A Guide to Preparing Lay Summaries

レイサマリー作成の手引き

Second Edition

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PPI JAPAN website
「治験・臨床研究を学ぶ」
[Learning about Clinical Trials and Research]
(Japanese)

PPI JAPAN

Introduction

The goal of the General Incorporated Association PPI JAPAN is to improve the understanding of medical care and the healthcare system in Japan among the people (general public), including patients and their families*, develop better treatments that actively reflect the perspectives of patients, their families, and the public, and promote the development of safe, secure, and highly satisfactory medical care.

We, as PPI JAPAN, are working to promote patient and public involvement* (PPI) activities in clinical research, which are being implemented in Europe. However, we feel that the current activities are not yet sufficient. There may be several major reasons for this situation, and one of them we believe is that it is more difficult for patients, their families, and the public to access clinical trial* information in Japan compared to Western countries.[a)]

In clinical trials conducted by pharmaceutical companies called *Chiken**, there have been significant restrictions on the disclosure of information on websites due to the potential of advertising and promoting unapproved drugs. However, in response to discussions at the Regulatory Reform Promotion Council[b)] and opinions from various stakeholders, including patient organizations, the Ministry of Health, Labour and Welfare issued[c)] a notice on 24 January 2023 titled “Handling of Information Provision Related to Clinical Trials” [1]. As a result, the environment for patients, their families, and the public to access clinical trial information is gradually improving. “Basic thoughts on the handling of information provision related to clinical trials" issued by the Drug Evaluation Committee of the Japan Pharmaceutical Manufacturers Association (JPMA) upon

a) For example, ClinicalTrials.gov (https://www.clinicaltrials.gov/) provides clinical trial information related to various diseases and symptoms not only to medical professionals and researchers but also to patients, their families, and the public. The Pharmaceutical Research and Manufacturers of America provides a guide on how to use ClinicalTrials.gov titled ‘How to use ClinicalTrials.gov’ (https://www.phrma-jp.org/library/clinicaltrials-gov20211001/) (cited 22 August 2024, only in Japanese).

b) The Cabinet Office provides information on the Council for the Promotion of Regulatory Reform meetings (https://www8.cao.go.jp/kisei-kaikaku/kisei/meeting/meeting.html) (cited 22 August 2024, only in Japanese).

c) In response to this notification, the JPMA has presented its “Chikennikakaru Johoteikyono Toriatsukainikansuru Kihontekina Kangaekata” [Basic thoughts on the handling of information provision related to clinical trials] (1 June 2023) (https://www.jpma.or.jp/basis/guide/information_20230601.html) (cited 22 August 2024, only in Japanese).

receiving this notification states, in the section on the registration and disclosure of information related to clinical trials, that the main purpose of disclosing trial results is to inform trial participants and the public. Since the recruitment for trial participation has already ended at the stage of result disclosure, it does not constitute any promotional aspect even it includes the name of the trial drug and the trial code, and that provision of clinical trial information is feasible regardless of whether it is registered at jRCT.

We, as PPI JAPAN, believe that patients, their families, and the public have the right to know not only the information about clinical trials themselves but also their results. We have established a working group as the first step to focus on disseminating clinical trial result summaries (called Lay Summaries), which are prepared in Europe as requirement. We held the "5th Seminar on PPI Activities in Japan" on 31 October 2022, where the participants discussed the topic of lay summaries. Before the workshop, we conducted a survey to assess the understanding of lay summaries among those who were registered for the workshop. Out of the 49 respondents, 38 were either 'completely unfamiliar with it' or 'had heard of it but did not know much about it'. That is, even among those who were interested in the topic and attended the workshop, the level of awareness was not so high. Comments from the participants after the workshop included, "I realized the importance of knowing about the clinical trial results," "I think lay summaries will attract more attention in the future," and "The advancement of medical care requires the collaboration of not only healthcare professionals but also patients and society; lay summaries are needed in Japan."

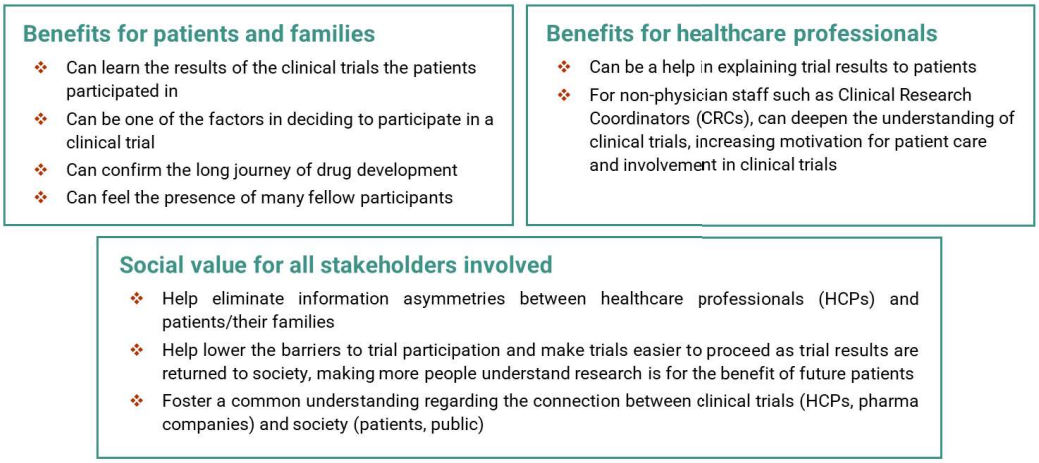

Figure 0 Benefits of Preparing Lay Summaries

In this context, any staff involved in drug development and clinical trials in pharma companies and research institutes that want to prepare lay summaries, as well as patients, their families, and healthcare professionals who wish to learn about them, a “Guide to Preparing Lay Summaries” has been developed to suit the Japanese context based on the Good Lay Summary Practice (GLSP) [2], which is a regulatory requirement for preparing lay summaries in Europe. We believe that disseminating this guide will accelerate the preparation and provision of lay summaries in Japanese, leading to benefits and value for people in various roles, as shown in Figure 0.

Before you read this guide:

In creating this guide, we emphasize the importance of “co-creation” and the relationship as “partners,” using the terms “patients and their families” and “healthcare professionals” without any honorifics often used in Japanese documents.

Furthermore, specialized terms within the main text are marked with an asterisk (*), and their meanings are provided in the glossary at the end of this guide (Section 6.2).

Column 1 What Is Information Asymmetry?

Originally a term in economics, information asymmetry refers to a situation of decision-making or imbalance of information in a market (for example, during a transaction) where one party (for example, the seller) has more or better information than the other party (for example, the buyer). In the medical field, there is a particularly noticeable disparity in the quantity and quality of information (knowledge gap) related to healthcare and pharmaceuticals between medical professionals (experts) and patients or their families (public), and healthcare decisions are made without proper sharing of information (knowledge).

Acknowledgement

In creating the first edition of this guide, we received many ideas and suggestions from the Japan Federation of Cancer Patient Groups members and those who participated in the workshop at the 8th PPI JAPAN Seminar Special Program (26 August 2023). Furthermore, we received many tips for improving the guide in the future from the participants at the 9th PPI JAPAN Seminar after the first edition was published (11 December 2023). This led to our decision to issue the second edition. We would like to express our sincere gratitude once again to everyone who contributed.

We, as PPI JAPAN, plan to continuously receive feedback from people in various roles, make revisions and improvements as needed, and raise awareness of the guide while creating opportunities for exchanging opinions with many others.

General Incorporated Association PPI JAPAN
Representative Director, Masaru Iwasaki

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Abbreviations

Abbreviation	Definition
CRC	Clinical Research Coordinator
CTIS	Clinical Trials Information System
EU	European Union
GLSP	Good Lay Summary Practice
JCOG	Japan Clinical Oncology Group
JPMA	Japan Pharmaceutical Manufacturers Association
jRCT	Japan Registry of Clinical Trials
PhRMA	Pharmaceutical Research and Manufacturers of America
PLS	Plain Language Summary
PMS	Post-Marketing Surveillance
PPI	Patient and Public Involvement
UMIN	University Hospital Medical Information Network

1. What Is Lay Summary

When clinical trials are completed, researchers involved in the trial often write medical papers and submit them to professional scientific journals. This contributes to the advancement of medical research and serves as a reference for patient treatment. Although reading these papers can provide information about the trial and its results, they are written for professionals and would be difficult for patients and their families to understand. To address this issue, lay summaries (Figures 1 and 2) are prepared to make the content of clinical trials accessible and understandable for patients and their families. The same document may also be referred to as layperson summaries or plain language summaries (PLS). However, in this context, the term lay summary will be used to align with the terminology used mainly by European regulatory authorities.

