GI Safety and Tolerability of Celecoxib

Some Considerations in Selection of Arthritis Anti-inflammatory/Analgesic Therapies

- Efficacy
  - Osteoarthritis
  - Adult rheumatoid arthritis
- Tolerability
  - Dyspepsia
  - Abdominal pain
  - Nausea
  - Non-GI symptoms
- Safety
  - GI (ulcers, ulcer complications)
  - Renal/cardiovascular
  - Platelet
  - Hemoglobin/hematocrit counts
  - Hepatic

GI Adverse Events Occurring in ≥ 2% of Celecoxib Patients

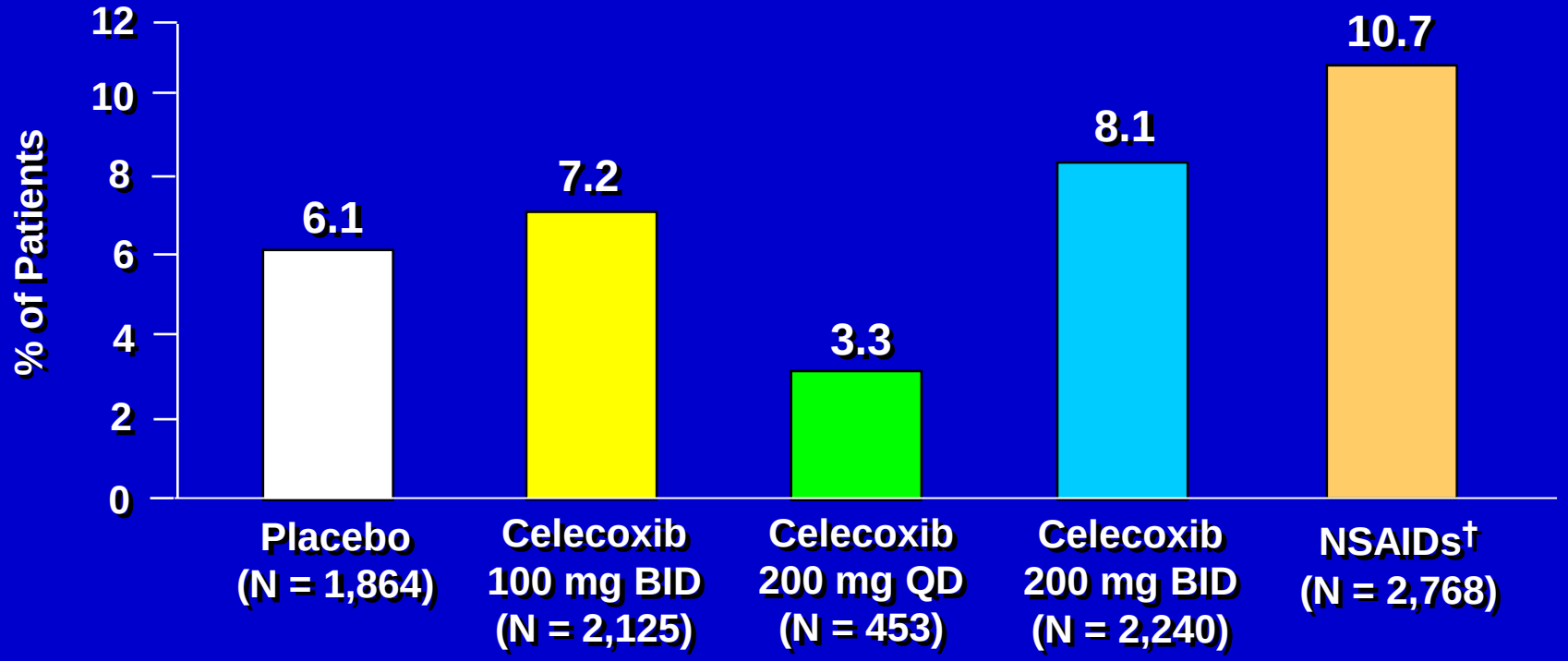
North American Arthritis Trials

GI event	Celecoxib 100 mg BID (N = 1,779) %	Celecoxib 200 mg QD (N = 453) %	Celecoxib 200 mg BID (N = 1,914) %	Placebo (N = 1,864) %	Comparator NSAIDs* (N = 2,098) %
Abdominal pain	3.4	2.0	5.2	2.8	8.2
Diarrhea	5.0	3.5	6.6	3.8	6.1
Dyspepsia	8.7	4.6	9.9	6.2	12.0
Flatulence	2.1	2.2	2.3	1.0	3.7
Nausea	3.6	2.4	3.7	4.2	5.6

Celecoxib is contraindicated in patients with known hypersensitivity to celecoxib. Celecoxib should not be given to patients who have demonstrated allergic-type reactions to sulfonamides; to patients who have experienced asthma, urticaria (hives), or allergic-type reactions after taking aspirin or other NSAIDs..

