This Week's Citation Classic™

CC/NUMBER 9
MARCH 4, 1985

Ezdinli E Z, Sokal J E, Crosswhite L & Sandberg A A. Philadelphia-chromosome-positive and -negative chronic myelocytic leukemia.
Ann. Intern. Med. 72:175-82, 1970.
[Div. Medicine, Roswell Park Memorial Inst., NY State Dept. Health, Buffalo, NY]

This paper is a retrospective analysis of 61 adult patients with chronic granulocytic leukemia (CGL), synonymous with chronic myelocytic leukemia, comparing the survival and disease characteristics of Philadelphia-chromosome-positive (Ph^{1+}) with the chromosome-negative subset (Ph^{1-}). The 18 Ph^{1-} patients were predominantly older males and had a median survival of only 8 months, as compared with the 40 months' median survival of the Ph^{1+} CGL. The presence of Ph^{1} chromosome in the myeloid cells of CGL is a favorable prognostic indicator. [The *SCI*® indicates that this paper has been cited in over 155 publications since 1970.]

Ediz Z. Ezdinli
Division of Hematology/Oncology
Department of Internal Medicine
University of Health Sciences
Chicago Medical School
North Chicago, IL 60064

December 6, 1984

This study originated as the result of a friendly argument with Joseph Sokal, then our department chief, who was committed to bettering the survival of patients with chronic granulocytic leukemia (CGL). I remember making an unkind and unsubstantiated statement to the effect that the new and complex regimens being tested had not improved upon the survival rates observed in the early part of the century, when the only treatment modality was splenic irradiation. I offered to (or may have been requested to) confirm this statement by reviewing the charts of all patients with CGL at the Roswell Park Memorial Institute, dating back to 1916.

The project was conducted when computers were not available for use by junior investigators and involved a detailed review of 206 charts and entry of various data on cumbersome work sheets. It proved to be a tedious but interesting undertaking. An upcoming American College of Physicians meeting provided the stimulus to analyze the data, but because of time constraints, the analysis was limited to a smaller subset, namely, the patients who had had chromosome analyses performed in Avery Sandberg's laboratory. Shortly after presentation at the meeting, the manuscript was submitted to *Annals of Internal Medicine* and expeditiously accepted for publication. (Incidentally, the median survival of the patients seen between 1916 and 1930 was 28 months; these additional data collect dust in a drawer.)

The diagnostic value of the Philadelphia chromosome (Ph^{1}) in CGL and its favorable prognostic implication had already been described.[1,2] Our study, conducted in the pre-banding era when the Ph^{1} was erroneously identified as a G21 rather than a G22 chromosome, confirmed these findings and reported a number of additional observations regarding the natural history of CGL and the significance of various disease features. It may have been cited repeatedly because it not only confirmed the value of chromosome study but also provided considerable additional information of practical importance to the clinician in a succinct presentation in a widely read medical journal. One can only speculate why a particular paper becomes a *Citation Classic*. What I have considered a very significant and pioneering study by our group, describing the occurrence of treatment-related myeloid leukemia in three patients with Hodgkin's disease, published a little earlier in the same journal,[3] has not gained this degree of recognition.

My principal interest prior to and since publication of this paper was and remains to achieve a better understanding of the lymphoproliferative disorders. It is rather amusing that my best-known publication should be in the area of myeloproliferative disease, a temporary diversion. This paper has even led to false rumors among our medical students and residents that I discovered the Ph^{1} chromosome. This, of course, was first reported from Philadelphia, in 1960, by Nowell and Hungerford.[4]

1. **Krauss S, Sokal J E & Sandberg A A.** Comparison of Philadelphia chromosome-positive and -negative patients with chronic myelocytic leukemia. *Ann. Intern. Med.* 61:625-35, 1964. (Cited 105 times.)
2. **Whang-Peng J, Canellos G P, Carbone P P & Tjio J H.** Clinical implications of cytogenetic variants in chronic myelocytic leukemia (CML). *Blood* 32:755-66, 1968. (Cited 180 times.)
3. **Ezdinli E Z, Sokal J E, Aungst C W, Kim U & Sandberg A A.** Myeloid leukemia in Hodgkin's disease: chromosomal abnormalities. *Ann. Intern. Med.* 71:1097-104, 1969. (Cited 90 times.)
4. **Nowell P C & Hungerford D A.** A minute chromosome in human chronic granulocytic leukemia. *Science* 142:1497, 1960. [See also: **Nowell P C.** Citation Classic. *Current Contents Life Sciences* 28(8):19, 25 February 1985.]