THE HOPE OF CLINICAL CANCER RESEARCH
An Address by Charles G. Moertel, M.D.

Upon Accepting the
Association of Community Cancer Centers'
Award for Outstanding Achievement
in Clinical Research
October 2, 1987

I am very grateful to be the first recipient of the clinical research award of the Association of Community Cancer Centers. This is especially important to me because it comes from you and those you represent who care for cancer patients in the communities of America.

As you know, my major effort, during what may be the most productive years of my life, has been to bring the hope of clinical cancer research to patients in their own communities, because I know that's the only way it can be brought to the vast majority of patients.

As you also know, this hope can only be realized by allowing oncologists in the community a major role in the design and conduct of these research programs. This seems self-evident now, but I am sure you all remember the battle cry ringing out from the ivory tower a decade ago, "Good clinical research can't be done by community oncologists" -- but, we had some pretty good fighters on our side, too, including you in this room and your colleagues.

Always in the front rank, leading the charge, was a close friend who was unable to show up today -- but I know Ed Moorhead is here. Then there is someone else who bears proud battle scars -- who I fight with now and again -- but not on this issue. This is Dr. Vincent DeVita. In supporting the community oncology program, he had to stand up to charges of wasting cancer research funds on politically motivated philanthropy. Certainly, however, his judgment has been vindicated.

Consider, if you will, the chaos that would exist today in the programs of the Division of Cancer Treatment if CCOP and CGOP were not in place contributing some 60 percent of patients entered on national protocols. Consider, if you will, the problems that would be faced tomorrow by the Division of Cancer Prevention and Control in initiating their hoped for large scale projects if they did not utilize this nationwide reservoir of thousands of physician investigators with direct access to tens of thousands of patients and with mechanisms of quality control and data logistics already in place.

Consider, if you will, the problems of trying to get an ever increasing National Cancer Institute budget, which largely supports basic laboratory research, approved by Congress and the American public if all we had to show them were cancer cures in the rodent population. I doubt if anyone today would seriously question that the community oncology efforts must be numbered among the most outstandingly successful in the history of the National Cancer Program.

From a personal standpoint, my community oncology colleagues and I in the North Central area have found the North Central Cancer Treatment Group (NCCTG) to be something very special. When we started, there was just no way that this group was supposed to succeed. During our first few years, we had either trivial budgets or no budgets. Our members had to pay their own way, and I don't know how they got this past their business managers. I had to beg, borrow, and steal from every pocket in sight to keep our operations office running.

But, with all this, the NCCTG has steadily grown and flourished. This group of community oncologists has set new standards in clinical research quality. Our total rate of patients entered on protocol who are lost to analysis -- ineligibilities, cancellations, lost to follow-up -- is less than three percent. Nobody else matches that record. Our community oncologists are very proud of it, because they worked hard to achieve it.

The majority of our protocols are devoted to the most common malignant diseases seen in the community -- gastrointestinal cancer, lung cancer, breast cancer. We do this without apology because this is the greatest need. At first our studies in these areas came up the usual negative results, but we kept plugging away and recently, as you know, we have been reporting some very exciting positive results, and we are just warming up.

One of our positive studies gave rise to a national intergroup trial in surgical adjuvant therapy of colon cancer that has just completed entry of some 1,300 patients, and our small group of community oncology clinics was right up there in accrual along with two giants. Next year we are anticipating a total group accrual of over 2,500 patients on cancer treatment and control protocols.

One might ask why has the NCCTG succeeded when so many other attempts at developing regional community clinic groups have failed? It's hard to come up

with a single answer, but I think one of the most important factors is that the NCCTG is run by community oncologists -- certainly with Mayo Clinic guidance, but Mayo doesn't have a vote in group policy or in approval of group protocols. This doesn't matter because we all work together in a spirit of mutual respect and, consequently, we have never had any major confrontations.

The primary motivation of everyone is clearly to conduct high quality clinical research that holds the greatest hope for our cancer patients. Some have voiced the fear that if a major cancer center encourages the development of clinical research in community clinics within its region this will choke off the flow of cancer patients to the major center.

Within our region, however, quite the opposite has been true. Our Mayo Clinic oncology referrals over the past decade have escalated at a more rapid rate than any other medical area within our institution. Since we have opened up clear lines of noncompetitive communication with the community clinics, referral is made easy for patients with more complex problems requiring the highly specialized sophistication of a major center.

On the other hand, when we at the Mayo Clinic see patients eligible for protocols that we know are being conducted by one of our group members located much closer to the patient's home, we do not hesitate to refer this patient to the group member. We know he will be receiving high quality clinical research care in a much more convenient and cost effective manner. In short, when this type of cooperative interaction is developed, the major cancer center wins, the community cancer center wins, and the biggest winner of all is the cancer patient.

You have seen that for most NCCTG publications and presentations a community oncologist is first author or standing on the podium. This type of experience is a memorable event for the community oncologist, and personally I get much more satisfaction from this than if I was standing on the podium myself. One of the most memorable moments of my life was when one of our NCCTG community oncologists was standing on the ASCO podium presenting what was probably the first paper he had ever presented in his life and showing why FAM didn't play in Peoria. Then he stood up strong to all the heat from famous academic oncologists.