Discontinuation Rates Due to Adverse Events*

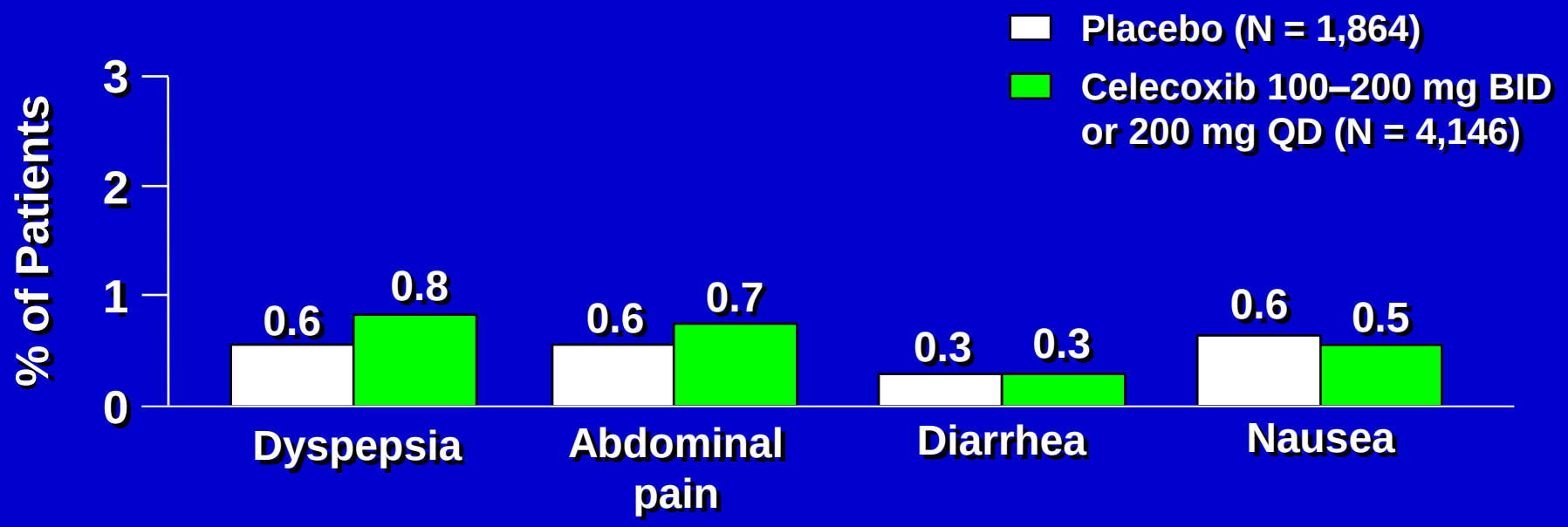
North American Arthritis Trials



*Includes any adverse events with an incidence ≥ 0.5% for any treatment group
†Diclofenac, naproxen, ibuprofen
Data on file. Searle, Skokie, IL.

Discontinuation Rates Due to GI Adverse Events

North American Arthritis Trials



Data on file. Searle, Skokie, IL.

Tolerability of Celecoxib

Summary

- Tolerability of celecoxib is similar to placebo
- Upper GI symptoms were generally mild to moderate

Most common side effects were headache (15.8%), dyspepsia (8.8%), upper respiratory tract infection (8.1%), diarrhea (5.6%), sinusitis (5.0%), and abdominal pain (4.1%). Side effects were generally mild.

