

U.S. DEPARTMENT OF  
HEALTH, EDUCATION, AND WELFARE  
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FOR RELEASE IN A.M. PAPERS  
Wednesday, October 16, 1963

The Department of Health, Education, and Welfare today released a report from the Director of the National Cancer Institute concerning his decision not to undertake clinical testing of Krebiozen.

The statement was accompanied by a report from the committee of cancer experts which reviewed the records of 504 patients treated with Krebiozen. The committee unanimously recommended against clinical testing of Krebiozen.

# # #

C O P Y

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TO : The Secretary

THROUGH: The Surgeon General and  
The Director, National Institutes of Health

FROM : The Director, National Cancer Institute

SUBJECT: Clinical Trial of "Krebiozen" Under National Cancer Institute  
Sponsorship

OCT 15 1963

In mid-August of this year, I appointed a committee to review clinical records on patients treated with "Krebiozen" and to recommend whether or not the National Cancer Institute should sponsor a clinical trial of "Krebiozen." The committee has been engaged in an extensive study of clinical records, microscopic slides, X-rays, and other records of these patients and has now completed its study and submitted a report to me. A copy of the report is attached.

The committee is unanimous in its conclusion that "Krebiozen" is ineffective as an anticancer drug and strongly recommends that no clinical trial be undertaken.

On the basis of this report, the findings of the Food and Drug Administration that "Krebiozen" is creatine and my own study of the extensive data previously submitted by Doctors Ivy and Durovic, I concur in the committee's findings and have determined that the National Cancer Institute will not sponsor or participate in a clinical trial of "Krebiozen."

As with any other potentially experimental drug, clinical trial of "Krebiozen" would have to be justified on one of three grounds. "Krebiozen" does not qualify on any one of the three.

The first basis upon which a drug might be considered for clinical trial is theoretical. The proponents of "Krebiozen" have advanced the theory that "Krebiozen" is a tissue hormone which inhibits the multiplication of cancer cells. The Food and Drug Administration has demonstrated that "Krebiozen" is not a tissue hormone but rather creatine, a normal component of the human body concerned primarily with muscle contraction.

The second basis for a clinical trial, and the one upon which most are based, is that the drug must possess consistently strong anticancer activity in experimental animals. "Krebiozen" does not qualify on these grounds.

The third basis is the accidental discovery that a drug has anticancer activity in human beings. If "Krebiozen" had been shown to possess such activity despite the failure to satisfy the other two justifications for trial, I would have been prepared to sponsor a controlled clinical trial after appropriate animal toxicity study and the development of a procedure for the control of the identity of the substance.

The committee's report of the 504 case records clearly establishes that "Krebiozen" does not possess any anticancer activity in man.

The National Cancer Institute has completed its consideration of "Krebiozen." There is no justification for a clinical trial, and from a scientific standpoint we regard the case closed.

## Report of the Review Committee

### EVALUATION OF KREBIOZEN CLINICAL RECORDS

#### Committee Membership

The Committee was chosen by the Director of the National Cancer Institute to review all available records concerning a selected group of patients treated with Krebiozen. The Committee was charged with determining, on the basis of an analysis of these clinical records, whether Krebiozen should be recommended for further clinical trial. All of the committee members have had extensive experience in the clinical problems of cancer, in particular experimental cancer chemotherapeutics, and represented the disciplines of surgery, internal medicine, pathology, radiotherapy, and endocrinology. Since a large number of breast cancer cases were submitted, several of the participants were selected because of their special interest and knowledge of this disease. The committee was composed of the following members:

Dr. Fred Ansfield  
Associate Professor of Surgery  
Cancer Research Division  
Department of Surgery  
University of Wisconsin Medical School  
Madison, Wisconsin

Dr. Harry Bisel  
Director, Pennsylvania Division  
American Cancer Society  
Assistant Professor of Medicine  
University of Pittsburgh  
School of Medicine  
Pittsburgh, Pennsylvania

Dr. Kirkland C. Brace  
Radiation Branch  
National Cancer Institute

Dr. Frank Dietrich  
Professor of Medicine  
University of Tennessee  
School of Medicine  
Chief, Medical Service  
Kennedy Veterans Administration Hospital  
Memphis, Tennessee

Dr. George C. Escher  
Associate Member  
Sloan-Kettering Institute for Cancer Research  
Associate Attending Physician  
Memorial Hospital for Cancer and Allied Diseases  
New York, New York

