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Looking for innovative digital solutions to optimize patient recruitment in IBD trials

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Dear Editors:

We read with great interest the article by Harris et al. reporting the Competition for Clinical Trials in Inflammatory Bowel Diseases[1]. The authors provide an alarming overview of the situation, with a drop in the last 20 years (1998-2018) of the average recruitment rate from 0.32 to 0.13 patients/site/month in moderate-to-severe ulcerative colitis (UC), and from 0.65 to 0.1 in moderate-to-severe Crohn's disease (CD). They present an in-depth analysis of the causes of this scourge and propose innovative solutions to try to overcome it, as well as opening new centers in new countries. However, this last point will further spread the problem and increase the already astronomical cost of IBD clinical trials. In addition, their proposals mainly focus on the level of complexity of the studies, whereas it is well known that there are 3 others bottlenecks in patient recruitment in clinical trials, at the level of the patient, the doctor and the participating center[2] [Figure 1].

As a national study group in IBD, the GETAID (Groupe d'Etude Therapeutique des Affections Inflammatoires Digestives, www.getaid.org) was previously threatened of bankruptcy when it was confronted to a lower than expected recruitment rate for a major trial we accepted

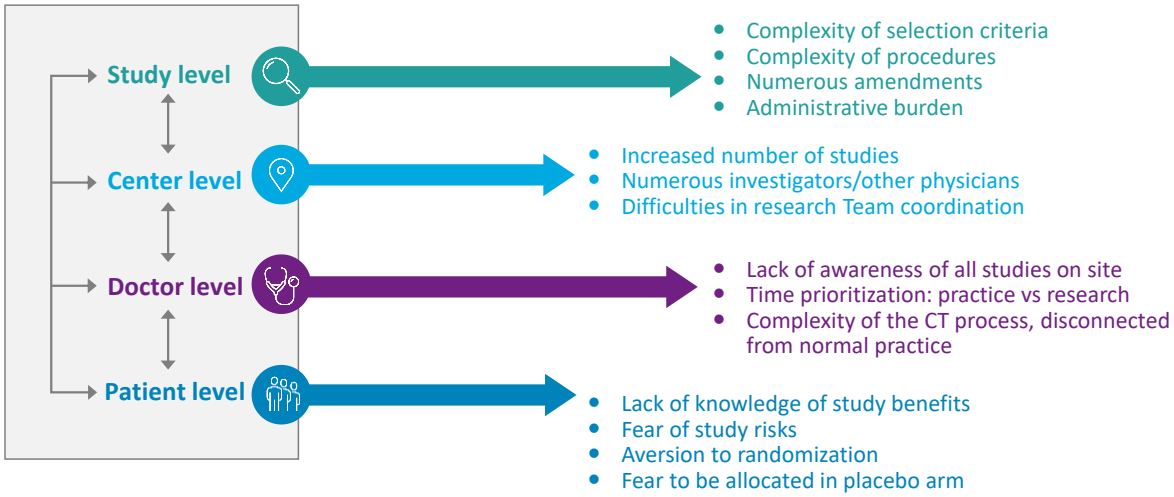

Figure 1 - Adapted from Oude Rengerink K et al. BMC Med Res Methodol 2010;10:85.

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to promote[3]. Considering that as a physician, it is very challenging to be aware of all ongoing trials onsite, to precisely know inclusion and exclusion criteria for these trials, and to find time available for recruitment tasks, we developed the CT-Scout™ solution, a multi-device web application that aims to optimize patient recruitment by enabling all physicians from one center, including non-investigators, to detect potentially eligible patients (www.ctma.fr). Identifying these patient, in real-time, by answering a simple and short questions in just a few clicks, allows physicians to check whether the patient matches with an ongoing CT on-site and, in that case, to send a notification to the research team which takes over the recruitment process[4]. Importantly, this solution, customized per site and including potentially all active trials, provides real-time data on recruitment in each site, increasing the visibility for all stakeholders from detection to randomization [Figure 2].

