Transcript of Rai Interview Part 1: Introduction

Gerald Marti: Good afternoon. We are fortunate this afternoon to have with us Dr. Kanti Rai to continue this series on the intellectual oral history of CLL. I've had the opportunity of meeting with Dr. Rai on two previous occasions and have some notes from that time.

Dr. Rai, I'm going to start with kind of three major divisions. One is that many of the investigators in chronic lymphocytic leukemia, in CLL, are not just experts in CLL, they are also hematologists, and they've had either parallel lives in other aspects of hematology. And in your case, before addressing CLL, I know there was at least two areas that you were active in. One was polycythemia vera—I think the original study group—and you've also had a long association with the treatment of acute leukemia. Acute myelogenous leukemia. So, I would like you to comment about your experience with those two areas if you will.

Kanti Rai: Thank you, Jerry, for reminding me that in addition to my interest in chronic lymphocytic leukemia, or CLL, I have had a strong interest as well in myeloproliferative diseases and in AML, or acute myeloid leukemia. In the chronic myeloproliferative disease category, as you pointed out, historically, my interest goes to the time, probably in the 1960s, when Dr. Wasserman had started—initiated—the PVSG, Polycythemia Vera Study Group. Dr. Wasserman was at Mount Sinai Hospital and Medical College in New York and he had organized a group of investigators throughout the country—throughout the world, really, who started the very first formal study of the natural history of polycythemia and worked toward standardizing the diagnostic criteria and then moved into finding the best possible treatment of this disease. And it was really very gratifying for me, as a young investigator, to be a part of that group because my own mentor, Dr. Gene Cronkite at Brookhaven National Laboratory, and my colleagues who were interested in P. vera, they all helped me immensely in becoming active in Dr. Wasserman's-led group. And whatever polycythemia study group did became for the time being, in that era—I'm talking about 1960s, 70s, 80s, and even up to early 90s—that we were able to put polycythemia vera on a firm footing and, before that, it was really a completely chaotic situation.

In AML, or acute myelocytic leukemia, I owe my interest in this fascinating disease to my, in another manner of speaking, another mentor, Jim Holland—Dr. Holland at Mount Sinai Medical Center. He was, when we first started our association, he still was at Roswell Park Cancer Institute in Buffalo. But during the time that I became involved in AML study, he had moved to New York, and he still continued to

remain the chairman of Cancer and Leukemia Group B. And it was then that in 1972, I believe, that I was asked to chair a large, randomized study to establish whether the 7 and 3 regimen which had just been proposed but had been tested only in a handful of patients, to conduct a large, randomized, multi-institutional group-wide—CALGB-wide—study to find out whether cytosine arabinoside given by continuous infusion over a 7-day period along with daunorubicin or the anthracycline used in AML then, given for 3 days successively, was superior to the same drugs given for 5 days and 2 days, respectively. And indeed, it was a very heady time because in the 1970s, we just did not know how to achieve the maximum incidence of complete remission, but we all knew that if we achieved a complete remission in AML we were offering a longer life expectancy to our patients. So that, it took us approximately 2 ½, 3 years to accrue the statistically needed number of patients, and I was very gratified because I learned a lot in clinical trials, the procedures, the requirements of discipline to get the data properly collected and analyzed, and to publish. And the statisticians in CALGB were most helpful and they became my teachers in a manner of speaking. And that launched me as a researcher, a clinical investigator in hematology.

Marti: I made a copy of the AML 7-3 paper[1] just to refresh your memory. Now, it's also my recollection that ASCO celebrated its 25th birthday, perhaps last year.

Rai: 50th.

Marti: 50th birthday.

Rai: It's that ASH celebrated in 2008 and ASCO did it a year before—

Marti: Before that.

Rai: I think—or a year after?

Marti: Anyway, I think in one or both of those celebrations, the treatment of AML—

Rai: Was—

Marti: Was highlighted.

Rai: Yeah.

Marti: And perhaps a series of papers leading up to this—

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[1] Rai KR, Holland JF, Glidewell OJ, et al. Treatment of acute myelocytic leukemia: a study by cancer and leukemia group B. *Blood*. 1981 Dec;58(6):1203-12.

Rai: Yeah.

Marti: Paper.

I basically wanted to document that—that in addition to CLL, you had wider hematological interest.

Rai: Oh yes. Yeah.

Marti: And perhaps in that sense, you have said that the staging of CLL—the clinical staging of CLL—was perhaps the beginning of the modern era of what we've come to learn about CLL.

Jumping ahead in the staging system, which we will come back to, I wanted to ask about—I think the major comparative study that might be parallel to AML would be the fludarabine-chlorambucil study, I believe from 2000 in the *New England Journal*.[2] Would you comment on how that came about, how that study came to be, the history behind it?

Rai: Yes, the point where in CLL, where we were in the early 90s, when fludarabine—it's really hard to believe that we have come more than 20 years since that time when fludarabine had become recognized as a very powerful drug in CLL and had been approved by the FDA for patients who had failed chlorambucil because chlorambucil continues to remain as the FDA-approved first-line treatment in chronic lymphocytic leukemia. What we did in CALGB was to test whether fludarabine indeed was a superior drug to chlorambucil in front-line treatment and it became an enormous effort. It required a lot of—practically a year of planning—fludarabine versus chlorambucil.

[2] Rai KR, Peterson BL, Appelbaum FR, et al. Fludarabine compared with chlorambucil as primary therapy for chronic lymphocytic leukemia. *N Engl J Med*. 2000 Dec 14;343(24):1750-7.