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The Use of Medical Marijuana in Cancer

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Abstract The use of medical marijuana in cancer care presents a dilemma for both patients and physicians. The scientific evidence is evolving, yet much of the known information is still insufficient to adequately inform patients as to risks and benefits. In addition, evidence-based dosing and administration information on medical marijuana is lacking. Medical marijuana is now legal, on some level, in 24 states plus the District of Columbia, yet is not legal on the federal level. This review addresses the current state of the research, including potential indications, risks and adverse effects, preliminary data on anticancer effects, as well as legal and quality issues. A summary of the clinical trials underway on medical marijuana in the oncology setting is discussed.

Keywords Marijuana · Cannabis · Cancer · Delta-9-tetrahydrocannabinol · Delta-9-THC · Tetrahydrocannabinol · THC · Cannabinoid · Cannabidiol · CBD · Endocannabinoid · Oncology · Dronabinol · Nabilone · Nabiximols

Introduction

Twenty years ago, California became the first state to make the use of cannabis products legal for medical use. On November 5, 1996, Californians approved the Ballot Proposition 215, which removed the state's criminal penalties relating to the medical use, possession, or cultivation of *Cannabis sativa*, (commonly known as "marijuana"), for patients when "deemed appropriate," provided they have "written or oral recommendation or approval of a physician" [1]. The general public has now voted in favor of the comprehensive use of medical marijuana in 24 states plus the District of Columbia, as well as an additional 16 states which have enacted laws allowing the use of "hemp oil," which is low in tetrahydrocannabinol (THC), but high in cannabidiol (CBD). This is a strong message to the medical community advocating for use, yet marijuana itself has not undergone the usual rigorous testing that would ensure safety and efficacy. In addition, medical marijuana lacks quality assurance and does not fall under the guidelines of FDA regulation.

In cancer care, medical marijuana presents a clinical conundrum for the individual physician and the oncology community at large. Many patients and caregivers inquire as to the potential benefit of medical marijuana at some point during the course of their cancer care. Oncology professionals are asked to describe the relative risks and potential benefits of a substance that has been used historically for medical use, as well as recreationally for years, but lacks the level of evidence for medical use that would make such a discussion as routine as providing education on other supportive care options. Patients are using medical marijuana and health care professionals are documenting that use, with questions still arising on how to address potential for adverse effects, drug interactions, dosing, routes of administration, and how to best navigate clinical decision-making.

Summary of Known Pharmacology

Cannabinoids are the active constituents of *C. sativa* and *Cannabis indica* species, mimic the effects of endogenous

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cannabinoids (endocannabinoids), activating CB1 (cannabinoid 1) receptors which exist primarily in the central nervous system and CB2 receptors found predominantly in immune cells [2••]. The cannabinoid receptors are part of the endocannabinoid system which function predominantly in modulating mood, memory, appetite, and pain sensation. There are thought to be approximately 100 cannabinoids in the cannabis plant, as well as about 400 non-cannabinoid compounds that originate from the secondary metabolism of cannabis, which are responsible for its biological activity [2••]. Delta-9-tetrahydrocannabinol, often simply referred to as THC, is the primary active ingredient in cannabis and its main psychoactive component. THC can induce feelings of euphoria, as well as have analgesic, antiemetic, anti-inflammatory, and antioxidant effects [3••]. CBD is one of the major secondary cannabinoids and may modulate THC. CBD has anxiolytic, antipsychotic, as well as anticonvulsive effects [3••].

Potential Indications

Several comprehensive review articles have been written in 2015 on cannabis and cancer. Abrams and Guzman co-authored an article in 2015 that reviews the history of cannabis as medicine as well as cannabinoid pharmacology and discusses the research that has been done on cannabinoids in cancer symptom management [2••]. In addition to the above, Kramer's review article provides summary tables comparing the research to date on effect of smoked marijuana on chemotherapy-induced nausea/vomiting, pain, and appetite/weight loss [3••]. Lastly, Whiting et al. performed a systemic review and meta-analysis of cannabinoids for medical use that included a total of 79 trials and 6462 participants. For symptom management, they found that cannabinoids had moderate-level quality evidence for the treatment of chronic pain. For chemotherapy-induced nausea and vomiting, there was low-quality evidence. Weight gain was evaluated for HIV infection, as there has not been research evaluating cannabinoids for weight gain in oncology patients, and low-quality evidence was found. Sleep disorders were also evaluated in a non-oncology population with low quality of evidence demonstrated [4••].

