centro ricerche cliniche di verona

Centro Ricerche Cliniche di Verona

RECENT ONCOLOGICAL PUBLICATIONS

The CRC is an ideal partner for every aspect of drug development (i.e. development plans, drug dose selection, appropriate pharmacodynamic or effective endpoints, the recruitment of suitable populations, tools to monitor drug safety and tolerability).

Recent Oncological Publications

Genome sequencing studies have shown that TGF-ß is the most mutated signal transduction pathway in pancreatic adenocarcinoma.

Galunisertib (LY2157299) is an orally administered small molecule that inhibits the TGF-ß receptor type 1 (R1) and the downstream signaling pathway.

The clinical data of the use of galunisertib in pancreatic adenocarcinoma derive, in particular, from the H9H-MC-JBAJ study, also conducted at Centro Ricerche Cliniche di Verona (CRC). From the data obtained from this trial it is clear that the use of the TGF-ß inhibitor drug has a favorable activity and an absolutely manageable toxicity profile. The biomarker analysis derived from this study showed that the subgroup of patients who benefit most from the combination treatment of galunisertib + gemcitabine is the one with the highest levels of cytokines involved in the recruitment of macrophages or regulatory T cells (MIP-1α, FOXP3, IP-10).

The use of the TGF-ß inhibitor in the treatment of advanced pancreatic adenocarcinoma was also tested in association with immunotherapy showing an acceptable toxicity profile and favorable anti-tumor activity (H9H-MC-JBEG trial).

The Centro Ricerche Cliniche played an important role in the definition and management of these two clinical trials.

- **Galunisertib plus gemcitabine vs. gemcitabine for first-line treatment of patients with unresectable pancreatic cancer.**
  Melisi D, Garcia-Carbonero R, Macarulla T, Pezet D, Deplanque G, Fuchs M, Trojan J, Oettle H, Kozloff M, Cleverly A, Smith C, Estrem ST, Gueorguieva I, Lahn MMF, Blunt A, Benhadji KA, Tabernero J. Br J Cancer. 2018 Nov;119(10):1208-1214. doi: 10.1038/s41416-018-0246-z. Epub 2018 Oct 15
- **Population pharmacokinetics and exposure-overall survival analysis of the transforming growth factor-ß inhibitor galunisertib in patients with pancreatic cancer.**
  Gueorguieva I, Tabernero J, **Melisi D**, Macarulla T, Merz V, Waterhouse TH, Miles C, Lahn MM, Cleverly A, Benhadji KA. Cancer Chemother Pharmacol. 2019 Nov;84(5):1003-1015. doi: 10.1007/s00280-019-03931-1. Epub 2019 Sep 3. PMID: 31482224
- **TGFß receptor inhibitor galunisertib is linked to inflammation- and remodeling-related proteins in patients with pancreatic cancer.**
  Melisi D, Garcia-Carbonero R, Macarulla T, Pezet D, Deplanque G, Fuchs M, Trojan J, Kozloff M, **Simionato F**, Cleverly A, Smith C, Wang S, Man M, Driscoll KE, Estrem ST, Lahn MMF, Benhadji KA, Tabernero J. Cancer Chemother Pharmacol. 2019 May;83(5):975-991. doi: 10.1007/s00280-019-03807-4. Epub 2019 Mar 18. PMID: 30887178

Approximately 50 percent of intrahepatic cholangiocarcinoma have at least one genetic mutation that drives their growth and may be the target of targeted drugs. Among these mutations, one of the most relevant is that of the Fibroblast Growth Factor receptor, also called FGFR-2 (present in about 15 percent of patients).

Treatment with an FGFR inhibitor drug, pemigatinib, has shown very promising results as a second line treatment (INCB 54828-202) and a randomized trial, that evaluates the same treatment in the first line setting, is ongoing (INCB 54828-302).

The Centro Ricerche Cliniche plays an important role in the conduction of both studies INCB 54828-202 e INCB 54828-302.

- **Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: a multicentre, open-label, phase 2 study.**
  Abou-Alfa GK, Sahai V, Hollebecque A, Vaccaro G, Melisi D, Al-Rajabi R, Paulson AS, Borad MJ, Gallinson D, Murphy AG, Oh DY, Dotan E, Catenacci DV, Van Cutsem E, Ji T, Lihou CF, Zhen H, Féliz L, Vogel A. Lancet Oncol. 2020 May;21(5):671-684. doi: 10.1016/S1470-2045(20)30109-1. Epub 2020 Mar 20. PMID: 32203698