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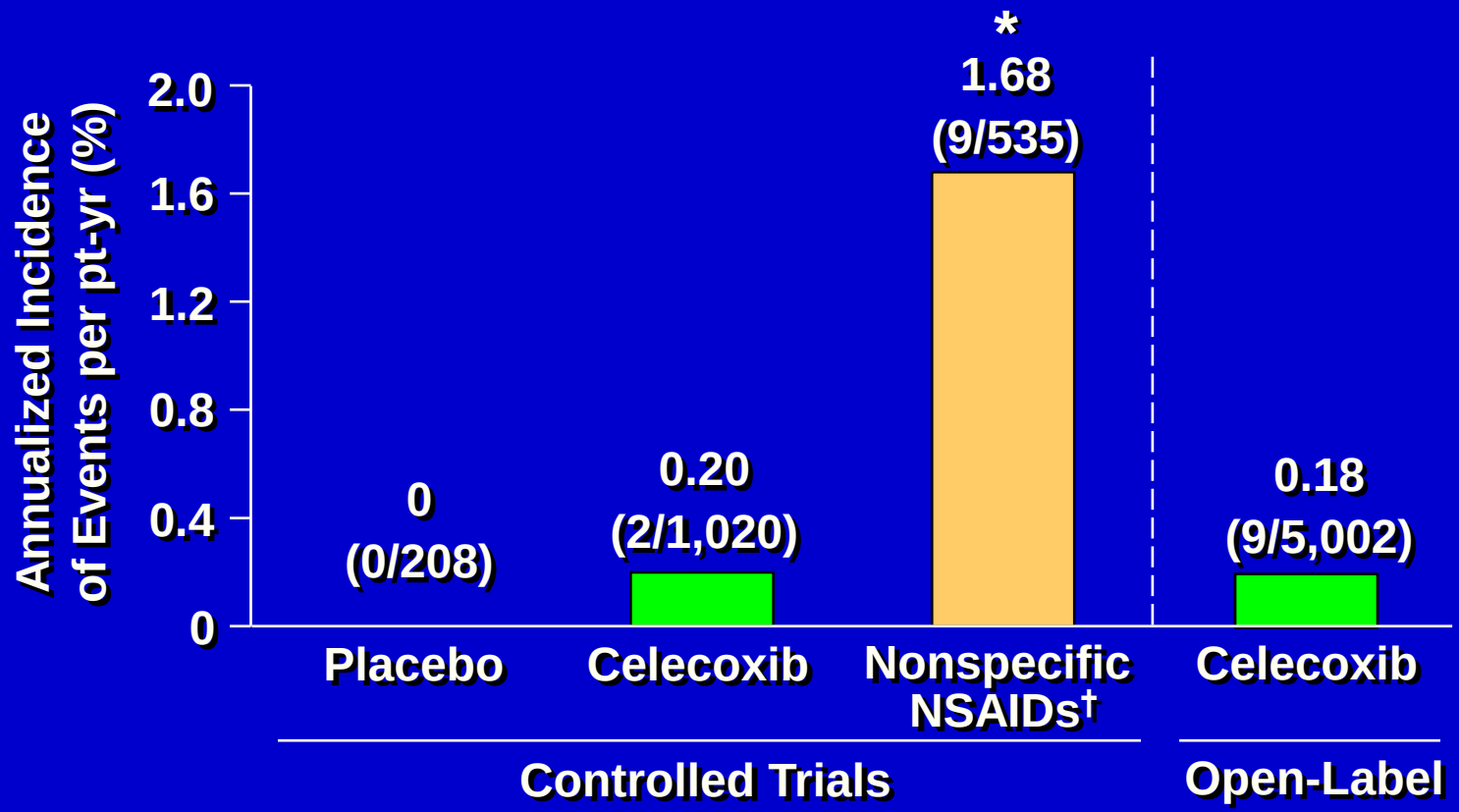
Incidence of GI Ulcer Complications