**Dr. Emil Frei, III**  
**Associate Scientific Director for**  
**Experimental Therapeutics**  
**Chief, Medicine Branch**  
**National Cancer Institute**

**Dr. David Grob, Assistant Dean**  
**Professor of Medicine**  
**State University of New York**  
**College of Medicine**  
**Director of Medical Services**  
**Maimonides Hospital**  
**Brooklyn, New York**

**Dr. Thomas Hall**  
**Senior Consultant in Oncology**  
**Lemuel Shattuck Hospital**  
**Associate Physician**  
**Children's Cancer Research Foundation**  
**Boston, Massachusetts**

**Dr. Donald Kayhoe**  
**Head, Medical Groups Section**  
**Clinical Branch, Collaborative Research**  
**National Cancer Institute**

**Dr. Alfred Ketcham**  
**Chief, Surgery Branch**  
**National Cancer Institute**

**Dr. Lyndon E. Lee, Jr.**  
**Associate Director, Research Service**  
**Coordinator, Research in Surgery**  
**Veterans Administration**  
**Washington, D. C.**

**Dr. Mortimer Lipsett**  
**Assistant Chief**  
**Endocrinology Branch**  
**National Cancer Institute**

**Dr. Gregory O'Connor**  
**Laboratory of Pathology**  
**National Cancer Institute**

**Dr. Kenneth Olson**  
**Professor of Medicine**  
**Albany Medical College**  
**Albany, New York**

**Dr. Albert H. Owens, Jr.**  
**Associate Professor of Medicine**  
**Johns Hopkins Medical School**  
**Director, Medical Oncology Unit**  
**Baltimore City Hospitals**  
**Baltimore, Maryland**

**Dr. Robert Bowdin**  
**Associate Professor of Surgery**  
**University of Pennsylvania Medical School**  
**Co-director Neoplastic Chemotherapy Clinic**  
**University of Pennsylvania Hospital**  
**Philadelphia, Pennsylvania**

**Dr. Juan A. del Regato**  
**Director, Penrose Cancer Hospital**  
**Colorado Springs, Colorado**

**Dr. Shirley Rivers**  
**Research Associate, Cancer Chemotherapy**  
**Veterans Administration Hospital**  
**Associate in Medicine**  
**Emory University School of Medicine**  
**Atlanta, Georgia**

**Dr. Albert Segaloff**  
**Professor of Clinical Medicine**  
**Tulane University School of Medicine**  
**Director of Endocrine Research**  
**Alton Ochsner Medical Foundation**  
**New Orleans, Louisiana**

**Dr. Bruce Shnider**  
**Associate Professor of Medicine**  
**Georgetown University School of Medicine**  
**Director of Tumor Service and**  
**Cancer Chemotherapy Research Program**  
**Georgetown Medical Division**  
**D. C. General Hospital**  
**Washington, D. C.**

**Dr. Jesse Steinfeld**  
**Associate Professor of Medicine**  
**Director, Cancer Chemotherapy Program**  
**University of Southern California**  
**School of Medicine**  
**Los Angeles, California**

**Dr. Grant Taylor**  
**Chief, Section of Pediatrics**  
**University of Texas**  
**M. D. Anderson Hospital and Tumor Institute**  
**Houston, Texas**

**Dr. T. Phillip Waalkes**  
**Associate Director for**  
**Collaborative Research**  
**National Cancer Institute**

**Mr. Emanuel Landau**  
**Statistical Consultant**  
**National Cancer Institute.**

#### Review Data

The Krebiozen Research Foundation had selected 504 of its case records of the more than 4,000 patients treated with Krebiozen. These records consisted primarily of forms prepared by the Krebiozen Research Foundation and returned at intervals to the Foundation by the practitioner who administered the Krebiozen. Copies of laboratory, X-ray, and pathology reports were included occasionally but not usually. The Foundation often added a case summary of its own with comments on the chronological course and with conclusions regarding the efficacy of Krebiozen. Information widely distributed by the Krebiozen Research Foundation regarding tumor type and response rate in 4,227 patients (1962 Report) was also available.