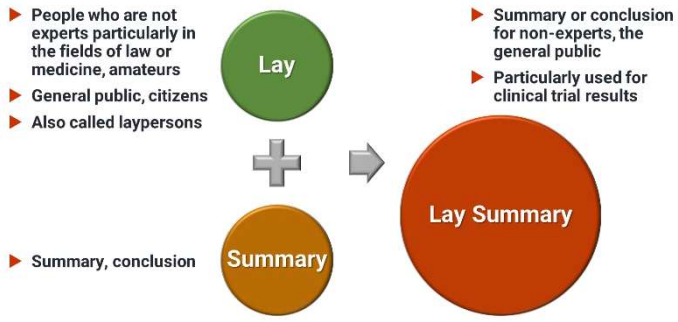

Figure 1 Meaning of Lay Summary

In Europe, the preparation of lay summaries became mandatory for all clinical trials under the Clinical Trial Regulation* (EU CTR536/2014) [3] issued on 16 June 2014. This regulation became enforced on 31 January 2022, and the submission (registration) of lay summaries is obligatory for new trials starting since 31 January 2023 and will be expanded for all ongoing and new trials from 31 January 2025. The prepared lay summaries will be registered in the Clinical Trial Information System* (CTIS)[d], the European clinical trial information system. Not only trial participants but also

d) https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system (cited 22 August 2024)

other patients, their families, and the public can access and view or download lay summaries along with trial information on the websites of global pharmaceutical companies and CTIS. However, many of the registered lay summaries are written in English. Although it is possible to read them in Japanese using translation software or apps, those translations may not always be easy to understand in Japanese.

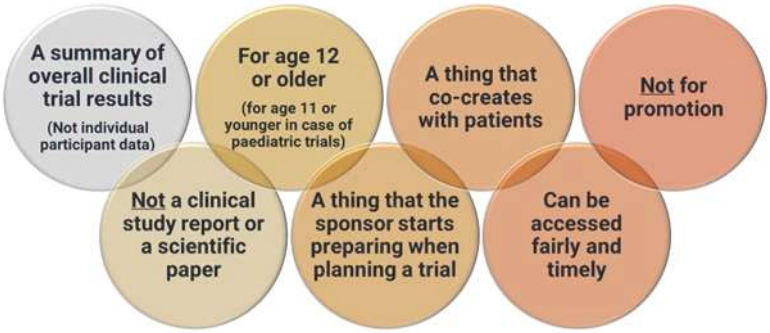

Figure 2 Lay Summary according to GLSP

In Japan, there is no obligation to prepare lay summaries for clinical trials. Pharmaceutical companies may create machine-translated Japanese versions of lay summaries prepared in Europe for multi-regional clinical trials* conducted in Japan. These summaries may be provided to trial participants through the medical institutions where the trials have been conducted, but they are not freely accessible to everyone. In a notification issued by the Ministry of Health, Labour and Welfare on 24 January 2023, "Handling of Information Related to Clinical Trials" [1], it was stated that companies could publish trial information registered in the Japan Registry of Clinical Trials* (jRCT)[e)] on their dedicated clinical trial websites, and that lay language can be used for this. In response to this, the JPMA has created a new guidance for providing information related to clinical trials [4]. It has been stated that when providing information to people who are seeking information related to clinical trials, the information registered in jRCT or University Hospital Medical Information Network (UMIN) can be provided via various media and methods in accordance with the above notification. In this guidance, it is explicitly stated the basic concept that lay summaries do not constitute any promotional aspect.

e) https://rctportal.niph.go.jp/en (cited 22 August 2024)

On 8 June 2023, there was a press conference at the Ministry of Health, Labour and Welfare Press Club announcing the launch of "Rinshoshikennni Minnaga Akusesushiyasui Shakaiwo Tsukurukai" [A Consortium for Creating a Society Where Everyone Can Easily Access Clinical Trials], which was initiated by patient groups, healthcare professionals, and researchers. The consortium aims to raise awareness, disseminate information, and educate (learn) about clinical trials, incorporating diverse voices, and to create a mechanism for a matching service for clinical trial information (a provision of push-type information)[f]. They are working towards renovating jRCT as a user-friendly information registry, and it is expected that the dissemination of lay summaries to patients, families, and the public will progress.

Recently, not only pharmaceutical companies but also physician-initiated clinical trials, such as those conducted by the Japan Clinical Oncology Group (JCOG), have been preparing lay summaries. On 10 March 2021, JCOG launched a patient and public involvement page on its website. As of 2 September 2023, for nine trials published in medical journals, summaries are made available to the media and the public with easy-to-understand figures and tables (Table 1). Lay summaries (Section 6.1 Examples) have been published for two trials released after 25 September 2023.[g]

Table 1 The JCOG Clinical Trials with Summaries for General Public

Date Released	Trial No.	Title
10 Mar 2021	JCOG1007	A randomized comparative trial* comparing resection of primary tumor plus chemotherapy with chemotherapy alone in incurable Stage IV colorectal cancer
8 Oct 2021	JCOG0603	Randomized study of hepatectomy+mFOLFOX6 vs. hepatectomy alone for liver metastasis of colorectal cancer

f) The press conference materials as well as proposals and requests prepared by Patient Cooperation Committee of the JPMA as the secretariat are available here: https://www.jpma.or.jp/information/patient/tsukurukai/index.html (cited 22 August 2024, only in Japanese)

g) https://jcog.jp/topic/general/jcog1305.html (cited 22 August 2024, only in Japanese)

Table 1 The JCOG Clinical Trials with Summaries for General Public (continued)

Date Released	Trial No.	Title
6 Dec 2021	JCOG0502	Randomized controlled trial of esophagectomy vs. chemoradiotherapy in patients with clinical stage I esophageal carcinoma
18 Mar 2022	JCOG1008	Phase II/III Trial of Postoperative Chemoradiotherapy Comparing 3-Weekly Cisplatin with Weekly Cisplatin in High-risk Patients with Squamous Cell Carcinoma of Head and Neck
12 Sep 2022	JCOG1213	Randomized phase III study of etoposide plus cisplatin combination therapy vs. irinotecan plus cisplatin combination therapy in advanced neuroendocrine carcinoma of the digestive system.
14 Mar 2023	JCOG1202	A phase III trial of S-1 vs. observation in patients with resected biliary tract cancer ASCOT: Adjuvant S-1 for CholangiOcarcinoma Trial
17 Apr 2023	JCOG1211	Confirmatory Trial of Segmentectomy for Clinical T1N0 Lung Cancer Dominant with Ground Glass Opacity based on Thin-section Computed Tomography
25 May 2023	JCOG1305	Non-randomized confirmatory study of interim PET-guided ABVD or ABVD/escalated BEACOPP regimen for previously untreated advanced stage Hodgkin lymphoma
7 Jul 2023	JCOG1704	A phase II study of systemic chemotherapy with Docetaxel, Oxaliplatin, and S-1 followed by surgery in advanced gastric cancer with extensive lymph node metastasis (Bulky/PAN-GC DOS NAC Phase II)
25 Aug 2023	JCOG1017	A randomized controlled trial comparing primary tumor resection plus systemic therapy with systemic therapy alone in metastatic breast cancer

Table 1 The JCOG Clinical Trials with Summaries for General Public (continued)

