Enhancing accessibility of study data: The development of a graphical abstract for lay summaries of clinical trial results

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Abstract
We describe the development of a graphical abstract for lay summaries of clinical trial results. The new graphical summary serves the same purpose for a lay summary as an abstract does for a scientific publication. Lay summaries are intended to inform the general public about the results of clinical studies. Consequently, they need to be understandable to people without specific knowledge of the disease or knowledge of the clinical research process. Visual displays have been shown to greatly support the understanding of complex data. With the support of patient organisations, we first determined the information items that were to be included in the graphical abstract and then transformed them into visual representations on a single page preceding the lay summary. Review and feedback from stakeholders and patient representatives helped derive a final graphical abstract template for all lay summaries across therapeutic areas. The generally positive feedback from patient representatives emphasises the usefulness of the graphical abstract in conveying key information of clinical trials.

Introduction
Lay summaries are short documents summarising the results of a clinical trial in a way that is understandable to the lay public. They are a new requirement introduced by the European Clinical Trial Regulation 536/2014 (EU-CTR) in 2014. According to the EU-CTR, a lay summary is to be provided for all clinical trials regardless of the clinical phase and therapeutic area, and irrespective of whether the trial was successful. The requirements regarding content of lay summaries are provided in Annex V of the EU-CTR in the form of a list comprising 10 items.[1]

Some aspects of the EU-CTR such as the central approval of clinical trials were intensively discussed with stakeholders before becoming part of the regulation. Conversely, the requirement for lay summaries was only included in the EU-CTR at a later stage and without broad consultation. A central component of the EU-CTR is a web portal that will facilitate the handling of all aspects of clinical trial application, review, and approval. In addition, this web portal will serve as a database for information on clinical trials. The idea is that the scientific summary, the lay summary, the protocol, and the clinical study report of one clinical trial are made available at a

single web location (§67 of the EU-CTR).[1] The central portal establishes a new interaction among sponsors, ethics committees, and regulatory authorities, i.e., for those that had also previously been part of the clinical research process. Lay summaries are the one new aspect of the regulation that is directly linked to patients and the general public.

For an innovative document such as the lay summary, the EU-CTR does not provide sufficient guidance for a successful and compliant implementation.[2,3] Many stakeholders, including sponsors of clinical studies and patient organisations, raised the need for more comprehensive guidance. Therefore soon after the publication of the EU-CTR, the Health Research Authority, a part of the National Health Service in the United Kingdom, was asked to coordinate the development of further guidance on the writing of lay summaries. A large stakeholder group was formed that developed detailed recommendations on the structure and content of lay summaries. The final version of the guidance became available as the "Recommendations of the Expert Group" in February 2018 (referred to as "expert recommendations" in the subsequent text).[4] The document consists of a section with general principles and two annexes with detailed guidance for the different parts of lay summaries. It provides clarifications on many aspects of the writing and design of lay summaries. Very importantly, the recommendations state that the primary audience of lay summaries is the general public. Consequently, lay summaries need to be written in a way that they are understandable to people without specific knowledge of the disease, the indication, or knowledge of the clinical research process. International surveys of adult literacy have demonstrated that average literacy levels are generally low. Across Europe, the average literacy level is 2 to 3 based on the International Adult Literacy Survey (on a scale from 1 to 5); level 3 roughly corresponds to a level attained after completing secondary school.[5-7] The stipulation that lay summaries need to be understandable to people with low literacy skills dominates all aspects of the guidance, particularly the sections on writing style, language, and use of numbers.

The expert recommendations also touch on the use of visuals and graphics in lay summaries. The use of "well-chosen and clearly designed visual aids" is encouraged.[4] This is in line with the understanding that the general public is the primary audience for lay summaries. People with low literacy levels find the processing of text challenging and their understanding is greatly helped by graphic displays. Research on medical instructions for patients has underlined the importance and helpfulness of visual aids.[8-11]

Going beyond the provisions of Annex V of the EU-CTR, the expert recommendations propose that a lay summary should have an abstract[4] to help readers decide whether they want to read the entire lay summary. The abstract should describe the purpose of the study, what was tested, the people who participated, the main results, and give information on safety (Annex 1

Box 1. Content of lay summaries as provided in Annex V of the EU-Clinical Trial Regulation.[1] (Reprinted under Creative Commons).

