Cannabis and Cannabinoid Use in Adult Patients During Active Cancer Treatment: Assessing Benefits and Harms

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On behalf of The Trans-NCI Cannabis and Cancer Research Interest Group (CCRIG)
## The Cannabis and Cancer Research Interest Group (CCRIG)

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- **Jeffrey White**
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Purpose of RFA

- There is a need for rapid infusion of multiple studies addressing cannabis and cannabinoid use:
  - Rapidly increasing availability and use of cannabis
  - Lack of available evidence base
  - Challenges to mounting clinical trials due to federal regulatory issues

- To support observational research studies to assess the benefits and harms of cannabis and cannabinoid use among cancer patients in active treatment
  - Provide evidence of the benefits and harms
  - Information required for future clinical trials
Definitions

Cannabis or cannabinoids refers to

- Cannabis plant (e.g., Marijuana)
- Cannabis-derived products / Cannabinoids
  - THC, CBD-only products
  - Prescription Cannabinoids (e.g., Dronabinol, Marinol, Syndros, Nabilone, Cesamet)
- Any other products made with or derived from cannabis

* For ease of this presentation, the term “cannabis” will be used to refer to “cannabis and cannabinoids”
Legal Landscape of Medical and Non-medical Cannabis Use
As of May 2022

- 37 states and DC: legalized cannabis for medical conditions
Available Delivery Methods

**Oral**

- Edibles, Drinks, Gum, Tincture, Pills, Ingestible Oils

**Inhalation (Smoking, Vaporizers)**

- Water Pipe, Joint, Dabs, Blunt, Vapes

**Topical**

- Spray, Cream, Patches, Bath Soaks
Reason for cannabis use among the survey respondents

24% (222/926) of cancer patients used cannabis to manage symptoms

# Potential Interaction Between Cannabis and Immunotherapy

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Population</th>
<th>Cancer Type</th>
<th>Immunotherapy Drug</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taha et. al. (2019)</td>
<td>140 patients</td>
<td>Advanced melanoma, non-small cell lung cancer, and renal clear cell carcinoma</td>
<td>Nivolumab</td>
<td>Decreased Response Rate</td>
</tr>
<tr>
<td>Bar-Sela et. al. (2020)</td>
<td>102 patients</td>
<td>Advanced-stage malignancy</td>
<td>Nivolumab, Ipilimumab, Durvalumab, Atezolizumab, Pembrolizumab</td>
<td>Decreased Time to Tumor Progression Decreased Overall Survival</td>
</tr>
<tr>
<td>Biedny et al. (2020)</td>
<td>104 patients</td>
<td>Advanced-stage malignancy</td>
<td>Nivolumab, Pembrolizumab</td>
<td>Decreased Overall Survival</td>
</tr>
</tbody>
</table>
Oncologist's practices and knowledge on medicinal cannabis

**Can it help?**
- Do studies show that cannabis can improve my symptoms?
- Can cannabis help to treat my cancer?

**Is it safe?**
- What are the risks of using cannabis?
- Is cannabis safe to use with opioids?

**Is it available?**
- What are the laws and in my state?
- What types of products are available?

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**Graph:**
- **Discussed with patients:** 79.8%
- **Recommended in the past year:** 45.9%
- **Sufficiently knowledgeable:** 29.4%

*(Braun, I.M., et al., J Clin Oncol, 2018)*
Knowledge Gaps

- How and why cancer patients are currently using cannabis?
  - Mode, dosage, frequency, and product type

- What are the benefits and harms of cannabis use among cancer patients associated with:
  - Cancer and its treatments
  - Comorbidities
  - Other medications (prescribed, complementary, and alternative medicines)
Purpose of RFA

- To support observational research studies to assess the benefits and harms of cannabis and cannabinoid use among cancer patients in active treatment

- NCI is seeking well-designed prospective cohort studies of cancer patients with solid or hematologic tumors, currently receiving treatment, comparing those using with those not using cannabis and cannabinoids
RFA Key Research Questions

- What adverse effects of cannabis and cannabinoid use are observed in cancer patients?