Date Released	Trial No.	Title
14 Nov 2023	JCOG1101	Nonrandomized confirmatory trial of modified radical hysterectomy for patients with FIGO stage Ib1 (< 2 cm) uterine cervical cancer (CC-MoRH)
13 Dec 2023	JCOG1404	A phase III study comparing gefitinib and inserted cisplatin and pemetrexed with gefitinib as a first-line treatment for patients with advanced non-squamous non-small-cell lung cancer harboring EGFR activating mutation (JCOG1404/WJOG8214L, AGAIN study)
8 Mar 2024	JCOG1611	Randomized phase II/III study of gemcitabine plus nab-paclitaxel combination therapy vs. modified FOLFIRINOX vs. S-IROX for metastatic or recurrent pancreatic cancer (GENERATE)
29 Mar 2024	JCOG2007	A Multicenter Randomized Phase III Study comparing Pembrolizumab + Platinum Combination Chemotherapy with Nivolumab + Ipilimumab + Platinum Combination Chemotherapy for Treatment-naive Advanced Non-Small Cell Lung Cancer without Driver Gene alteration (Pembro + Chemo vs Nivo + Ipi + Chemo Phase III (NIPPON))
11 Apr 2024	JCOG1314	A randomized controlled phase III study comparing docetaxel, CDDP and 5-FU with CDDP and 5-FU in patients with metastatic or recurrent esophageal cancer (MIRACLE study)
8 May 2024	JCOG1607	A phase III study comparing T-DM1 with pertuzumab, trastuzumab and docetaxel in elderly patients with advanced stage HER2 positive breast cancer (JCOG1607, HERB TEA study)
29 May 2024	JCOG1409	A phase III study of minimally invasive vs. open esophagectomy for thoracic esophageal cancer (JCOG1409, MONET trial)

Please note that a lay summary is a report of the overall results of a trial, not a report on individual trial participant data. If you want to know more about the trial results, please refer to the published papers and/or other sources.

2. Elements of Lay Summary

In the GLSP, the following 10 elements [2] that must be included in a lay summary (Table 2):

Table 2 Ten Elements That Must Be Included in Lay Summary

1. Clinical trial identification	6. Adverse reactions and their frequency
2. Name and contact details of the sponsor	7. Overall results of the clinical trial
3. General information about the clinical trial	8. Notes on the outcome of the clinical trial
4. Population of trial participants	9. Information on future relevant clinical trials
5. Investigational medicinal products used	10. References to additional information

1. **Clinical trial identification:** Trial title, registration information such as the clinical trial plan number in jRCT[h)].

2. **Name and contact details of the sponsor:** Information such as inquiry contact for when patients and families who have read lay summaries need clarifications or have questions about its content. It is desirable to have this information listed if possible. It is also desirable to inform that people can receive necessary answers via email address or on the website, etc.

3. **General information about the clinical trial:** The content of the trial, such as the rationale, background and objectives, design (e.g., placebo-controlled double-blind comparative trial), trial sites, and trial period. If possible, it is desirable to make it easy to understand by visualizing it.

4. **Population of trial participants:** Disease name, severity classification, inclusion/exclusion criteria*, etc. Age (e.g., children or elderly), disease status, and comorbidities are important information for accurately understanding trial results.

h）https://rctportal.niph.go.jp/en (cited 22 August 2024)

5. **Investigational medicinal products used:** Describe the type of medicinal product (investigational drug) whose efficacy and side effects were confirmed in the trial (e.g., oral medication, injectable medication). In comparative trials, it is necessary to describe the medicinal products or treatments used as comparators. For medicinal products, do not include promotional information.

6. **Adverse reactions and their frequency:** List serious side effects first, followed by the number and frequency (%) of other common side effects. It is desirable to make it easy to understand by preparing a list.

7. **Overall results of the clinical trial** [i)]**:** Clearly show the results related to the primary endpoint(s)*. It is desirable also to describe secondary endpoints such as patient-reported outcomes* assessments and quality of life* related assessments. However, some secondary endpoints may be difficult to judge, and care should be taken to ensure that readers do not emphasize such results. It is desirable to use easy-to-understand figures, tables, and infographics* for presenting results rather than just listing them in text.

8. **Notes on the outcome of the clinical trial:** Describe to what population the trial results are applicable and if there are any limitations to the applicability.

9. **Information on future relevant clinical trials:** Describe any follow-up trials (long-term trials) or other related trials that have been disclosed or are in progress.

10. **References to additional information:** Provide links to public clinical trial information registry sites and other websites where the trial results can be viewed. Ensure readers are not inadvertently directed to promotional advertisements or one-sided (biased) information. In addition, in the case of being printed on paper, consider including a two-dimensional code in addition to URL.

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i) A lay summary provides a summary of the overall clinical trial results (or part of it) and does not provide data of an individual participant.

3. Preparing A Lay Summary

3.1 Basic Approaches to Preparation

The primary readers of lay summaries are the public who are affected by diseases in some way. Specifically, the following people are assumed:

- People who have participated in clinical trials
- Members of patient organizations and patient advocacy groups that communicate with patients
- Patients considering new treatments
- Family members, partners, and caregivers (care partners) of patients

The background knowledge of the intended readers varies, and the content required depends on the target disease. For example, it is necessary to use words and expressions that younger children can understand in pediatric diseases. In diseases related to visual impairment, expressions that do not rely on visual information (such as audio) are required.

When preparing a lay summary, it is necessary to be aware of the main readers, the type of disease targeted by the clinical trial, and who will be reading it. Having a concrete image of the background of the people you want to read it in advance makes it easier for the entire preparation team to share the direction. In addition, it is expected that understanding of clinical trials will deepen through smooth communication between patients and medical professionals, such as doctors and clinical research coordinators* (CRCs), using lay summaries.

In this guide, we assume that the main target is adults with general knowledge who have not received any specialized education in medicine. When preparing a lay summary in practice, please consider additional measures appropriate for the target readers.

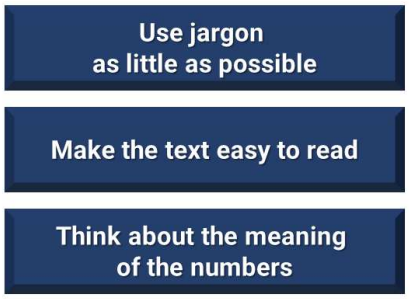
Considering the past tendency for the results of trials that did not achieve the expected outcomes not to be published (this biased information is called publication bias*), information disclosure is now institutionalized on a global scale. The mandatory implementation of lay summaries in Europe is one of these efforts. Lay summaries are not only prepared for successful (or completed as planned) trials. Knowing the results of unsuccessful trials (such as those that were terminated midway for some reason or those that could not demonstrate the expected therapeutic effects) is also a public right. It provides important information for patients, families, and the public in making

treatment choices[j].

In Japan, there is a system called post-marketing surveillance* (PMS) that verifies the risks and benefits of newly approved drugs and treatments after the launch. PMS is not applicable under GLSP but consider the benefits of information for patients and families and prepare a lay summary.

When preparing a lay summary, it is necessary to be conscious of “readability” and “visual clarity” and not just rely on words but actively use illustrations, photos, diagrams, tables, and infographics. Aiming to prepare a better lay summary, Section 3.1.1 discusses the use of terms, Section 3.1.2 discusses layout and graphic design, Section 3.1.3 shows the competencies and knowledge for preparing and understanding lay summaries, and Section 3.1.4 explains how patients and the public should participate in the preparation of lay summaries.

3.1.1 Lay Language



There are three principles when using lay language. Several tools[k] are available online to check the difficulty level of sentences.

1） Use jargon as little as possible

Specialized terms and abbreviations can be very effective for concisely expressing content. However, sentences with many of these terms can be difficult to understand for people without specialized education. It is important to choose and use simple words instead of specialized terms and abbreviations. However, this does not mean you should never use technical terms or abbreviations. You can actively use words that are better to

j） Information such as the direction of future development based on the trial results and the reason for discontinuing the trial is important for patients, but there may be cases where it is difficult to disclose details from the perspective of protecting the company's intellectual property rights.

k) As examples of such tools, the followings are available: “Yasashii Nihongo Yasanichi Checker Shosaiban (Kenkyushamuke) [Easy Japanese Yasanichi Checker Detailed Version (for Researchers)]”. “‘Yasashii Nihongo’ KAKEN Group” ["Easy Japanese” Scientific Research Group]. http://www4414uj.sakura.ne.jp/Yasanichi/index.html, Japanese Text Readability Management System: jReadability. https://jreadability.net/sys/terms_of_use?lang=ja, “Kanji Kensaku System” [*Kanji* Search System]. Nara University of Education. http://denki.nara-edu.ac.jp/~yabu/edu/kanji/kanji3.html, “Shogakusei/Chugakuseino Kanji Checker” [*Kanji* Checker for Elementary and Junior High School Students]. https://kanji.gramin.jp/#/ (all cited 22 August 2024, only in Japanese).

know when explaining the content of a trial and words that appear frequently. When using them, it is necessary to provide a clear explanation the first time they are used. Adding annotations and explaining terms in context will also make them easier to understand.