As mentioned in Table 1 below, several types of cannabis-derived pharmaceuticals are available in the USA and Canada. Dronabinol, which is a schedule III controlled substance, and nabilone, which is a schedule II drug, are approved in the USA, and nabiximols (not US Food and Drug Administration approved) is available in Canada. Table 1 summarizes the potential indications of cannabis in cancer care and includes the information on dose ranges that have been studied.

Risks and Adverse Effects

The short-term adverse effects for smoked cannabis are well described in a recent review by Zhang and Ho (2015) and include the following which may occur approximately 30 min after consumption and usually lasting for 2–4 h: anxiety or agitation, illusions, feelings of depersonalization, hallucinations, paranoid ideation, temporal slowing as well as impaired judgment/attention as well as red eyes, dryness of the mouth, tachycardia, and increased appetite. Of note, cannabis may impact cognition for as much as 5–12 h after smoking. In addition, for consumption in high doses, acute confusion, hypotension, hypothermia, and even psychosis may occur [5]. Oral consumption of cannabis may not cause significant symptoms as the bioavailability is significantly reduced [5]. There is a lack of data overall for oral or mucosal cannabis risks and adverse effects, beyond what is described in the prescribing information for the approved drugs dronabinol and nabilone. The most common side effect for oral administration appears to be fatigue and dizziness [6].

Other adverse effects associated with cannabis include risk of anxiety, depressive disorder, exacerbation of manic syndromes in those with bipolar disorder, increased risk of schizophrenia and psychosis, and cannabis hyperemesis syndrome (a paradoxical effect associated with long-term use) [5]. Additional risks are from potential vascular effects, including cannabis-induced arteritis, posterior circulation stroke, and myocardial infarction [5]. Heavy smoking of marijuana is associated with large airway inflammation and may cause symptoms related to chronic bronchitis; however, occasional use of marijuana does not appear to be a risk factor for chronic obstructive pulmonary disease [7]. Potential metabolic effects include adipose tissue insulin resistance, and there is one case report of pancreatitis [5].

Of note, there is an additional risk for inhaled cannabis. A variety of microorganisms can be present on cannabis leaves and flowers which when inhaled could expose potentially immunocompromised oncology patients to the risk of opportunistic pulmonary infections, primarily from inhaled molds [8].

Metabolism of Cannabis and Potential Drug Interactions

Minimal data is available for cannabis and potential drug interactions. Smoked cannabis may induce CYP1A2 (cytochrome P-450 1A2), although the ability of cannabinoids administered via oral or mucosal routes to specifically provoke this effect is uncertain [9]. There is a lack of human data for THC or CBD inhibition and induction of CYP-450 isoenzymes, but preclinical studies indicate a low risk of clinically significant drug interactions [9].

Table 1 Potential indications of cannabis in cancer care [4••]

Potential indication evaluated	Level of evidence	Intervention	Dose evaluated in studies	Approved drug availability in the USA	Dose evaluated of approved drug
Nausea/vomiting due to chemotherapy	Low	THC	5–60 mg/day (either 1×/day or every 4–6 h)	Dronabinol (synthetic THC)	5–30 mg/day (1–4 doses per day, most common, 2 doses)
				Nabilone (synthetic cannabinoid derivative mimicking THC)	0.5–8 mg (most common dose 2 mg bid)
Chronic pain and spasticity	Moderate	Cannabis	Vaporized 1.29 or 3.53 % concentration: 4 puffs after 1 h then 4–8 puffs after 3 h	None—although nabiximols is licensed for use in other countries	
		THC	Capsules—same dose as above		
			1–5 cigarettes smoked (potency when reported ranged from 2.5 to 9.4 %		
Appetite/weight loss (only studied in HIV/AIDS)	Low			Dronabinol	2.5–10 mg bid
Sleep	Low			Nabilone (nabixomols outside of the USA)	0.5–8 mg (most common dose 2 mg bid)
Anxiety disorder	Very low	CBD (active cannabinoid)	200–800 mg/day capsules	None	None

Summary of Potential Cancer Risk

Smoked cannabis does contain many of the same carcinogens as tobacco; however, marijuana is typically smoked less frequently than tobacco and in smaller quantities. In addition, marijuana is consumed via oral and mucosal routes of administration, which complicates analysis of potential long-term cancer risk as the studies to date have been with smoked cannabis. The most recent studies are summarized below.

