changed, if possible, before considering TG-lowering drug therapy.

Continued Therapy: Laboratory studies should be performed periodically to measure the patient's TG levels during Omacor therapy. Omacor therapy should be withdrawn in patients who do not have an adequate response after 2 months of treatment.

Information for Patients:

Omacor should be used with caution in patients with known sensitivity or allergy to fish.

Patients should be advised that use of lipid-regulating agents does not reduce the importance of adhering to diet.

Laboratory Tests:

In some patients, increases in alanine aminotransferase (ALT) levels without a concurrent increase in aspartate aminotransferase (AST) levels were observed. Alanine aminotransferase levels should be monitored periodically during Omacor therapy. In some patients, Omacor increased low-density lipoprotein cholesterol (LDL-C) levels. As with any lipid-regulating product, LDL-C levels should be monitored periodically during Omacor therapy.

Drug Interactions:

Anticoagulants: Some studies with omega-3-acids demonstrated prolongation of bleeding time. The prolongation of bleeding time reported in these studies has not exceeded normal limits and did not produce clinically significant bleeding episodes. Clinical studies have not been done to thoroughly examine the effect of Omacor and concomitant anticoagulants. Patients receiving treatment with both Omacor and anticoagulants should be monitored periodically.

Cytochrome P450-Dependent Monooxygenase Activities: Omega-3-fatty acid containing products have been shown to increase hepatic concentrations of cytochrome P450 and activities of certain P450 enzymes in rats. The potential of Omacor to induce P450 activities in humans has not been studied.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

In a rat carcinogenicity study with oral gavage doses of 100, 600, 2000 mg/kg/day by oral gavage, males were treated with omega-3-acid ethyl esters for 101 weeks and females for 89 weeks without an increased incidence of tumors (up to 5 times human systemic exposures following an oral dose of 4 g/day based on a body surface area comparison). Standard lifetime carcinogenicity bioassays were not conducted in mice.

Omega-3-acid ethyl esters were not mutagenic or clastogenic with or without metabolic activation in the bacterial mutagenesis (Ames) test with *Salmonella typhimurium* and *Escherichia coli* or in the chromosomal aberration assay in Chinese hamster V79 lung cells or human lymphocytes. Omega-3-acid ethyl esters were negative in the *in vivo* mouse micronucleus assay.

In a rat fertility study with oral gavage doses of 100, 600, 2000 mg/kg/day, males were treated for 10 weeks prior to mating and females were treated for 2 weeks prior to and throughout mating, gestation and lactation. No adverse effect on fertility was observed at 2000 mg/kg/day (5 times human systemic exposure following an oral dose of 4 g/day based on a body surface area comparison).

Pregnancy Category C:

There are no adequate and well-controlled studies in pregnant women. It is unknown whether Omacor can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Omacor should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Omega-3-acid ethyl esters have been shown to have an embryocidal effect in pregnant rats when given in doses resulting in exposures 7 times the recommended human dose of 4 g/day based on a body surface area comparison.

In female rats given oral gavage doses of 100, 600, 2000 mg/kg/day beginning two weeks prior to mating and continuing through gestation and lactation, no adverse effects were observed in the high dose group (5 times human systemic exposure following an oral dose of 4 g/day based on body surface area comparison).

In pregnant rats given oral gavage doses of 1000, 3000, 6000 mg/kg/day from gestation day 6 through 15, no adverse effects were observed (14 times human systemic exposure following an oral dose of 4 g/day based on a body surface area comparison).

In pregnant rats given oral gavage doses of 100, 600, 2000 mg/kg/day from gestation day 14 through lactation day 21, no adverse effects were seen at 2000 mg/kg/day (5 times the human systemic exposure following an oral dose of 4 g/day based on a body surface area comparison). However, decreased live births (20% reduction) and decreased survival to postnatal day 4 (40% reduction) were observed in a dose-ranging study using higher doses of 3000 mg/kg/day (7 times the human systemic exposure following an oral dose of 4 g/day based on a body surface area comparison).

In pregnant rabbits given oral gavage doses of 375, 750, 1500 mg/kg/day from gestation day 7 through 19, no findings were observed in the fetuses in groups given 375 mg/kg/day (2 times human systemic exposure following an oral dose of 4 g/day based on a body surface area comparison). However, at higher doses, evidence of maternal toxicity was observed (4 times human systemic exposure following an oral dose of 4 g/day based on a body surface area comparison).

Nursing Mothers:

It is not known whether omega-3-acid ethyl esters are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Omacor is administered to a woman who is breastfeeding.

Pediatric Use:

Safety and effectiveness in pediatric patients under 18 years of age have not been established.

Geriatric Use:

A limited number of patients over 65 years of age were enrolled in the clinical studies. In the pooled analyses, safety and efficacy findings in subjects over 60 years of age (approximately 25% of the study population) did not appear to differ from those of subjects less than 60 years of age.

OMACOR® (omega-3-acid ethyl esters) Capsules

ADVERSE REACTIONS

Treatment-emergent adverse events reported in at least 1% of patients treated with Omacor 4 g per day or placebo during 8 randomized, placebo-controlled, double-blind, parallel-group studies for HTG are listed in Table 2. Adverse events led to discontinuation of treatment in 3.5% of patients treated with Omacor and 2.6% of patients treated with placebo.