Because the material provided by the Krebiozen Research Foundation was inadequate for scientific evaluation, the FDA undertook the collection of complete medical records of all the cases submitted by the Foundation. This involved for each patient, whenever possible:

- 1) Copies of hospital and doctors' records; laboratory, pathological, X-ray, surgical, and autopsy reports; and death certificates
- 2) Pathology slide preparations

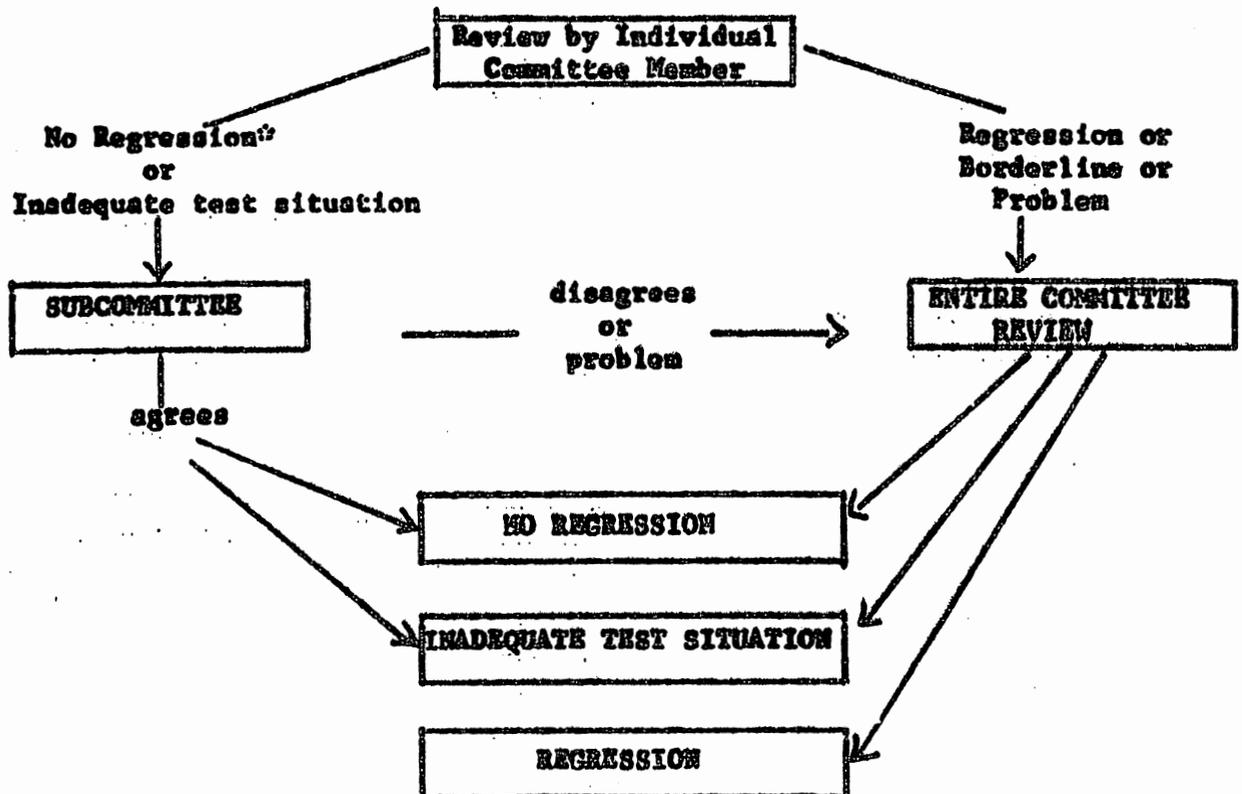
- 3) X-rays
- 4) Report of interviews with all physicians involved in caring for the patient
- 5) Report of interviews with living patients
- 6) Report of interviews with relatives and friends of patients.

A regional representative of the FDA personally conducted each interview and, following a specific protocol, sought answers to a comprehensive group of questions.

### Review Procedure

Working with this total information on each patient, a Committee member, using a 13-page worksheet, tabulated all pertinent data with particular emphasis on factors related to objective measures for evaluation. The Committee member then rated each case in terms of objective regression and subjective response.

In addition to individual evaluation, each case was reviewed either by the entire committee or by a subcommittee following the scheme diagrammed below:



\*See page 6 for definitions.

