

## How to optimize the effectiveness of anticancer therapy

Hepatocellular carcinoma (HCC) is the most common type of liver cancer. HCC is a public health problem worldwide because of its high incidence and its poor prognosis with high cancer-related mortality. In the majority of cases, patients were diagnosed with HCC with advanced stage and among them, and physician proposed only systemic therapies in this situation. Today, only a single agent (Sorafenib, Nexavar®) is approved for patients with advanced disease. HCC was considered compared to other cancer types an orphan disease regarding validated systemic therapies. Many physicians and pharmaceutical firms tried to find another treatment as effective as sorafenib for patients with HCC. Therefore, many clinical trials have been conducted worldwide to test some drugs in comparison to sorafenib in patients with advanced HCC. The last compound evaluated was an oral agent called, "linifanib." In a large international study, the linifanib was compared to the recommended treatment "Sorafenib." The results of this study showed that linifanib has evidence of efficacy in some patients with HCC (It permits stabilizing cancer for a long time, controlling tumor evolution and for some patients it reduces tumor size). Unfortunately, the linifanib failed to improve the overall survival of these patients, unlike sorafenib.

We have some comments and explanations regarding these negatives results. In this study, the linifanib showed a high proportion of toxicities including hypertension, cutaneous toxicities. The physicians have to reduce the dose of the treatment or to stop it in a high proportion of patients. We believe that the dose chosen for this study was not so good for these patients. In fact, we consider that every patient is different and instead of the fixed dose, a dose calculated according to the patient's body weights should have been proposed. Usually, patients with cancer lose their skeletal muscle mass, called "sarcopenia", over the time and toxicities of treatment may increase in such situation.

In some patients, linifanib can handle the appearance of ascites and some neurological disorders. These symptoms are serious in patients with cancer developed on cirrhosis. The treatment should be stopped under these conditions and, therefore, the benefit of the treatment may be less.

The linifanib was not effective for HCC, in a part because of the high exposure of patients to the fixed dose chosen for the study (They have a low body mass index, a low skeletal muscle mass, and the liver do not normally work because of cirrhosis).

The physician could be aware of these concepts when they conduct clinical studies for patients with HCC, and we advise to pay attention to the behavior of drugs in the organism and to study it carefully in this population of patients.

### Publication

[Negative Trials for Foreseeable Safety Reasons in Advanced Hepatocellular Carcinoma: How Long Are We Going to Take Lightly Pharmacokinetics of Tyrosine Kinase Inhibitors?](#)

Bouattour M, Rousseau B, Wassermann J, Payancé A, Huillard O

*J Clin Oncol. 2015 Aug 1*