Safety of greater than 3 days of therapy with parecoxib injection in the management of postoperative pain

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INTRODUCTION

- Multi-modal pain management that includes parenteral non-opioid analgesics is strongly recommended in fast-track surgery protocols.[1]
- Current guidelines recommend non-steroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2-specific inhibitors (coxibs) to improve postoperative analgesia and decrease opioid consumption and opioid-related side effects.[2]
- Parecoxib is an injectable coxib used for the management of acute postoperative pain.[3]
- Most patients receive parecoxib treatment for 2-3 days following surgery.[3]
- However, certain surgeries (eg, gastrointestinal) or circumstances (eg, when a patient is debilitated) require parenteral administration of analgesics beyond 3 days.
- The current analysis assessed the clinical safety of parecoxib for the management of postoperative pain when administered for >3 days.

METHODS

- An examination of 28 randomized, placebo-controlled trials of parecoxib for the management of postoperative pain identified 3 trials in which patients could have received parecoxib for >3 days.
  - Study designs for each of these trials are shown in **Table 1**.
- Data from these 3 studies was pooled and the frequency of all treatment-related adverse events (AEs) was calculated for the placebo and parecoxib treatment groups.
- Specific analyses were also conducted to examine the frequency of specific, predefined, potentially serious events commonly associated with NSAIDs and/or coxibs, including thrombotic or embolic cardiovascular events, serious gastrointestinal events, and serious renal events.

RESULTS

Table 1. Studies included in the analysis

Surgery type	Parecoxib treatment[a]
Total hip arthroplasty[4]	• All patients received 40 mg IV parecoxib followed by 20 mg IV parecoxib on Day 1. • Patients were then randomized to receive IV placebo, 20 mg IV parecoxib QD, or 20 mg IV parecoxib BID on Days 2-5.
Lower abdominal gynecologic[5]	• All patients received 40 mg IV parecoxib followed by 20 mg IV parecoxib on Day 1. • Patients were then randomized to receive IV placebo or 20 mg IV parecoxib BID on Days 2-5.
General[b,6]	• Patients were randomized to receive placebo or active treatment on Days 1-10. • Active treatment consisted of an initial 40 mg IV dose of parecoxib followed by 20 mg IV doses of parecoxib every 12 hours through at least Day 3. • Beginning on Day 4, or later if patients could not tolerate oral medication, patients in the active treatment group received 20 mg oral valdecoxib through Day 10.

[a] Day 1 refers to day of surgery.
[b] Procedure types included major orthopedic, abdominal, gynecologic, non-cardiac thoracic, and primary cancer resection.
BID = twice daily; IV = intravenous; QD = once daily.

- 358 patients received parecoxib for >3 days, including 63/320 (19.7%) in the hip arthroplasty study, 92/211 (43.6%) in the gynecologic study, and 203/525 (38.7%) in the general surgery study.
- 318 patients received placebo for >3 days.
- Mean duration of treatment was 4.1 days for parecoxib and 4.2 days for placebo in the 3 combined studies.
- Basic patient demographics for both treatment groups are shown in **Table 2**.

Table 2. Patient demographics

	Placebo n=318	Parecoxib n=358
Gender, n (%)		
Male	112 (35)	131 (37)
Female	206 (65)	227 (63)
Race, n (%)		
White	303 (95)	344 (96)
Black	7 (2)	7 (2)
Asian	1 (0)	0 (0)
Not listed	7 (2)	7 (2)
Age, years		
Mean	52.4	53.7
SD	13.9	13.7
BMI, kg/m^2		
Mean	27.3	27.1
SD	4.9	4.9

BMI = body mass index; SD = standard deviation.

- The occurrence of treatment-emergent AEs was similar between treatment groups and, with the exception of constipation, all AEs occurred in <1% of patients (**Table 3**).
- The only AEs to occur in ≥0.5% of patients in the parecoxib group, and at a higher frequency than placebo, were nausea, vomiting, dizziness, fatigue, incision site vesicles, and bloody discharge (**Table 3**).
  - Each of these events occurred in only 1-2 more patients in the parecoxib group compared with the placebo group.
- There were no reports of thrombotic or embolic cardiovascular events in either group.
- There were no reports of gastrointestinal perforations, ulcerations, hemorrhage, or obstructions in either group.
- There was 1 (0.3%) report of oliguria in the parecoxib group.

Table 3. Most common treatment-emergent AEs[a]

Event, n (%)	Placebo n=318	Parecoxib n=358
Any AE	31 (9.7)	37 (10.3)
Constipation	5 (1.6)	5 (1.4)
Nausea	0 (0.0)	2 (0.6)
Vomiting	1 (0.3)	2 (0.6)
Dizziness	0 (0.0)	2 (0.6)
Fatigue	0 (0.0)	2 (0.6)
Insomnia	2 (0.6)	2 (0.6)
Tachycardia	0 (0.0)	2 (0.6)
Incision site vesicles	1 (0.3)	2 (0.6)
Bloody discharge	0 (0.0)	2 (0.6)
Diarrhea	2 (0.6)	1 (0.3)
Headache	2 (0.6)	1 (0.3)
Chills	2 (0.6)	0 (0.0)

[a] Occurring in ≥0.5% of patients in either treatment group.
AE = adverse event.

CONCLUSIONS

- The occurrence of AEs in patients receiving parecoxib following a variety of surgical procedures for >3 days was low and similar to those receiving placebo.
- The occurence of specific, predefined, potentially serious AEs commonly associated with NSAIDs and/or coxibs was also low with parecoxib treatment.

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DISCLOSURE

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