Japan Clinical Oncology Group (JCOG)

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Japan Clinical Oncology Group (JCOG) is a cooperative oncology group with the aims of conducting, developing, coordinating and stimulating clinical research in Japan on the treatment of cancer and related problems. The purpose of JCOG is to establish and improve the standard of cancer treatment, mainly in solid cancer, through the testing of new therapeutic regimens or combined modalities, using drugs that are newly-approved or already commercially available. Research sponsored by JCOG is accomplished mainly through the execution of large, prospective, randomized, multicenter, clinical trials. In this way, JCOG facilitates the passage of new clinical trial discoveries into state-of-the-art treatment.

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ORGANIZATION OF JCOG, COOPERATIVE CLINICAL STUDY GROUPS AND JCOG COMMITTEES

The organization of JCOG is shown in Fig. 1, which depicts the relationship between the Operations Office, the Steering Committee, the JCOG Data Center, the Clinical Trial Review Committee (CTRC) as an institutional review board and the Independent Monitoring Committee (IMC) that monitors and reviews efficacy and safety data from on-going clinical trials. The clinical study groups consist of the Lymphoma Study Group (LSG), Japan Esophageal Oncology Group (JEOG), Lung Cancer Study Group (LCSG), Lung Cancer Surgical Study Group (LCSSG), Gastrointestinal Oncology Study Group (GIOSG), Gastric Cancer Surgical Study Group (GCSSG), Breast Cancer Study Group (BCSG) and Gynecological Cancer Study Group (GCSG). JCOG membership included more than 600 physicians belonging to about 200 medical institutions as of November 1997.

In developing standard treatments with the ultimate goal of curing cancer, multicenter cooperative clinical trials are needed. In order to expedite the application of advances in clinical research to cancer treatment, it is necessary for investigators to collaborate in cooperative clinical trials. The trials must be carried out systematically with the cooperation of extensive monitoring and coordinating systems. In order to facilitate clinical trials of cancer treatment, a project entitled ‘A Study on the Multidisciplinary Treatment for Solid Cancer’ was started in 1978, which was designated by the President of the National Cancer Center (NCC) (Hichiro Ishikawa [1978-84], Takashi Sugimura [1984-91], Keiichi Suemasu [1992-94] and Kaoru Abe [1994-present]) and has been supported since then by a Grant-in-Aid for Cancer Research, chaired by the President of the NCC, from the Ministry of Health and Welfare. The project was chaired by Keiichi Suemasu, MD, Deputy Director, National Cancer Center Hospital (NCCH) between 1978 and 1987 and then by Masanori Shimoyama, MD, who served as Chief of the Medical Oncology Division (1988-91), Deputy Director (1992-93), NCCH, Director, NCCH East (1994) and finally Director, Nagoya National Hospital (1995-present). In this project the first cooperative clinical study groups, LSG chaired by Masanori Shimoyama, MD, which includes the T- and B-cell Malignancy Study Group (TBMSG) and Lymphoma Clinico-Pathology Panel (LCPP), and JEOG chaired by Norihumi Iizuka, MD, were formed in 1978, then LCSG by Nagahiro Saijo, MD in 1982, which consists of two subgroups, East Japan LCSG (EJ-LCSG) and West Japan LCSG (WJ-LCSG), GCSSG by Toshihumi Nakajima, MD in 1984, GIOSG by Minoru Kurthara, MD and BCSG by Kaoru Abe, MD in 1985, LCSSG by Mitsuho Ohta, MD in 1986, Autologous Bone Marrow Transplantation Study Group (ABMTSG) by Kensei Tobinai, MD in 1990, which was later absorbed into the LSG and BCSG in 1996, and GCSSG by Ryoichi Tsunematsu, MD in 1995. In 1985, a Constitution and Bylaws for these groups were adopted which provided for the CTRC and the IMC (1). The office of the two Committees was housed at the NCCH, Tokyo. Scientific and ethical guidelines for generating and conducting protocols of these groups were also established in 1985 (1). All protocols of the JCOG trials

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are reviewed and approved by the CTRC and all on-going trials are monitored every 6 months by the IMC. A Joint Committee of CTRC and IMC fills the role of the Steering Committee, which is responsible for directing the activities of a designated project of JCOG and for the conduct of multicenter clinical trials in JCOG. The Joint Committee was renamed and became the Steering Committee in 1997. Each of the JCOG Committees held meetings regularly every 6 months until recently, but since early 1997 they have been held every 3 months.