Maybe our region of the country is unique -- maybe all of this is not exportable -- but it does seem reasonable to believe that the cooperative spirit developed within the NCCTG might be modelled as a foundation stone for similar efforts by others. Of one thing I'm sure -- no one can ever tell me that good clinical research can't be done by community oncologists.

Beyond any question, the community oncologists of this country, as exemplified by the ACCC membership, have been remarkably accomplished over the past decade. You have won some very difficult political battles, and you have proven your right to be winners by demonstrating responsible performance.

With all of this, however, past accomplishments are like candles in the wind -- they flicker brightly for a moment, but then they are out, and they only serve to light our first few few steps as we move ahead.

Take just a moment to be proud, but then devote yourself to the problems of tomorrow, and how these are to be met. As you know, unless you continue to seek challenge, the strong organization you have built will quickly degenerate into an impotent old boys' club. I am going to offer you several challenges, which I hope you will take on because I feel they are crucial to the future of medical oncology and clinical cancer research. These are challenges that you can meet within your own ranks. Superficially, this may sound easy since you have so successfully battled the external dragons. I can assure you, however, that the internal demons may be much more difficult to exorcise.

I would first suggest to you that strong winds of socioeconomic change are blowing, and we in oncology will soon find ourselves right in the epicenter of this storm. Costs of health care delivery are in the eyes of many indefensibly high. When we as oncologists dole out, on a routine basis, treatment for drug resistant cancers that is either minimally effective or not effective at all, and when we do this at a very high cost, we are placing ourselves in an extraordinarily vulnerable position.

I know that right now, major legal actions are being undertaken by two of the largest health insurers of this country, and the focus of these actions is their refusal to pay for unestablished cancer therapy. I think it is more than coincidence that both have elected to take on the same specific therapy for the same specific tumor -- interferon for renal cell cancer. One must suspect that they intend these actions to be precedent setting. The possible fall out from such precedent is mind boggling to contemplate. If third parties only agree to pay for proven effective treatment, our clinical cancer research program would grind to a halt. Indeed, even today most health insurance contracts specifically state that research treatment is not covered. It takes little imagination to visualize the scenario when Medicare rates inevitably go up.

Consider what might happen the next time the automobile industries write up their health contracts when these industries are already averaging some $1500 per automobile to pay health care benefits and

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when their cars are becoming increasing less competitive with foreign imports. I think we have been far too slow proacting constructively to this inevitable crisis. Many think naively that we can simply tell the third-party carriers how great and noble cancer research is, and how, in the interest of future generations, it is their responsibility to support this research. Their response will be, "Yes, we agree cancer research is terribly important -- we hear you -- but someone else is going to have to pay for it, because the voice of people paying our bills is louder than yours."

I think it is possible to preserve third-party support of legitimate clinical cancer research treatment, but only if we present convincing evidence that this is sound economic practice. To accomplish this, we are going to have to give a little. We must join with the carriers in reaching constructive compromises.

As a start, I would suggest we could support their efforts to withhold payment for the routine practice administration of unproven and ineffective treatment, e.g., weekly 5-FU as surgical adjuvant therapy for colon cancer, FAM, or anything else for advanced pancreatic cancer, and Lord knows what all for advanced non-small cell lung cancer. As a trade off, we might hope to obtain their approval for treatment of these patients under nationally approved research protocols.

As further inducement, we could also agree to carefully scrutinize these protocols to eliminate unnecessary costs. In all honesty most protocols are overburdened with expensive examinations that really aren't essential for the fundamental protocol objectives, e.g., serial bone scans, serial CT scans. These are seldom necessary to find out whether a patient is going to live longer or better, which should be the primary objectives of the usual Phase III trials conducted in the community setting.

We could let our voice be heard in opposition to such maneuvers as the treatment IND recently enacted by the politically appointed leadership of the Food and Drug Administration responding to politically motivated pressure from the Office of Management and Budget. Simply stated, this represents an obvious maneuver to obtain third-party payment for a non-research administration of very costly drugs, which have no established safety or effectiveness. In essence, it shifts the cost of new drug development from the stockholders of the small and emerging high tech drug companies and places these costs directly on the back of an already overburdened health insurance industry. Whereas turning these so-called "promising" but unproven drugs loose on the general public may have appeal to the oncologist who's willing to treat with anything and shuns research involvement, such an action will unquestionably be damaging to the oncologist who is committed to participating in carefully controlled research trials to prove the value of hopeful new drugs.

Even though it may hurt a bit, I think we must now join with third-party carriers in making mutually acceptable changes that will best meet the hopes and needs of the cancer patient today and tomorrow. If we just sit back passively and then react after the fact, I'm afraid we might find that very damaging changes have been irreversibly established.

