Beginning with the January 1976 issue, Cancer Chemotherapy Reports changed its name to Cancer Treatment Reports; and in July, Dr. Bruce Chabner became its new Editor-in-Chief. The journal now publishes articles relating to all aspects of cancer treatment, as well as relevant brief reports, correspondence and commentaries.

January and February

The January issue reports several trials of combination chemotherapy in solid tumors. Von Eyben et al. (Finsen Institute, Copenhagen, Denmark) noted one complete and six partial responses in 33 patients (30 previously untreated) with advanced colorectal carcinoma treated with 5-FU, DTIC, BCNU and vincristine (VCR). Responses were more frequent among patients with recently detected (i.e., smaller) tumors. Beretta et al. (World Health Organization, Milan, Italy) report the results of a large randomized cooperative study of patients with advanced malignant melanoma in Europe using the following regimens: (A) DTIC, VCR, BCNU; (B) DTIC, VCR, hydroxyurea; or (C) DTIC, actinomycin D (ACT-D), BCNU. Among 274 evaluable patients, regimens A and C were superior to B in inducing complete remissions (9.3 percent and 16.4 percent versus 1.1 percent), although no differences in overall response rate were noted. Of interest was the failure of BCNU to affect or delay CNS involvement. Lloyd et al. (University of Arizona College of Medicine, Tucson, Arizona) report encouraging response rates in metastatic ovarian (61 percent) and endometrial (67 percent) carcinoma using an adriamycin (ADR)/cyclophosphamide (CTX) combination in a Phase II study. Finally, Wiernik et al. (Baltimore Cancer Research Center, National Cancer Institute, Baltimore, Maryland) report the results of daunorubicin alone versus a four-drug combination (daunorubicin, cytosine arabinoside, 6-thioguanine and pyrimethamine) in acute non-lymphocytic leukemia. In this randomized trial, 33 patients receiving the single agent had response rates and median survival similar to those of 33 patients treated with the four drugs. Further, the pyrimethamine-containing regimen did not avert meningeal relapse. This rather important study demonstrates that combination therapy consisting of multiple active drugs may not be superior to a single agent in a responsive disease. It calls to mind the necessity for concern in the current polypharmacy of cancer treatment: empirically derived drug combinations may not interact synergistically.

Finally, Olweny et al. (Uganda Cancer Institute, Kampala, Uganda) report activity of ICRF-159 in patients with Kaposi's sarcoma. This adds yet another agent to the growing list of active drugs in the treatment of this disease (others are CTX, ACT-D, vinblastine, DTIC, BCNU and BLM).
The February issue contains the Proceedings of the Sixth New Drug Seminar on DTIC sponsored by the Division of Cancer Treatment of the National Cancer Institute.

March and April

The results of several important clinical trials are described in the March issue. Unequivocal evidence of VCR activity in small cell carcinoma of the lung was demonstrated by Dombernowsky et al. (Finsen Institute, Copenhagen, Denmark) in a Phase II trial; no cross resistance to CCNU, CTX or methotrexate was noted.

Rosenstock and Donaldson (Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania) report a total lack of objective response in 13 children with acute leukemia in relapse treated with VM-26. Solomon et al. (University of Tennessee Memorial Research Center and Hospital, Memphis, Tennessee) describe antitumor activity of an ADR-containing combination in a patient with malignant carcinoid. They document response using serial 67gallium scintography. Benjamin and co-workers (M.D. Anderson Hospital and Tumor Institute, Houston, Texas) undertook a Phase I-II study using ACT-D in a single dose, as opposed to the usual five-day schedule. Since the plasma half-life of this compound is 36 hours, intermittent high-dose schedules similar to those employed for ADR would appear rational. A recommended total dose of 2 mg./m² produced less hematologic and gastrointestinal toxicity than that usually observed on a five-day schedule. Clinical responses were observed in patients with advanced cancer in this trial. The use of this new schedule in pediatric tumors and sarcomas should be explored since the economy of single-vs-multiple-dose therapy is considerable.

Two reports of lung cancer therapy appear in the March issue. Edmonson, reporting on behalf of the Eastern Cooperative Oncology Group, reported no therapeutic advantage in a CCNU-nitrogen mustard (HN2) combination, compared to HN2 alone in squamous (109 patients) or large cell (114 patients) histologic types. Edlis et al. (Veterans’ Administration Lung Cancer Study Group) undertook a trial evaluating the effect of heparin and coumadin anticoagulation in patients with lung cancer receiving CTX. They report no benefit of anticoagulation (response rate of five percent in 19 patients) and serious hemorrhagic complications in two patients, one of whom died. An editorial on the role of anticoagulation in cancer chemotherapy will appear in a forthcoming issue of the journal.

Richman and co-workers (M.D. Anderson Hospital and Tumor Institute, Houston, Texas) report the results of a chemo-immunotherapy trial in 35 patients with head and neck cancer. A combination of BLM, ADR, CCNU, VCR and HN2 (BACON) was used and the effect of weekly BCG
by scarification was studied. The response rates were similar
(50 percent for BACON; 40 percent for BACON plus BCG).
Of interest was the observation of three complete responses
in six patients with carcinoma of the nasopharynx. BCG
appeared to prolong survival (median 30.5 vs 13.5 weeks),
but the mechanism by which this occurs (immune stimula-
tion, reduction of toxicity) remains speculative.

The Proceeding of the Symposium on the Metabolism and
Mechanism of Action of CTX (sponsored by the Chester
Beatty Research Institute, London, England) is presented in
the April issue.

May and June

The May issue reports several experimental and clinical re-
sults of considerable interest. Using flow microfluorometry
to measure tumor cell distribution in the cell cycle, Maruyama et al. (University of Kentucky, Lexington, Ken-
tucky) studied the perturbation of in vivo cell kinetics in a
murine lymphoma model treated with HN2, BCNU, hy-
droxyurea and radiation. They noted recruitment of cells into
S phase induced by hydroxyurea and BCNU, with a G1 block
(noted also by others) three days after administration of the
latter. Cell-cycle traverse was greatly perturbed by all
agents. The strategy of such cell recruitment in scheduling
cycle-active agents has been validated in animal studies
using nitrosoureas and 5-FU.

Several clinical trials reported in this issue deserve men-
tion. In a randomized trial of 243 evaluable patients with
metastatic melanoma studied by the Central Oncology
Group, a response rate of 17 percent for DTIC alone was
observed. Responding patients had more drug toxicity but
better survival than non-responders, but response or survival
were not related to patient sex or lesion site. The addition
of a nitrosourea, VCR, and hydroxyurea in various combina-
tions did not improve the response rate. These results corrob-
orate the data reported by Beretta et al. in the January issue
(vide supra). Bellet et al. (American Oncologic Hospital,
Philadelphia, Pennsylvania) also report a trial of DTIC
versus BCNU plus VCR in 50 patients with metastatic mela-
noma in which primary response rates were 29 percent and
23 percent respectively. Of the 26 patients switched to the
alternate therapy, a 19 percent response rate was noted
overall. Thus, while DTIC and the nitrosoureas induce use-
ful responses alone, their combined activity is apparently not
additive. These trials serve as a further reminder that combi-
nation chemotherapy is not always better than single agent
therapy.

The June issue contains the Proceedings of the Seventh
New Drug Seminar on the Nitrosoureas sponsored by the
Division of Cancer Treatment, National Cancer Institute.