## Evaluation Standards

The most important criterion necessary to assess the effectiveness of a specific cancer therapy is the presence of measurable disease. Most frequently used are tumor masses, either directly accessible or clearly outlined on X-ray film, which can be followed and serially measured during the course of treatment. However, because of the importance given to subjective improvement attributed to Krebiozen, e.g., pain relief, the exact role and significance of subjective changes seen during therapeutic trials should be understood. The use of subjective response in evaluating the effectiveness of an agent without reference to objective regression is treacherous. In clinical trials of antitumor agents conducted by experienced investigators, subjective response is recorded and evaluated but is considered important only if paralleled by objective improvement. In addition, the majority of such patients are receiving drugs for the control of symptoms. Moreover, the administration of any new agent almost invariably improves the patient's outlook and hope for some period of time.

### A. Objective Criteria

Three categories were used in determining the final status of each patient:

1. Objective regression: A significant regression of a proven neoplasm occurring while the patient was receiving Krebiozen as the only antitumor agent. In accordance with nationally accepted criteria, tumor regression is considered significant if a 50% or greater decrease in the product of measured diameters occurs. At the same time, no new lesions should appear, nor should tumor growth progress elsewhere. The vast majority of the cases did not have serial measurements recorded. In such instances the practitioner's statement of definite tumor decrease was accepted and the patient was classified as showing an objective regression unless contrary evidence existed in the clinical records to indicate that the other criteria had not been met.
2. No regression: An absence of significant objective regression, as defined above, while the patient was receiving Krebiozen as the only antitumor therapy.
3. Inadequate test situation: A broad category of conditions in which some feature of the case made an objective evaluation of Krebiozen impossible.
  - a. Concurrent or immediately prior antitumor therapy

- b. No histologic diagnosis of cancer
- c. No residual cancer (following previous therapy) upon initiation of Krebiozen treatment
- d. Other, e.g. inadequate data.

In each of the above four situations, no decisions regarding the efficacy of Krebiozen can be made. For example, with concurrent therapy, a specific treatment of demonstrated value, it is impossible to distinguish between the effects of Krebiozen and the other modalities of therapy whether the patient's tumor progresses, remains static, or regresses. In some instances such treatment known to exert antitumor effects over a six to eight week period was given immediately before Krebiozen administration. Such cases were placed in the "Inadequate test situation" category.

#### B. Subjective Criteria

In considering subjective effects, a number of factors including degree of disability, pain, narcotic requirement, and other symptoms such as nausea, vomiting, dyspnea, and vertigo were considered. These were evaluated in light of concurrent and prior specific, symptomatic and supportive therapies, e.g., blood transfusions, oxygen, narcotics, and antiemetics. In no instance was subjective improvement alone considered evidence of an objective remission.

#### Findings

##### A. Objective

Of the total 504 cases, 288 fulfilled the necessary conditions so that the effects of Krebiozen could be evaluated. The remaining 216 fell in the "Inadequate test situation" category. Of the latter, 101 had had concurrent antitumor therapy, 50 had no histologic diagnosis of cancer, 49 had no residual malignancy at the time Krebiozen was started, and for 16 the data were inadequate.

Of the former 288 cases, 273 when evaluated, on the basis of the criteria indicated above, showed no significant regression.

Two of the remaining 15 patients were considered to meet the criteria for objective regression. Patient 68 had an abdominal mass which at the time of surgery was determined by frozen section to be a malignancy. The exact type could not be classified and permanent sections were not obtained for a more definitive diagnosis. Consequently, the Committee could not be certain of the nature of the disease in this case. Following the operation in 1951 the patient received X-ray therapy and thereafter was treated with Krebiozen. As of the latest report the patient was apparently living and well. Patient 163 had an adenocarcinoma of the stomach which regressed. The diagnosis was made from a biopsy obtained at surgery in

August of 1954. The patient was treated with five injections of Krebiozen over a 4-week period in September 1954. No other therapy was given. Subsequent abdominal surgery in May 1956 for suspected gall bladder disease disclosed no evidence of carcinoma.

For the remaining 13 patients, although included as regressions, doubts existed as to whether or not they should be considered in this category. The matter was complicated because the tumor changes for some were of a very equivocal nature and there were questions concerning the actual amount of decrease in tumor size, the true validity of the measurements or statements given, and the precise status of the disease. Inadequate documentation often made accurate assessment difficult. Nevertheless, the Committee classified the 13 patients as regressions despite the obscure conditions. The attached Table A is presented to give a clearer picture of the disease status of each one of the 15 patients and to indicate the problems surrounding the objective evaluation of the 13 questionable cases.

