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Informed Consent Procedure in Clinical Trials Promoted by the Hospital: Knowledge and Perceptions of Primary Care Physicians

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ABSTRACT

Objectives: To evaluate Primary Care Physician's (PCP) awareness degree concerning their patient's participation in Clinical Trials (CT) analyze the communication methods used and obtain physicians personal views.
Methods: Authors performed a cross-sectional observational study that included CTs approved by the Institutional Review Board at a Regional University Hospital (n=78). Among these 37 CTs were selected. PCPs involved in these trials received a questionnaire regarding aspects of the CTs in which their patients participated. The communication systems established in the study protocols were analyzed.
Results: Out of 89 PCPs contacted, 82.1% were aware of their patient's participation in CTs. The information reached them through verbal communication from the participant (56.3%). PCPs also accessed it through electronic medical records (EMR) (34.0%). A majority (97.4%) considered being informed about the participation of their patients in CTs should be compulsory.
Conclusion: Communication of patients' participation in CTs fundamentally takes place through a verbal interaction between patients and their doctor. PCPs consider that the preferred method of communication would be an alarm system in the patient's EMR.

Keywords: Clinical research, Sponsor, Electronic medical record, Safety

BACKGROUND

Drug randomized controlled clinical trials (RCTs) are the primary scientific method used to gather the maximum degree of evidence regarding the effectiveness of new treatments [1,2]. For respecting the participant's autonomy and well-being, it is mandatory to obtain an informed consent form (ICF) from the beginning of the trial, as indicated in the Declaration of Helsinki [3] and other related documents [4-6].

The Guidelines on Good Clinical Practice (GCP) recommend to inform the primary care physician (PCP) of the patients' involvement in clinical trials (CTs) [7]; however, in the CT protocol and the ICF, this is not always clearly stated [8,9]. Although some ICFs encourage participants to consult/inform their respective PCPs when becoming enrolled in a clinical trial (CT), or even state that

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investigators should communicate this information, the inclusion of the PCP in the ICF process is not regulated.

In Spain, a significant number of CT participants are cancer patients [10], who often present multiple comorbidities for which they frequently visit their PCP. To ensure good clinical practice when prescribing a new medication for these patients,
as well as for safety issues, PCPs should be aware of the participation of patients in CT and should have information about the CT protocol characteristics. This information is critical during the interpretation of new signs or symptoms that may be related to the administered drug under study.

Our Ethics Committee (EC) is currently working on establishing a formal procedure to inform PCPs of a patient's participation in a CT. This procedure should ensure confidentiality for both the participant and the trial sponsor and, in this regard, the electronic medical record appears to be an adequate tool, without neglecting other systems such as the provision of participation cards or letters from the Principal Investigator (PI) to the PCPs. As a preliminary step in the establishment of this new procedure, our EC carried out a study to determine the extent to which sponsors and PIs would be willing to inform PCPs about the participation of their patients in a CT [11]. The results revealed that 69% of the ICFs reviewed considered the possibility of notifying PCPs (in 46 out of 67 clinical trials). In general, the information that the PCPs were receiving their patients participate in a CT was somewhat limited. It also became apparent that there was high variability among the methods that were employed to convey such information.

Nonetheless, CT participants widely acknowledged that their PCPs were aware of their inclusion in a CT and noted that the electronic medical record was their preferred method for this information to be given to their PCP. However, this study did not analyze the compliance and effectiveness of the communication between the PI and the PCP regarding CTs managed from the specialized medical care area. The PCPs' views on the participation of patients in CTs conducted by specialists was not examined either.

The present study aimed to analyze the PCPs' degree of knowledge of their patient's participation in CTs and their preferences about how they should be informed of such involvement.

METHODS

We performed an observational cross-sectional study. All CTs that had recruited patients between January 2014 and February 2017, and that was still ongoing at that time, were selected for the study. The Hospital Universitari Arnau de Vilanova Ethical Committee approved the study that complied with the Declaration of Helsinki.

We identified a total of 37 trials that met the inclusion criteria. By analyzing the patients' Hospital Clinical Record and participation records (n =155), their respective PCPs were identified (n = 89 physicians since some physicians had more than one patient within CTs). We designed an anonymous questionnaire and cover letter to contact the selected PCPs, and these were sent by internal mail from the Primary Care Management of the healthcare organization.

The questionnaire mentioned above asked doctors about several questions as their degree of knowledge regarding the participation of their patients in CTs and how they received this information. Second their interest in being provided with such information and what they would consider as the ideal method to use to broadcast this information. A time limit of one month was given for answers to be received (17/03/2017- 17/04/2017). In investigators treated anonymously and ensured confidentiality. **Figure 1** shows an outline of the conduction of the study.

