

IND SAFETY REPORT: INITIAL WRITTEN REPORT

TO: Division of Drug Oncology Products, Center for Drug Evaluation and Research, FDA

FAX: 301-796-9845

1. IND NUMBER
61010

2. AGENT NAME
CCI-779 (temsirolimus, Torisel®)

3. DATE
June 24, 2011

4. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION
L. Austin Doyle, MD, Senior Investigator for Investigational Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI

6. PHONE NUMBER
301-496-1196

7. FAX NUMBER
301-402-0428

8a. PROTOCOL NUMBER (AE#)
GOG-0086P (AE# 1314479)

8b. AE GRADE: AE
Grade 3: Joint effusion

9. PATIENT IDENTIFICATION
046-0086P-026

10. AGE
72 years

11. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT
The patient is a 72-year-old female with endometrial adenocarcinoma who experienced grade 3 joint effusion while on a phase 2 trial utilizing the investigational agent temsirolimus in combination with paclitaxel and carboplatin. The patient began the investigational therapy on February 17, 2011, and received her last dose of temsirolimus on May 27, 2011 (Cycle 5, Day 8), and the last doses of paclitaxel and carboplatin on May 20, 2011 (Cycle 5, Day 1). On June 9, 2011 (Cycle 5, Day 21), the patient presented to the clinic with left ankle pain, erythema, and swelling. The patient also had a fever (102°F) the night before, which was controlled by Tylenol®. She was admitted for further evaluation. X-ray examination did not show evidence of fracture or dislocation of the left ankle. Her synovial fluid analysis suggested acute inflammation. No crystals were observed in the synovial fluid. Culture results from blood and synovial fluid were negative. Her uric acid was 4.4 mg/dL (reference range: 2.0-6.0 mg/dL) and her erythrocyte sedimentation rate was more than 140 mm/hr (reference range: 0-30 mm/hr). Asymmetric polyarticular inflammatory arthritis was considered. Depo-Medrol® and oxycodone were given. The patient was discharged on June 12, 2011, when her symptoms resolved. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.

13. DOSE, ROUTE, AND SCHEDULE

Cycle = 21 Days
Temsirolimus: 25 mg IV over 30 minutes on Days 1 and 8 (starting with Cycle 2 for those patients entering post surgery) × 6 cycles. Maintenance Therapy (Cycles 7+): Temsirolimus 25 mg IV over 30 minutes weekly on Days 1, 8, and 15 (Note: Patients to receive maintenance treatment until disease progression or until adverse events prohibit further therapy).

14. DATES OF TREATMENT

The patient began the investigational therapy on February 17, 2011, receiving the last dose of temsirolimus on May 27, 2011 (Cycle 5, Day 8), the last doses of carboplatin and paclitaxel on May 20, 2011 (Cycle 5, Day 1).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 2731.
There have been no other cases of joint effusion reported to the NCI through AdEERS as serious adverse events for temsirolimus.

16. COMMENTS

Paclitaxel: 175 mg/m² IV over 3 hours on Day 1 × 6 cycles; Carboplatin: AUC = 5 IV over 30 minutes on Day 1 × 6 cycles

AT THIS TIME, NO OTHER INFORMATION IS AVAILABLE. IF UPON FURTHER INVESTIGATION RELEVANT INFORMATION BECOMES AVAILABLE, THEN A FOLLOW-UP REPORT WILL BE SUBMITTED IN ACCORDANCE WITH 21CFR 312.32 (d) (2).

DISCLAIMER per 21 CFR 312.32 (e): THIS SAFETY REPORT DOES NOT NECESSARILY REFLECT A CONCLUSION OR ADMISSION BY THE CTEP IDB SENIOR INVESTIGATOR/SPONSOR THAT THE INVESTIGATIONAL AGENT/THERAPY CAUSED OR CONTRIBUTED TO THE ADVERSE EXPERIENCE BEING REPORTED.