Reducing the frequency of using *kanji* (Chinese letters) as much as possible gives an impression of simplicity and ease of understanding. When using *kanji*, using characters learned in elementary and middle school is preferable. At the very least, limiting kanji usage to the level of commonly used characters for high school graduates is a good idea.

Some words require caution, even if they are commonly used. For example, the term “standard treatment” is understood by medical professionals as “the best treatment currently available based on scientific evidence” [4]. However, many people generally perceive it as “general treatment” or “ordinary treatment”. It is necessary to actively replace such words with a clearer description to prevent misunderstandings. In the case of “standard treatment”, it is preferable to express it as “the best treatment currently available (based on scientific evidence)”.

2） Make the text easy to read

Shorter sentences are easier to understand. It is recommended to break down sentences into smaller parts, aiming for no more than 40 characters per sentence. Also, it is better to keep paragraphs short, aiming for about 200 characters.

Furthermore, using active voice and affirmative form makes the expression clearer. For example, change the expression “It was shown to be XX.” to “It showed XX." Change the expression "The possibility of being XX cannot be denied." to "There is a possibility of being XX." These adjustments make the text easier to read.

Considering the provision of information through video and audio, it would be better to be conscious of writing in a way that can be understood just by listening.

3） Think about the meaning of the numbers

In the research world, it is necessary to convey numerical values accurately and in detail. However, this is not always the case for general audiences. Sometimes, the meaning of a number may not be well understood just by its size.

For example, if the blood albumin concentration is expressed as 4.0 g/dL, it may be difficult for someone unfamiliar with blood test results to understand whether this is high or low. Try to convey

the meaning of the number within the context, such as “The blood albumin concentration is 4.0 g/dL, which is within the normal range.”

Additionally, there is a risk that numbers can be easily understood but taken out of context. It is better to indicate accurate numbers, but it is also necessary to decide whether to express specific numbers for values valid only under certain conditions or with no meaning.

For example, in the case of the blood albumin concentration mentioned earlier, if the value of 4.0 g/dL has significant meaning, it should be included. However, suppose it is sufficient to know that it is within the normal range. In that case, it may be easier to understand by expressing it as “within the normal range” without specifying the number.

3.1.2 Points to Consider in Layout and Graphic Design

The overall layout and graphic design are also important in preparing a visually clearer and more understandable summary.

1） Actively use displays and illustrations

Instead of relying solely on text, using displays and illustrations actively can make it easier to understand. The most important results should be expressed using displays or illustrations. Ideally, the overall content should be understandable through displays and illustrations alone and reading the text should provide more profound knowledge.

2） Use headings and bullet points

Having clear headings that show the content of a paragraph briefly makes it easier to read. It is also convenient to quickly understand where something was where when looking back. Parallel information should be presented in bullet points, making understanding what is being compared easier.

3） Increase font size and add margins

Using larger fonts and leaving ample line spacing and margins is important. The use of universal design (UD) fonts is recommended. Filling the page with small text creates an impression of

difficulty. The font size in high school textbooks is about 10.5 to 14 points. Using 12 points as a standard is a good idea. Be mindful of leaving margins for readers to write notes.

4） Do not use many colors

Consider people with color vision impairments and opt for expressions that do not rely on color. Moreover, using fewer colors gives a cleaner, easier-to-read impression. Ideally, use no more than four colors.

5） Emphasize text

If the text becomes too long, use bold, underlining, or italics to make it stand out. However, it is generally not recommended to write long sentences.

6） Consider the overall volume

There is no set volume for a lay summary. However, a certain amount of content is necessary to summarize clinical trial results in an understandable and somewhat detailed manner. As a guideline, try to prepare a summary within six A4-sized pages.

7） Check an accessibility

To make it easy to read for people with disabilities, various considerations are necessary, such as adding alternative texts to images and adjusting layouts. It would be good to use features built into the document creation software (i.e., Microsoft 365, Adobe Acrobat) to check the accessibility of the created lay summary.

3.1.3 Necessary Competencies and Knowledge

The following competencies [2] are listed in GLSP for preparing excellent lay summaries:

1. **Scientific knowledge:** Scientific knowledge is indispensable for preparing lay summaries. You must understand basic knowledge about diseases and treatments and the latest research results.
2. **Familiarity with source documents:** Using reliable references is important for providing accurate information. Skills in evaluating and selecting literature are required.
3. **Disease and patient/trial participant population:** Lay summaries convey information about

specific diseases and patient groups, so it is necessary to understand their characteristics. Knowledge about the onset and progression of diseases, symptoms, and treatment methods is required.

4. **Clinical research methodology:** Understanding the methods of clinical trials is essential for appropriately interpreting and conveying trial results. It is important to know about trial design and the reliability of trial results.

5. **Safety of the intervention under Investigation:** Appropriate terminology and judgment are required when including information about the safety of treatments and drugs in lay summaries. Knowledge and the ability to interpret side effects and risks are necessary.

6. **Statistical knowledge:** Basic knowledge of statistics is necessary to interpret statistical data and judge the reliability of results. An understanding of statistical significance* is required.

7. **Communication and language skills:** Lay summaries aim to convey information in an easy-to-understand manner to patients and the public. Creativity in wording and expression is necessary to explain professional information in an easy-to-understand manner.

8. **Skills for quality control and accuracy checks:** The ability to check the accuracy and consistency of information, such as comparing the numbers listed with the original data, is required to ensure the quality and accuracy of the lay summaries prepared.

9. **Legal and regulatory knowledge:** There are legal regulations for medical care and clinical trials. Knowing these regulations is important in preparing lay summaries.

10. **Visual and design skills:** Visualizing information in an easy-to-understand manner is important for helping understand lay summaries. Basic knowledge of graphic design and methods of expressing visual information need to be learned.

11. **Skills for validation of content:** The ability to integrate opinions and feedback from patient groups and other stakeholders and prepare lay summaries is required. It is important to consider the needs and perspectives of various stakeholders.

12. **Attitudes and collaboration skills:** Collaboration with multiple experts and stakeholders is necessary for preparing lay summaries. Ease of working in a team and interest in mutual communication are required.

To better understand summaries, it would be good to acquire the following knowledge:

1. **Knowledge of statistics:** Various displays and graphs are used in lay summaries to show trial results. It is also important to understand how to read these data and indicators that show reliability as well as the criteria for judging statistical significance.

2. **Purpose and design of clinical trials:** It is important to understand the purpose of clinical trials and how they are conducted. Knowledge about methods of evaluating efficacy and safety is desirable.

3. **Balance of benefits and risks:** Clinical trials evaluate the balance between therapeutic effects (benefits) and side effects (risks). Understanding the benefits and risks of treatment and the ability to make appropriate judgments are desirable.

4. **Rights and protection of trial participants:** In clinical trials, the rights of participants and the protection of personal information are important. Understanding the rights of participants and involvement in clinical trials from an ethical perspective are desirable.

5. I**nterpretation of results and understanding of bias:** In interpreting the results of clinical trials, it is necessary to consider the impact of bias. Evaluating the reliability of results and making appropriate interpretations are desirable.

Educational programs[l)] for patient and public involvement are helped in learning this knowledge. The toolbox provided by the European Patients' Academy on Therapeutic Innovation (EUPATI), a patient advocacy organization to provide education for therapeutic innovation in Europe, explains various terms related to drug development and patient and public involvement.[m)]

With these competencies and knowledge, you can understand, and appropriately prepare, and evaluate lay summaries.