1.	Clinical trial identification (including title of the trial, protocol number, EU trial number and other identifiers);
2.	Name and contact details of the sponsor;
3.	General information about the clinical trial (including where and when the trial was conducted, the main objectives of the trial and an explanation of the reasons for conducting it);
4.	Population of subjects (including information on the number of subjects included in the trial in the Member State concerned, in the Union and in third countries; age group breakdown and gender breakdown; inclusion and exclusion criteria);
5.	Investigational medicinal products used;
6.	Description of adverse reactions and their frequency;
7.	Overall results of the clinical trial;
8.	Comments on the outcome of the clinical trial;
9.	Indication if follow-up clinical trials are foreseen;
10.	Indication where additional information could be found.

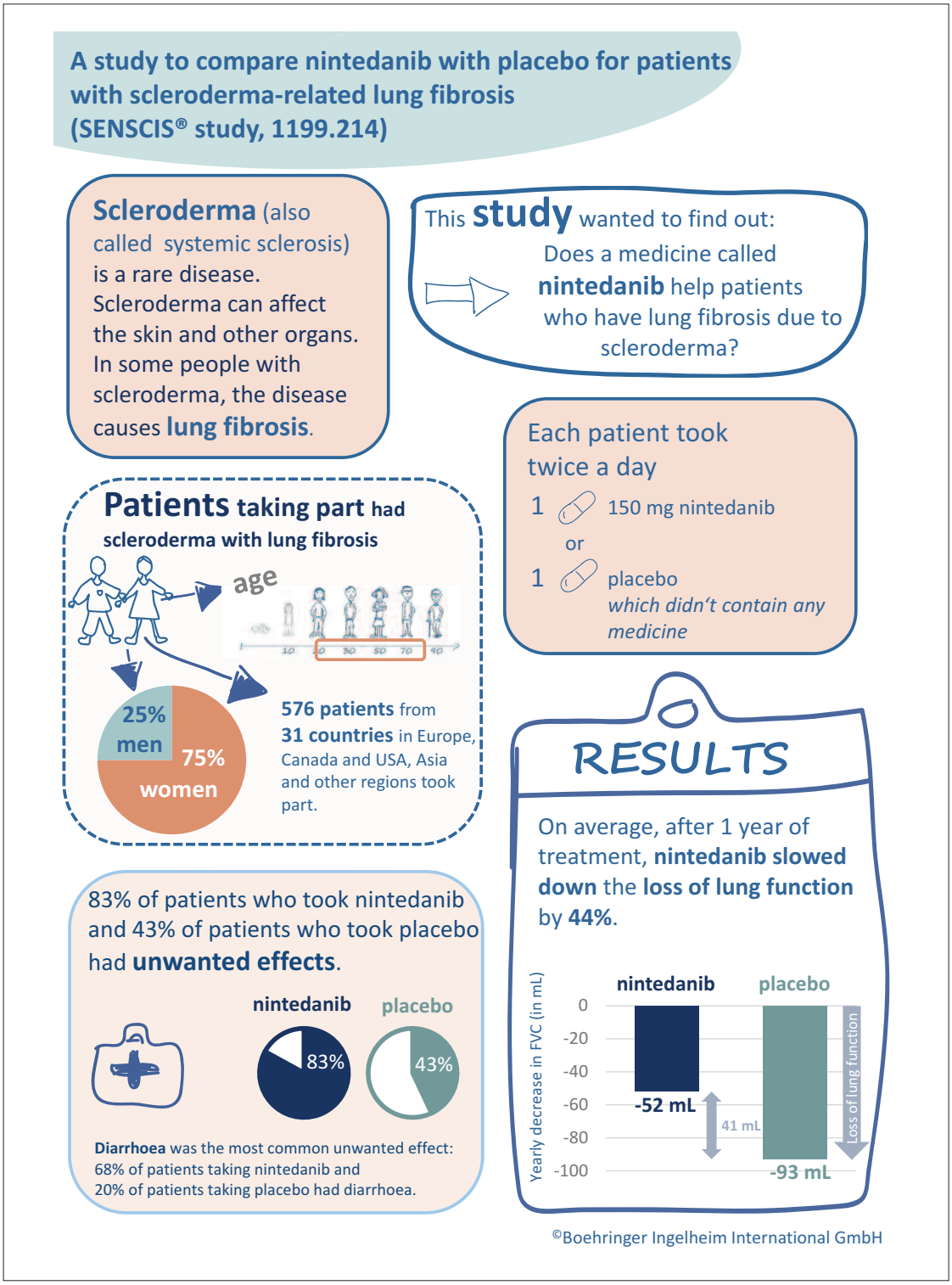

Figure 1. Example of a graphical abstract preceding a lay summary. (Reprinted with permission.)
NB: The full lay summary is available at the Boehringer Ingelheim trial results website (https://trials.boehringer-ingelheim.com/trial_results/clinical_trials_overview.html)

of the Expert Recommendations).

Using the expert recommendations as a basis, we first identified those items that constitute the key information of a study for a general audience. The next step was the determination of the appropriate level of data aggregation. We fine-tuned our conclusions in discussions with internal stakeholders, patient representatives, and patient organisations.

Subsequently, we transferred these information items into graphical representations. Our idea was to create a graphical abstract that serves the same purpose for a lay summary as an abstract does for a scientific publication. This entails a limitation of the content of the graphical abstract to highly aggregated data and statements. To ensure a harmonised format across different trials and therapeutic areas, we developed a template for the graphical abstract. The initial template was used to create the first version of a graphical abstract, which was then reviewed by representatives of different patient organisations. Their feedback and input helped us to make improvements and shaped the development of the final template so that it aligned with the needs of patients.

Design principles for the graphical abstract

In line with the expert recommendations and the requirements of the EU-CTR,[4] we based our

development on the notion that a graphical abstract must be strictly non-promotional. That also meant that the overall appearance, the "feel", and the content of the graphical abstract should be distinctly different from any marketing material used for the medicine under study. We consciously aimed at a sketchy, non-glossy appearance of the graphical abstract; something a clinical investigator might draw to illustrate the results of a study in a conversation with a patient or study participant.

