April 2008 Volume 134 ■ Number 4 ■ Suppl 1

Supplement to

Gastroenterology

www.gastrojournal.org

Digestive Disease Week®
and the
109th Annual Meeting of the
AGA Institute

May 17-22, 2008, San Diego, CA

- Program of the Annual Meeting of the AGA Institute, the American Association for the Study of Liver Diseases, the Gastroenterology Research Group, the Society for Surgery of the Alimentary Tract, and the American Society for Gastrointestinal Endoscopy
- Abstracts of Papers Accepted by the AGA Institute
- Abstracts of Papers Accepted by the American Association for the Study of Liver Diseases
- Abstracts of Papers Accepted by the Society for Surgery of the Alimentary Tract

BOUND VOLUMES

For information on bound volumes write to Elsevier, Periodicals Department, 6277 Sea Harbor Drive, Orlando, Florida 32887-4800.

ABSTRACTING/INDEXING SERVICES

GASTROENTEROLOGY is abstracted/indexed in *Biological Abstracts, CABS, Chemical Abstracts, Current Contents, Excerpta Medica, Index Medicus, ISI, Nutrition Abstracts,* and *Science Citation Index.*

REPRINTS

For orders of 100 reprints or more, contact: Commercial Reprints, 360 Park Avenue South, New York, New York 10010-1710, fax (212) 633-3820; e-mail: reprints@elsevier.com.

DISPLAY ADVERTISING

All display advertising must conform to the policies outlined in the current 2008 rate card. Contact the Advertising Representatives (Cunningham Associates, 201-767-4170) for additional information or to request a copy of the rate card.

CLASSIFIED ADVERTISING

Space for both display and line classified advertisements is available. See classified advertising section (in the back of the journal) for details.

CUMULATIVE INDEXES

Cumulative indexes are available from Elsevier, 1600 John F. Kennedy Boulevard, Suite 1800, Philadelphia, Pennsylvania 19103-2899.

STATEMENT OF RESPONSIBILITY

The ideas and opinions expressed in GASTROENTEROLOGY do not necessarily reflect those of the AGA Institute, the Editor, or the Publisher. Publication of an advertisement or other product mention in GASTROENTEROLOGY should not be construed as an endorsement of the product or the manufacturer's claims. Readers are encouraged to contact the manufacturer with any questions about the features or limitations of the products mentioned. Neither the AGA Institute nor the Publisher assumes any responsibility for any injury and/or damage to persons or property arising out of or related to any use of the material contained in this periodical. The reader is advised to check the appropriate medical literature and the product information currently provided by the manufacturer of each drug to be administered to verify the dosage, the method and duration of administration, or contraindications. It is the responsibility of the treating physician or other health care professional, relying on independent experience and knowledge of the patient, to determine drug dosages and the best treatment for the patient.

PERMISSIONS

GASTROENTEROLOGY: GASTAB 134(4) A1–A914(2008)
ISSN 0016-5085

TABLE OF CONTENTS

GI complications in Spain. Methods: Setting: 10 general hospitals in Spain attending ~ 3.000.000 people. All patients hospitalized due to GI events with diagnostic codes registered in the Minimum Basic Data Set that describe GI complication events (AJG 2005) occurring at each participating hospital from Jan 1, 1996, to Dec 31, 2005, have been included in the study. All codes identifying either upper, lower or non-defined (e.g. gastrointestinal bleeding) sources of GI events have been validated. Results: A total of 30,498 patients had 34.544 events in 10 years. There were clear decreasing trends in the crude rate of upper GI events from 77/100,000 people in 1996 (59.6% of all GI events) to 39/100,000 people (39.9% of GI events) in 2005*, and increasing trends in the crude rate of lower GI events from 10 cases/100,000 people (7.9% of GI events) in 1996 to 27/100,000 people (27.9% of GI events) in 2005*. Occurrence of cases with non-specific codes was stable over time. Validation reviewing original clinical charts (6726 = 22% of all 30,498 patients) showed that the source of the event in patients with non-defined GI codes (n=4492) was located in the upper GI tract in 51% of cases, 28% in the lower GI tract whereas the rest remained undefined. This suggests that of all hospitalization due to GI events, 56% were upper GI events, 38% lower GI events and 6 % undefined in the year 2005. Data from validation review of charts revealed that compared to upper GI events, lower GI events were more severe (dead rate 5.5% vs 8.7%*), had longer duration of hospitalization (7.8±8.4 vs 11.5±13.9 days*) and higher impact on resource utilization (Group related diagnosis weight= 1.3±1.2 vs 1.9±2.2*). Overall, recorded NSAID/ASA use was higher in the elderly (> 65 y.o.), was similar in elderly men with either upper or lower GI events (36.7% vs 31.6%), but not in elderly women (42% vs 31.5%*). Conclusions: Over the last 10 years, there was a clear decreasing trend in the rates of hospitalizations due to upper GI complications in contrast with an increasing trend of lower GI complications. The clinical impact and severity of hospitalizations due to lower GI events were greater than those of upper GI events, and among the elderly, a third of lower GI events were associated with NSAID/ASA use. (*p <0.0001; chi-square test).

