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Dear Editor-in Chief,

In number 7/2 issue (June 1999) of Archive of oncology an interesting article appeared written by Đorđević and coauthors ″Breast cancer: epidemiological research preliminary results″, pp.55-59. The article covers, in part, a ″hot″ topic of chemoprevention of breast cancer by tamoxifen. However, their results and experience on using tamoxifen in prevention of breast cancers open some serious questions concerning methodology of such trials.

Aims of the study are confusing, four aims are unusual for any type of the clinical research. What was specific aim of chemoprevention study? What were the end points?Authors stated that they are ″challenged to start a study″ by the following experience: ″We had a group of patients... 70% decrease in risk of developing breast cancer in contralateral breast...″ What was the number of that ″challenging″ group of patients, who were the controls and many other details are important and need to be stated. All of the results concerning tamoxifen chemopreventive action were shown in abstract section. It is of minor problem that the references were cited in Abstract form?!The incidence of side effects on tamoxifen was 0, and this is the first report with such statement. We are aware that long term tamoxifen use is followed by some serious life-threatening side effects: including endometrial cancer, pulmonary metabolism, stroke and deep vein thrombosis.Dose of 10 mg tamoxifen for 15 days and 15 days of, deserves special attention. There is no rational for choosing such a dosage of tamoxifen. Pharmacokinetics data of tamoxifen are well known. Terminal half-life of tamoxifen is 7 days approximately and half-life of its main active metabolite, N-desmethyl-tamoxifen, is 14 days. Tamoxifen reaches steady-state in plasma after at least 3-4 weeks of treatment and N-desmethyl-tamoxifen needs 8 weeks of continuos therapy. In addition, minimal effective dose of tamoxifen is 20 mg per day. The authors chose half of minimal effective dose without explaining why. During the 15 days of treatment, the active principle of drug did not reach effective and steady-state levels in plasma. And then the drug application interrupted!? Drug-free period, that follows (15 days) was just enough to return tamoxifen plasma-levels to zero. In conclusion, treatment subjects received half-dose of investigation agent during half-time of trial period. Such schedule was never used before in any type of study with tamoxifen. What was author's rationale for such dose and schedule of tamoxifen? More over, the use of Tamoxifen as chemopreventive agent is ″off-label″ in Yugoslavia. Such usage of drugs needs the approval of health authorities. Authors did not state who approved the study Protocol. Approval of the Ethics Committee must be stated.There is no methodology of the statistics, use. What was the power of the study, estimated sample size, randomization assignment procedure etc. Doing chemoprevention study is one of the challenging issues in clinical trials in oncology. Anyone who read the report of P-1 study, Fenretinide trial or similar trials will know what I am talking about. Additional minor things are the references that do not follow the rules of the Journal and, even, the reference numbers are not in correspondance with the statement in the text. Ii would be interesting to see whhether anything of the above mentioned was noticed by the reviewers of the article?

The Archive of oncology is the only journal in the field of oncology in our country. We are all responsible for the quality of the articles published if we want our journal to be high on the international level.

Best regards,

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Robert SCHAEFER

Dear Mr Baltić,

EPREX®/ERYPO® (epoetin alfa), known as efficacious drug in cancer chemotherapy, orthopedic surgery and chronic renal failure, is now available for more cancer patients. Janssen-Cilag has received an expanded indication to market EPREX-ERYPO in Europe, and is now awaiting implementation of the approval by the European countries on national level.

We would be happy if you see a chance to cover the news in your media.

Yours sincerely,
Robert Schaefer

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*B*eerse, Belgium, March 31, 2000 - Janssen-Cilag announced today that it has received an expanded indication in Europe via the manual recognition procedure to market EPREX®/ERYPO® (epoetin alfa) for the *″tretment of anemia and reduction of transfusion requirements in adult patients receiving chemotherapy for solid tumors, malignant lymphoma or multiple myeloma at risk of transfusion as assessed by the patient's general status (eg cardiovascular status, pre-existing anemia at the start of chemotherapy)″*.

Previously, the use of EPREX/ERYPO in Europe was restricted to cancer patients receiving platinum-containing chemotherapy. The European Member States reached the decision to aprove the extended indication on February 10, 2000. Janssen-Cilag is now awaiting implementation of the approval at the national level by the competent authorities.

Approval for the expanded indication was based on two large multi-center, placebo-controlled trials of 520 cancer chemotherapy patients in Europe. Published results from one of the trials determined that *″epoetin alfa is highly effective in increasing hemoglobin, reducing transfusion requirements, reducing fatigue and increasing energy, acitivity levels and overall quality of life in cancer patients receiving non-platinum chemotherapy*[1]*″*.

EPREX/ERYPO is a genetically engineered version of erythropoietin, a naturally occurring hormone produced by the kidney that stimulates bone marrow to produce red blood cells. The main function of red blood cells is to carry oxygen needed for energy throughout the body. Anemia is an abnormally low level of red blood cells, and is assessed primarily through measurements of hemoglobin and hematocrit values.

In addition to cancer chemotherapy, EPREX/ERYPO is approved in Europe for the treatment of anemias associated with adjunctive therapy in autologous blood pre-deposit programs and reduction of allogeneic blood exposure in orthopedic surgery. EPREX/ERYPO is widely used for patients with chronic renal failure.

Epoetin alfa has been used to treat more than three million patients worldwide. It has proven to be effectie with a good safety profile when administered according to the prescrubing information.

Janssen-Cilag is a member of the Jonhson & Jonhson family of companies.

[1] *Littlewood TJ, et al. Proc ASCO 1999; 18:574a.*