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CONNECT-ClinicalTrials: An Empirical Study on Establishing an Online Consultation System for Clinical Trial Enrollment Using a Communication Application Among Medical Professionals

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Research Article

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Abstract

Background

Clinical trial participation among patients with cancer remains limited, with particularly low rates in Japan. Structural challenges, including “drug lag” and “drug loss,” along with limited patient access to trial information and physician time constraints, hinder trial enrollment. Therefore, the National Cancer Center Hospital (NCCH) developed CONNECT-ClinicalTrials (COnsultation system of Nationwide oncology medical NEeds with online Communication Tool in Clinical Trials), a multicenter initiative leveraging the Join® communication platform to facilitate early trial eligibility assessments and streamline patient referrals.

Methods

This observational, non-interventional study aimed to evaluate the implementation of CONNECT-ClinicalTrials. Participating physicians from cooperating institutions submit patient data via Join®, enabling NCCH specialists to assess trial eligibility. Eligible patients may be formally referred to and enrolled in clinical trials. The data collected include patient demographics, clinical history, trial participation outcomes, and physician satisfaction. The primary endpoint is the proportion of referred patients enrolled in any clinical trial within three months of consultation. The study assessed 150 participants over two years, with follow-up extending to one year post-enrollment. The observed trial participation rate will be compared with the predefined threshold using binomial testing and Clopper–Pearson confidence intervals.

Conclusion

CONNECT-ClinicalTrials offer a scalable digital solution to enhance clinical trial access and mitigate disparities in trial enrollment. By improving inter-institutional communication and pre-screening efficiency, the system may contribute to reducing drug development delays in Japan and promoting equitable access to investigational therapies. CONNECT-ClinicalTrials could potentially be a national model for integrating community and academic cancer care in precision oncology.

1. Background

1.1. Background and Rationale

Despite significant advancements in cancer therapeutics, the number of patients participating in clinical trials remains low. Indeed, only 6.3% to 7.1% of patients with cancer are enrolled in treatment trials, with participation rates ranging from 18.9% to 21.6% at NCI-designated cancer centers and 3.6% to 5.7% at

regional facilities[1]. When including all study types (biospecimen collections, registries, and genetic studies), 21.9%–25.4% of patients with cancer participate in at least one clinical study.

In Japan, participation in such programs remains limited. At the National Cancer Center Hospital (NCCH), a leading oncology institution, only 366 of 4,209 patients (8.69%) who presented for an initial consultation in 2023 participated in clinical trials or related activities. Notably, of the 176 patients referred specifically for clinical trial consultation, only 26 (15%) were enrolled in a trial, which falls short even when compared with the United States' benchmarks. In the remaining 85% of patients, the reasons for not being linked to a trial include referral of patients with poor performance status or ineligibility due to comorbidities (31%), followed by 13% of patients without a referrable trial, and 6% without a target lesion for whom a trial could not be proposed.[2]

Japan also faces structural challenges of "drug lag"—delayed domestic approval of therapies available internationally—and "drug loss," wherein therapies approved abroad are never developed or marketed in Japan. These issues are particularly pronounced in oncology. As of March 31, 2024, 128 drugs approved in the United States or Europe have not been approved in Japan and 70 lack Japanese indications.[3]

One root cause of these challenges is Japan's limited inclusion in global trials. Oncology drug development is being spearheaded by pharmaceutical venture companies without a Japanese presence, resulting in limited access (Fig. 1). [4]

Factors determining the inclusion of Japan in multinational studies include the country's drug pricing policies aimed at cost containment, regulatory complexity, and the logistical burden of patient recruitment. [5,6]

To address these issues, multistakeholder collaboration across industries, governments, and academia is essential to facilitate clinical trial registration at key academic and research institutions.

