The Fundamentals of Oncology

A clinical focus session dedicated to the fundamentals of oncology placed the procedures performed by interventional radiologists engaged in cancer care into a broader context, and addressed challenges encountered in the pursuit of evidence on the effectiveness and safety of the various therapies used, underscoring the importance of clinical involvement.

Prof. Sandrine Faivre (Lausanne/CH) provided a broad introduction to **conventional chemotherapy**. The main classes of agents involved in colorectal cancer include alkylating agents, which interact with the DNA of tumour cells to impair their proliferation; anti-metabolites, such as 5-FU, which integrate into the DNA molecule; and anti-topoisomerases, which target the DNA's repair enzymes. By contrast, taxanes, a more recent class of agents, interact with microtubules, inhibiting their depolymerisation. The main side effects include myelosuppression, which may manifest as neutropenia, which increases the risk of infection. Prof. Faivre noted that, for advanced colorectal cancer patients, survival rates were limited to six months before chemotherapy was introduced. Today, especially when combined with targeted therapies, survival extends beyond two years. Dr. Faivre also indicated that for chemo-sensitive disease, chemotherapy is the main systemic treatment for advanced stages, and is used as an adjuvant therapy for localised stages after surgery. She also emphasised that chemotherapy effects require radiological evaluation every three months.

Prof. Faivre's second lecture focused on **targeted therapy**, which relies on scientifically designed drugs to block relevant biological tumour targets. For advanced HCC, not considered chemotherapy-sensitive, Sorafenib, a VEGFR-inhibitor, is the only medical therapy approved as a first-line treatment. For liver metastases from colorectal cancer, which is chemo-sensitive, two agents are mainly used in combination with chemotherapy: an anti-proliferative agent (cetuximab) and an anti-angiogenic agent (bevacizumab). The safety profile of targeted therapy differs from that of chemotherapy, with skin and vascular toxicity mainly observed. Complications can include necrosis and bleeding; while rare, this can be potentially severe. Finally, the efficacy of combining targeted therapies with IR techniques (ablation, TACE and RE) has not yet been validated outside of trials, and such an approach does increase the risk of adverse reactions. Additional trials are needed to properly gauge the risks and benefits.




Dr. Eric François (Nice/FR) outlined the **differences between Phase I, II and III clinical trials**. Phase I studies represent the first administration of a new drug (or a new combination of drugs) to humans. In the oncological context, no healthy volunteers are included, and the studies are generally proposed to patients who have no hope of improvement with traditional treatment. The main objective is to determine the recommended dose for future trials. Phase II trials, the most common in oncology, seek to demonstrate sufficient efficacy in specific clinical situations, with an acceptable tolerance profile. Phase III trials, which include both superiority and non-inferiority trials, aim for both tolerance and efficacy. Phase IV studies occur post-approval, and seek to analyse results in real practice, including detecting rare and/or late toxicities. While the scientific level of these trials is not very high, they can provide very useful data for clinical practice.

Prof. Riccardo Lencioni (Pisa/IT) discussed **defining response in interventional oncology trials**, focusing on HCC. The goal of oncological treatments is to improve survival, and, for the past fifteen years, this has been evaluated by means of the RECIST criteria, which focus on tumour shrinkage. This approach does not work in interventional oncology, which induces necrosis, a development not paralleled by changes in tumour size, at least not in the early follow-up stages. Five years ago, modified criteria, known as mRECIST, were implemented. These introduced the concept of a "viable" tumour, and outlined recommendations for image interpretation of HCC in cirrhosis, which involves changes that can result in incorrect determinations of progression. Mostly scrutinised in the context of TACE thus far, mRECIST appears to better capture changes in tumours that have clinically meaningful implications. However, it is still of limited use for purposes of comparing results of clinical trials.

Dr. Riad Salem (Chicago, IL/US) explained **how endpoints in interventional oncology may differ from medical oncology trials**. He outlined the clinical and radiological endpoints generally used for trials involving interventional oncology, noting potential differences between endpoints with local therapies and systemic therapy. He then explained how typical IO endpoints (PFS, local recurrence rate) are defined, and discussed their validity in oncology.

*Presentations are available at **www.esir.org***