The second challenge I would put to you is that of accrual on high priority, nationally approved clinical cancer research protocols. You fought hard to be a part of the National Cancer Program, but having achieved this, you now hold the responsibility for productive performance. The data, which the CCOPs themselves supplied, show that among patients actually eligible for cancer treatment protocols, at most one patient of three and as few as one of ten are actually entered on protocols. We must presume that the same is true for the CGOP, and I'm not at all sure that university cancer centers do much better.

As a result, important clinical cancer research questions are taking far too long to answer, and hope for tomorrow's cancer patient is intolerably delayed. I find this hard to understand since I can think of nothing more boring or less satisfying than pushing routine 5-FU for gastrointestinal cancer, routine CMF for breast cancer, or routine whatever for lung cancer.

On the other hand, I know of nothing more exciting or enriching to clinical practice than to be actively contributing to clinical research. The extra time involved might bring your tax bracket down a notch, but I think the trade is worthwhile.

I would hope that the ACCC would take primary leadership in implementing measures to enhance protocol entry by community oncologists. Certainly, however, all of us who are a part of the National Cancer Program can make a contribution. The National Cancer Institute can give a major assist through measures to improve public recognition of research contributions made by the community oncologist, and particularly to facilitate this recognition on a local level.

Legitimate publicity offered through news media could do a great deal towards counteracting the full page or TV spot advertisements used by those who wish to commercialize alleged "research" cancer treatment. Major efforts should be made to educate the public on the value to themselves of participating in clinical trials. They should be strongly reassured that rather than being guinea pigs, they will obtain the most hopeful cancer care available and obtain it from the hands of physicians who are sufficiently knowledgeable and caring to devote a major portion of their time to improving treatment results for cancer patients now and in the future.

Probably the most single helpful assist the NCI administrators could offer to increase accrual on high priority protocols is to discontinue the practice of publishing protocol recipes in the PDQ system. To the oncologist who tries to enter a patient on such a protocol, there is nothing more discouraging than to lose

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his patient to the competition down the block who flashes up the recipe on a computer screen and shows the patient that he can offer exactly the same new treatment without making the patient a research subject, without randomization, and with the NCI showing him how to do it. How much better it would be if the protocol recipe was replaced with the names of the patient's community oncologists entrusted by the NCI with active participation in the protocol.

Those of us allowed the position of scientific leadership in cooperative groups could also encourage protocol entry by eliminating needless protocol complexities and initiating measures to facilitate practical conduct. Forms could be greatly simplified by dropping requests for great quantities of information that are never analyzed and are in no way pertinent to the primary protocol objectives. Superfluous monitoring visits and expensive testing could be dropped. We could ensure that someone knowledgeable was always promptly available for questions so that the community oncologist wouldn't have to make a half-dozen phone calls to get a definitive answer.

In the NCCTG we've found it very helpful to prepare separate protocol abstracts for the physician, the oncology nurse, and the data handler, which completely and succinctly cover their respective responsibilities in protocol conduct -- much more convenient than asking each of them to search through a 40-page protocol. All of these procedures conserve physician time and our NCCTG members have told us time is the single greatest obstacle to protocol entry.

Realizing, however, the frequent intractibility or ineptitude of those of us bestowed with national leadership recognition, you should not hesitate to move ahead on your own. Scheduling new and potential study patients at your less frenetic time of day will certainly be more conducive to protocol entry. You might wish to consider prepared audiovisual material -- not as a substitute for patient contact, but as a supplement to enhance patient understanding and to conserve your time for more individualized attention.

Certainly one of the most essential members of a clinical research team is a well trained and highly motivated study assistant who can identify potential protocol patients, facilitate multidisciplinary coordination, preschedule appropriate testing and return appointments, assist in form preparation and editing, and gather and forward the right material to the research base at the right time. For the oncologist participating in clinical research, such an individual should be just as much an automatic item on the clinic overhead as the receptionist or the secretary. These tasks should not be assigned to the spare time of an already overburdened oncology nurse.

Finally, I would challenge you to take an active, innovative, leadership role in cancer control research. At your urging, and to support your efforts in this area, the National Cancer Institute has devoted a substantial budget for both CCOP and CGOP cancer control participation. This should be your bag. You chose commmunity clinical practice because you had a commitment, not just to dispense cytotoxic drugs, but to meet the overall needs of cancer patients and to guide your communities in measures of cancer detection and cancer prevention. You are in the best position to define the needs of your patients and your communities. Your experience should be exerted in designing feasible approaches to meet these needs, and you should be the prime drivers in ensuring that these protocols meet their accrual objectives in a timely fashion. You will undoubtedly find your oncology nurses highly qualified in these areas and eager to push you along. They should be allowed commensurate responsibility in the conduct of cancer control protocols.

If I have done anything to deserve the award you have given me today, I feel it is that I have always regarded routine cancer treatment as bad cancer treatment. I've felt hope and excitment in clinical cancer research, and I've tried to transmit these to my patients. Most of them have died, but we've shared the satisfaction of knowing that we fought the good fight. I wish this satisfaction on you. ■

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