From a patient's perspective, limited access to trial information and psychological barriers are the major deterrents to enrollment. Approximately 84.3% of patients seek clinical trial information from their oncologist, followed by clinical trial physicians (47.4%), family physicians (22.2%), and other healthcare providers (12.9%).[7] Misconceptions are also a major challenge, with many patients perceiving clinical trials as experimental endeavors rather than a component of quality care. This is compounded by time constraints among practicing physicians who may lack the capacity to search for trials or engage in discussions with patients.[8]

To mitigate these challenges, an online consultation system may facilitate advanced sharing of patient information and the early estimation of eligibility and reduce unnecessary referrals. This approach may increase enrollment efficiency and reduce mismatches between trial availability and patient suitability.

In response, the NCCH developed an online consultation platform— COnsultation system of Nationwide oncology medical NEeds with online Communication Tool in Clinical Trials (CONNECT-ClinicalTrials)—

based on the Join® application. This system enables medical professionals to share the clinical data of patients seeking trial enrollment to facilitate early assessment of eligibility and improve access to investigational therapies. CONNECT-ClinicalTrials (NCCH2403, UMIN ID: UMIN000056850) was officially launched as a multicenter initiative to evaluate the effectiveness of this digital consultation infrastructure.

1.2 Join®

Join® is a communication application developed by Allm Inc. for medical professionals to facilitate seamless and secure information sharing among healthcare providers. It is integrated with hospital systems such as Picture Archiving and Communication Systems (PACS), allowing clinicians to access and share medical images, such as magnetic resonance imaging (MRI) and computed tomography (CT) scans, via a standard-equipped DICOM viewer. This functionality enables remote consultations, permitting specialists to provide treatment advice even off-site, thereby enhancing interhospital collaboration and expediting patient care delivery.[9]

Join is certified as a medical device in multiple regions, including Japan (PMDA: Class II), the United States (FDA: Class I), Europe (CE: Class I), and Brazil (ANVISA: Class I). As of February 2022, the application has been implemented in over 1,000 medical institutions across 30 countries, contributing to the establishment of a global medical network to improve healthcare quality and address disparities in medical resource distribution.[8]

2. Methods

2.1. Study Design

As illustrated in Fig. 2, attending physician A, cooperating medical institution (hereafter referred to as “Attending Physician A”), submits patient information and consultation details to the National Cancer Center Hospital (NCCH) via the Join® online consultation platform. Upon submission, a unique registration number is generated, comprising the institution number, order of registration at that institution, Clinical Consultation Trial (CCT), and an overall study identifier (e.g., 0101CCT01).

The NCCH reviews the submitted consultation and responds via Join® regarding patient eligibility for ongoing clinical trials.

A designated research physician from the corresponding department at the NCCH makes the final determination. If the patient is deemed potentially eligible and expresses interest, the cooperating institution may proceed with formal referral to the NCCH. For documentation purposes, the patient’s registration number should be indicated in the referral letter to confirm participation in the study.

Subsequently, a physician at NCCH (hereafter referred to as “Attending Physician B”) will provide a full explanation of the relevant clinical trial, obtain informed consent, and initiate patient registration for

participation.

In addition, medical professionals from cooperating institutions that utilize the system will be surveyed using a questionnaire to evaluate their satisfaction and user experience with the platform.

Although this system supports treatment option evaluation and clinical trial screening, the final clinical decision-making remains the responsibility of Attending Physician A. Responses generated via the consultation system do not constitute medical directives; thus, this study does not involve any interventional procedures and will be conducted as a non-interventional observational study.

As described in Fig. 3, the secretariat pays the participating sites for research, and the evaluation points for payment are calculated based on the following three cases:

1. Number of consultations through Join® from each facility (filling in the primary screening sheet, filling in the secondary screening sheet).
2. Number of patients consulting the NCCH for a specific proposed clinical trial.
3. Number of patients participating in the proposed clinical trial.

Funding for the research is provided by the Secretariat to each medical institution based on funds submitted by pharmaceutical companies that have pledged to participate in the research.

2.2. Eligibility Criteria

The study population includes patients whose consultations are managed through the Join® system and healthcare professionals who provide consultations through systems belonging to institutions classified as cooperating medical institutions. These institutions are defined as those providing only existing samples and clinical information. No exclusion criteria are applied in this study.