- How is cannabis and cannabinoid use, including dose, frequency of use, and different types and sources of cannabis and cannabinoid products associated with improving cancer patients’ symptoms?

- How is cannabis and cannabinoid use associated with cancer patients’ use of medications to manage symptoms from their cancer or cancer-related treatments?
RFA Key Research Questions (Cont.)

- What mitigating or enhancing effects of cannabis and cannabinoid use are observed in cancer patients with regards to cancer therapies and medications used for symptom management?

- What are the biological effects of cannabis and cannabinoid use during cancer treatment?
Cannabis/Cannabinoid Use
Demographics
Clinical and disease characteristics
Co-morbidities

Date of Diagnosis

Cannabis/Cannabinoid use and patterns

Cancer therapies and concomitant medications

Potential Outcomes:
• QOL
• Symptoms
• Medication reductions
• Adverse Events
• Survival Outcomes
• Biomarkers of effect (e.g. liver, kidney, inflammatory markers)

Symptom surveys
Biological specimens (e.g. blood)
Justification for RFA and Cooperative Agreement

- No awarded grants on the harms and benefits of cannabis and cannabinoid use in cancer patients
- Urgent need to collect this information to inform clinical trials
- Ensure diverse populations across different U.S. states, care settings, cancer sites, stages, and outcomes
- Substantial program involvement to enhance research collaborations across studies through sharing surveys, data and resources
- Specialized scientific review with expertise in the clinical epidemiology of cannabis and cannabinoid cancer research
RFA Mechanisms

- FY 2023:
  - 4 U01 grants (5 years)
  - 1 U24 Coordinating Center (5 years)
## Proposed Budget

<table>
<thead>
<tr>
<th></th>
<th>FY 23</th>
<th>FY 24</th>
<th>FY 25</th>
<th>FY 26</th>
<th>FY 27</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Costs U01 grants</strong> (4 grants)</td>
<td>$3.3M</td>
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<td>$3.3M</td>
<td>$3.3M</td>
<td>$16.5M</td>
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<tr>
<td><strong>Total Costs U24 grant</strong> (1 Coordinating Center)</td>
<td>$800,000</td>
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<td>$800,000</td>
<td>$800,000</td>
<td>$4.0M</td>
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<tr>
<td><strong>Total Costs</strong></td>
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<td><strong>$4.1M</strong></td>
<td><strong>$20.5M</strong></td>
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</table>
Clarifications in Response to BSA Subcommittee Feedback

- **Patient Reported Outcomes (PROs):** Emphasize a patient-centered approach, prospective follow-up and PROs will be collected over time.

- **Biological Markers of Effects:** Refers to biological mechanisms of action potentially affecting cancer therapy, such as liver/kidney function and inflammatory markers.

- **Future Clinical Trials:** Funded observational studies can inform relevant endpoints, appropriate patient populations, possible harms, and potential cannabis products, doses and delivery methods to be tested in future trials.

- **Active Treatment:** includes surgical patients as well as those undergoing radiation and/or other systemic adjuvant therapy. Follow-up of patients can extend beyond initial "active treatment" time period.

- **Population Based Recruitment:** SEER and many State registries allows for rapid case ascertainment, in addition to integrated healthcare systems.
Potential Impact

- Assess How And Why Cancer Patients Use Cannabis
- Identify The Benefits And Harms
- Contribute Evidence To Clinicians And Patients
- Provide Information To Design And Conduct Clinical Trials
Recent New Funding Opportunity (FY 2023)

- Notice of Special Interest (NOSI) (NOT-CA-22-085): **Basic Mechanisms of Cannabis and Cannabinoid Action in Cancer**
  - To promote research in understanding the mechanisms by which cannabis and cannabinoids affect cancer biology, cancer interception, cancer treatment and resistance, and management of cancer symptoms
  - Applies to due dates on or after June 5, 2022, and subsequent receipt dates through May 8, 2027
  - R01, R03, R21, K01, K08, K22, K99/00
QUESTIONS?