



HAL
open science

**RADIOLOGICAL AND PATHOLOGICAL RESPONSE
TO NEOADJUVANT NIVOLUMAB IN PATIENTS
WITH BCLC A HCC TREATED BY CURATIVE
PERCUTANEOUS IRREVERSIBLE
ELECTROPORATION: PRELIMINARY REPORT
FROM THE FRENCH MULTICENTRE PHASE 2
NIVOLEP TRIAL.**

Pierre Nahon, Olivier Seror, Frederic Oberti, Solohaja Faniaha Dimby,
Christophe Aube, Jean-Frederic Blanc, Herve Trillaud, Philippe Merle, Agnès
Rode, Eric Assenat, et al.

HAL Id: hal-03903631

<https://hal.science/hal-03903631>

Submitted on 20 Feb 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

► **To cite this version:**

Pierre Nahon, Olivier Seror, Frederic Oberti, Solohaja Faniaha Dimby, Christophe Aube, et al.. RADIOLOGICAL AND PATHOLOGICAL RESPONSE TO NEOADJUVANT NIVOLUMAB IN PATIENTS WITH BCLC A HCC TREATED BY CURATIVE PERCUTANEOUS IRREVERSIBLE ELECTROPORATION: PRELIMINARY REPORT FROM THE FRENCH MULTI-CENTRE PHASE 2 NIVOLEP TRIAL.. ILCA Annual Conference, 2020, Sep 2020, Bruxelles, Belgium. hal-03903631

Radiological and pathological response to neoadjuvant Nivolumab in patients with BCLC A HCC treated by curative percutaneous irreversible electroporation: preliminary report from the NIVOLEP trial (NCT03630640)

Pierre Nahon¹, Olivier Seror¹, Frédéric Oberti², Solohaja Faniaha Dimby^{3,4}, Christophe Aubé², Jean-Frédéric Blanc⁵, Hervé Trillaud⁵, Philippe Merle⁶, Agnès Rode⁶, Eric Assenat⁷, Boris Guiu⁷, Mohamed Bouattour⁸, Zohra Talib³, Annick Tibi⁹, Julien Calderaro¹⁰, Marianne Ziol¹, Eric Vicaut³

¹APHP Avicenne, Bobigny, France, ²CHU Angers, ³APHP Fernand Vidal, ⁴SAMM (EA 4543), Université Paris 1 Panthéon Sorbonne, PARIS, France, ⁵CHU Bordeaux, ⁶CHU Lyon, ⁷CHU Montpellier, ⁸APHP Beaujon, ⁹APHP Ageps, ¹⁰APHP Henri Mondor

Email: pierre.nahon@aphp.fr

Background and Aims: Irreversible electroporation (IRE) is a percutaneous ablation which induces tumour cells apoptosis. It has been shown to be safe and effective for curative ablation of HCC located near vascular or biliary trunks. The preservation of the tumour microvasculature and extracellular matrix favours infiltration by anti-tumoral immune cells. Given these immunomodulatory changes, neoadjuvant and adjuvant immunotherapy might act in synergy with this non-thermal ablative technique to improve HCC curative management.

Method: The NIVOLEP trial is a French multicentre (n=6) phase 2 trial aimed at recruiting 50 patients with BCLC A HCC eligible for IRE and high-risk of recurrence (single lesion >3 cm or multiple). Patients consecutively received: 1) 2 neoadjuvant Nivolumab infusions (every 15 days); 2) curative IRE procedure; 3) 12 adjuvant Nivolumab infusions (every 30 days) during one year. All HCC nodules were biopsied at inclusion then during IRE procedure to assess neoadjuvant Nivolumab impact on tumour biology. The present data report preliminary results of the neoadjuvant phase in the first 20 included patients as assessed by sequential radiological and pathological examination before and after 2 Nivolumab infusions.

Results: 37 HCC nodules (uni-nodular 9, bi-nodular 5 and tri-nodular 6 patients, mean size: 31.4 mm) in 20 patients (mean age 69 yrs, males 90%, cirrhosis: 70%, baseline AFP: 56 ng/mL, AFP >50ng/mL: 10%) were considered. No Grade 3 or 4 adverse events related to Nivolumab infusions were reported. Following neoadjuvant Nivolumab, radiological response defined by an objective reduction in nodule(s) size(s) was observed in 11 (29%) (complete response in 0 nodules). One patient experienced progression and was ineligible for IRE. The 19 other patients underwent successful curative IRE procedure. Among these 37 nodules, 17 paired pre- and post neoadjuvant Nivolumab HCC biopsies from 15 patients were analyzed. Pathological response pattern was observed in 3/17 nodules (17%), characterized by tumor regression, replaced by fibrosis with mixed inflammatory infiltrate including foamy macrophages and heavy peritumoral and intratumoral lymphocyte infiltration. These 3 nodules also had radiological response. Additionally, significant increase of peritumoral and intratumoral infiltrating lymphocytes, without evidence of tumor regression zone were observed in 4 other nodules. Overall, 9/17 (53%) had either radiological or pathological modification following Nivolumab infusion.

Conclusion: Neoadjuvant Nivolumab in BCLC A HCC patients eligible for IRE was safe and did not delay ablation procedure. Induced radiological and pathological changes were reported in a substantial number of patients suggesting antitumoral and/or immunomodulation effect of neoadjuvant immunotherapy for liver cancer. **NCT03630640**

Figure:

