Clinical trials under the spotlight

Clinical trials, their results and their implementation were among the hottest topics discussed at the 2019 annual meeting of the European Network for Light Ion Hadron Therapy (ENLIGHT), hosted by the University of Caen (Normandy, France) and the cancer treatment centre, the Centre François Baclesse, of Caen in July. An entire session – session five – was dedicated to a broad discussion of trials that were ongoing in Europe and beyond.

European results and progress were offered from studies at the Heidelberger Institut fur Radioonkologie (HIRO), Germany, known in English as the Heidelberg Institute for Radiooncology, and at the Centro Nazionale di Adroterapia Oncologica (CNAO) or the National Centre for Oncological Hadrontherapy in Italy. A talk on the subject was presented by Roberto Orecchia (CNAO). He provided a thorough and critical overview of the European (Heidelberger Ionen Therapie (HIT), or the Heidelberg Ion Therapy Center, and CNAO) results obtained so far in clinical research, regarding mainly carbon ion therapy. Worldwide, a total of 63 clinical trials have been carried out in carbon ion radiation therapy (CIRT), but 84% were non-randomised. Nearly all of these trials recruited adults only (86%), while one trial (2%) exclusively studied children. So far, most trials have been conducted in Japan (60%), Germany (25%), China (11%), and Italy (2%). One randomised trial (2%) of radioresistant tumours is running collaboratively in France and Italy. Interestingly, the primary endpoint for the majority of clinical trials (51%) was adverse events (13 trials) or toxicity and/or dose response (19 trials), followed by local control in 15 trials (24%), progression-free survival in nine trials (14%), and overall survival in only seven trials (11%). Despite recent international consensus for a model-based approach to particle-beam therapy that includes patient selection, nonrandomised trials based on highly selected patients are inadequate to provide high-level evidence for the efficacy of CIRT that is required to justify the construction of new facilities. Thus, further efforts are needed to facilitate patient accrual to phase III randomised trials, improve collaboration between national and international investigators and to create a registry, to facilitate definitive comparisons.

Roberto Orecchia presents the results of clinical trials in Europe.

Piero Fossati (MedAustron, Austria) spoke regarding **MedAustron development of CIRT and the continuation of proton therapy** (PT), and, based on the time course of this work, he discussed a comprehensive set of clinical programmes mainly based on PT. He gave some details regarding low-grade glioma (PT), prostate (PT), chordomas with a very interesting Bayesian design (CIRT) and pancreatic carcinoma (CIRT). As a whole the MedAustron plan is managing a four-fold portfolio of trials:

i) A "Registry-Study": prospective data evaluation with 90 - 100% recruitment of patients treated at MedAustron;
ii) National disease-specific clinical studies implemented at MedAustron and developed in collaboration with Austrian oncology groups;
iii) Multicentre trial participation with international proton centres; and
iv) Multicentre trial participation with international carbon-ion centres (HIT, CNAO, National Institute of Radiological Sciences in Japan, etc.).

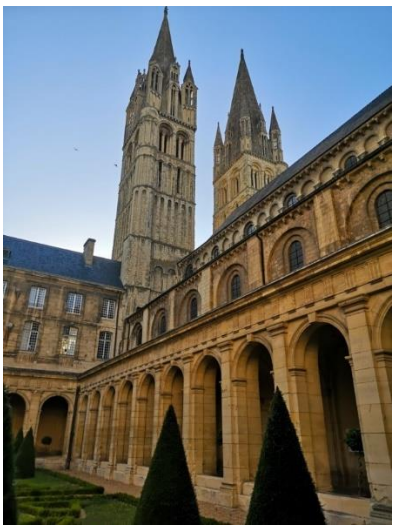
Piero Fossati also shared with the participants the astonishing history of CIRT in treatment of pancreatic carcinoma based on the experience of NIRS and other Japanese centres. Two-year overall survival is reaching 40% to 50%. This compares with the most aggressive chemo-radiotherapy with photons, which hardly obtains about 20%. However, these results are similar to Folfirinox results – notice that the latter can only be achieved for those patients who may tolerate it! He discussed the US National Cancer Institute's call for a project that is issuing a Chinese phase I trial, and the CIPHER project with Texas University in Dallas, US, and the NIRS, activated at the end of May 2019.

Piero Fossati after treating his first patient with carbon-ion in MedAustron in discussion with Robert Orecchia.

In the same sessions, participants could also hear the latest advances of the randomised trial called **PHRC-ETOILE** (France-Italy). Jacques Balosso (Grenoble, Caen, Archade) presented in detail this well-known trial of carbon ion radiotherapy versus photons or proton radiotherapy (PHRC-ETOILE_ULICE), which is a collaboration between Lyon University Hospital and CNAO to set up the first transnational randomised trial for CIRT. It was activated at the end of 2017. About 16 centres in France are contributing to the recruitment of patients who are treated at CNAO when randomised in the CIRT arm. The eligible cases are sarcomas, spine or sacrum chordomas and adenoid cystic carcinoma of head and neck.

A software application for **radiotherapy hypoxia dose painting** was presented by Michaël Gérard (Centre François Baclesse, Archade) replacing a report on the European Particle Therapy Network. This very technical software presentation demonstrated that hypoxia-guided dose painting was possible and would be part of fast-approaching optimisation tools for photon therapy as well as particle therapy, as also shown by Walter Tinganelli (GSI Helmholtz Centre for Heavy Ion Research, Darmstadt, Germany).

The need for randomised clinical trials in particle therapy was stressed by Enrico Clementel (European Organisation for the Research and Treatment of Cancer, EORTC), who offered a very comprehensive presentation on the **role and goals of EORTC.** He specifically discussed all the painful topics regarding the difficulties of obtaining the high level of proof necessary to buy medical devices, as is the case for particle therapy.



The meeting took place in beautiful Caen, where the participants could enjoy the incredible architecture of the city

Find out more about the various presentations and the latest reports on clinical trials at the meeting's website: https://indico.cern.ch/event/783037/timetable/#all.detailed

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