114

Combination of a Cyclooxygenase (COX)-2 Selective NSAID and a Proton Pump Inhibitor for Prevention of Gastroduodenal Ulcers in Very High Risk Patients: A One-Year, Double-Blind, Randomized Trial

Francis K. L. Chan, Bing-yee Suen, Vincent W. Wong, Justin Wu, Joseph JY Sung

Background & Aims: Among patients with arthritis who had prior ulcer bleeding, we previously showed in a randomized trial that none receiving celecoxib plus esomeprazole had recurrent ulcer bleeding in 1 year. While endoscopic ulcer remains to be an important surrogate for ulcer complications, it is uncertain if this treatment strategy could eliminate recurrent gastroduodenal ulcers in these very high risk patients. We studied the ulcer incidence and factors predicting ulcer recurrence in a prospective, double blinded trial of patients with prior ulcer bleeding. Methods: Consecutive patients who presented with NSAID-associated ulcer bleeding were screened. Patients were enrolled after their ulcers had healed and a test for *Helicobacter pylori* was negative. All patients were given celecoxib 200 mg twice daily. They were randomly assigned to receive 20 mg of esomeprazole twice daily (combined-treatment group) or a placebo (control group) for 12 months. Patients underwent endoscopy if they developed recurrent bleeding. Those without recurrent events underwent endoscopy at their last follow-up visit. The endpoint was recurrent endoscopic and/or bleeding ulcers. Analysis was by intention to treat. Results: 273 patients were enrolled, 221 (81%) underwent endoscopy (111 in the combined-treatment group and 110 in the control group). The cumulative incidence of recurrent bleeding ulcers was 0% in the combined-treatment group and 8.9% in the controls (difference, 8.9; 95% CI, 4.1 to 13.7; p=0.0004). The cumulative incidence of recurrent endoscopic ulcers was 6.7% in the combined-treatment group and 16.8% in the controls (difference, 10.1; 95% CI, 1.4 to 18.8; p=0.02). Combining bleeding and endoscopic ulcers, 6.7% in the combined-treatment group and 25.9% in the controls had recurrent ulcers in one year (difference, 19.2; 95% CI, 9.8 to 28.6; p<0.0001). Significant dyspepsia (hazard ratio, 11.0; 95% CI, 3.8 to 31.5), treatment assignment (hazard ratio, 7.6; 95% CI, 2.9 to 20), concomitant low-dose aspirin (hazard ratio, 2.4; 95% CI, 1.1 to 5.1), and ulcer diameter greater than 2 cm (hazard ratio, 2.4; 95% CI, 1.1 to 4.9) independently predicted ulcer recurrence. Conclusion: Combined treatment with a COX-2 selective NSAID and a proton-pump inhibitor did not totally eliminate ulcer recurrence in patients with very high gastrointestinal risk.

116

A Single Tablet Multilayer Formulation of Enteric-Coated Naproxen Coupled with Non-Enteric-Coated OMEPRAZOLE Is Associated with a Significantly Reduced Incidence of Gastric Ulcers vs. Enteric-Coated Naproxen: A Prospective, Randomized, Double-Blind Study

Jay L. Goldstein, Mark B. Sostek, John G. Fort, Dennis S. Riff, Ying Zhang, John R. Plachetka

Introduction: Co-prescribed enteric-coated (EC) proton pump inhibitors (PPIs) reduce the incidence of gastric ulcers (GUs) associated with NSAID use. Long-term adherence to such co-therapy is suboptimal and new approaches are needed to help ensure full medical benefit, which may be lost due to non-adherence. The efficacy and safety of a single tablet formulation, PN200, which provides sequential delivery of non-EC omeprazole 20 mg + EC naproxen 500 mg was compared with EC naproxen 500 mg alone (twice daily use for both). **Methods:** A 6-month, randomized, double-blind, parallel-group, multicenter study included *H. pylori*-seronegative patients who required chronic NSAIDs and were at risk of NSAID-associated GUs (18-49 y/o with a Hx of GU or duodenal ulcer (DU) within the past 5 yrs, and/or ≥50 y/o). Major exclusion criteria included use of antisecretory agents/misoprostol within 14 days. Patients were randomized to either PN200 bid or EC naproxen 500 mg bid. EGD was performed at baseline, 1, 3 and 6 months. The primary endpoint was the proportion of patients developing a GU (≥3 mm diameter with depth) during the 6-month study. Secondary endpoints included incidence of DU, tolerability and safety. **Results:** Baseline demographics were similar between groups. The table shows the results of the ITT population (randomized patients who had no baseline ulcer and received ≥1 dose of study drug) and additional results of the sub-population of patients who concomitantly received low-dose (≤325 mg) ASA. The proportion of patients discontinuing due to UGI adverse events was 4.4% for PN200 and 10.8% for EC naproxen (p=0.012). **Conclusion:** This multicenter concept trial demonstrates that non-EC omeprazole + EC naproxen in a single tablet formulation significantly reduce the incidence of GUs and DUs in the overall population (RR for GU, 72%), and in those with concomitant ASA therapy (RR for GU, 73%). This approach may add to the treatment armamentarium for patients at risk of NSAID-associated GU, and address adherence to GPA co-therapy.