In three instances, patients 72, 157, and 143, the tumor regression was of very short duration and followed by death due to metastatic disease. The latter fact indicates that although regression was noted in one anatomic site, the disease was progressing simultaneously in other areas. Essentially the same is true for patient 51, whose records show that while the lung nodules due to a hypernephroma decreased, metastatic involvement of the central nervous system became apparent and persisted during Krebiozen administration. It should be noted that the pulmonary lesions of a hypernephroma may become smaller on occasion even though no specific antitumor therapy is given.

Of the 13 patients, 4 had breast cancer. Patient 149 had a reported metastatic tumor growth in the fundus of one eye. This small lesion regressed during the period she received Krebiozen. Periodically within the same time interval, the patient was also given hormonal agents which are known to produce objective regression in breast cancer. The exact dates she received these latter materials were not recorded but their administration might logically be considered concurrent therapy.

Upon examination of the histologic slides of the tumor of patient 449 by expert pathologists, the diagnosis was made of a rare type of breast tumor which in all known instances had never metastasized. In addition, this patient and patient 141 as well had biopsies taken of their tumor masses during Krebiozen treatment. Such excisions alone, by actual measurement, could have been a factor in the recorded regression. Patient 362 is reported to have had a complete regression of a breast cancer, although the duration of the regression and actual onset of disease is not documented.

Patient 425 had a fibrosarcoma, Grade I. The malignant potential

of this tumor is considered highly uncertain.

Patient 308 had a neuroblastoma partially resected at the age of 5 months. Several reports in the medical literature substantiate the fact that this malignancy, particularly in patients under one year of age, may spontaneously regress or change to a benign tumor.

Patient 165 had histologically documented melanoma of the face in 1946 and of the elbow in 1951 which were excised. Krebiozen was administered in 1951 for an un-biopsied nodule of the leg which disappeared. Patient 439 also had a melanoma and received Krebiozen seven years after the original diagnosis. Krebiozen therapy was continued for 21 months until the patient died with widely metastatic disease.

Patient 177 died of metastatic cancer 1 year and 9 months following Krebiozen therapy. No X-rays or radiologists' reports were available for review to verify the disappearance of the mediastinal metastasis reported to have occurred while the patient was receiving Krebiozen.

#### B. Subjective

Of the 421 patients who could be evaluated on the basis of subjective symptoms, 44 patients showed subjective improvement. However, as previously pointed out, the use of subjective response in evaluating the effectiveness of an agent without reference to objective regression is extremely unreliable in assessing the true status of malignant disease.

#### C. Toxicity

The administration of the ampuled Krebiozen was associated with definite toxic effects in 35 cases. In most instances only induration and inflammatory granulomas at the injection sites were noted. In some cases the pain associated with these lesions necessitated discontinuance of further injections. Abscesses or sloughs occurred in six patients. There was little evidence of systemic toxicity, although one patient who died with broncho-pneumonia was found to have lipid deposits scattered through the lungs, heart, liver, and spleen, possibly due to the large amount of mineral oil administered.

#### Conclusion

On the basis of data reviewed and objective criteria employed to assess antitumor response, it is the unanimous opinion of the Review Committee that Krebiozen is ineffective as an antitumor agent. In a very small number of patients, tumor regressions of varying degrees were seen during Krebiozen treatment. The validity of the majority of these regressions is subject to question for several different reasons. It is the opinion of the Committee that the nature, degree, and number of effects noted are what one might expect in any large random sample of cancer patients. The Committee strongly recommends that no clinical trial of Krebiozen be undertaken.