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l) Well-known examples include 'PE (Patient Engagement) Expert Learning Course' for patients and the public offered by Ji4pe.tokyo (https://ji4pe.tokyo/intro-course.html), and Clinical Trial Ambassador Project by YORIAILab Inc. (https://www.yoriailab.com/clinical-trial-ambassador) (cited 22 August 2024, only in Japanese).

m) The toolbox provided by EUPATI, a European patient education organization, can be read in Japanese (accessible from the PPI JAPAN website: https://www.ppijapan.org/eupati_toc [cited 22 August 2024, only in Japanese]).

3.1.4 Patient and Public Involvement in Preparing Lay Summaries

When preparing lay summaries, it is important to consider insights from various perspectives. Collaboration with not only medical professionals but also patients, families, and the public is strongly recommended. Involving patients and families with the same disease experience is not always necessary. By verifying the content's readability, ease of understanding, and validity from diverse perspectives, lay summaries become more understandable for patients, families, and the public. Under the rules established by each company sponsoring clinical trials, devise the participation of appropriate individuals.

Column 2 How PPI Can Be Initiated?

Recently, there has been an increase in efforts to seek the insights of patients and their families in the early stages of clinical development and finalize trial protocols based also on their perspectives. How to plan and implement collaboration with patients can be found in the Japan Pharmaceutical Manufacturers Association's "Guidebook for Drug Development Reflecting Patient Voices" [5, 6, 7] and the Japan Agency for Medical Research and Development's "Patient Participation (PPI) Handbook" [8].

When collaborating with patients, it is necessary to clarify the content of the collaboration and the compensation. It is important to consider whether the ideas of the patient community are widely represented in the collaboration and to take into account the code of conduct in the pharmaceutical industry. The Council for International Organizations of Medical Sciences (CIOMS) also prioritizes collaboration with a broader patient community (patient organizations, patient groups) rather than individual patients receiving treatment. [9]

Which part of the trial is most important for patients, families, and the public to know may not be noticed from the perspective of medical professionals. Therefore, it is important to reflect the insights of patients and their families as much as possible through collaboration with them. Although it may not be possible to fully reflect the insights of patients and their families from the perspective of resources within the clinical trial sponsors, legal systems, and regulations, collaborating in preparing lay summaries can provide (i.e., co-create) something that meets their needs as much as possible.

When preparing summaries, the informed consent document, which explains the protocol for trial participants (patients) and their families, can be utilized. Since the informed consent document explains the content of the trial in an easy-to-understand manner for patients and their families, it is practical to use the descriptions in the lay summaries as well. This ensures consistency in the explanation of the trial.

3.2 Timing of Preparation

Consider what content to include in the lay summary at the trial planning stage (i.e., preparing the trial protocol).

In GLSP, it is mandatory to publish the lay summary within 12 months after the trial ends[n)] (within 6 months for trials targeting children and within 30 months for phase 1 trials) [2]. When multi-regional clinical trials involving Japanese medical institutions are conducted in Europe, the lay summary (in English or languages of the countries in Europe where the trial was conducted) is published according to this deadline. It is strongly desired that the Japanese version be published simultaneously to ensure that information reaches Japanese patients and the public fairly and timely. The points to consider for the timing of provision depending on the trial design and situation are as follows:

- The timing of publication does not depend on the trial results.
- For trials that are terminated midway, the date of termination is used as the basis.
- For trials with an interim analysis as the primary endpoint analysis (standard in oncology clinical trials), the date when data collection required for the primary endpoint analysis is completed may be used as the basis.
- For long-term trials (extension trials, outcome trials, etc.), PMS, and epidemiological studies, individual consideration is needed to ensure accurate and reliable trial information is shared appropriately.
- For trials providing unapproved drugs on humanitarian grounds to patients who do not meet the trial eligibility criteria (also called expanded clinical trials), the same approach as regular clinical trials is taken.

n) The date when the last participant (patient) in the trial completes his/her final visit (examinations or consultations to complete the trial), referred to as Last Subject Last Visit, or a later date as defined in the trial protocol.

Column 3　Why A Longer Grace Period for the Disclosure of Phase 1 Trials?

In Phase 1 trials (also called clinical pharmacology trials), which do not target a specific disease, the focus is on the safety (tolerability) and pharmacokinetics of a new drug. Usually, this examination is conducted through a combination of multiple trials, and due to inclusion of highly confidential information for trial sponsors related to the drug's composition and mechanism of action, consideration is given to the timing of the disclosure of the results. [10]

There may be cases where clinical trial sponsors must make judgments based on the individual trial situation. For example, there may be concerns that the 30-month provision period for phase 1 trials is too long. The first thing to consider is ensuring that Japanese patients, their families, and the public can access clinical trial results “fairly and timely”.

When publishing trial results as a medical paper, preparing a plain language summary (PLS)[o)] for the public may be possible. In that case, using the PLS as a substitute for the lay summary could be considered. However, there are no standardized rules for PLS across journals (publishers). If the content shown in this guide cannot be fully covered, preparing a separate clinical trial lay summary is desirable. From the perspective of access to clinical trial information, journals that allow open access*, Japanese full-text translations[p)] and PLS are recommended (in general, as a supplement or a web-content).

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o）For PLS of scientific papers and conference presentations, PFMD（https://patientfocusedmedicine.org/）provides a how-to guide “Plain language summaries (PLS) of peer-reviewed publications and conference presentations: practical ‘How-To’ Guide for multi-stakeholder co-creation”（https://pemsuite.org/How-to-Guides/WG5.pdf）(cited 22 August 2024).

p) A supplementary material of a full Japanese translation, created in a similar format to the main body of an English academic paper.

Column 4　PLS of Medical Papers Is Similar But Not Identical to Lay Summary

Recently, some medical and clinical papers reporting the results of clinical trials also provide a plain, easy-to-understand summary as a supplemental material. These are often referred to as Plain Language Summaries (PLS). Medical papers transmit important messages from a medical perspective based on clinical trial data. Some provide an overview of the trial results, while others delve deeply into a part of them. And they do not necessarily contain all the elements required in a lay summary. The purpose is the same, to convey the content to patients and their families, but the content varies. Some PLS are planned and created together with patients or patient organizations to reflect the perspective of patients and their families.

3.3　Preparation and Review Procedures

The lay summary of each clinical trial is generally prepared following a process like the one shown in Figure 3. The GLSP recommends standardizing the preparation process and templating [2], but the specific approach is left to the discretion of the clinical trial sponsor. In the case of multi-regional clinical trials, including European countries, English is generally the first language, so a Japanese version needs to be prepared for review by Japanese stakeholders. What is important here is not just designing a good translation but also designing and providing a lay summary that meets the needs of Japanese patients and their families. To give the trial results to those who need them as quickly as possible, it is important to do what can be done in advance rather than starting preparations after the results are obtained. A lay summary is prepared based on whether the trial results are available. For parts that do not depend on the results, such as the trial design, keeping the preparation of the lay summary in mind when writing the informed consent document can also help utilize its content.