A small statistical section was set up in 1989. At this opportunity, all clinical study groups, committees and a statistical section were integrated into an organization which was named the Japan Clinical Oncology Group (JCOG) in 1990. The Chairperson of JCOG has been Masanori Shimoyama, MD since that time. The JCOG Operations Office, under the direction of the JCOG Chairperson, is located at the institution where he is now posted, i.e. the Nagoya National Hospital, Nagoya.

The Constitution and Bylaws were amended and the guidelines were also revised twice in 1989 (2) and 1995 (3,4). JCOG toxicity grading criteria (5), which were a modified and expanded version of the National Cancer Institute Common Toxicity Criteria (NCI-CTC) used in the USA, were adopted in 1991. After completion of the international version of the NCI-CTC, now being updated throughout, it will be adopted by JCOG in 1998. A Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting in JCOG (6) was provided and executed in 1996, although partly amended in 1997.

**PROTOCOL**

Approximately 10 new JCOG protocols per year are approved by the CTRC. The collected protocols have been published annually for JCOG members and so far 10 issues have been provided to members. Over 100 protocol studies have been conducted by eight clinical groups. At present, about 30 protocols are active in accrual of patients. It is agreed by the JCOG Chairperson and all members of JCOG Committees that all protocols recently approved will be open as soon as possible to the Internet through the Cancer Information Service of the National Cancer Center in Japanese. In addition, the Editorial Board of the Japanese Journal of Clinical Oncology (JJC0) invites JCOG to describe the outline of each JCOG protocol, on-going and newly approved, in English. Thus, JCOG will be able more rapidly to provide information on its clinical cancer research activities to non-member clinical investigators and patients on a national and international basis to establish the standard of cancer treatment.

**FROM THE JCOG STATISTICAL CENTER TO THE PRESENT JCOG DATA CENTER**

JCOG requires the presence of a statistical center to serve as another coordinating system providing comprehensive assistance from the massive input of data to the output of results. The JCOG Statistical Center, under the direction of Masanori Shimoyama, MD, was planned in 1989 and had almost been established by 1993 as a result of his research efforts in the development of a computerized system for the management and analysis of data from clinical trials conducted by JCOG (7). The research project to establish the JCOG Statistical Center was chaired by Masanori Shimoyama, MD and was supported by a Grant-in-Aid for Basic Research from the Science and Technology Agency between 1991 and 1993. The project is on-going and aims to improve its function with the support of a Grant-in-Aid for the Second-term 10-Year Strategy for Cancer Control from the Ministry of Health and Welfare (1994). The chief investigator was Masanori Shimoyama, MD in 1994, Shoichiro Tsugane MD, Chief, Epidemiology and Biostatistics Division, National Cancer Center Research Institute (NCCRl) East in 1995 and 1996 and has been Naohito Yamaguchi, MD, Chief, Cancer Information Service of the National Cancer Institute (NCCRl) East since 1997.

The JCOG Statistical Center was housed at NCC, Tokyo in 1989, moved to NCCRI East, Chiba in 1995 and has been rehoused at NCCRl, Tokyo since 1996. The Director of the JCOG Statistical Center was Masanori Shimoyama, MD from 1989 to 1996 and since then has been Naohito Yamaguchi, MD. The JCOG Statistical Center has a system fully equipped with the necessary functions including patient registration, management and analysis of data from clinical trials, records from management, monitoring report generation and several information services. The system is called the JCOG Database System. In addition to this system, the JCOG Statistical Center plays a major role in protocol generation for assisting with study design, sample size calculation and case report form generation.
The data from the patients registered in JCOG trials are principally managed by the JCOG Statistical Center. Patients' data from about 30 on-going and 30 follow-up protocols are monitored twice a year and the results are summarized as monitoring reports, which are assembled in their respective clinical groups and provided immediately to their respective members for quality control of data. All monitoring reports of all clinical study groups are collected in book form once or twice a year and these books are provided to all JCOG members to maintain the high quality of the trials.