TABLE A

Patients Evidencing Tumor Regression While on Krebiozen

Patient	Age when Kreb. st.	Sex	Diagnosis	Reported Tumor Regression		Comments
				Character	Duration	
51	69	F	Hypernephroma	Decrease in size of Pulmonary Metastases	5 Mo.	After tumor regression, pulmonary metastases again increased in size while the patient was still on Krebiozen. Signs of CNS metastases appeared about the time Krebiozen was started and persisted with varying severity until the patient's death, said to be due to cerebral hemorrhage or embolus. It could not be determined whether autopsy was performed. The clinical picture suggests that while regression occurred in the lung masses, metastatic disease was progressing in the CNS. In addition, pulmonary lesions of hypernephroma are known to decrease in size on occasion even though specific therapy has not been given.
66	12	M	Grade IV malignant intra-abdominal neoplasm of undetermined primary site	>50% decrease in tumor mass on multiple occasions while on Krebiozen	June 1951 to present	The exact type of tumor represented by this case was never determined. Only frozen sections were obtained and no permanent slides prepared. Consequently, the committee could not assess the true nature of the disease. Post-operatively the patient received x-ray therapy and thereafter was given Krebiozen. At the last report the patient was living and apparently well.
72	21	F	Fibrosarcoma left sacrum	>50% decrease in mass of tumor in two areas	10 days	16cc. Krebiozen was given over a 10-day period, during which tumor regression was noted. The patient died on 10th treatment day of metastatic disease. The rapid decline and death of the patient due to cancer, despite regression of the tumor masses, suggest that malignant disease was progressing elsewhere.

Patient	Age then Kreb. sto.	Sex	Diagnosis	Reported Tumor Regression		Comments
				Character	Duration	
141	55	F	Adenocarcinoma of breast	Complete Regression	1 year	The patient was said to have been free of disease for 1 year. A number of areas, including the breast mass, were biopsied during the period of Krebiozen therapy. The possibility must be considered that such biopsies may have been a factor in the recorded decrease in tumor size. A chest X-ray during the period of complete regression revealed a suspicious pulmonary infiltrate suggesting that tumor growth was occurring in the lung. The patient died, probably while on Krebiozen, 5 years after diagnosis.
143	47	M	Adenocarcinoma of colon	>50% decrease in palpable abdominal mass	2 months	During the 4 months following the regression, the tumor mass again increased in size, although Krebiozen therapy was continued. The patient died shortly thereafter.
145	46	F	Malignant melanoma of face	Nodule on lower extremity disappeared	Disease diagnosed in 1946. Krebiozen given August 1951. Patient living at last report.	The patient had histologically documented melanoma of the face in 1946, and of the elbow in 1951. She was given 5 cc's of Krebiozen from August to November 1951 for a non-biopsied lesion of the lower extremity, consequently the exact nature of the nodule is unknown. This disappeared. She received multiple courses of I <sup>131</sup> before and after Krebiozen. This latter therapy with I <sup>131</sup> is of questionable value.

Patient	Age When Kreb. st.	Sex	Diagnosis	Reported Tumor Regression		Comments
				Character	Duration	
169	44	F	Infiltrating duct cell carcinoma of breast with lymph node metastases.	Disappearance of metastatic lesions in fundus of the eye and retinal reattachment.	3 months	The patient with metastatic breast cancer was bedridden and blind with a detached retina and metastases in the fundus when Krebiozen was started. The patient received steroids and ACTH as well as Krebiozen and died 7 months after initiation of Krebiozen therapy, apparently from carcinomatosis. The possibility that the hormonal agents may have been a factor in the regression noted must be considered.
157	51	M	Teratocarcinoma	Disappearance of pulmonary metastases	8 weeks	Following a brief regression, pulmonary metastases reappeared. Increasing doses of Krebiozen had no effect. Transient regression followed repeated courses of radiotherapy but the patient died of progressive disease.
177	34	M	Seminoma	Mediastinal metastasis said to have disappeared	1 year	Disease recurred and the patient died of metastatic cancer 1 yr. 9 months following completion of Krebiozen therapy. No x-rays or radiologist's reports were available for review.
183	38	M	Adenocarcinoma Stomach	Complete regression	Diagnosis 1954 Krebiozen 1954 Living and well at present time.	Inoperable adenocarcinoma of stomach was found in 1954. No tumor was found at re-exploration in 1956.

Patient	Age when Kreb. started	Sex	Diagnosis	Reported Tumor Regression		Comments
				Character	Duration	
303	11 mo.	F	Neuroblastoma, retroperi- toneal	Complete re- gression of re- current abdominal disease and metastatic disease	1962 to present	This female infant had an 80-90% resection of a neuroblastoma at age 5 months. With the appearance of abdominal recurrence, supraclavicular and mediastinal metastases, Krebiozen was started in March 1962 and by September 1962 there was no evidence of disease. It should be noted that in patients under one year of age this malignancy on occasion regresses or changes to a benign tumor.
302	67	F	Scirrhous adenocarcinoma of breast.	Complete regression.	?	Cancer, first symptomatic in ? 1949, was diagnosed in 1957. The patient had no therapy before Krebiozen which was given in 1958 over the 7-month period during which complete disappearance of the mass was said to occur. The duration of remission is unknown although the patient died 8 months after completion of Krebiozen therapy 18 months after diagnosis.
425	36	F	Fibrosarcoma Grade I of thigh	Complete dis- appearance of 4" x 4" lesion, left thigh.	Diagnosis 1944 Last Krebiozen Dec. 1954. Living at last report.	After multiple surgical procedures and courses of irradiation between 1944 and 1952 the patient presented in 1953 with a lesion on the thigh which was not biopsied. The exact nature of the lesion here is unknown. If a fibrosarcoma Grade I, it would be of questionable malignant character. During the period of Krebiozen administration, the lesion disappeared leaving only a defect in the area.

**Reported  
Tumor Regression**

Patient	Age when Kreb. std.	Sex	Diagnosis	Character	Duration	Comments
439	42	F	Malignant melanoma of lower extremity	Lesion on lower extremity said to have disappeared	Months	Melanoma initially treated in 1945, continued to recur despite excisional and X-ray therapy until 1952 when Krebiozen was started. Krebiozen therapy was continued for 21 months until the patient died with widely metastatic disease. Apparently the tumor was a very slow growing malignancy. Nevertheless, the question arises whether or not progression was occurring elsewhere at the same time regression was noted for the lower extremity lesion.
445	70	F	Adenoid cystic carcinoma of breast	>50% reduction in tumor size reported	Living from time of diagnosis in 1958 to present	Following a year of Krebiozen therapy, two biopsies of the lesion were made: one measured 3 x 2.8 x 1.8 cm.; the other 4.5 x 4 x 2.5 cm. Such large biopsies could well have accounted for a very substantial decrease in tumor mass. The original mass size was reported as 10 x 16 cm. Upon further review, the specimen was felt to represent an adenoid cystic carcinoma, an extremely uncommon lesion which, in the experience of the Armed Forces Institute of Pathology, has not been observed to metastasize.

## APPENDIX

Table 1 - shows the distribution of the 504 cases according to primary site with a breakdown into categories for evaluation as determined by the Review Committee.

Table 2 - indicates the number of objective regressions for those primary sites containing 10 or more patients who fulfilled the requirements for an adequate test situation.\* For comparison, the total number of patients treated with Krebiozen as of the 1962 Report is shown for the same sites.

Table 3 - is the same as Table 2 but for primary sites of less than 10 acceptable test patients.

\*All patients were included in this category unless the nature of the experimental conditions made an objective evaluation of Krebiozen impossible as stated under "Inadequate test situation" on Page 6.

TABLE 1

DISTRIBUTION OF KREBIOZEN CASES BY PRIMARY TUMOR SITE  
AND TEST SITUATION

Primary Tumor Site	No. Subm.	Adequate Test Situation	Inadequate Test Situation				
			Total	Concurrent Therapy	No Path. Diag. of Ca.	No residual Cancer	Other
Total	504	288	216	101	50	49	16
Brain & Cord, Primary	17	6	11	4	4	3	0
Breast	180	93	87	39	12	9	7
Cervix Uteri	6	3	3	0	0	2	1
Colon	49	33	16	3	3	10	0
Duodenum & Small Intest.	2	1	1	0	0	1	0
Esophagus	1	0	1	0	0	1	0
Gallbladder	1	0	1	0	1	0	0
Head & Neck	6	3	3	1	1	1	0
Kidney; Ureter	10	6	4	1	0	2	1
Larynx	2	1	1	0	0	1	0
Liver & Bile Ducts	5	5	0	0	0	0	0
Lung; Bronchus	22	19	3	0	1	2	0
Nasopharynx	6	6	0	0	0	0	0
Ovary <sup>1/</sup>	19	11	8	6	1	1	0
Pancreas	15	10	5	1	4	0	0
Prostate	11	2	9	7	2	0	0
Rectum	23	20	3	0	3	0	0
Salivary Glands	2	2	0	0	0	0	0
Stomach	24	12	12	1	5	5	1
Testes	6	5	1	1	0	0	0
Thyroid	3	1	2	0	0	2	0
Tongue	3	3	0	0	0	0	0
Urinary Bladder	10	6	4	2	0	2	0
Uterus	8	6	2	0	0	2	0
Vagina; Vulva	2	1	1	0	0	1	0
Undetermined Site	20	11	9	3	4	1	1
Hodgkin's	2	0	2	2	0	0	0
Lymphosarcoma	2	1	1	1	0	0	0
Melanoma	8	6	2	1	0	1	0
Osteogenic Sarcoma; Bone; Spine	12	8	4	3	1	0	0
Sarcomas - Soft Tissue	7	1	6	1	0	1	4
Acute Myelocytic Leuk.	2	0	2	2	0	0	0
Misc. Abdom. Malig. <sup>2/</sup>	3	3	0	0	0	0	0
Mediastinum, Undifferen.	1	1	0	0	0	0	0
Misc. Skin Cancer <sup>3/</sup>	2	1	1	1	0	0	0
Neuroblastoma	3	1	2	1	0	1	0
No. estab. diag. of Malig.	9	0	9	0	8	0	1