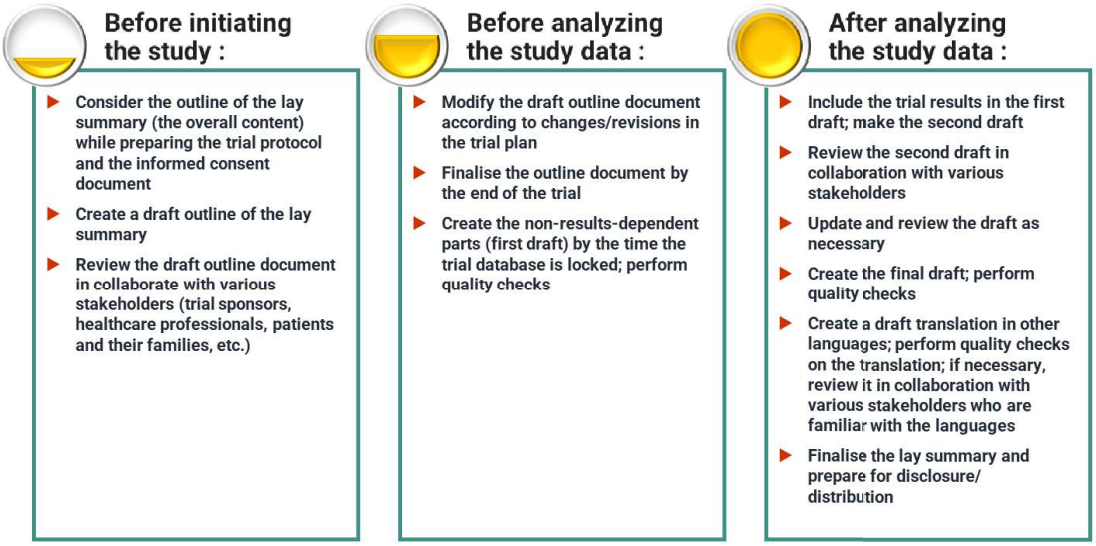


Figure 3 Steps to Prepare a Lay Summary

Even when a Japanese version of a lay summary is prepared, the quality of the translation is not always good. In clinical trials where global pharmaceutical companies are the sponsors, companies are cautious about regulatory and compliance* risks related to the content of the lay summary to ensure consistency with what is required by regulations in Europe. As a result, translations may be literal and not easy to understand. The GLSP explicitly states the convenience of using figures, illustrations, and infographics for clear expression [2]. However, what is prepared in Europe may not be easy or people in other regions to understand. While it is not easy to fully consider cultural backgrounds, the Japanese version must be easy to understand (easy to read and visually clear) for its readers. In addition to the checklist provided in the “A Guide to Conveying Medical Research in an Easy-to-Understand Manner (March 2023 Edition)” [5], it is important to pay attention to the following three points when translating into Japanese:

- Make sentences as natural as the Japanese language
- Simplify expressions without changing the content
- Rewrite extended noun expressions into sentences that include predicates

To improve the quality of the translated version, it is recommended to conduct checks involving translation experts.

4. Providing A Lay Summary

4.1 Current Status and Challenges

In Japan, lay summaries (Japanese version) of clinical trials sponsored by pharmaceutical companies are provided only to the trial preparations. Some companies may make them accessible through their websites. Still, in most cases, the provision is left to the trial investigators, and the cooperation of the investigators (or the staff of the medical institution conducting the trial) is essential for participants to know about the trial results. As an example of physician-led clinical trials, JCOG publishes lay summaries on a publicly accessible website (Section 6.1 Case Studies). On the other hand, when pharmaceutical companies conduct clinical trials in European countries, lay summaries are widely provided to the public as regulatory requirements. There is an issue of information disparity due to regional or language differences.

Information disclosed under European regulatory requirements can be accessed from anywhere in the world (although it is generally written in English or languages within the European region). This means that regardless of whether one is eligible to receive a lay summary (Japanese version) in Japan, they can access the lay summaries published in Europe. With the widespread use of advanced translation software, accessible English lay summaries can also be read. However, one cannot necessarily expect a reading in “natural” Japanese.

At the 2023 American Society of Clinical Oncology (ASCO) conference, a two-dimensional barcode for the lay summary was introduced at the end of the presentation. Patients and advocates who attended the conference seemed to access the lay summary at such moments. To make lay summaries more understandable and user-friendly, preparing support tools such as videos and audio guides is also useful.

According to the Ministry of Health, Labour and Welfare notification, “On the Handling of Information Provision Related to Clinical Trial” [1], there is little meaning in continuing to provide information in a limited manner as is currently done, and efforts by clinical trial sponsors can improve access to lay summaries for patients, families, and the public. This will also help alleviate the inconvenience of accessing foreign websites to obtain information. Currently there are companies that are creating lay summaries (Japanese version) as standard and widely publishing them on jRCT and corporate clinical trial information sites for patients and the public seeking clinical trial information. As such publication progresses, there may be an increase in inquiries to

treating physicians from patients who have viewed the information. There is room for improvement in providing lay summaries through trial investigators. Needlessly physicians should fully understand the purpose of the lay summary and the needs of trial participants and be proactive in distributing them. On the other hand, after the clinical trial has ended and time has passed, there is a possibility that the participant no longer sees the investigator, and there may be few or no opportunities to receive the lay summary. Procedures such as contacting treating physicians by the investigator or CRC at the trial site or contacting trial participants by phone, email, or mail are also necessary. It is essential to include whether to receive a lay summary in the informed consent document, and both the clinical trial sites and participants should be aware of how to provide and receive lay summaries.

4.2 Future of Lay Summaries in Japan

Generally, companies are considered widely disclosing information about treatments under development against industry rules. However, as indicated earlier in the Ministry of Health, Labour and Welfare notification “Handling of Information Provision Related to Clinical Trials” [1], it is expected that the provision of clinical trial information, including lay summaries, to patients, their families, and the public will progress. As a result, more people will better understand the progress of development of new treatment methods and, if necessary, consider participating in clinical trials more efficiently. However, in Japan, there is no requirement to prepare a lay summary. There is no place where patients, their families, and the public can easily access all existing lay summaries. Bringing the provision of lay summaries to a level comparable to that in Europe is a topic that needs to be realized through further discussions with regulatory authorities and industry associations.

As the number of lay summary cases increases in the future, we would like to broadly consider lay summaries that consider various disease backgrounds and readers (for example, the bereaved families of patients who participated in the trial).

5. References

1) Ministry of Health, Labour and Welfare, Pharmaceutical Safety and Environmental Health Bureau, Compliance and Narcotics Division. “Chikennikakaru Johoteikyono Toriatsukainitsuite” [Handling of Information Provision Related to Clinical Trial] (Notification 0124 No. 1). 24 January 2023 (in Japanese)

2) European Commission Directorate-General for Health and Food Safety. Good Lay Summary Practice (GLSP). 4 October 2021.

3) Regulation (EU) No 536/2014 of The European Parliament and the Council of the European Union. 16 April 2014.

4) Japan Pharmaceutical Manufacturers Association, Drug Evaluation Committee, Drug Evaluation Sub-committee. “Kanja Oyobi Ippanshiminwo Taishotoshita Chikennikakaru Johoteikyono Yoryo, Third Edition” [A Guideline for providing information related to clinical trials targeting patients and the general public, Third Edition]. November 2023. (in Japanese)

5) How to Disseminate Medical Research Results in an Easy-to-Understand Manner, Second Edition. March 2023. (in Japanese)

6) Japan Pharmaceutical Manufacturers Association, Drug Evaluation Committee, Drug Evaluation Sub-committee. “Kanjanokoewo Ikashita Iyakuhinkaihatsu – Seiyakukigyoniyoru Patient Centricity” [Drug Development Reflecting Patient Voices - Patient Centricity by Pharmaceutical Companies]. June 2018. (in Japanese)

7) Japan Pharmaceutical Manufacturers Association, Drug Evaluation Committee, Drug Evaluation Sub-committee. “Kanjanokoewo Ikashita Iyakuhinkaihatsu – Seiyakukigyoga Patient Centricity-nimotozuku Katsudowo Jusshisurutameno Guidebook” [Drug Development Reflecting Patient Voices: A Guidebook for Pharmaceutical Companies to Implement Activities Based on Patient Centricity]. September 2019. (in Japanese)

8) Japan Pharmaceutical Manufacturers Association, Drug Evaluation Committee, Drug Evaluation Sub-committee. “Kanjanokoewo Ikashita Iyakuhinkaihatsu – Seiyakukigyoga Patient Centricity-nimotozuku Katsudowo Suishinsurutameno Communication Guidebook” [Drug Development Reflecting Patient Voices: A Communication Guidebook for Pharmaceutical Companies to Promote Activities Based on Patient Centricity with Patient Organizations]. September 2019. (in Japanese)

9) Japan Agency for Medical Research and Development. PPI Guide Book. 6 October 2022 (the original Japanese version published 31 March 2019).

10) Council for International Organizations of Medical Sciences. Patient involvement in the development, regulation and safe use of medicines. 2022.

11） Brown C, Leithold L, Sroka-Saidi K, Schindler T. Lay summaries for Phase I trials in healthy volunteers. Medical Writing. 2020;29(4):24-29.

12） Higashijima J, Fujisawa K, Muto K. Patient and Public Involvement in Observational Studies Using Human Materials and/or Data: Experiences and Future Perspectives in Japan. Journal of Science and Technology Studies. 2020;18:97-107. Japanese.

