

# Lumiracoxib Introduction Mathias Hukkelhoven PhD

## JOINT MEETING OF THE ARTHRITIS ADVISORY COMMITTEE AND THE DRUG SAFETY AND RISK MANAGEMENT ADVISORY COMMITTEE

February 16-18, 2005, Hilton Gaithersburg, 620 Perry Parkway, Gaithersburg, Maryland.

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### Highlights

- **LARGE DATABASES ON LUMIRACOXIB, IBUPROFEN & NAPROXEN:** The Novartis lumiracoxib program also provided large ibuprofen and naproxen databases.
- **EACH DRUG HAS A UNIQUE BENEFIT-RISK PROFILE:** Each non-selective and COX-2 selective NSAID has an individual benefit-risk profile, and lumiracoxib has a unique “GI and CV safety profile”.
- **PRESENTATION TO FOCUS ON CHRONIC USE DATABASE:** Lumiracoxib has been investigated for several indications, but the Novartis presentation will focus on chronic indications, with data on 34,000 patients in 22 clinical trials of 1 week or longer.
- **LARGE (>18,000 PATIENT) TARGET TRIAL:** These data include the TARGET trial in over 18,000 patients (the largest NSAID trial ever performed) and a trial that used “400 mg daily dosing, which is 4 times the dose for which approval will be sought”.
- **LARGE META-ANALYSIS (34,000 PATIENTS):** In addition, the results of a meta-analysis of all 22 clinical trials will be presented.
- **GI BENEFIT WITH NO SIGNIFICANT GI RISK:** The results show “a definitive GI benefit with lumiracoxib in the non-aspirin population. In addition, the CV meta-analysis of all lumiracoxib studies at no point revealed a significant CV risk”.

### Presentation Text

Thank you. Dr. Wood, Dr. Gibofsky, Dr. Gross, members of the FDA Advisory Committees, FDA, and Guests: Good

morning. My name is Mathias Hukkelhoven and I am responsible for Global Regulatory Affairs at Novartis.

On behalf of Novartis, I would like to thank you for the opportunity to review the gastrointestinal and cardiovascular safety data that we have gathered in our clinical development program for lumiracoxib.

As a part of the program, we have also gathered one of the largest databases of clinical trial data with ibuprofen and naproxen.

Allow me to remind you of the reason that the COX-2 selective NSAIDs were developed. In the U.S. alone, there are approximately 100,000 hospitalizations, and as we heard yesterday, 16,000 deaths annually that are caused by GI adverse events. Deaths due to NSAIDs are among the leading causes of death in the U.S.

Our presentation will make the following key points. Each non-selective NSAID and COX-2 selective inhibitor has a benefit-risk profile that must be considered individually.

The Novartis development program provides clinically informative safety data for lumiracoxib as well as for ibuprofen and naproxen.

The GI and CV safety profile for lumiracoxib differs from non-selective NSAIDs and other COX-2 selective inhibitors.

We have investigated the use of lumiracoxib for several indications, but our presentation today will focus on the safety data accumulated for chronic indications. We have conducted 22 clinical trials of 1 week or longer in which 34,000 patients were enrolled.

The largest of the clinical studies was the TARGET outcome study. This is the largest outcome study ever conducted for an NSAID or COX-2 selective inhibitor with 18,325 patients enrolled. It is important to note that this study was conducted at 400 mg daily dosing, which is 4 times the dose for which approval will be sought.

This 1-year study compared lumiracoxib to two different NSAIDs - naproxen and ibuprofen.

We will also present a meta-analysis of cardiovascular safety of all 22 long-term lumiracoxib studies.

Our presentation will demonstrate that there is a definitive GI benefit with lumiracoxib in the non-aspirin population. In addition, the CV meta-analysis of all lumiracoxib studies at no point revealed a significant CV risk.

I would like to introduce today's presenter Dr. Patrice Matchaba from our Clinical Research Department. In addition, we have a few advisers with us who will be able to answer specific questions. These are Dr. Michael Farkouh, a cardiologist from NYU; Dr. Raymond Hirschberg, a nephrologist from UCLA; and Dr. Thomas Schnitzer, a rheumatologist from Northwestern.

Drs. Farkouh and Schnitzer were the lead authors on the TARGET CV and GI publications that were published this past September in the Lancet. I would now like to turn the podium to Dr. Patrice Matchaba.

# Presentation Slides

Note: Some of the slides presented may not be included below.

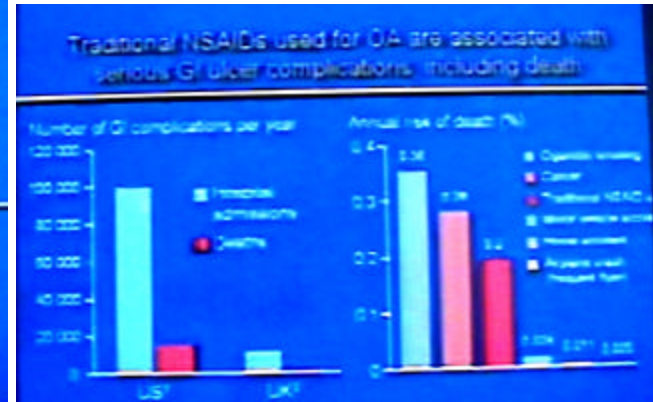


Joint Meeting of the Arthritis and the Drug Safety and Risk Management Advisory Committees

Gastrointestinal and Cardiovascular Safety of Lumiracoxib, ibuprofen, and Naproxen

February 17, 2005

Matthias Hukkelhoven, PhD  
Senior Vice President and Global Head  
Drug Regulatory Affairs  
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### Key points

- Each NSAID/COX-2 selective inhibitor has a benefit-risk profile that must be considered individually
- Novartis development program provides clinically informative safety data for lumiracoxib, ibuprofen and naproxen
- Safety profile of lumiracoxib differs from non-selective NSAIDs and other COX-2 selective inhibitors

### Presentation overview

- Presentation of TARGET study
  - Largest (18,325 patients) GI outcomes study conducted in OA patients
  - Compared lumiracoxib to naproxen and ibuprofen
  - Lumiracoxib dose is 4x the recommended chronic OA dose
- Presentation of comprehensive meta-analysis of CV safety
  - Includes all completed randomized controlled clinical trials of lumiracoxib with durations ≥ 1 week (27 trials, 33,533 patients)
- Definitive GI benefit in non-aspirin population
- No significant CV risk in meta-analysis of all lumiracoxib (including 1 week)

### Participants

- Presentation: Patrice Matchaba, MD  
Global Medical Director, lumiracoxib program
- External clinical experts
  - Michael Farkouh, MD  
Cardiologist, NYU Medical Center
  - Raimund Hirschberg, MD  
Nephrologist, Harbor-UCLA Medical Center
  - Thomas Schitzer, MD, PhD  
Rheumatologist, Northwestern University Feinberg School of Medicine