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### DW-MRI Guided Dose Escalation Improve Local Control of Locally Advanced Nasopharyngeal Carcinoma treated with Chemoradiotherapy

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**Purpose/Objective(s):** We aim to investigate the feasibility and efficacy of dose escalation guided by DW-MRI in locally advanced NPC.
**Materials/Methods:** 230 patients with locally advanced NPC treated with IMRT at Sichuan cancer hospital between January 2010 and January 2015 were enrolled in this retrospectively study. All the patients were treated with all-course of simultaneous integrated boost-IMRT. DW-MRI guided dose escalation with 2.2-2.5Gy/F, q.d. for 1-3 days or 1.2-1.5Gy/F, bid for 1-3 days were prescribed to 123 patients. Survival and complication of the patients were evaluated and multivariate analysis was performed.
**Results:** The median follow-up of patients in the DW-MRI guided dose escalation group and the conventional group were 48 months (range 8-88 months) and 52 months (range 6-90 months) respectively. The 5-year OS, DMFS, PFS and LRFS of patients in the dose-escalation group and the conventional group were 88% vs 82.5% ($p = 0.244$), 86.1% vs 83.3% ($p = 0.741$), 82.2% vs 76.6% ($p = 0.286$) and 89.1% vs 80.1% ($p = 0.029$) respectively. Multivariate analysis showed that dose escalation was independent prognostic factor for LRFS (HR 0.386, 95% CI 0.163-0.909, p = 0.03).
**Conclusion:** DW-MRI guided dose escalation is a feasible strategy to improve local control of locally advanced NPC patients. The treatment-related complications were tolerable.
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## 3985

### NBTXR3 Radiation Enhancing Hafnium Oxide Nanoparticles Activated By Radiotherapy In Combination With Anti-PD-1 Therapy: A Phase I Study

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**Purpose/Objective(s):** Immune checkpoint inhibitors (ICIs) are being increasingly used to improve patient outcomes across different cancer types. However, the response rate to ICIs remains low (~15%), indicating the need for novel strategies to improve treatment outcome. Emerging evidence suggests that radiation therapy (RT) could potentially enhance the antitumor response and provide synergy with ICIs. RT dose and ultimate efficacy are however limited by toxicity related to exposure of healthy tissues. The first-in-class radioenhancer NBTXR3, administered by direct intratumoral injection, is designed at the nanoscale to increase RT dose deposition within tumor cells and RT-dependent tumor cell killing, without increasing toxicity to surrounding normal tissue. Preclinical and early clinical data suggest NBTXR3 activated by RT can trigger an anti-tumor immune response, producing 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 and produce a systemic response sufficient to increase the proportion of ICI responders or convert ICI non-responders to responders.
**Materials/Methods:** This multicenter, open-label, phase I trial [NCT03589339] will evaluate safety and tolerability of R3/RT/PD-1 in three cohorts: (1) Locoregional recurrent or recurrent and metastatic head and neck squamous cell carcinoma (HNSCC) amenable to re-irradiation of the HN field, (2) Lung metastases, or (3) Liver metastases, both from any primary cancer eligible for anti-PD-1 treatment. Approximately two-thirds of patients in each cohort will be anti-PD-1 non-responders. NBTXR3 injected volume is based on a percentage of baseline gross tumor volume (GTV).
**Results:** The primary objective is to determine the R3/RT/PD-1 recommended phase 2 dose in each cohort. Secondary objectives are to evaluate anti-tumor response (objective response rate; ORR), 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, as well as mRNA and cytokine immune marker profiling. Recruitment is ongoing. To date, three patients have been treated, one in cohort 1 and two in cohort 2.
**Conclusion:** NBTXR3 activated by RT induces an anti-tumor immune response which may convert immunologically "cold" tumors into "hot" tumors. In combination R3/RT/PD-1 holds the potential to increase the proportion of ICI responders or convert ICI non-responders to responders.
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### Radiation Treatment Breaks: Are They Detrimental to Outcomes for Oropharyngeal Carcinoma Treated with Definitive Chemoradiation?

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**Purpose/Objective(s):** Varying practices exist to account for radiation treatment breaks (rTBs) resulting from institutional holidays during treatment of oropharyngeal squamous cell carcinoma (OPSCC) cancer patients undergoing concurrent chemoradiation (CRT). Studies in radiation biology suggest that local therapy delays may result in accelerated repopulation of residual tumor cells, however the clinical effects of this model in the setting of concurrent systemic therapy are unclear. We, therefore,