13） Japan Pharmaceutical Manufacturers Association. Guidelines for Collaboration with Patient Organizations. 25 May 2022 Revised. Japanese.

14） Japan Pharmaceutical Manufacturers Association, Drug Evaluation Committee, Drug Evaluation Sub-committee, Taskforce 7. “Chikenniokeru Patient Reported Outcomes – Rinshokaikatsutantoshanotameno PRO Riyono Tebiki” [Patient Reported Outcomes in Clinical Trials - A Guide to Using PROs for Clinical Development Professionals -]. June 2016. (in Japanese)

15） The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. General Principles for Planning and Design of Multi-Regional Clinical Trials (E17). 12 June 2018.

16） Ministry of Health, Labour and Welfare. Ministerial Ordinance on Good Post-marketing Study Practice for Drugs] (Ministry of Health, Labour and Welfare Ordinance No. 171). 20 December 2004. (in Japanese)

17） The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. ICH Harmonised Tripartite Guideline: Statistical Principles for Clinical Trials (E9). 30 November 1998.

18） The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. Choice of Control Group and Related Issue in Clinical Trials (E10). 27 February 2001.

6. Appendices

Lay Summary Case Studies (Section 6.1)

As an example of physician-led clinical trials, we are reprinting a lay summary document (Japanese) provided by JCOG with their permission. In JCOG, the consideration of lay summaries is carried out through collaboration between healthcare professionals and patients. The clinical trial presented as examples was not conducted in Europe, but its lay summary includes all the elements required by GLSP.

Global pharmaceutical companies have already widely published many lay summaries in accordance with the European regulatory requirements. There are also examples of animated videos and comic versions. However, not all of them are translated into Japanese. As mentioned in Section 4.1, the provision of lay summaries (Japanese version) in Japan is currently in most cases limited to clinical trial participants (patients), so posting case studies of pharma-sponsored clinical trials (Japanese version) is not permissible. In the future, if we obtain case studies (Japanese version) permitted to disclose, we plan to add them to this document.

Glossary (Section 6.2)

We have compiled a list of technical terms that you should know to understand lay summaries and that are specifically defined in this guide and provide a simple explanation for each of them. Each term explained here is marked with an asterisk (*) in the main text where it first appears.

6.1 Case Studies

JCOG1305[q)]

JCOG
Japan Clinical Oncology Group

JCOG1305

初発進行期ホジキンリンパ腫治療の非ランダム化検証的試験

結果のまとめ

JCOG1305 試験へのご参加ありがとうございました！

ホジキンリンパ腫に対する治療に関する臨床試験（JCOG1305）にご参加いただき、誠にありがとうございました。

このたび、データ解析を行い、試験の主要な結果を 2022 年 12 月に開催された国際学会（米国血液学会）で発表しました。試験にご参加いただいた皆さまにご報告します。

1. この臨床試験の経緯について

この臨床試験は、「ホジキンリンパ腫」と診断された方を対象として、有効性が高い治療法を調べることを目的としています。具体的には以下の治療選択の効果を調べました。

① ABVD（エービーブイディ）療法を 2 コース行った後に PET（ペット）検査（中間 PET）を行います。

- ABVD 療法が十分に効いている場合は ABVD 療法を 4 コース行います。
- 十分に効いていない場合は別の治療（増量 BEACOPP（ビーコップ）療法）に切り替えます。

② それぞれの治療後にリンパ腫病変が残っている場合には放射線療法を行います。

※治療後に効果判定を行い、病変が残っている場合には放射線療法を行います
（放射線療法を受けた患者さんは、増量 BEACOPP 療法では 1 人、追加 ABVD 療法では 2 人でした）

治療名	使用薬剤
ABVD 療法	ドキソルビシン、ブレオマイシン、ビンブラスチン、ダカルバジン
増量 BEACOPP 療法	ブレオマイシン、エトポシド、ドキソルビシン、シクロホスファミド ビンクリスチン、プロカルバジン、プレドニゾロン

JCOG1305 試験に参加されたみなさまへ 2023 年 3 月 10 日 JCOG リンパ腫グループ 1 / 4

q）Can be downloaded from the JCOG website https://jcog.jp/topic/general/jcog1305.html (cited 22 August 2024, only in Japanese).

JCOG1305 (continued)

2. 結果について

2022 年 6 月のデータ解析では、2015 年 11 月 20 日から 2020 年 2 月 1 日に登録された 93 人の患者さんを対象として解析しました。

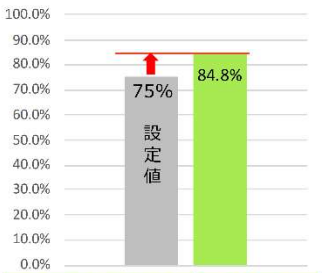
解析(1)すべての登録患者さんを対象として集計する **2 年無増悪生存割合**※

解析(2)中間 PET が陽性の患者さんを対象として集計する **2 年無増悪生存割合**※

※2 年無増悪生存割合（登録から 2 年後に病気が悪化することなく生存している人の割合）

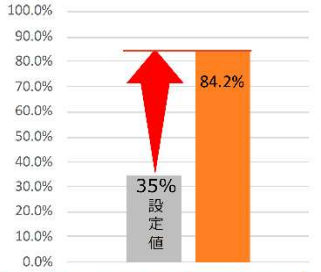
すべての登録患者さんを対象として集計した 2 年無増悪生存割合が 75%を上回ること、中間 PET が陽性の患者さんを対象として集計した 2 年無増悪生存割合が 35%を上回ることを調べる設定で、105 人の患者さんの登録を目標としました。

主な結果（1）無増悪生存割合
すべての患者さん（92人）



2年無増悪生存割合	84.8%
80% 信頼区間	79.2-88.9
95% 信頼区間	75.7-90.7

主な結果（2）無増悪生存割合
中間PET陽性患者さん（19人）



2年無増悪生存割合	84.2%
80% 信頼区間	69.7-92.1
95% 信頼区間	58.7-94.6

主な結果（1）登録患者さん全体の 2 年無増悪生存割合が 75%を上回りました

解析の結果「すべての登録患者さんを対象として集計した 2 年無増悪生存割合が 75%を上回る」が満たされ、**「ABVD 療法 2 コース後の中間 PET 検査の結果、効果が十分でない場合に強い治療に切り替える」という治療が有効であること**が示されました。

主な結果（2）中間 PET 検査陽性患者さんの 2 年無増悪生存割合が 35%を上回りました

解析の結果、「中間 PET 検査が陽性であった患者さんを対象として集計した 2 年無増悪生存割合が 35%を上回る」が満たされ、**「中間 PET 検査の結果、効果が十分でない時に行う増量 BEACOPP 療法」も有効であること**が示されました。

JCOG1305 試験に参加されたみなさまへ 2023 年 3 月 10 日 JCOG リンパ腫グループ 2 / 4

JCOG1305 (continued)

3. 副作用について

もっとも懸念していたブレオマイシンによる肺毒性（肺機能障害）は 9 人の患者さんに起こりました。9 人のうち 6 人の患者さんで、肺毒性出現後にブレオマイシンを中止しましたが、肺毒性のために死亡された患者さんはいませんでした。

その他の副作用として、高トリグリセリド血症（高脂血症の一種）、肝機能障害（AST（肝酵素）上昇）、心嚢液貯留を伴う心タンポナーデ（心臓のまわりに水が溜まって心臓が圧迫される）が計 3 人（3%）の患者さんで起こりました。骨髄抑制（白血球減少、好中球減少、リンパ球減少）はいずれも予想していた範囲内であり回復しています。

二次がんとして、びまん性大細胞型 B 細胞性リンパ腫が 1 人（1%）の患者さんに発生しました。

	肺毒性	骨髄抑制		
		白血球減少	好中球減少	リンパ球減少
導入 ABVD 療法	2%	11%	46%	8%
追加 ABVD 療法	5%	12%	37%	1%
増量 BEACOPP 療法	16%	100%	100%	100%

4. この臨床試験でわかったこと

この臨床試験の結果、ABVD 療法 2 コース後の中間 PET 検査の結果により治療を替える（効果が十分ではない時に増量 BEACOPP 療法（6 コース）に変更する）ことが有効であることがわかりました。