The graphical abstract is intended both to invite readers and to provide them with a high-level summary of the study. Therefore, we limited it to one page and placed it at the beginning of the lay summary, i.e., where an abstract of a publication is also located. After having viewed the graphical abstract, the readers should be able to decide whether they want to continue reading the full lay summary.

The graphical abstract should not only be visually appealing to attract readers but also be able to hold their attention. To achieve this, we decided to present the content information in several distinct panels, leaving as much white space as possible. Each panel presents a single aspect of the lay summary content such as demographics, disease information, study aim, efficacy, and safety. They are independent so that each panel can be understood without reference to others. The panels are arranged in a logical order but we did not introduce a fixed sequence. The readers should be free to go through the content at their discretion.

We varied the shapes, line styles, and background colours of the different panels to enhance the visual appeal. However, we were mindful that too much playfulness might be associated with a non-serious, non-scientific intention.

Since the information is to be conveyed graphically, the amount of text was reduced to a minimum. Variations in font features (style, size, colour, and highlight forms) make certain words stand out from the rest of the text. These words serve as visual focal points and "headings" for the different panels. They enable readers to skim the graphical abstract and focus on the content area that they are most interested in.

Content of the graphical abstract

Since the graphical abstract was to be the first page of the lay summary, we decided to start it with the lay title of the clinical study. We routinely develop lay titles for all clinical studies based on the full scientific title and the final study protocol. The lay titles are also used for other study-related documents such as Informed Consent Forms and for the posting on ClinicalTrials.gov.[12] Having the lay title as the first element on the page allows the reader to judge quickly whether the study is relevant for them. Encompassing the suggestions of the expert recommendations,[4] we include the following elements in a graphical abstract:

- Disease description: a short description of the disease under study. This panel provides the reader with high-level information on the disease and complements the information provided in the lay title.
- Study aim: a short description of the study objective
- Demographics: a depiction of key inclusion criteria, age range, gender distribution, and location of study participants. We use a pie chart for the depiction of the gender distribution and sketches of human age characteristics to depict the age requirements.
- Information on the medicines that are studied: name and dose, mode of administration.
- Information on safety outcomes: adverse reactions as required by Annex V of the EU-CTR. Since the term adverse reaction is not familiar to lay readers, we chose "unwanted effect" instead. The frequencies of the unwanted effects in all treatment groups are visualised by pie charts.
- Information on the outcome of the protocol-specified primary endpoint: the results of all

treatment groups are shown graphically by bar charts.