In 2013, Callaghan et.al. found initial longitudinal evidence that cannabis use might elevate the risk of lung cancer in a 40-year population-based cohort study using Cox regression analysis with an $n = 44{,}284$. Even after a statistical adjustment for tobacco and alcohol use as well as socioeconomic status and respiratory conditions, a lifetime use of cannabis smoked more than 50 times was found to have more than a twofold risk of developing lung cancer over the 40-year follow-up period (hazard ratio 2.12, 95 % CI 1.08–4.14) [9]. However, the other six studies on risk of lung cancer from cannabis appear to not support an association. This may be due to the relatively smaller amount of marijuana smoked as compared to tobacco, as mentioned above [10].

Cannabis smoking and the incidence of bladder cancer were evaluated by the California Men's Health study cohort in a study published in 2015, which followed a multiethnic cohort of 84,170 men aged 45–69 years for 11 years. Thomas et.al. found that 89 of the cannabis users (which was 0.03 % of the participants) developed bladder cancer as compared to 190 participants who did not report cannabis use ($P < 001$). Interestingly, after adjusting for age, race, or ethnicity, as well as body mass index, those that used cannabis only were associated with a 45 % reduction in bladder cancer incidence (HR, 0.5; 95 % CI, 0.31–1.00). However, using tobacco only was associated with an increased risk of bladder cancer (HR 1.52; 95 % CI, 1.12–2.07) [11].

In head and neck cancer, research on marijuana and cancer risk has been conflicting, with reports on both increased and decreased risk. There are three case-controlled studies showing increased risk for testicular cancer with marijuana use [summary ORs, 1.56; 95 % (CI), 1.09–2.23 for higher frequency and 1.50 (95 % CI, 1.08–2.09) for >/=10 years] [12]. There is inadequate data to draw any conclusions for cancers occurring at other sites.

Potential Anticancer Effects

Recent preclinical studies have demonstrated a number of interesting therapeutic applications of cannabis as a potential anticancer agent. Chakravarti et al. elaborate on the antiproliferative and anti-angiogenic activity that has been identified in vitro as well as in vivo in different models of cancer [13]. Cannabinoids have been shown to play a role in regulating key cell signaling pathways that are involved in cell survival,

invasion, angiogenesis, and metastasis [13]. In the last year, several interesting studies have provided more specific clues as to the potential mechanisms. For example, Orellana-Serradell et al. detected the presence of cannabinoid receptors on prostatic cancer cells and then evaluated the effect of the in vitro use of synthetic cannabis analogues [14]. They found a dose-dependent inhibitory effect, including increasing levels of activated caspase-3 and a reduction in the levels of Bcl-2 confirming activation of apoptosis. In addition, they observed an endocannabinoid-modulated activation of the ERK pathway and a simultaneous decrease in the activation of the AKT pathway [14], suggesting that endocannabinoids may have activity in the treatment of refractory prostate cancer. A recent review by McAllister et al. revealed that CBD has been shown in animal models to inhibit progression of glioblastoma, breast, lung, prostate, and colon cancer [15]. The conclusions of these studies are very preliminary, but indicate a further area of research which may uncover further uses of cannabinoids and/or their synthetic analogues in cancer care as having additional therapeutic benefit.