2.3. Objectives and Outcome Measures

2.3.1. Data Collection via the Join System

(1) Initial data entry items

Patient preferences and social context: interest in clinical trials and welfare status

Basic clinical information (primary)

Age, sex, cancer type, performance status (PS), oxygenation, laboratory values, comorbidities, previous treatment (number and type of regimens), diagnosis, current medical history, and nutritional intake status

(2) Additional Items (if preliminary eligibility is confirmed)

Secondary clinical information

Presence and location of metastasis, current regimen name, date of last anticancer therapy, presence of target lesions, gene panel testing status, and relevant imaging data (e.g., CT and MRI)

2.3.2. Post-referral Follow-Up

The coordinating office will follow up with Attending Physician B to determine the trial participation status within 3 months of the patient's initial NCCH visit. Physicians will select one of the following responses:

Participated in a clinical trial (interventional or non-interventional)

→ Date of enrollment, trial classification, whether the patient enrolled in the trial recommended via Join, and whether the treatment was guided by cancer genome profiling will be collected.

No trial available at the time of referral (e.g., full enrollment)

Ineligible for available trials owing to clinical factors (e.g., poor PS and comorbidities)

Note any changes in the patient's condition since joint registration.

Awaiting trial candidacy

Other details (e.g., ongoing treatment locations) will be collected for responses (2) and (3).

2.3.3. Cooperating Institution Feedback

Three months after referral, a satisfaction survey will be administered via Join® to Attending Physician A at each cooperating institution.

2.4. Sample Size and Recruitment

2.4.1. Primary Endpoint

The primary endpoint is the proportion of patients referred via the Join-based consultation system who are subsequently referred to the NCCH and enrolled in any clinical trial (interventional or non-interventional) within 3 months of referral, regardless of whether the trial was initially proposed via Join® .

2.5. Data Collection and Management

Based on the preliminary hypotheses (Section 2.2.1), a threshold clinical trial participation rate of 9% and an expected rate of 17% are assumed. With a one-sided $\alpha = 0.05$ and power $(1-\beta) = 80\%$, the estimated required sample size is 150 patients.

Planned enrollment: 150 participants

Enrollment period: ~2 years (approval date through December 2026)

Follow-up period: 1 year following the final enrollment

Overall study duration: ~3 years (approval date through December 2027)

2.6. Planned Statistical Analysis

Principal Analytical Methods:

(A) Perform a binomial test to assess the null hypothesis: “The true participation rate is ≤ 9%.” Significance level: one-sided α = 0.05.

C. Estimate the Participation Rate and Its 90% and 95% Confidence Intervals, using the Clopper-Pearson Exact Method Based on a Binomial Distribution

3. Conclusion

The CONNECT-ClinicalTrials study presents a novel, systematic approach to enhance clinical trial accessibility and participation by implementing an online consultation platform that facilitates real-time communication and information sharing between referring institutions and central cancer hospitals. By enabling early assessment of trial eligibility through the Join® system, this model overcomes key logistical and informational barriers that have historically limited patient enrollment in oncology clinical trials in Japan.

Our protocol outlines a non-interventional, observational framework designed to evaluate the feasibility, efficiency, and satisfaction associated with a digital consultation system. The study further seeks to quantify clinical trial participation rates following system-based referrals and identify factors associated with successful trial enrollment.

This initiative has significant potential to reduce “drug lag” and “drug loss” in Japan by improving the visibility of investigational therapies and facilitating timely patient referral to appropriate clinical trials. Moreover, the system fosters collaboration between community-based and specialized oncology centers, supporting a more equitable and streamlined approach to precision cancer care.

CONNECT-ClinicalTrials is a potential scalable model for nationwide implementation, providing a foundational strategy for optimizing trial matching, accelerating trial accrual, and improving access to innovative therapies for patients with cancer.

Declarations

Acknowledgment

This study received no funding. We would like to thank all participating hospitals and participating pharmaceutical companies.

Conflict of interest

Although this study is not a clinical study on human subjects, this study was approved by the Institutional Review Board of the National Cancer Centre (Tokyo, Japan) [No. 2024-231].

