# Combination Studies

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# NANORAY-1100: A phase I study of NBTXR3 activated by radiotherapy in patients with advanced cancers treated with anti-PD-1 therapy.

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**Abstract**

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**Background:** Most cancer patients present resistance to immune therapy; only approximately 15% of patients respond to immune checkpoint inhibitors (ICI). Strategies able to increase ICI response are thus of great interest. Radiotherapy (RT), by acting as an immunomodulator is a good candidate to increase the proportion of ICI responders. However, RT dose and ultimate efficacy are limited by potential toxicity to healthy tissues. NBTXR3, a first in class radioenhancer administered by intratumoral injection, has been designed at the nanoscale to increase RT energy dose deposition within the tumor. The result is increased radiation-dependent tumor cell killing, without increasing radiation exposure of healthy tissues. Preclinical and early clinical data suggest NBTXR3 activated by RT can increase the anti-tumor response yielding both local and systemic (abscopal) effects. We hypothesize that NBTXR3 activated by RT, in combination with anti-PD-1 therapy (R3/RT/PD-1), will act synergistically to maximize the local RT effect while also producing a systemic effect sufficient to increase the proportion of ICI responders or convert ICI non-responders to responders. **Methods:** NANORAY-1100 [NCT03589339] is a multicenter, open-label, phase 1 study to evaluate safety and tolerability of R3/RT/PD-1 in three cohorts: (1) Locoregionally recurrent or recurrent and metastatic head and neck squamous cell carcinoma (HNSCC) amenable to re-irradiation of the HN field, (2) Lung metastases from any primary cancer eligible for anti-PD-1, or (3) Liver metastases from any primary cancer eligible for anti-PD-1. Approximately two-thirds of each cohort will be composed of anti-PD-1 non-responders. NBTXR3 injection volume is based on a percentage of gross tumor volume (GTV) determined by central review. The primary objective is to determine R3/RT/PD-1 RP2D. Secondary objectives are to evaluate anti-tumor response (objective response rate; ORR) of R3/RT/PD-1, safety and feasibility of NBTXR3 injection, and NBTXR3 body kinetic profile. Exploratory objectives will assess biomarkers of R3/RT/PD-1 response, including PD-L1 status by IHC, mRNA and cytokine immune marker profiling. Clinical trial information: NCT03589339.



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