5. この臨床試験が計画された経緯

ホジキンリンパ腫に対する標準治療は、ABVD 療法です。ABVD 療法は多くの患者さんに治癒が期待できる治療ですが、2015 年時点で、十分に効かない患者さんがいることもわかっていました。しかし、この試験を計画した時も 2023 年現在もまだ、治療を始める前に ABVD 療法が効かない患者さんを見分ける方法は見つかっていません。

そこで、ABVD 療法を 2 コース行った後に、ABVD 療法の効果を調べ、効いていない場合には別の強力な治療に切り替えることで、より多くの患者さんで治癒が得られないかと考え、世界中のリンパ腫治療の専門家が検討を重ねてきました。その中で当時もっとも期待されていたのが、ABVD 療法を 2 コース行った後に、「PET検査」を行って、治療が効いていないと判断された場合に、より強い治療「増量 BEACOPP 療法」に替える方法でした。

そのため、JCOG のリンパ腫グループは、治療途中の PET 検査の結果により治療を変更することが本当によい治療であるのかを詳しく調べるため、この臨床試験を行いました。2015 年 11 月 20 日に登録を開始し、2020 年 2 月 1 日までに 93 人の患者さんが登録されました。

JCOG1305 (continued)

6. この臨床試験の今後の予定と掲載サイト情報について

●今後の予定

この臨床試験の結果は、2022 年 12 月に開催された国際学会（米国血液学会）で発表いたしました。今後、論文公表を予定しています。

また、現在 10 年間の追跡調査期間中です。引き続き、追跡調査へのご協力をお願い申し上げます。追跡調査の結果は 2031 年冬を目途に国際学会で発表、論文公表を予定しています。

※　学会発表、論文公表ではあなたを特定できる情報は含みません。

●掲載サイト情報

この臨床試験の概要は以下のサイトにて公開しています。

jRCT 臨床研究等提出・公開システム情報：jrct.niph.go.jp

臨床研究実施計画番号　jRCTs031180218

https://jrct.niph.go.jp/latest-detail/jRCTs031180218

検索サイト「JRCT」で検索→**臨床研究等提出・公開システム**

jRCT サイトで「JCOG1305」で検索

JCOG ウェブサイト試験概要：www.jcog.jp

http://www.jcog.jp/document/1305.pdf

※　臨床研究等提出・公開システム、JCOG ウェブサイトではあなたを特定できる情報は含みません。

改めて、JCOG1305 試験にご参加頂いたことに感謝を申し上げます。

＜用語解説＞

無増悪生存割合	試験に登録してから病気が悪くなることなく生存している患者さんの割合
PET 検査	がん細胞はとどまることなく活発に増殖しているため、大量の栄養素を必要とし、正常細胞に比べて 3～8 倍のブドウ糖を取り込むとされています。PET 検査はこの性質を利用しています。
PET 陽性	PET 陽性とは、ホジキンリンパ腫の腫瘍細胞にブドウ糖がたくさん集まっていることを表します。PET が陽性であれば腫瘍細胞が残っていて治療があまり効いていない可能性があります。

JCOG1305	Interim PET に基づく初発進行期ホジキンリンパ腫に対する ABVD 療法および ABVD/増量 BEACOPP 療法の非ランダム化検証的試験	
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6.2 Glossary

Term	Definition in This Guide
Bias	Deviation in research data. A non-random deviation between true data and observed data. The ICH E9 guideline (5, 17) defines bias in statistics as "the systematic tendency of any factors associated with the design, conduct, analysis and evaluation of the results of a clinical trial to make the estimate of a treatment effect deviate from its true value." Synonym: deviation
Chiken	The Japanese term that refers to a clinical trial to obtain manufacturing approval for a new drug from the government. A "investigator-initiated clinical trial" is a trial led by a physician rather than a pharmaceutical company. (5) Synonyms: clinical trial, interventional trial, clinical study
Clinical Study	In Japan, this is an umbrella term including clinical trials and *chiken*. (5)
Clinical Trial	A study to confirm whether a drug, etc., can be used as a treatment by investigating its effects on the human body. (5) Synonyms: *chiken*, interventional trial, clinical study
Clinical Trial Coordinator	A person who manages and cares for patients participating in a clinical trial and supports physicians, nurses, and others conducting the trial. A contact point for patients during the trial.
Clinical Trial Information System	A system for centrally managing information on clinical trials conducted in the EU and European Economic Area, introduced with the adoption of EU CTR536/2014.[r)]
Clinical Trial Regulation	A new regulation to harmonize the notification, evaluation, and supervision processes for clinical trials conducted in the EU and European Economic Area countries (EU CTR536/2014). (3)

r) https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system (cited 22 August 2024)

Term	Definition in This Guide
Complication	Another disease caused by a certain disease. (5)
Competency	Behavioral characteristics that lead to high performance, including basic abilities, specialized knowledge and skills, and ways of thinking required for a job.
Compliance	The act of conducting business and other activities by companies and other organizations without deviating from laws, ethics, and other social norms.
Double-blind	A method in which all trial participants, investigators and the trial sponsor are unable to know the trial treatment that the participants receive. It is used to limit conscious and unconscious bias in the trial conduct and the interpretation of the trial results. (17)
Family	Includes not only people with traditional blood and marital relationships, but also people who share and support the patient's life. This includes people who do not physically live with the patient. Synonyms: (in pharmaceutical development) caregiver, care partner (in general, not as a profession)
Inclusion/Exclusion Criteria	The minimum conditions for selecting appropriate study participants. It is important to keep the number of selection criteria to a minimum, as having too many can make it difficult to select study participants. Common items include age, gender, and primary endpoint criteria. Exclusion criteria are conditions to avoid when selecting appropriate study participants. These criteria are set to minimize bias in trial results and to consider the safety of study participants. (17) Synonym: eligibility criteria
Infographics	A concise representation of complex information or data that can be visually understood.

Term	Definition in This Guide
Multi-regional Clinical Trial	Clinical trials intended for registration and conducted in multiple regions under a single protocol. (15)
Open Access	The practice of making academic papers freely accessible.
Outcome	This refers to both study results and study endpoints. From this, it is also used as an endpoint showing what the condition of a disease finally became (sometimes years later) as a result of the treatment. (5) Synonym: endpoint
Patient and Public Involvement	A practice that aims to conduct research and development by considering the opinions and perspectives of patients and the public, with researchers and patients/the public collaborating to produce better social, scientific, and ethical outcomes. (12, 13) Synonyms: (In Western countries and pharmaceutical companies) Patient Engagement, patient involvement
Patient-Reported Outcomes	Symptoms and quality of life as assessed by patients themselves. Relatedly, outcomes assessed by people other than patients or healthcare professionals, such as patients' family members or caregivers, are called Observer Reported Outcomes. (5, 14)
Placebo Control	A placebo control is a trial design that compares with a placebo to confirm the presence or absence of the effect of a new treatment and the degree of side effects. Using a placebo control does not mean not being treated, but means that a placebo is used in addition to standard treatment (added on top). A placebo is a fake drug that looks and tastes like a real drug but has no effect of the drug. (5,18)
Post-Marketing Surveillance	A survey conducted to confirm the safety and effectiveness of pharmaceuticals and medical devices after they have been approved and used in routine clinical practice. (16)

Term	Definition in This Guide
Primary Endpoint	An item that can provide the most clinically appropriate and persuasive evidence directly related to the main objective of a clinical trial. (17) Synonym: primary variable
Quality of Life	The state of life that a person can be satisfied with when he/she can no longer live his/her normal life due to illness, aging, and/or treatment. (5)
Randomized Comparative Trial	A trial in which study participants are randomly assigned into two or more groups to confirm the effects of treatments, etc. “Randomly assigned” means “drawing lots with the same probability to determine which group to join,” which allows for a fair comparison of effects and a highly reliable study. (5) Synonym: randomized comparative controlled trial
Secondary endpoint	An additional endpoint related to the main study objective (the primary endpoint), or an endpoint related to the secondary objective. (17) Synonym: secondary variable
Statistical significance	This indicates the possibility that the detected difference is not due to chance is extremely high. (5,17)

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