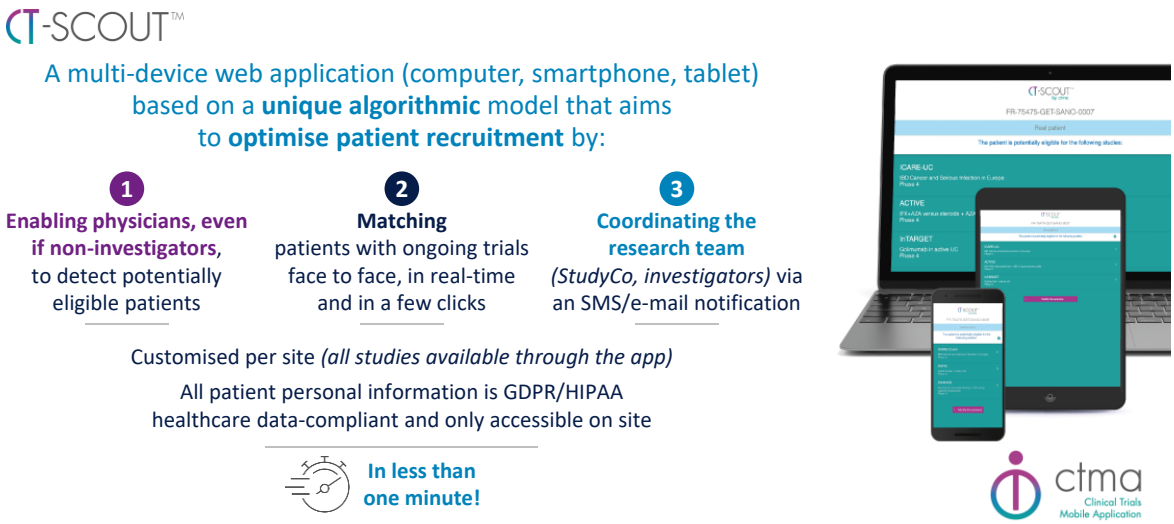

Figure 2 – The CT SCOUT™ solution

We recently conducted a study aiming to compare the number of patients enrolled in two phase III clinical trials HICKORY[5] and BERGAMOT[6] evaluating the efficacy and safety of etrolizumab in UC and CD in sites equipped or not with CT-Scout™ [7]. These results were presented as an oral communication during the UEGW 2019. Briefly, it was a multicenter, prospective, open-label, observational study including all sites opened for over 6 months. Recruitment figures were provided by the sponsor, which considered all French sites equipped with CT-Scout™ and sites in other countries not equipped with CT-Scout™ at the time of study launch. The primary endpoint was the mean number of patients randomized per site in both studies. Secondary endpoints were the mean number of patients randomized in each study. Patients who signed informed consent form (screened) and those finally randomized were compared in sites equipped or not with CT-Scout™ using a one-way ANOVA followed by post-hoc Tukey and Mann-Whitney tests. During the observational period of 40 months (Sept 2015 - Dec 2018), 644 and 289 patients were screened and randomized in 134 sites in both trials, respectively. 21 sites in France were equipped with CT-Scout™ and were compared to the 113 sites non-equipped with the app, located in Belgium (n=14), Germany (n=41), Spain (n=19), United Kingdom (n=26) and Israel (n=13). There were 307 and 149 patients in 78 sites for Hickory, and 337 and 140 patients for Bergamot in 102 sites. The mean number of patients screened and randomized per site in sites equipped and non-equipped in both studies was 7.55 and 3.05 ($p<0.001$) and 3.79 and 1.27 ($p<0.001$), respectively. For Hickory, they were 9.17 and 3.14 ($p<0.001$) and 5.17 and 1.28 ($p<0.001$), respectively. For Bergamot, they were 5.94 and 2.97 ($p=0.003$) and 2.41 and 1.26 ($p=0.009$), respectively. The mean number of patients detected and selected with the app was 13.9 and 15.9 and 9.2 and 5.9, for Hickory and Bergamot, respectively [Figures 3, 4].

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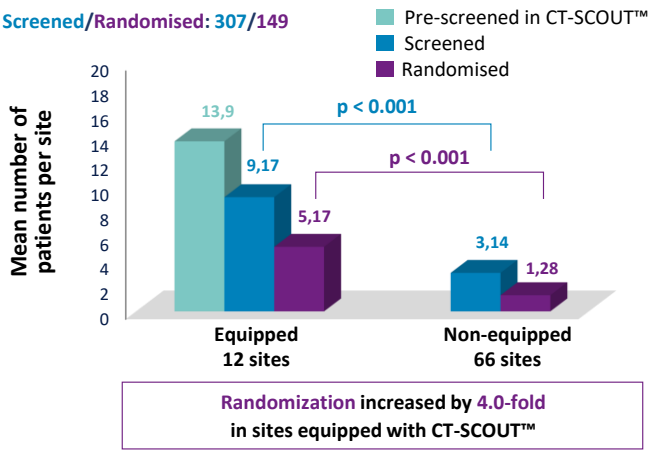

Figure 3: Comparison of patient recruitment in a phase 3 Ulcerative Colitis clinical trial (Hickory study) depending on the use or not of the CT-SCOUT™ application over a 40-month observational period (Sep. 2015 - Dec. 2018)

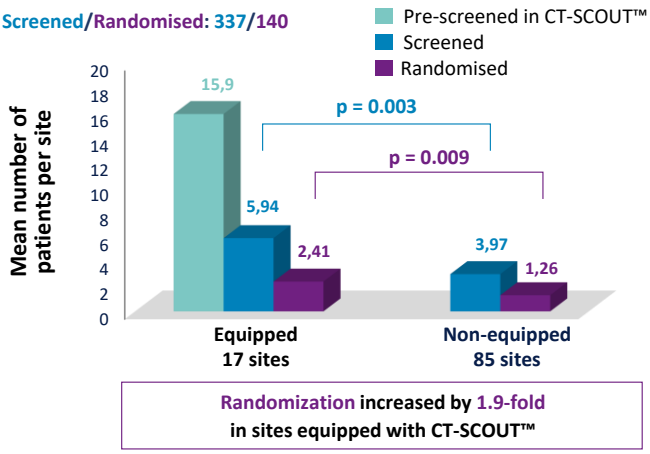

Figure 4: Comparison of patient recruitment in a phase 3 Crohn's disease clinical trial (Bergamot study) depending on the use or not of the CT-SCOUT™ application over a 40-month observational period (Sep. 2015 - Dec. 2018)

So, the switch from pre-screened to screened patients was lower in Bergamot, raising interesting questions that need to be addressed, and in phase with the results reported by Harris et al.[1]. We therefore demonstrated a significant increase in patient recruitment in IBD clinical trials, with randomization rates twice to four times higher in equipped sites compared to non-equipped ones. We work therefore on a similar platform accessible from patients' association web-site (Totem4me) giving to each patient the opportunity to test himself and in case of matching, to be referenced to a site having the ongoing recruitment trial using geolocation. Based on these findings, we believe that such innovative solutions should be extended worldwide to contribute to solve the challenging issue of insufficient patient recruitment in IBD and non-IBD clinical trials.

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Abbreviations

CT, Clinical trials; IBD, Inflammatory bowel diseases; UC, ulcerative colitis; CD, Crohn's disease

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