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Original Research

Organisational factors influencing early clinical trials enrollment: Gustave Roussy experience

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Abstract ***Purpose:*** Enrolment process influences the likelihood of patients' inclusion in early clinical trials (ECT) through social, medical and organisational factors.
Patients and Methods: All patients referred from 2008 to 2016 to the Drug Development Department (DITEP) of Gustave Roussy (GR) were reviewed. Referring physician, organisational factors, medical and socioeconomic characteristics for patients were analysed. Multivariate analysis was performed with regard to those factors. A telephone survey was conducted on a sample of referring physicians located outside GR (N = 142).
Results: Between 2008 and 2016, 8694 requests were received with 49% from external physicians. Here, 4517 were male patients with a median age of 58 [49–66] years (range 18–85). Tumour types were gastrointestinal (28%), lung (19%), breast (9%) and gynaecologic (8%). Mean enrolment rate was 37% (ranging from 24 to 45%). From 2008 to 2016, the enrolment rate decreases from 39% to 24%. In the meantime, DITEP trials portfolio evolves with the part of precision medicine trials increase from 12% to 40%. Factors that were significantly associated with a lower likelihood of being enrolled were referral from an external physician (OR 0.15 s.16–0.21]) compared to a physician from DITEP and year of the request (2.74 [1.8 –2.9] 2008 versus 2016). The enrolment rate and the number of patients addressed have a high

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variability regarding referring physicians, which is little explained by characteristics as training, previous experience or attitude regarding ECT.
Conclusion: Beyond patients' individual characteristics, we show that organisational and professional factors have a major impact on likelihood of enrolment in ECT.

1. Introduction

Recent transformations of cancer research emphasise the role of early clinical trials (ECT) (phase I and II) in drug development [1]. Beyond the controversies on their therapeutic status [2], the equality of chance for patients to get access to those trials becomes a matter of public concern [3] as they are increasingly seen as an opportunity of therapeutic benefits [4,5]. Nevertheless, barriers in referral and enrolment challenge the equity of access. The literature shows that women [6,7], ethnic minorities [4,8], older patients [9,10] or lower socioeconomic status [4] are less likely to be referred and/or included. Various explanations are identified from the physical or anticipated condition linked to ageing and pathologies [11], the financial burden or cultural factors [12].

Studies dedicated to ECT enrolment focus mainly on patients [8,13]. However, organisational factors have been shown in clinical trials to impact the situation of the patients [14–16]. The central role of the physician in the treatment decision-making process to address patients has also been clearly identified [13,17]. Nevertheless, those studies rarely concern ECT specifically and tend to isolate patients' and physicians' actions without considering existing interactions [18]. Investigating the enrolment process leads to consider altogether individual, medical, professional and organisational factors. This is all the more needed that precision medicine is changing the constraints on patients enrolment, [19] which consequences are yet little investigated [20,21].

In this retrospective study, we analyse the impact of both patient's characteristics and selection process on the enrolment likelihood at DITEP, the largest French ECT dedicated drug development department.

2. Methods

2.1. Patients

The Drug Development Department DITEP at Gustave Roussy (Villejuif, France) is one of the 16 centres certified by the French NCI (INCa) to undertake ECT ("CLIP^2"). The recruitment process for patients at GR has been formalised in three steps to ensure systematic review and broaden the access. The first step (S1) consists in a pre-screening form available online about patient's health information, completed by the referring physician. If the patient does not fill the requirements or if there is no available trial, the refusal is notified to the referring physician.

In case of a positive answer, a medical visit is planned for complementary examinations and presentation of the trial's characteristics. During this second step (S2), consent may be given directly or delayed, depending on the situation, e.g. additional assessments or reflection time requested by the patient.

The third step (S3) is dedicated to the screening period, and the medical evaluation required by the trial. If the requirements are not met any longer (withdrawal of consent, disease evolution, new contraindications), the patient is not eligible and considered as 'screening failurë (SF).

Requests for joining a trial at the DITEP are systematically registered since 2008. For each patient, gender, address, birth date, disease, status (external or internal to GR), referring physician and the evaluation of the request are classified by decision date. Ethical information collection is not allowed in France. Some information is only available since 2012: reason for negative answer and screen failure. Reasons of refusal have been manually recoded, and addresses have been geo-localised using an online governmentally run database and matched with French micro-geographic areas IRIS (aggregated units for statistical information) from the INSEE (National Institute of Statistics and Economic Studies). This allows the calculation of a deprivation index at the communal level (IDA), [22] which is obtained with the first dimension of a principal component analysis (PCA) of five variables (incomes, housing situation, unemployment rate, level of education and rate of mono-parental family) divided in a 5-step scale following the French population distribution ranging from IDA-q1, the most deprived, to IDA-q5, the most privileged.

2.2. Physicians

A telephone survey has been conducted in 2013 on a sample of N = 143 external physicians who have referred at least one patient to the DITEP between 2007 and 2013. The questions focused on their opinions about ECT and their current professional situation to test if the rate of referral and the probability of enrolment were correlated to the attitude toward early clinical trials.