To the best of our knowledge, there was no validated questionnaire for the objectives of our work, as it had a particular purpose that required very directed and specific questions. The survey was specifically designed for this study. The questionnaire was initially created by two of the researchers, making a short, simple questionnaire that should be easy to understand and fill for the recipients (to increase the probability of response). These two researchers evaluated the validity and understandability of the survey items by consensus. Answers were exhaustive and mutually exclusive. All the investigators assessed its efficacy by completing the survey. After that, the entire team discussed the issues observed, and the final document was constructed.

RESULTS

Responses were obtained for 46% (41/89) of the questionnaires sent to the PCPs. It should be noted that some of the multiple-choice questions in the survey allowed more than one answer. A total of 82.0% of the physicians were aware that some of their patients were participating in a CT, and of these, 75.0% believed they could recall the number of patients (they remembered a total of 93 participants).

Results are presented in **Figure 2**. A total of 28.0% of the PCPs declared to be aware via a letter provided by the patient and 34% through the patient's Electronic Medical Record (EMR). However, no alert system is in place, which means physicians must actively search for the information. Any of the PCP interviewed received PI letter communicating the recruitment of the patient in a CT.

PI informed PCP of patient inclusion in a CT only in 6% of the cases, and the sponsor did so in 6% of the cases. Of the PCP surveyed, 56% stated that they had been informed through other systems, for example, verbal communication from the patient during the medical visit.

A clear majority of physicians (97.4%) considered that it was essential to be informed about their patients' participation in CTs and that this should not be optional

(74.0%). However, 18.0% considered that it should be the patient, the one who should decide about this communication and 5.0% believed it was for the PI to determine.

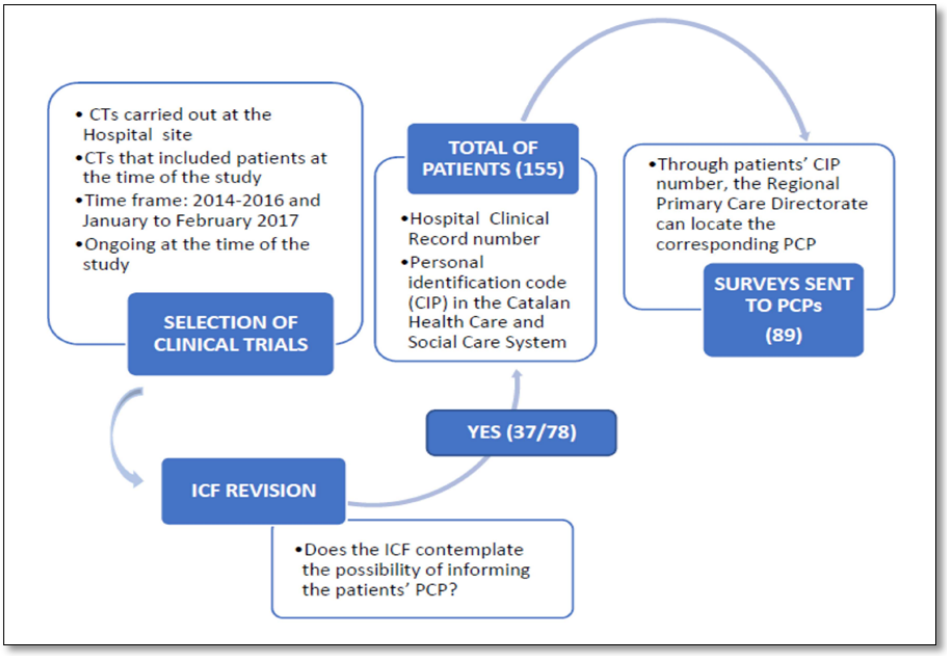

Figure 1. Study design and methodology.
CT: clinical trial; PCP: primary care practitioner