The major change to occur in 1996 was the relocation of the JCOG Statistical Center at NCCRI, Tokyo under the direction of newly appointed Director, Naohito Yamaguchi, MD. The JCOG Statistical Center was renamed and became the JCOG Data Center in 1997. Following grant submission and initiation of activities, the present JCOG Data Center began functioning in July 1997. Over the ensuing year, the JCOG Data Center has been developing into the finest statistical resource center in existence, as evidenced by the quality of its work, the level of scientific and intellectual interchange and total commitment to excellence.

ACTIVITIES

JCOG will continue to strive for excellence in clinical cancer research efforts. JCOG publications in English in books and peer-review journals are listed in the Appendix. This cannot be accomplished without the dedication and commitment of each JCOG member, whether that individual is a physician, biostatistician, study coordinator, data manager or in an administrative position. As of October 1997, there are on average 10 new protocols each year open for accrual in eight cooperative clinical study groups. Accrual has reached approximately 1000 patients per year and there are a total of more than 12,000 patient records in the database. However, the accrual rate is not increasing from the level of the past 3 years because of problems with resources such as research nurses, data managers and research funds. In tandem with increasing our accrual, we hope to continue our reputation for innovative clinical cancer research trials, high-quality data acquisition and the publication of Group efforts. Based upon the growth of the Group since its inception in 1985, the JCOG is expected to continue as a leader in conducting cooperative cancer clinical trials.

PROBLEMS TO BE SOLVED IN THE NEAR FUTURE

There are only a few biostatisticians and study coordinators and almost no research nurses are available at present in Japan. JCOG studies are extremely limited under these circumstances. There are five major reasons for these problems. First, there is a problem with the educational system in medicine, namely too few biostatistics divisions in medical colleges and universities. Second, there are no educational and training systems for research nurses, study coordinators and data managers. Third, medical facilities for clinical trials are inadequate, so that they are not sufficiently established in hospitals and medical institutions to allow good clinical trials of high quality to be conducted. Fourth, financial support from the Government of Japan for clinical trials is insufficient, so that it would be impossible to employ research nurses, study coordinators and data managers on adequate salaries even if they did exist. Fifth, regulations for personnel expenses from research funds are too rigid, i.e. they impose legal controls on low salaries without health insurance, worker's compensation insurance and commutation allowance.

Problems other than those of the educational system need to be solved urgently, with deregulation for personnel expenses from research funds being especially essential. This is the most important first step in improving the clinical trial system in JCOG and throughout Japan. The establishment of adequate numbers of qualified medical institutions for cancer clinical trials is also an urgent issue. We must also make great efforts to improve the cancer clinical trial system and to support and encourage qualified investigators and research associates with on-the-job training.

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References

Lymphoma Study Group (LSG)

**JCOG8701**

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Other cooperative studies of LSG on diagnosis, treatment, etiology and epidemiology of lymphoma


Japan Esophageal Oncology Group (JEOG)

**JCOG8201**

**JCOG8073**

**JCOG8807**

**JCOG8503**

**JCOG8806**
Other cooperative studies of JEOG


Lung Cancer Study Group (LCSG)

JCOG8502


JCOG8803


JCOG8809


JCOG9011


JCOG9110


Other cooperative studies of LCSG


Gastrointestinal Oncology Study Group (GIOSG)

JCOG8501


JCOG8804


JCOG9001


Other cooperative studies of GIOSG


Breast Cancer Study Group (BCSG)

JCOG9107


Autologous Bone Marrow Transplantation Group (ABMTG)


Gynecological Cancer Study Group (GCSSG)

JCOG8601