Table 2. Adverse Events in Randomized, Placebo-Controlled, Double-Blind, Parallel-Group Studies for Hypertriglyceridemia that Used Omacor 4 g per Day

BODY SYSTEM Adverse Event	Omacor (N = 226)		Placebo* (N = 228)	
	n	%	n	%
Subjects with at least 1 adverse event	80	35.4	63	27.6
Body as a whole				
Back pain	5	2.2	3	1.3
Flu syndrome	8	3.5	3	1.3
Infection	10	4.4	5	2.2
Pain	4	1.8	3	1.3
Cardiovascular				
Angina pectoris	3	1.3	2	0.9
Digestive				
Dyspepsia	7	3.1	6	2.6
Eructation	11	4.9	5	2.2
Skin				
Rash	4	1.8	1	0.4
Special senses				
Taste perversion	6	2.7	0	0.0

Adverse events were coded using COSTART, version 5.0. Subjects were counted only once for each body system and for each preferred term.

*Placebo was corn oil for all studies.

Additional adverse events reported by 1 or more patients from 22 clinical studies for HTG are listed below:

BODY AS A WHOLE: Enlarged abdomen, asthenia, body odor, chest pain, chills, suicide, fever, generalized edema, fungal infection, malaise, neck pain, neoplasm, rheumatoid arthritis, sudden death, and viral infection.

CARDIOVASCULAR SYSTEM: Arrhythmia, bypass surgery, cardiac arrest, hyperlipemia, hypertension, migraine, myocardial infarct, myocardial ischemia, occlusion, peripheral vascular disorder, syncope, and tachycardia.

DIGESTIVE SYSTEM: Anorexia, constipation, dry mouth, dysphagia, colitis, fecal incontinence, gastritis, gastroenteritis, gastrointestinal disorder, increased appetite, intestinal obstruction, melena, pancreatitis, tenesmus, and vomiting.

HEMATOLOGIC-LYMPHATIC SYSTEM: Lymphadenopathy.

METABOLIC AND NUTRITIONAL DISORDERS: Edema, hyperglycemia, increased ALT, and increased AST.

MUSCULOSKELETAL SYSTEM: Arthralgia, arthritis, myalgia, pathological fracture, and tendon disorder.

NERVOUS SYSTEM: Central nervous system neoplasia, depression, dizziness, emotional lability, facial paralysis, insomnia, vasodilatation, and vertigo.

RESPIRATORY SYSTEM: Asthma, bronchitis, increased cough, dyspnea, epistaxis, laryngitis, pharyngitis, pneumonia, rhinitis, and sinusitis.

SKIN: Alopecia, eczema, pruritis, and sweating.

SPECIAL SENSES: Cataract.

UROGENITAL SYSTEM: Cervix disorder, endometrial carcinoma, epididymitis, and impotence.

DRUG ABUSE AND DEPENDENCE

Omacor does not have any known drug abuse or withdrawal effects.

OVERDOSAGE

In the event of an overdose, the patient should be treated symptomatically, and general supportive care measures instituted, as required.

DOSAGE AND ADMINISTRATION

Patients should be placed on an appropriate lipid-lowering diet before receiving Omacor, and should continue this diet during treatment with Omacor. In clinical studies, Omacor was administered with meals.

The daily dose of Omacor is 4 g per day. The daily dose may be taken as a single 4-g dose (4 capsules) or as two 2-g doses (2 capsules given twice daily).

HOW SUPPLIED

Omacor (omega-3-acid ethyl esters) capsules are supplied as 1-gram transparent soft-gelatin capsules filled with light-yellow oil and bearing the designation OMACOR in bottles of 60 (NDC 65726-424-15) and 120 (NDC 65726-424-27).

Recommended Storage:

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature]. Do not freeze. Keep out of reach of children.

Rx only

Revised: January, 2006

Distributed by:
Reliant Pharmaceuticals, Inc.
Liberty Corner, NJ 07938



Address Medical Inquiries to:

Reliant Medical Inquiries
c/o PPD
2655 Meridian Parkway
Durham, NC 27713-2203
or Call: 877-311-7515

© 2006 Reliant Pharmaceuticals, Inc.

4241S-01
14241401-S
PRINTED IN USA

INDEX OF ADVERTISERS

Abbott Laboratories	
Corporate	6
TriCor	11-12
AstraZeneca LP	
Crestor	39-40
Bayer Healthcare, LLC	
Aspirin	25
Daiichi Sankyo, Inc.	
Benicar	36a-36d
GlaxoSmithKline	
Coreg CR	16a-16b, 17
Medtronic, Inc.	
Pacemaker	15-16
Novartis Pharmaceuticals Corporation	
DiovanHCT	3-4
Lotrel	29-31
Pfizer Inc.	
Caduet	20-23
Reliant Pharmaceuticals, Inc.	
Omacor	33-34
Scios Inc.	
Natrecor	4a-4d
Unetixs Vascular, Inc.	
Corporate	13
University of Pittsburgh Medical Center	
Corporate	9