Funding

None

Author contributions

TShimoi, SK and KY designed and organised the study. In addition to these three, TY, RI, Tshibata, MI and HI and KN are responsible for the study management; YS, ST and TSakano are involved in the study as employees of Allm Inc, including providing JOIN. All members were involved in the preparation of this paper and approved the final version.

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Tables

Table 1 is available in the Supplementary Files section.

Figures

Figure 1. Recent Drug Development and Time Schedule

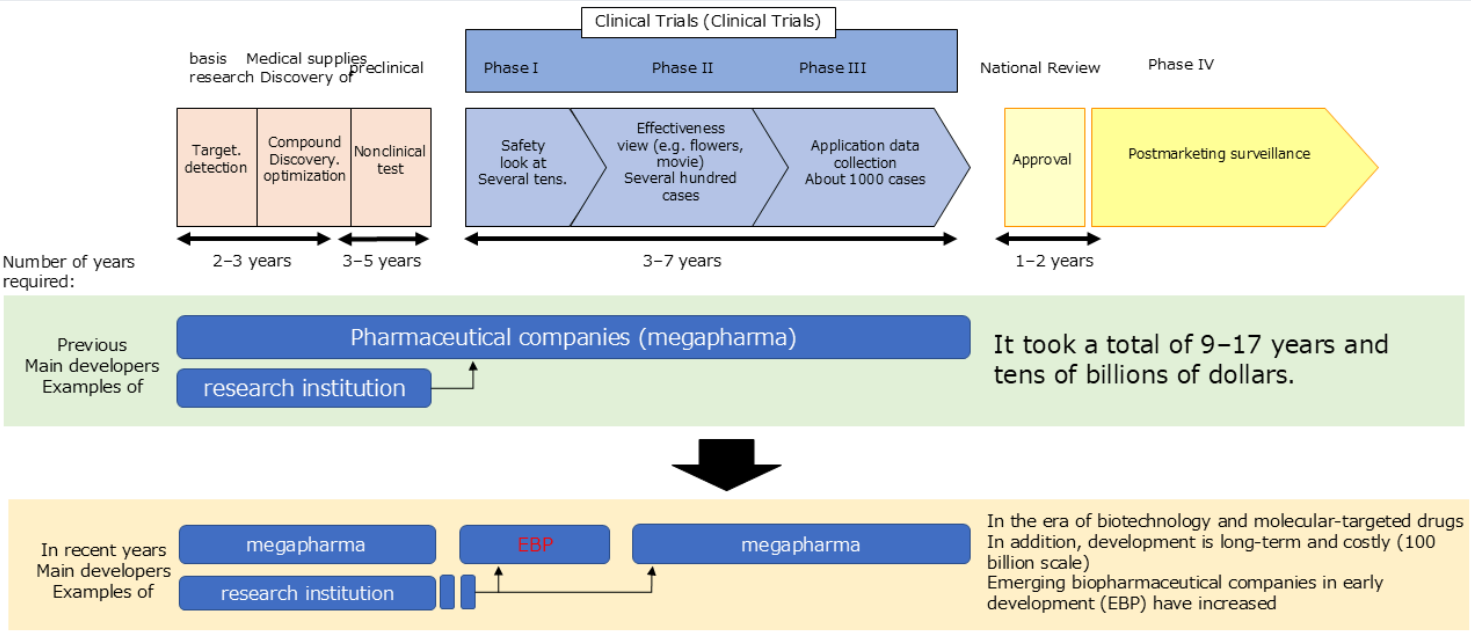


Figure 1

Recent drug development and time schedule. Historically, discovering and approving a compound as a drug required 9–17 years and expenses of hundreds of millions of dollars. However, in the era of biotechnology and molecular-targeted drugs, development has become long-term and expensive (in the order of billions of dollars). This has led to drug losses in Japan, with emerging biopharmaceutical companies increasingly undertaking early-stage -stage development.

