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Relationship between Cannabis Use and Opioid Use in Patients with Cancer Metastatic to Bone in a Large Multicenter Cohort from a State with Legalized Adult Non-Medical Cannabis

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Purpose/Objective(s): Patients with cancer who use cannabis frequently note pain as a reason for their cannabis use. Available data do support cannabis use for management of pain in some settings, though the effectiveness of cannabis for cancer-associated pain is less clear. Based on limited data, some have suggested that cannabis might be used as an alternative to opiates for management of cancer-related pain. We sought to determine the relationship between cannabis use and opioid use in a multicenter cohort of patients undergoing radiotherapy for bone metastases.

Materials/Methods: On January 1, 2021, questions about cannabis use were added to Michigan Radiation Oncology Quality Consortium (MROQC) questionnaires for bone metastasis patients. Pain scores, opioid use, social, demographic, and disease characteristics were also prospectively collected. A multivariable model using logistic regression identified associations between recent cannabis use and opioid use, accounting for relevant patient and disease characteristics.

Results: Since questions on cannabis were introduced, 2,096 patients have been enrolled. A total of 1143 of 2096 (54.5%) completed questionnaires about recent cannabis use; 1912 of 2096 (91%) completed questionnaires about current opioid use; and 1064 of 2096 (51%) completed both. Among those who completed both, 132 of 1064 (12%) reported recent opioid and cannabis use, 320 of 1064 (30%) reported recent opioid but not cannabis use, 57 of 1064 (5%) reported no recent opioid but recent cannabis use, 281 of 1064 (26%) reported no recent opioid or cannabis use, and the remaining individuals (274/1064 [26%]) declined to answer cannabis use questions by selecting "decline to answer". In a multivariable model, cannabis use [OR = 2.11 (95% CI = 1.37, 3.26) $P = 0.001$], along with pain score [Score 1-3 vs 0, OR = 2.32 (95% CI = 1.36, 3.94); Score 4-7 vs 0, OR = 6.55 (95% CI = 4.06, 10.6); Score 8-10 vs 0, OR = 11.20 (95% CI = 6.32, 19.8), $P < 0.001$], NSAID use [OR = 1.66 (95% CI = 1.17, 2.37) $P = 0.005$], prior systemic therapy [OR = 0.54 (95% CI = 0.37, 0.78) $P = 0.005$], and number of metastatic lesions [3-5 vs 1-2, OR = 1.57 (95% CI = 0.95, 2.26); 5-10 vs 1-2, OR = 1.54 (95% CI = 0.91, 2.59); 11+ vs 1-2, OR = 3.26 (95% CI = 2.06, 5.15) $P < 0.001$] predicted opiate use while age, gender, and race did not.

Conclusion: Patients with bone metastases frequently use cannabis, opioids, or both. Though it has been suggested that cannabis availability might reduce opioid use among patients with cancer, our finding that cannabis use predicts opioid use does not support this hypothesis. These data suggest a more complex relationship between cannabis use and opioid use in this population. Further study is needed to assess risks of concurrent cannabis and opioid use and to explore patient rationale for concurrent usage.

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Time-Synchronized Immune-Guided Partial Tumor Irradiation: Proof-of-Principle Trial (NCT04168320)

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Purpose/Objective(s): Partial tumor irradiation (PTI) is a novel immunomodulatory concept which adds to the direct cell-killing radiation effects an additional component of immune-mediated tumor cell-killing. PTI consists of 3 key principles: (1) neutralizing the immunosuppressive, central hypovascularized, and hypometabolic tumor segment, (2) preserving the peritumoral immune microenvironment (PIM) as OAR, and (3) delivering the treatment at precisely planned times, individually tailored for each patient based on homeostatic oscillations of immune activity (time-synchronized immune-guided radiotherapy). We hypothesized that PTI would generate radio-immunogenic effects thereby enhancing patient prognosis. The primary endpoint: bystander and abscopal responses rate.

Materials/Methods: This is a mono-centric, prospective, two-arm, phase 1 proof of principle trial including 22 patients with complex unresectable bulky tumors and at least 1 untreated metastatic site, deemed unsuitable for standard radiotherapy experiencing disease progression despite systemic therapies. Hypovascularized and hypometabolic tumor segment, delineated using the c.e. CT and FDG-PET-CT, was targeted with 10 Gy x 3 at 70% sparing the PIM. 2 weeks prior PTI, each patient had 7 serial blood draws assessing CRP, LDH and lymphocyte/monocyte ratio to determine each patient's idiosyncratic immune activity cycle. First 11 patients (arm 1) PTI was delivered at an estimated "less reactive day" and to last 11 patients (arm 2) at "most reactive day." In selected patients, residual tumors, radiation-spared PIM and unirradiated abscopal tumor sites were surgically removed for immunohistochemistry (IHC) and cell-death inducing genes (CDIG) analysis.

Results: PTI exhibited significant radio-immunogenic effect (Tab. 1). Arm 2 demonstrated superior outcomes across nearly all treatment aspects. A higher proportion of long-term survivors were from arm 2 (55%, median follow-up of 54 months) compared to arm 1 (27%, median follow-up of 43 months). IHC and CDIG revealed significant anti-tumor-directed-activation of the immune system.