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Letter

Responding to the challenges of international collaborations between the east and the west – report of the first JCOG–EORTC symposium and a perspective from young JCOG and EORTC investigators

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Abstract

International/intercontinental collaboration is necessary to set up new innovative clinical trials for cancer treatment. However, the infrastructure, especially Asia–Europe academic partnerships, to enable such collaboration has not been fully structured and differences and similarities between the research groups have not been well studied. In 2015, collaboration started between the biggest cancer research organizations in Asia and EU, Japan Clinical Oncology Group (JCOG) and European Organisation for Research and Treatment of Cancer (EORTC). Following the first pilot collaboration study, the first scientific symposium took place in December 2017 in Tokyo. Before the symposium, a working visit for EORTC investigators from the Early Career Investigator initiative (ECI), willing to develop projects within the JCOG–EORTC partnership, was held. In addition to the digest of the working visit and symposium, we aimed to describe the differences and similarities between the two groups and to identify key factors for collaboration from the perspective of the young investigators of the networks. These findings are described in this article.

Key words: JCOG–EORTC, ECIs, EORTC fellowship

Introduction

Nowadays international collaborations are strategically important to take up the challenges of modern clinical research such as, but

not limited to, multidisciplinary quality assurance programs and subgroup fragmentation of diseases. Intergroup studies, notably those done between the Europe and North America have changed

practice and/or brought additional knowledge (1–3). Such collaboration between Europe and Asia is essential to allow knowledge development and cross expertise.

Based on this background, since 2015, the Japan Clinical Oncology Group (JCOG) and the European Organization for Research and Treatment of Cancer (EORTC) have been working together to promote partnership in research and to identify strategies for successful collaborations between the East and the West (4,5). The JCOG is the largest multicenter clinical study group for cancer in Japan which is mainly funded by national research grants (6–8). The EORTC is the largest international clinical research organization in the Europe, conducting multidisciplinary clinical trials in all tumor types. The first pilot collaborative study, the EORTC1527/JCOG1609INT/ESSO02 [Diffusion-weighted Magnetic Resonance Imaging Assessment for Liver Metastasis to improve surgical planning (DREAM) (NCT02781935)], has already recruiting patients with colorectal liver metastases since 2016 (9,10).

As part of this effort, the first JCOG–EORTC Clinical Research Symposium was held in Tokyo in December 2017. The purpose of this symposium was to deepen the mutual understanding about the current perspectives of both cooperative groups and strengthen this initiative to promote further collaborative projects. Common scientific strategies and unmet needs that could be translated into potential clinical trials were discussed at the meeting. This symposium was linked with the Early Career Investigator initiative (ECI), which provided an opportunity of travel grants for young EORTC investigators willing to develop projects within the JCOG–EORTC partnership. This was a unique opportunity to motivate the young investigators to come up with new collaboration projects.

In this article, as well as the digest of the symposium, and the site visit of ECIs and EORTC visiting Japanese medical fellows, the differences and similarities between the two groups are assessed, including key factors for successful collaboration.

Digest of JCOG–EORTC symposium

In the two-days meeting, several topics were discussed from both the JCOG and EORTC side, respectively. On Day 1, the overview and experience of international clinical trials in both groups were discussed. It was identified that both academic cooperative groups have similar structures, moreover the flexible EORTC structure implementing international clinical trials was presented. Details regarding structures in both groups have been described elsewhere (5). At the end of the session, the results of surveys sent to key JCOG and EORTC investigators were presented and indicated that, despite the existing challenges, the majority of investigators in both territories are supportive of international collaboration. The result of surveys will be published in another report. Next, translational research infrastructures were also discussed to find ways for future collaborations. In both JCOG and EORTC, unique biobanking infrastructures, JCOG biobank system and SPECTA platform as well as internal Advisory Committee for translational research, have already been incorporated. Although there are still some challenges for collaboration to overcome, such as shipping of materials and regulatory matters, it has been agreed that it is already time to start working on collaborative translational research using the materials each group already has.

On Day 2, the similarities and differences were discussed from the statistical point of view. Two educational topics were presented from each group; Adaptive design from EORTC and statistical

measures for time-to event from JCOG. Then standard statistical methodology was compared and discussed. Discussion topics were; one-sided test vs. two-sided test in superiority setting, timing of event for progression free survival, policy for interim analysis and population for analysis (Intent to Treat vs. per-protocol). It has been concluded that differences of statistical methodology in each group were minor and they were basically similar. Afterwards strategies of three disease-oriented groups in JCOG and EORTC (gastrointestinal, lung and brain) and examples of ongoing clinical trials were presented. Lastly, in the panel discussion, the key factors to success for this collaboration were discussed to enable future collaboration. First, it has been agreed that mutual communication such as attendance of disease group meetings in both groups is the first step for collaboration to share common clinical questions and to establish a worldwide network. Second, it has been agreed that there is an urgent need to develop the infrastructure which can facilitate international collaboration. Financial resources to cover the activities such as networking, management of trials, and centralization and quality assurance of human biological material and other type of data such as imaging scans, should be secured. Therefore, it has been agreed that, to achieve these factors, both groups need to assess the feasibility of research questions early on, in terms of financial and regulatory aspects and aim to achieve common solutions. Furthermore, everybody agreed that a good common clinical research question should come first.

