Research initiated and conducted at the community level is not easy. Community based oncologists are limited in their access to investigational drugs, the number of suitable projects that can be undertaken is limited, and it is difficult to publish results of studies conducted outside of large, well known institutions. Despite all these obstacles, we suggest there is a strong role for the community physician as an initiator of innovative clinical research activities.

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Letter to the Editor...

COMMUNITY INITIATED RESEARCH A NOTE OF CAUTION

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With the demonstration of the high performance level of community oncologists in clinical trials,[1,2] there can no longer be any doubt of the major contribution that this large reservoir of investigators, given adequate resources, can make to the national cancer research program. Beck and Hart propose that this demonstrated expertise can be taken one step further and lead to significant clinical trials being initiated and performed in single community institutions.

We agree that there is no intrinsic reason that an investigator who chooses to practice in a community setting cannot generate and answer good scientific questions. We fear, however, that there are very real constraints to accomplishing that goal. If these limitations are not taken into account, we may witness a profusion of studies that are asking relatively insignificant questions or lack the patient populations (statistical power) or analytic capabilities (subset analyses) to answer a clinically important question. The real tragedy, of course, will be that these patients, under the care of these competent investigators, will be lost to major trials that would significantly contribute to oncologic knowledge.

The design of a good research protocol requires that the scientific question be based on a firm foundation of basic and clinical research. Unfortunately, community oncologists, given the unrelenting demands of their practices, often do not have the time to adequately survey literature devoted to the basic sciences. Of even more importance, their clinical, rather than laboratory, orientation may not allow them to properly evaluate the contribution of animal or cell system studies. The implications of modulations of biochemical pathways, derivation of pharmacokinetically timed schedules, or alterations in cell membrane transport systems, may not be apparent to investigators who are not constantly exposed to this body of data. Since this information is not routinely utilized in the design of community-based studies, the opportunity to incorporate innovative approaches based on bench research is often missed.

For the purposes of protocol design, the community oncologist's familiarity with past or current clinical studies may also be deficient. Most community oncologists derive their information from standard journals, which give them superb information for providing the most up-to-date accepted treatment to their patients. Most of these articles reflect work that was completed a year before publication. By the time these studies appear in print, the next generation of research studies that were derived from these results have been well under way for some time. Similarly, although the oncologist usually attends ASCO or ASH meetings, the information from other major meetings, NCI workshops, specialized symposia, or guest lectures by active investigators is usually not consistently available.

Thus, although community oncologists can feel secure that they possess the necessary information to offer their ptients state-of-the-art care, this information may not be adequate for the derivation of new protocols. The posing of research questions is often based on data that is not yet applicable to standard patient care. Is there an on-going trial that would make a proposed trial superfluous? Was there a pilot study presented in a seminar that offers new opportunities? Did an informal contact reveal that a proposed regimen was ineffective or unexpectedly toxic? Without this knowledge of preliminary, negative, or less well-known clinical trials findings, the community oncologist may lack the background crucial to the formulation of significant studies.

The result of this lack of access to supporting data is that community oncologists tend to design studies, which are minor variations of previously reported regimens. These variations are often not of benefit, since they do not represent significant differences in the therapeutic regimen. Given the relatively limited populations available at even the largest community center, the studies are usually pilot studies with confidence limits that are so broad that they preclude meaningful interpretation.

It is not unusual to find that the only conclusion that can be drawn is that the new regimen will have to be studied in a large randomized study if any realistic evaluation is to be made. This type of pilot study does not provide any useful data, and oncologic science would have been much better served had the community oncologist placed his patients in a multi-institutional trial. We must also emphasize that it is equally regrettable when NCI-approved comprehensive cancer centers and cooperative oncology research groups conduct serial pilot studies employing minor treatment modifications rather than evaluate promising new therapies in appropriate multi-institutional trials.

To see if this perspective is a fair one, we have analyzed abstracts relating to the treatment of non-small cell lung cancer in the 1987 Proceedings of the American Society of Clinical Oncology. Of 37 abstracts utilizing conventional or experimental agents, 16 studies were performed by institutions that were community-based or university centers, and that were not NCI-designated centers. We have grouped these two types of hospitals since we felt that they have a similarity in their patient bases and emphasis on clinical oncology practice. Table 1 lists the studies, the accrual rates, and the overall response rates reported.

While we would admit that these studies represent a variety of modifications, and that some of them asked other questions, the sum total of these trials is that they probably have not contributed in any meaningful way to the cancer research effort. The majority of the studies are variations of known platinum regimens, and several are identical treatments. The studies averaged only 25 patients per trial, making evaluation very difficult. The combined results of these 408 patients would probably have yielded significant information if they had all been entered on one large randomized trial.

Since the studies do not represent a systematic progression from previous studies, there is no real opportunity for the development of sequential modifications or follow-up trials. Several of the studies took 2-3 years to complete, thus tying up data collection resources for a considerable length of time. The abstracts do not allow us to comment on whether these studies were accomplished with less laboratory data than those performed in cooperative groups, but the issue should be to have all clinical research, at whatever level, use only those tests absolutely necessary for answering the scientific question.

Finally, many of the reported response rates appear higher than one would expect in non-small cell lung cancer. Whether this represents selection biases, differences in response criteria, or chance variation cannot be determined in these small pilot trials. Given all these considerations, the conclusion from this analysis must be that, for the most part, these studies have not been able to provide information that other investigators can use in designing new studies or caring for patients.

In conclusion, we do not disagree with Beck and Hart's thesis, but we suspect that oncologists will continue to play a relatively minor role in producing original research at the community level. This in no way detracts from the overwhelming impact they are having on answering the major questions that are being addressed by the major groups and centers. Expansion of this evolving collaboration should be fostered and supported, since the cooperation maximizes the strengths of all the participants.

References

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TABLE 1
Clinical Trials in Non-Small Cell Lung Cancer
by Community and Non-NCI Designated University Centers -- 1987

Regimen	# Eval.	% CR+PR
CDDP, FU	21	33
CDDP, FU	17	47
CDDP, FU, RT	46	85
CDDP, FU, LEUCOVORIN	16	16
CDDP, FU, MITO	24	38
CDDP, FU, MITO, RT	24	ALL
CDDP, VLB, VP-16	26	34
CDDP, VLB, VP-16	44	43
CDDP, VLB, VP-16, CLEO, CTX, MTX	18	11
CDDP, VLB, MITO	36	62
CDDP, VP-16, RT	20	80
CDDP, VP-16, ADRIA	37	48
CDDP, VP-16, ADRIA, BLEO vs.	19	41
CDDP, VCR, MTX, BLEO		31
CDDP, VINDESINE	21	65
FU, MITO, LEUCOVORIN, MTX	29	38
13-CIS RETINOIC ACID	10	10
TOTAL PATIENTS	408	