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ESTRO 2023 Biology Track – Pre-meeting Course

Making the most of radiation therapy combination strategies

The radiobiology pre-meeting course chaired by Laure Marignol and Ludwig Dubois was aimed to enable participants to understand the challenges of designing clinical protocols that could maximise the benefits of radiation therapy combination treatments for cancer patients. The course could also have been called "How to increase the effectiveness of radiotherapy". The aim was not to catalogue new or existing techniques but to question how these techniques could be used in combination with various tools to help us to take better care of patients suffering from cancers. The tools that were considered were artificial intelligence (AI), biological biomarkers and radiation dose optimisation. The course ended with a concrete example of a de-escalation strategy that could be used to treat human papilloma virus (HPV): the statistical analysis of radiation-drug interaction.

One major current theme is the integration of AI into the clinical routine. This topic was addressed first by Heiko Enderling, who considered the development of mathematical models that are based on the interactions of a tumour with its immune environment. He spoke about clinical trials that had investigated how tumour-immune interactions could be combined with treatment adaptations that were based on mathematical models. However, input data such as clinical and/or biological data are required before such treatments can be used, as AI and mathematical modelling rely on such data to function.

The development of biomarkers was discussed by Anna Dubrovska as a key issue in radiotherapy treatment not only to reduce the toxicity caused to healthy tissue but also to define the radiosensitivity of the tumour. Biomarkers associated with physiological processes that are linked to cancer can be used as diagnostic, prognostic, or predictive tools. The combination of biological information with clinical and pathological parameters of patients in the form of models that are based, for example, on fluid biopsies can help to explain the heterogeneity of treatment responses and may enable improved stratification of patients.

Another strategy that has been proposed as a method to improve patient stratification is the use of imaging, in particular PET or MRI, to better identify radioresistant tumours. A demonstration of tumour hypoxia signatures was a good example of what these new strategies could bring to radiation oncology. However, as Daniela Thorwarth pointed out, very few studies have been performed to investigate the use of these imaging markers as prognostic labels for the improvement of radiotherapy. Karl Butterworth then explained that the development of biomarkers, whatever their nature, could not be achieved without the use of pre-clinical biological models to test the efficacy and safety of novel drug radiotherapy treatments.

After lunch, the programme made a transition to look at more clinically orientated issues through dose adjustment. Ala Yaromina, Clare Von Neubeck, and Steffen Lock provided an overview of different radiation dose optimisation strategies. Besides describing different radiation modalities such as dose painting techniques, proton therapy, hadron therapy, and dose modelling through the use of tumour control probability and normal tissue complication probability models, they provided insight into evidence of the benefit of dose optimisation strategies.

A concrete application of the combination of these strategies was presented for oropharyngeal squamous cell carcinoma by Sandra Nuyts and Vincent Grégoire. They highlighted the link between the use of biological markers and improved prognoses through their explanation of strategies to radiosensitise HPV-positive head and neck squamous cell carcinomas based on DNA repair proteins as targets. Other strategies to de-escalate treatment intensity that had been tested in clinical trials were presented.

The key aim of treatment through the use of this or that therapeutic strategy is to eradicate the tumour while preserving healthy tissue. This was the nub of the issue, because side effects reduce the quality of patients' lives and can even be life-threatening. It was highlighted by Rob Coppes in the final section of this pre-meeting course.

In conclusion, this course pointed out some possibilities to combine radiation strategies with other treatment tools; however, it also highlighted the gaps in knowledge regarding their application in a clinical routine. These gaps must be addressed in order to design truly adapted radiotherapy protocols.

Sandrine PEREIRA, PhD
R&D director
Neolys Diagnostics
Entzheim, France