Figure 2. Trial design and Research implementation system

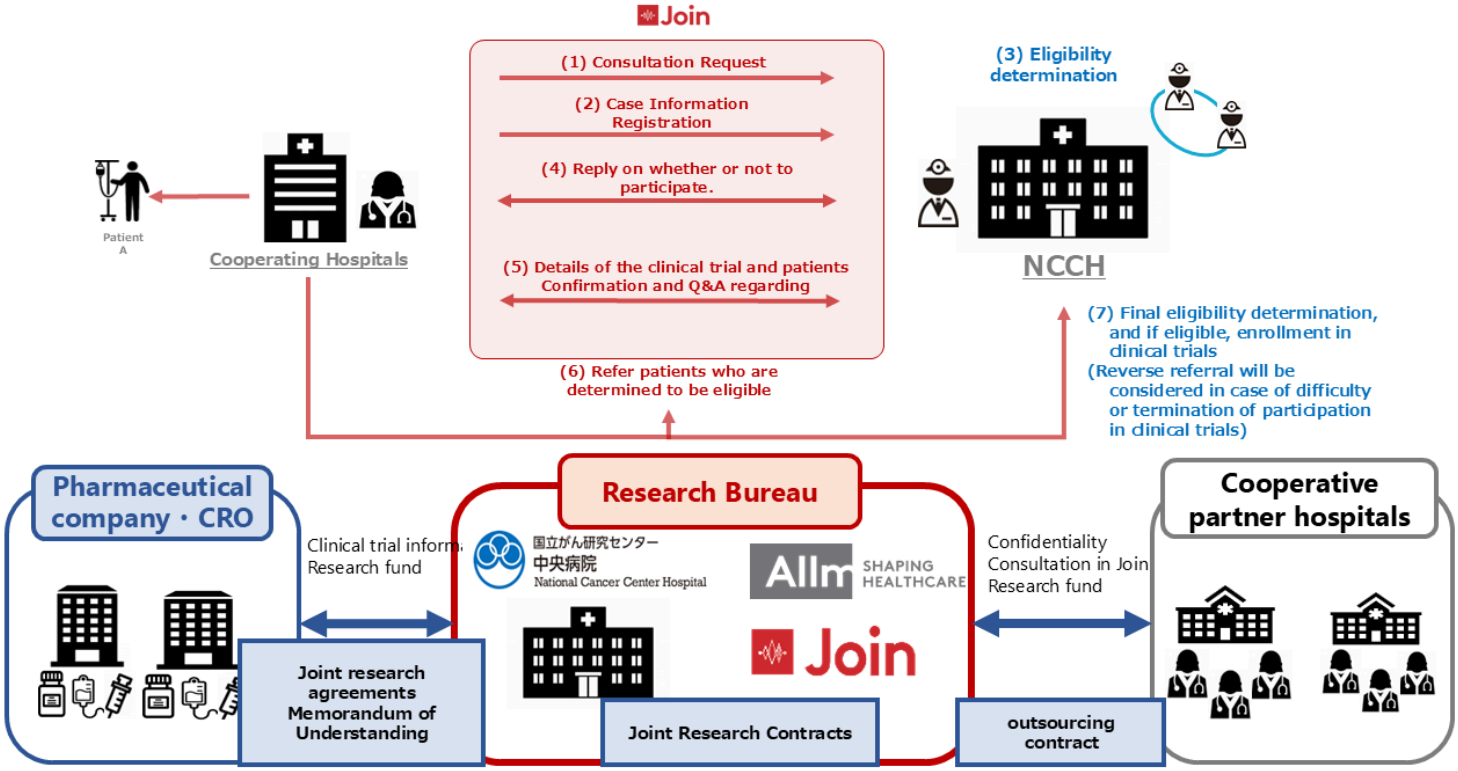


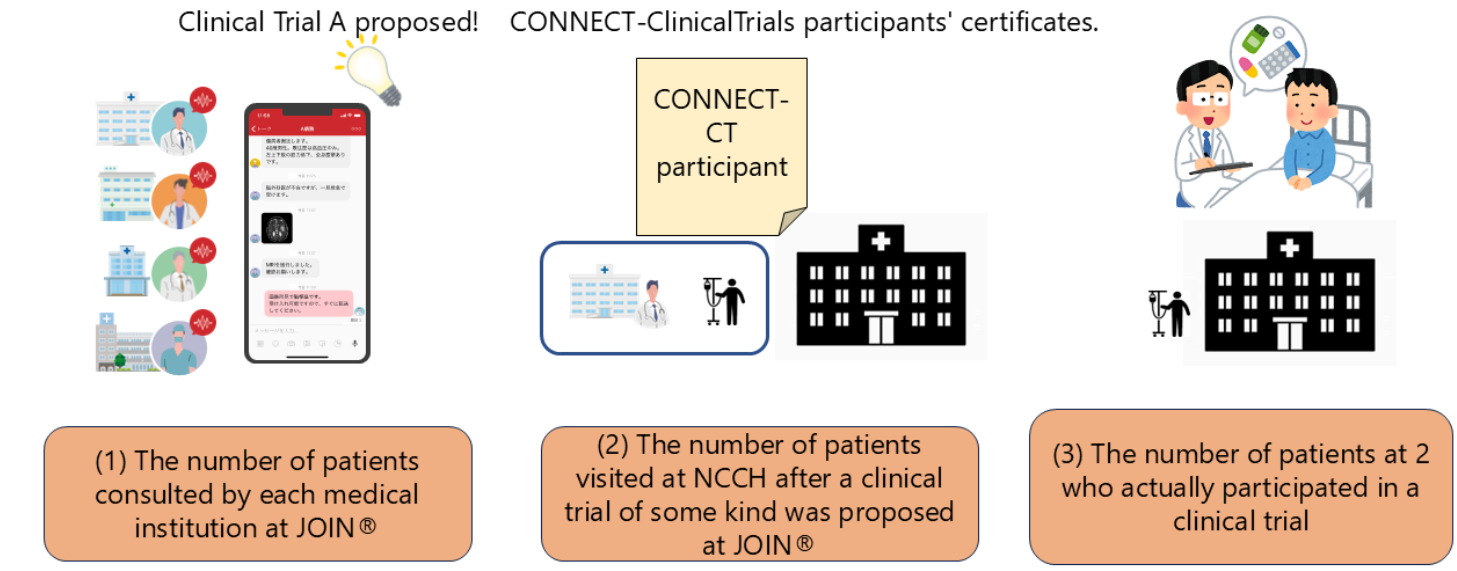
Figure 2

CONNECT ClinicalTrials trial design and Research implementation system.

CONNECT ClinicalTrials is a study in which patient and clinical trial information are exchanged between hospitals. In this study, JOIN® is used to reach patient referral in the following six steps: 1) a consultation request is made by the collaborating healthcare organization to the NCCH about the patient; 2) patient information is sent from the collaborating healthcare organization to the NCCH; 3) the NCCH physician determines whether a possible clinical trial proposal exists and checks eligibility; 4) On Join®, the NCCH doctor determines whether the patient is eligible to participate in a clinical trial; 5) The NCCH doctor asks additional questions regarding the clinical trial and the patient to the cooperating healthcare organization doctor; 6) the patient is referred to the NCCH.

Half of the diagram describes the research structure. NCCH and Allm are the research secretariats for this study. Pharmaceutical companies, CROs, and research partner hospitals contract with the research secretariat to participate in the study.

Figure 3. Scheduled payment of research expenses to CONNECT-ClinicalTrials participating facilities



3

Figure 3

Scheduled payment of research expenses to CONNECT-ClinicalTrials participating facilities. In this study, research funds are made available to collaborating medical institutions according to the calculated results based on the three phases: 1) the number of patients consulted by each medical institution at JOIN®; 2) the number of patients visited at NCCH after a clinical trial of some kind was proposed at JOIN®; the patients provide a certificate of participation in CONNECT-ClinicalTrials at the time of NCCH referral; 3) the number of patients seen in point 2 who actually participated in a clinical trial.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- 20250522Table.docx