<sup>1/</sup> One of these cases was shown at autopsy to be metastatic carcinoma from the breast.

<sup>2/</sup> Includes - Mesothelioma, Neurofibrosarcoma, and Sympathicoblastoma.

<sup>3/</sup> Includes - One patient with epidermoid cancer of hand, and one with squamous cell cancer of penis.

TABLE 2

**OBJECTIVE REGRESSION CATEGORY  
(FOR SELECTED PRIMARY TUMOR SITES - LARGE SAMPLES)**

Primary Tumor Site <sup>1/</sup>	NUMBER OF PATIENTS				
	Total <sup>2/</sup> Treated	Total Submitted by K.F.	Fulfilled Adequate Test Situation		
			Total <sup>3/</sup>	No Objective Regression	Objective Regression
Breast	870	180	93	89	4
Colon	463	49	33	32	1
Lung	340	22	19	19	0
Ovary	228	19	11	11	0
Pancreas	177	15	10	10	0
Rectum	237	23	20	20	0
Stomach	286	24	12	11	1
Undetermined Site	102	20	11	10	1

<sup>1/</sup> For sites with 10 or more cases fulfilling the requirements for an adequate test situation

<sup>2/</sup> Source: "Report on Krebiozen, An Agent for the Treatment of Cancer, 1962", Krebiozen Research Foundation, Table 1, Page 9

<sup>3/</sup> As determined by Review Committee in present study of 504 cases.

TABLE 3

**OBJECTIVE REGRESSION CATEGORY**  
(FOR SELECTED PRIMARY TUMOR SITES - SMALL SAMPLES)

Primary <sup>1/</sup> Tumor Site	NUMBER OF PATIENTS				
	Total <sup>2/</sup> Treated	Total sub- mitted by K.F.	Fulfilled Adequate Test Situation		
			Total <sup>3/</sup>	No Objective Regression	Objective Regression
Osteogenic Sarcoma	23	12	8	7	1
Brain <sup>4/</sup>	178	17	6	6	0
Kidney, Ureter	116	10	6	5	1
Nasopharynx	48	6	6	6	0
Urinary bladder	107	10	6	6	0
Uterus	71	8	6	6	0
Melanomas	115	8	6	4	2
Liver & Bile Duct	62	5	5	5	0
Testes	31	6	5	5	0
Cervix-Uteri	147	6	3	3	0
Misc. Abdominal <sup>5/</sup> malignancy		3	3	3	0
Prostate	130	11	2	2	0
Salivary Glands	21	2	2	2	0
Duodenum & Small intestines	19	2	1	1	0
Larynx	26	2	1	1	0
Thyroid	18	3	1	1	0
Vagina; vulva	10	2	1	1	0
Lymphosarcoma	44	2	1	1	0
Sarcomas	115	7	1	0	1
Neuroblastoma <sup>5/</sup>		3	1	0	1
Misc. Skin <sup>5/</sup>		2	1	1	0
Mediastinum undiff. <sup>5/</sup>		1	1	1	0

<sup>1/</sup> For sites with less than 10 cases fulfilling the requirements for an adequate test situation.

<sup>2/</sup> Source: "Report on Knebixon, An Agent for the Treatment of Cancer, 1962", Table 1, Page 9

<sup>3/</sup> As determined by Review Committee in present study of 504 cases.

<sup>4/</sup> Includes Brain and Cord, primary, and Brain metastases

<sup>5/</sup> Not listed in 1962 Report.