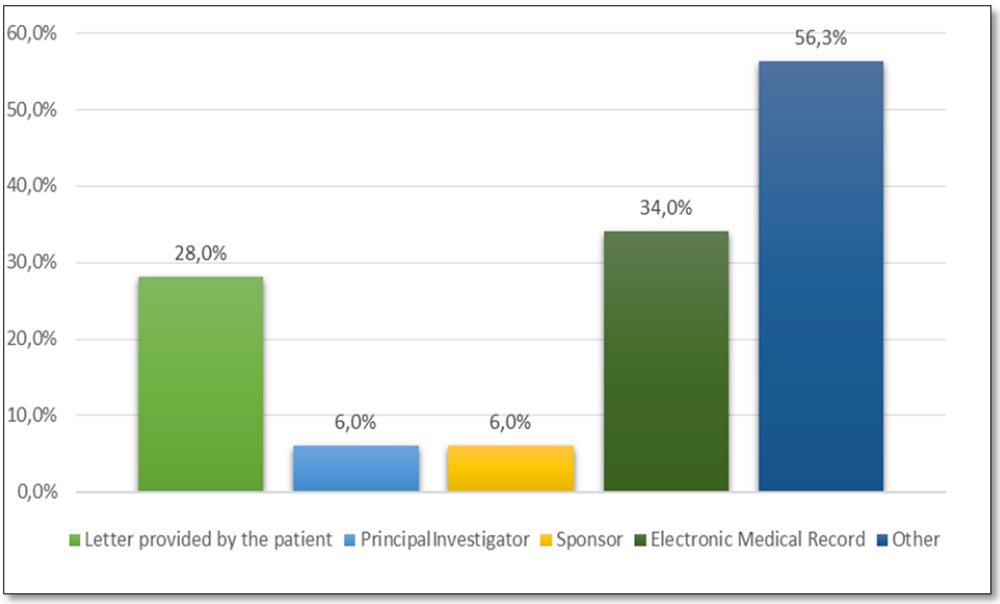

Figure 2. Communication method through which Primary Care Physicians were informed of their patient´s participation in a clinical trial. The multiple-choice questions of the questionnaire sent out allowed more than one answer.

Figure 3 shows the PCPs' preferences regarding the means of communication with the PIs. There is evidence to prove that a majority of PCPs would prefer to receive such notification through an alarm or signal in the patients' EMR (61.5%) or a letter delivered by the principal investigator (35.9%). Communications provided by the patient or by the investigator were the least preferred (25, 5% and 17, 9% respectively). The last option considered was communication by the sponsor. No physician expressed a preference which differed from those suggested.

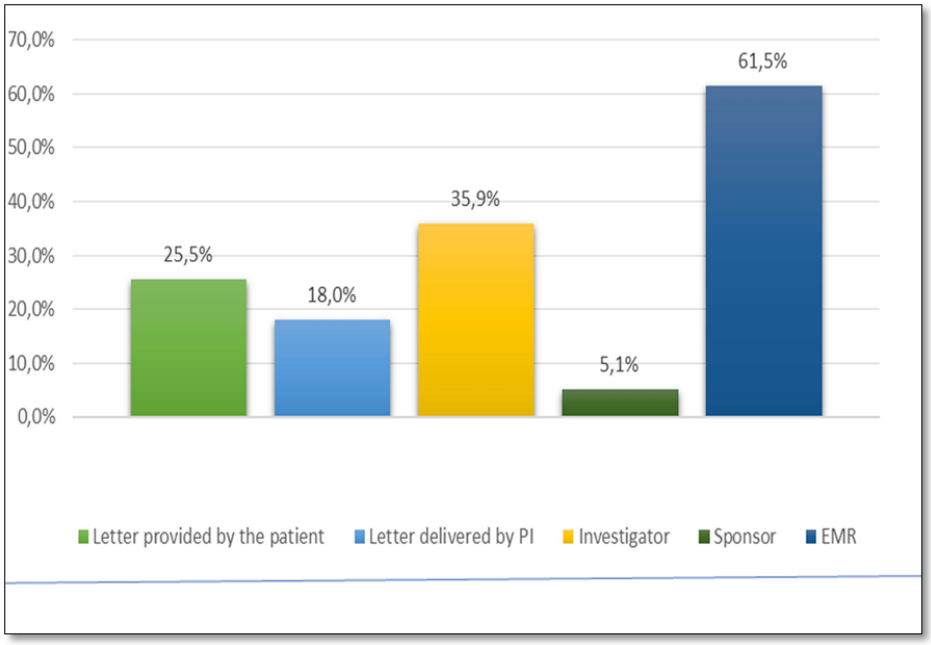

Figure 3. Primary care physicians' preferences regarding the means of communication for being informed of their patients' participation in clinical trials. The multiple-choice questions of the questionnaire sent out allowed more than one answer.

Finally, we should note that the questionnaire allowed the option of giving an open opinion, and 20.0% of PCPs made use of this possibility. A total of 5.1% stated that they felt uninformed, while 12.8% stressed the importance of the matter and 2.6% believed that it should be mandatory to inform the PCP at the time of signing the ICF.