We write all texts in plain language using short, simple, and neutral sentences. Since abbreviations are usually not known to lay readers, we avoid using them in the graphical abstract.

Other considerations

The information in lay summaries and in graphical abstracts needs to be presented objectively. To retain the credibility of lay summaries for the general public, anything promotional must be strictly avoided. This notion is strongly emphasised in the expert recommendations.[4] To ensure objective scientific content, we have developed internal guidance documents for the writing of lay summaries and graphical abstracts. The key elements are:

- The content of the graphical abstract is strictly factual.
- In line with the expert recommendations, we limit the presentation of efficacy results to the protocol-specified primary endpoint.
- We provide numeric data for the primary endpoint and for the key safety observations to enable the readers to link the information provided in the graphical abstract to the scientific summary or the results posted on ClinicalTrials.gov.
- The standards of ethical publishing are observed in the graphical representations of the results, e.g., the axes of bar charts and pie charts are appropriately labelled and the results of all treatment groups are shown.
- All statements are made in neutral language; emotional words and expressions as well as superlatives are avoided.
- The different content elements such as efficacy results and safety results are presented in a balanced way.

For people with limited numeracy skills, decimal numbers are difficult to understand. Therefore, we only present full numbers in the graphical abstract, i.e., we apply conventional rounding rules wherever possible. Numerical data are supported by graphical presentations.

We consider the graphical abstract and the full lay summary as forming one document. Both are contained in a single file and are posted as one pdf-file (examples are available at https://trials.boehringer-ingelheim.com/trial_results/clinical_trials_overview.html). The highly aggregated data in the graphical abstract are complemented by more detailed data and descriptions in the lay summary. The single file format is also important because our lay summaries comprise a disclaimer called "Important notice" that also applies to the graphical abstract. The disclaimer states that the lay summary presents only the results of a single study and that it cannot represent the entire knowledge about a drug. Other studies may have different results. In addition, the disclaimer alerts the readers that they should not change their therapy on reading the lay summary and that they should always consult with their physician.

Challenges

One of the challenges in designing and writing graphical abstracts is the choice of the appropriate level of aggregation. To be useful for the general public, lay summaries are limited in the amount and depth of information that can be provided and this applies even more to the graphical abstract. We try to meet the challenge of describing objective scientific information for lay audiences within a limited space by following clear rules (see above) and by involving patient representatives in the review of lay summaries. The use of the template in conjunction with following clear instructions ensures high-quality graphical abstracts. For complex trials and trials with unclear results, the graphical abstract may need to deviate from the template.

Scientifically and ethically, it is most appropriate to present the results of the primary endpoint as the key efficacy outcome. The primary endpoint is the assessment for which the study was designed and for which it was powered to show differences in a confirmatory way. Therefore, the expert recommendations require that the primary endpoint data are always shown.[4] Secondary endpoints are evaluated in an exploratory way and studies commonly evaluate large numbers of secondary endpoints. Given the space limitations of a graphical abstract, the inclusion of secondary or even tertiary endpoints amounts to a selection and may lead to presenting only those results that are favourable for the drug. This is ethically and scientifically questionable, as studies are usually not powered to show differences in secondary endpoints. In addition, the issue of multiple testing and adjustment of the significance levels needs to be considered before reporting them. However, sometimes, secondary endpoints capture patient-relevant observations. A solution to this would be the inclusion of secondary endpoint data in a lay summary but under a separate heading and with a statement that no firm conclusions can be drawn.

Conclusions

We have developed a new graphic format to present the key information of a study to patients. The graphical abstract summarises the data in a lay summary similar to what an abstract does for a scientific publication in a visually appealing way. We have tested the graphical abstract with patient representatives from various disease areas. The feedback to the overall idea of an abstract preceding the lay summary has been positive and patient reviewers have found the graphical display helpful and attractive. We therefore believe that this new format can increase the attractiveness of lay summaries and thus help to more adequately inform the general public about the results of clinical studies.

Disclaimers

The opinions expressed in this article are the authors' own and not necessarily shared by their employer or EMWA.

Conflicts of interest

The authors declare no conflicts of interest.

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