	Survival analysis and cumulative observed ulcers [%; (n)]			
	GU		DU	
	PN200 (n=206)	EC naproxen (n=203)	PN200 (n=206)	EC naproxen (n=203)
1 month	3.4% (7[a])	10.3% (21)	0.5% (1[a])	5.4% (11)
3 months	5.1% (10[a])	23.1% (40)	0.5% (1[a])	8.9% (16)
6 months	8.3%[b] (15[a])	29.4% (48)	0.5%[b] (1[a])	10.8% (18)
	Survival analysis and cumulative observed GU by ASA use [%; (n)]			
	PN200 + ASA (n=56)	PN200 No ASA (n=150)	EC naproxen + ASA (n=52)	EC naproxen No ASA (n=151)
6 months	10.4% (5)	7.6% (10)	39.0% (15)	26.5% (33)

[a]For observed incidence p<0.01 at 1 month and p<0.001 at 3 and 6 months (CMH test); [b]for survival analysis at 6 months p<0.001 between groups for GU and DU (log-rank test)

117

Physicians Fail to Provide Protective Co-Therapy for High GI Risk Patients Taking NSAIDs—Even with Direct Interactive Communication and Free PPI: Results of a Prospective Outcomes Trial

Loren . Laine, Laurine Connors, Marie R. Griffin, Sean P. Curtis, Christopher P. Cannon

We assessed the success of strategies designed to optimize adherence to guidelines for co-therapy in NSAID users with increased GI risk in a large, prospective, double-blind outcomes trial. **METHODS**: Arthritis patients ≥ 50 yrs were randomly assigned to diclofenac (75 mg bid) or etoricoxib (60-90 mg qd). Reminders that protective therapy (PPI or misoprostol) should be provided to patients with GI risk factors (age > 65 yrs; prior ulcer or hemorrhage; use of steroids, anticoagulants or aspirin) were presented at initial investigator meetings and in the protocol. Omeprazole was provided at no charge. Midway through the study, an intervention was performed: investigators received a form for each patient with a risk factor reminding them to provide co-therapy; if they did not, they were required to return the form stating the reason. **RESULTS**: 23,504 were enrolled (14,029 prior to the intervention). 15,235 (65%) patients had ≥ 1 risk factor and 7913 (52%) of them received PPI or misoprostol (> 99% PPI). Table 1 shows results relative to time of intervention. The main reasons for not providing co-therapy were physician judgment (52%) and patient refusal (42%). **CONCLUSIONS**: Approximately 50% of NSAID users with GI risk factors are not given protective co-therapy—even if prescribers are reminded repeatedly and the cost of therapy is not an issue. Direct communication requiring written response increased adherence to guidelines modestly. Physicians prescribed prophylaxis most often in those with a prior ulcer or hemorrhage and those with multiple risk factors. Achieving high levels of adherence to guidelines will be difficult. Our results support the need for patient and physician educational programs and pharmacy systems that require prescribers to consider additions (e.g., PPI) and/or substitutions (e.g., coxib) in high GI risk patients prescribed NSAIDs.

Table 1. Proportion of patients with risk factors who received PPI or misoprostol

Risk Factor	All patients enrolled pre-intervention (N=14,029)	All patients enrolled post-intervention (N=9,475)	Pre → post intervention results in the group of patients who enrolled pre-intervention and remained in study 6 mos post-intervention (N=10,026)
Any risk factor	4374/9347 (47%)*	3539/5888 (60%)	2879/6515 (44%) → 3976/6515 (61%)*
Age > 65	2764/6226 (44%)*	2177/3773 (58%)	1780/4251 (42%) → 2518/4251 (59%)*
Age > 75	854/1878 (45%)*	545/928 (59%)	481/1156 (42%) → 670/1156 (58%)*
Prior ulcer or hemorrhage	695/1040 (67%)**	445/610 (73%)	446/693 (64%) → 551/693 (80%)*
Steroid use	480/970 (49%)*	599/949 (63%)	282/631 (45%) → 391/631 (62%)*
Anticoagulant use	28/58 (48%)**	25/34 (74%)	18/33 (55%) → 25/33 (76%)
Aspirin use	2608/4926 (53%)*	1853/2671 (69%)	1726/3436 (50%) → 2239/3436 (65%)*
1 risk factor	2459/5865 (42%)*	2179/3982 (55%)	1666/4204 (40%) → 2404/4204 (57%)*
2 risk factors	1644/3111 (53%)*	1169/1673 (70%)	1058/2101 (50%) → 1402/2101 (67%)*
3-4 risk factors	271/371 (73%)**	191/233 (82%)	155/210 (74%) → 170/210 (81%)

Proportions shown are number receiving co-therapy/number with risk factor * p < 0.00001 pre vs. post-intervention ** p < 0.05 pre vs. post-intervention