DISCUSSION

This study gives us an estimate of the PCPs' degree of knowledge about their patients' participation in CTs. Our research shows that most physicians receive such information verbally through the patient. This method may lead to incomplete or distorted information. However, it is probably the most frequently used route due to the interpersonal relationship and trust that exists between patients and their primary care physician [12]. In fact, in a study conducted by our research group in 2016, 70% of the patients reported having communicated their participation in a CT to their PCP in person [11].

The present study shows that the means of communication with PCPs about the participation of their patients in CTs is an aspect to be clarified in the ICF. This clarification is paramount to ensure patients' safety, to avoid interference of concomitant medication in the clinical trial results and to provide adequate medical care. Although CTs are mainly run in the hospital setting, PCPs know their patients better and are the gateway to accessing the health system.

According to their disease, opinions, character and social environment, each individual can respond differently to their inclusion in a CT. Factors such as whether a CT is performed in the field of cancer or diabetes, whether participants have a higher education, or indeed their socioeconomic situation or their possibilities of accessing health resources, may have an influence. All of these aspects can have a bearing on the understanding of the study protocol, the study follow-up and, ultimately, the results of the CT and even the participant's well-being [12,13].

EMR allows for the exchange of information on all relevant CT aspects between PCPs and specialist physicians [14,15]. According to our results, this would be the PCPs' preferred method of communication when obtaining information about the participation of their patients in CTs (of note, it would be desirable that an alarm or signal be showed in the EMR system to warn of the patients' participation in a CT). Other communication methods have been proposed, such as the hospital discharge report [16].

As shown in the previous study of our research group [11], the majority of patients considered communication with their PCP of paramount importance. The preferred method of notification was the EMR, coinciding with the PCPs' opinion. Besides, PCPs point out the importance of knowing what kind of medicines their patients are receiving during the CT; to this end, the EMR should include the CT information leaflet or a link to the CT information online. This link to the CT information appears in the Spanish Registry of Clinical Trials, which is a public database that serves as a source of information regarding CTs performed in Spain and can be accessed free of charge from the Spanish Medicines Agency website (AEMPS) [17]. It could also be found at ClinicalTrials.gov which is an NIH website that

provides patients, family members, health professionals, researchers and the public with easy access to clinical trial information on a wide range of diseases and conditions [18].

It is also of note that in certain types of CTs, due to the nature of medication administered, duration of the study and health department conducting it (pathology, patient characteristics, other), it would be relevant that this information reaches the PCP. All clinical trials selected for this study tested drugs and mainly oncologic medication, which may have influenced the degree of communication with the PCP. However, we believe that PCPs should be informed of their patients' participation in CTs in a systematic way. Also, the ICF should specify the chosen communication path to inform the PCP (letter, EMR, personally) and periodical evaluations should be performed by ECs to ensure that the investigators perform the procedure correctly.

Our results are similar to those of Giménez et al. [19]. This study, conducted in a close healthcare system, established that in 50.0% of ICFs, patients were advised to consult with their respective PCP, 96.0% of PCPs considered that receiving such information is essential and only 33.0% received it. A total of 60.0% of physicians remembered having patients participating in clinical trials and, in 76.0% of cases, it was the patient who reported it to the doctor [19]. A total of 85.0% of PCPs showed dissatisfaction with the information received [19].

The main limitation of this study is that it has been carried out in a healthcare setting with a specific organization that may be different from others. Therefore, the survey results may not be universally applicable. We agree that PCPs are the closest specialists to the patient in any kind of organization and that their collaboration can facilitate the recruitment and support process, as well as the follow-up of patients in CTs [20]. They could also play the role of an educator [21] or counsellor [22] to facilitate the understanding of the ICF since several studies have shown suboptimal ICF understanding [23,24].

CONCLUSION

The results obtained in this study indicate that, while respecting the autonomy and confidentiality of the patient, a regulated and reliable system of communication with the corresponding PCP regarding the participation of their patients in CTs promoted in the field of specialized care should be contemplated. In this regard, nowadays, most PCPs are informed verbally through the patient and this system can lead to incomplete or distorted information.

Communication through the electronic medical record allows the exchange of facts and data between both levels of care. It would be the preferred way for PCPs to learn of the participation of their patients in a CT.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Hospital Universitari Arnau de Vilanova Ethical Committee approved the study.

AVAILABILITY OF DATA AND MATERIAL

The datasets used are available from the corresponding author on reasonable request.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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AUTHORS' CONTRIBUTIONS

All authors read and approved the final version of this manuscript.

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