



- Hepatic resection and liver transplantation have been considered the treatments of choice for curative purposes. However, fewer than 40% of patients are suitable candidates for surgery, and the rate of recurrence after curative surgery is high.
- Chemoembolization and ablation techniques such as radiofrequency, microwave ablation or cryoablation are currently being considered as potential effective local treatments in patients with HCC smaller than 3 cm in diameter. However, the antitumor efficacy drops drastically with bigger tumors
- Irreversible electroporation (IRE), a soft tissue ablation technique based on the administration of electric fields to create permanent nanopores in the cell membrane and induce tumor cell death, is being considered as an alternative ablative therapy for tumors located close to vital structures.
- Clinical trials have shown that IRE is safe but still inefficient for long-term control of disease. Thus, further development is needed for a better long-term control of tumor growth.
- The lack of long-term efficacy of this technique might be due to its poor capacity to induce an adequate inflammatory reaction that might favor the induction of an anti-tumoral immune response
- IRE ablation may cause the release of tumor-specific antigens. However, it does not induce a favorable inflammatory condition to facilitate DC maturation and thus, tumor antigen release is not adequately exploited to induce an anti-tumor immune response.
- In this scenario, we proposed a therapeutic strategy based on the combination of intratumoral injection of the immunogenic adjuvant Poly-ICLC (a dsRNA analog mimicking viral RNA) followed immediately by IRE in the same zone of the adjuvant administration.
- **1st Indication:** Non-resectable hepatocellular carcinoma (with single or multiple tumor lesions)
- **Other Indications:** Non-resectable solid cancers.

## Approach

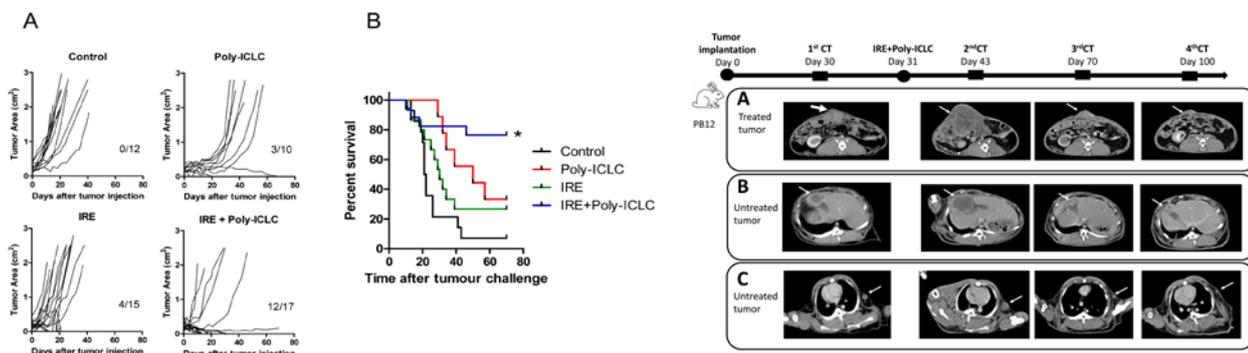
- Improvement of the anti-tumor effect of the irreversible electroporation technique by combining it with the injection of an immunological adjuvant to prime the induction of an anti-tumor immune response. Proof of concept in models of hepatocarcinoma in mice and in rabbits.

## Key concepts

- Irreversible electroporation (IRE) in combination with a Poly-ICLC adjuvant has a therapeutic effect in a murine model for hepatocellular carcinoma.
- IRE in combination with a Poly-ICLC adjuvant has a therapeutic effect in rabbits bearing hepatocellular carcinomas.

## Validation

- Irreversible electroporation (IRE) in combination with a Poly-ICLC adjuvant has a therapeutic effect in animal models for hepatocellular carcinoma.



**Treatment of Hepa.129 tumor cells by irreversible electroporation plus Poly-ICLC.** Mice were challenged with Hepa.129 tumor cells s.c and at day 7-10, when tumors reached 5 mm in diameter, they were treated i.t. with Poly-ICLC, irreversible electroporation (IRE, 2500v), by the combination of IRE plus Poly-ICLC or left untreated (control group). \*, P < 0.05.

**Follow up of tumour growth in rabbits.** Rabbit PB12 presented a liver tumour (Panel B) with extrahepatic dissemination (abdominal wall (Panel A) and axillary node (Panel C)). The lesion located in the abdominal wall (Panel A) was treated with IRE plus poly I: C, whereas the intrahepatic lesion (B) and the axillary nodes (C) were left untreated.