Data From ~13,000 Patients in Phase II–III Trials

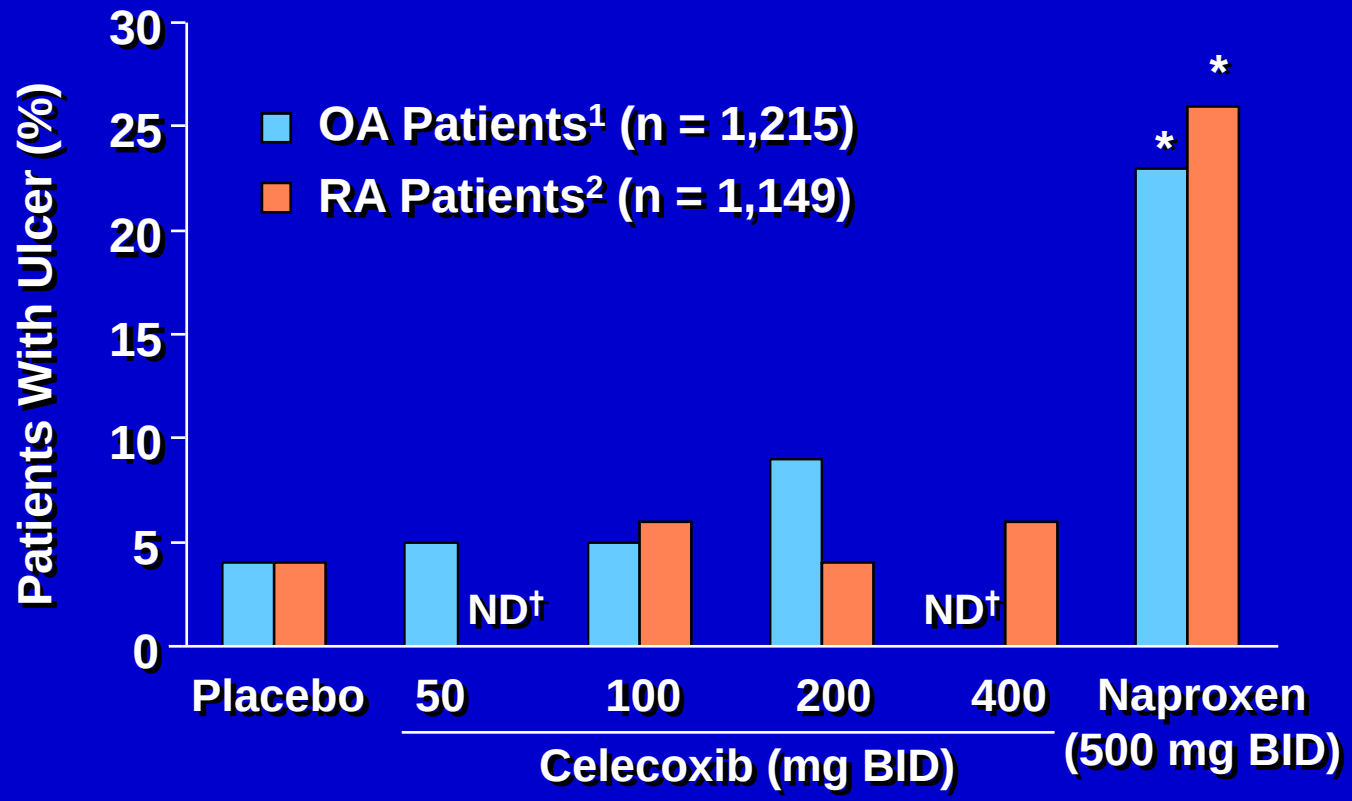


Celecoxib has not been studied in pregnant women. Celecoxib should therefore only be used during pregnancy when the potential benefits outweight the potential risks.

*$P < 0.05$ vs celecoxib
†Naproxen, diclofenac, or ibuprofen
Goldstein, et al. *Am J Gastroenterol.* 2000;95:1681–1690.

Incidence of GI Ulcers

After 12 Weeks of Treatment (Trials 021[1] and 022[2])



The correlation between findings of endoscopic studies and the incidence of clinically serious upper GI events has not been fully established.

*$P < 0.001$ vs all other treatments

†ND = not done

1. Data on file. Searle, Skokie, IL.
2. Simon, et al. *JAMA*. 1999;282:1921–1928.

Upper GI Safety of Celecoxib Summary

- Endoscopic ulcer incidence is significantly lower with celecoxib than with therapeutic dosages of comparator non-specific NSAIDs.[1]
- Symptomatic ulcers and ulcer complications (ie, bleeding, perforation, gastric outlet obstruction) are clinically important events.[2]

The correlation between findings of endoscopic studies and the incidence of clinically serious upper GI events has not been fully established. Serious GI toxicity can occur with or without warning symptoms with NSAIDs.

1. Simon, et al. *JAMA*. 1999;282:1921–1928.
2. Silverstein, et al. *Ann Intern Med*. 1995;123:241–249.

SUCCESS-I Study
Healthcare Resource Utilization

- Randomized, multicenter, double-blind 12-week trial (SUCCESS-I in OA) designed to reflect standard clinical practice
- Treatment arms include daily doses of celecoxib 200 mg, celecoxib 400 mg, naproxen 1000 mg, or diclofenac 100 mg
- Healthcare resource utilization is primarily driven by the evaluation of drug intolerance and the management of upper GI ulcer complications

SUCCESS-I
The Largest Multinational OA Study

Celecoxib was associated with fewer GI events versus pooled comparator NSAIDs (naproxen and diclofenac)[1]	
75% fewer	ICU hospitalizations
52% fewer	GI hospitalizations
86% fewer	Blood transfusions
34% fewer	Physician office visits for upper GI complications
45% fewer	Specialist visits for upper GI complications

1. Goldstein JL, Eisen G, Stenson W, et al. Celebrex significantly reduces gastrointestinal-related healthcare resource utilization compared to NSAIDs: SUCCESS-1 in osteoarthritis (OA) trial [abstract]. *Arthritis Rheum*. 2001;44(suppl):Abstract 503.

Celecoxib GI Tolerability and Safety Summary

- Tolerability of celecoxib is similar to placebo
- Endoscopic ulcer incidence is significantly lower with celecoxib than with therapeutic dosages of comparator non-specific NSAIDs
- In the SUCCESS-I study, celecoxib was associated with fewer GI events versus pooled comparator NSAIDs (naproxen and diclofenac)
- The CLASS study further confirms the upper GI safety profile of celecoxib

The correlation between findings of endoscopic studies and the incidence of clinically serious upper GI events has not been fully established. Serious GI toxicity can occur with or without warning symptoms with NSAIDs.