The experiences of EORTC ECIs and Japanese EORTC fellows

Research fellowships and site visits by young investigators might be one of the efficient ways to foster reciprocal understanding of each other's culture and research environment. As part of JCOG–EORTC symposium, several ECIs were enabled to visit a Japanese cancer center and to attend the symposium. ECIs were requested to submit the application forms including their research collaboration ideas and winners were selected based on the score of the application forms. The score was given carefully and impartially based on (1) purpose to join this program, (2) passion for collaboration, (3) academic background, (4) quality of idea of collaboration project, (5) experience of collaboration experience and (6) quality of application form, by the JCOG–EORTC steering committee members. Six ECIs were selected and visited Japanese hospitals for 3–4 days. During their visits, they discussed similarities and differences between their hospital and the Japanese visit hospital. A medical oncologist and a pulmonologist from the EORTC lung group who visited the thoracic oncology division in National Cancer center Hospital, Tokyo, mentioned the higher incidence of early stage cancer in Japan compared to Europe. They also mentioned genomic differences as Epidermal Growth Factor Receptor (*EGFR*) mutated lung cancer is more common in Japan. Furthermore, differences in drug metabolism in Japanese and Caucasians may lead to different standard drug doses and other adverse events. Regarding radiotherapy, a young radiation oncologist from the EORTC radiation group and European Society for Radiotherapy and Oncology (ESTRO) noticed that the patient population receiving radiotherapy is different (30% in Japan and 60% in Europe), probably due to a Japanese focus on surgery and a higher percentage of early disease in Japan due to screening. A young surgeon from EORTC GI group and European Society and Surgical Oncology (ESSO) who visited hepatobiliary and Pancreas division pointed out the difference in the

historical role of surgeons. He mentioned that while in Europe, the medical oncologist has been working closely together with the surgeon, the Japanese surgeons seem to integrate these two disciplines, as clinical oncology remains a fairly 'young discipline' in Japan. These aspects should be fully recognized and considered in a collaboration project.

On the JCOG side, since 2015, three Japanese fellows already experienced the actual clinical trial situation in Europe through an EORTC medical fellowship. Japanese young investigators mentioned that not only scientific aspects, but also operational aspects are needed to understand in collaboration. They said that since Japan is a 'homogeneous' country in many senses, Japanese have to understand the complicated and diverse Europe regulations and difficulty of financial support in pan-Europe clinical trials (5,11,12). It took some time to launch the first pilot trials due to preparation time for translation and contracts. Despite the several differences mentioned, all the ECIs and Japanese EORTC fellows concluded that it is first step to know the differences and similarities between the Europe and Asia for successful EORTC–JCOG collaboration which can affect the practice of all over the world.

Summary and future perspective

The main objective of this exercise was to address the needs for clinical trial collaboration and where Asia can enter in such initiatives. In this symposium, the similarities and differences between the two groups were fully discussed; the two groups are similar in the basic structure of headquarters, translational research infrastructures and standard statistical methodology, but they differ in the standard treatment in some disease groups, the infrastructure facilitating international clinical trials, details of statistical methodology, regulatory process and financial support. These have been addressed in a previous collaboration paper (5). Additionally, during the symposium, it has been agreed that mutual communication should be maintained across disease groups to facilitate development of transversal projects with common scientific questions. This will potentially open more opportunities for collaboration and financing. Both groups need to be vigilant in obtaining alternative sources of funding academic pursuits. Lastly, the working visit by ECIs made us realize that such personal and dynamic interaction across cultures is one of the most effective ways to bridge the gap between the two groups. For young investigators it is easier to come up with clinical questions relevant for both groups when they have the chance to be engaged with experts and mentors and when they are exposed to different working environments early in their career. Furthermore, by giving young investigators opportunities to be involved in the management of clinical trials, they can better understand clinical unmet needs or operational issues across countries. Such knowledge and understanding are critical for a sustainable Asian-European collaboration. An example of the active involvement of an ECI in a clinical trial is in the EORTC lung cancer group which appoints a young investigator for each new trial to manage the clinical trial together with a senior investigator.

Several initiatives are ongoing to further expand the portfolio between JCOG and EORTC. First, the opportunity for further communication has already been prepared. A second JCOG–EORTC symposium related to quality of life has taken place last September 2018. In disease group level, EORTC–JCOG exchange program has been already started. Some Japanese investigators have been invited to the disease group meeting to share their thoughts. Additionally, several Japanese applicants are now under negotiation with EORTC

headquarters for the future EORTC medical fellow. Through these exchange initiatives, the chance to come up with attractive common clinical question will certainly increase. After increasing the opportunity for mutual communication, the next step is to secure the grants. To make this initiative visible, one of the solutions may be to invite fund bodies such as pharma companies to the future symposium for encouraging them to find the value of our collaboration and getting support from them. The advantage of the combined networks of EORTC and JCOG must be used as a leverage to seek for funding and support internationally.

Conclusion

With the working visit and the first joint scientific symposium, several challenges have been identified such as differences in standard treatments and regulatory matters including financial support. However, we have reasons to be optimistic because through a series of these collaborative projects, we found that we have a common vision and mission for practice changing, high quality clinical trials. The field of cancer research is evolving very fast so that academic networks like JCOG and EORTC need to work together to define and direct the future of cancer research. The exchange program, such as ECI program and EORTC fellowship is one of the routes to bridge the gap between the Asia and Europe and to foster the international academic trial platform which helps conducting global intercontinental clinical research smoothly.

Appendix

All authors of this articles are below:

Kozo Kataoka, Orit Kaider-Person, Bernd Kasper, Patrick Starlinger, Carmela Caballero, Jessica Menis, Lizza E. Hendriks, Mitsumi Terada, Laurence Collette, Junko Eba (JCOG Data Center/operations office, National Cancer Center, Japan), Kenichi Nakamura, Denis Lacombe and Haruhiko Fukuda.

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Conflict of interest statement

None declared.

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