Legal Issues Surrounding Medical Marijuana

The legal concerns regarding medical marijuana are complex, and the rapidly changing legal and legislative environment around this issue creates the risk that information presented here may be quickly outdated. However, we will attempt to point out key issues physicians need to understand more fully in order to appropriately advise their patients. The primary legal issue is that marijuana (*C. sativa*), THC, and CBD derived from *C. sativa* are all classified as schedule I controlled substances under the federal Controlled Substances Act (CSA) of 1970 and, as such, may not be prescribed for any purpose outside of an appropriately registered clinical trial [16–18]. To be classified under schedule I, a drug or substance must meet the following criteria:

1. The drug or other substances have a high potential for abuse.
2. The drug or other substances have no currently accepted medical use in treatment in the USA.
3. There is a lack of accepted safety for use of the drug or other substances under medical supervision.

Other examples of schedule I substances include the following: heroin, lysergic acid diethylamide (LSD), 3,4-methylenedioxymethamphetamine (ecstasy), and mescaline (peyote).

Much confusion exists as to the differences between marijuana and hemp, which is primarily grown for its fiber, used in textiles, paper, and rope manufacturing. Hemp differs from marijuana in that it is cultivated primarily for its fiber, seed, and oil and therefore employs varieties and cultivars of *Cannabis* sp. most suited to those end uses, and which also have lower THC, and in some cases CBD. All three *Cannabis* spp., *C. sativa* L., *C. indica*, and *Cannabis ruderalis* can be grown for hemp, although due to its shorter height, *C. ruderalis* is less suitable for fiber purposes. However, some strains of *C. ruderalis* are reportedly high in CBD content, while being low in THC content [19]. The American Herbal Products Association employs the following definitions [20]:

Cannabis	Means any of the aerial parts [exposed to air] of a plant in the genus *Cannabis* and does not mean hemp.
Hemp	Means any part of a plant in the genus *Cannabis*, whether growing or not, with a delta-9 tetrahydrocannabinol [THC] concentration of not more than 0.3 (three-tenths) percent on a dry weight basis.

The CSA definition for "marihuana" [sic] as a schedule I substance specifically includes "all parts of the plant *Cannabis sativa* L., whether growing or not" [21]. Since THC is also listed separately in schedule I, a product containing THC derived from any *Cannabis* sp. would be considered a schedule I substance. However, CBD is not listed individually as a schedule I substance, and therefore, many producers of "high CBD/low THC" oils describe their products as "hemp oil" derived from *C. ruderalis*.

Federal law regulates the importation, manufacture, distribution, possession, and improper use of all controlled substances, as well as the transportation of controlled substances across state lines [22]. However, beginning in 1996, a total of 24 states plus the District of Columbia have passed comprehensive medical marijuana laws, and an additional 16 states have enacted "low THC, high CBD" laws [23–25] [see Table 2]. In nearly all of these states, a physician must certify that the patient has a debilitating condition which qualifies under state laws for the use of medical marijuana. These laws typically require a physician to have a bona fide physician-patient relationship with the patient prior to certifying them for medical marijuana use. This is most often described as ongoing responsibility for the assessment, care, and treatment of the patient's debilitating medical condition or a symptom of their debilitating medical condition, and being reasonably available to provide follow-up care. Physicians should be aware that this is a rapidly changing area of the law and would be well advised to seek legal counsel regarding the current status of medical marijuana laws in their state and local jurisdiction.

On October 19, 2009, then, US Attorney General Eric Holder announced formal guidelines for federal prosecutors in states which have adopted medical marijuana laws. These enforcement guidelines, while not changing existing federal law regarding marijuana, did effectively alter priorities for the use of federal investigative and prosecutorial resources.

Table 2 State medical marijuana laws [23–25]

State	Year	Physician responsibility	Unrestricted oncology use	Recognizes patients from other states	Comprehensive quality requirements
Comprehensive laws					
Alaska	1998	Certify Dx and benefit	Yes	No	No
Arizona	2010	Certify Dx and benefit	Yes	Yes	Partial
California	1996	Certify Dx and benefit	Yes	No	Yes
Colorado	2000	Certify Dx and benefit	Yes	No	Yes
Connecticut	2012	Certify Dx and benefit	Yes	No	Yes
Delaware	2011	Certify Dx and benefit	Yes	Yes	Yes
District of Columbia	2010	Certify Dx and recommend	Yes	No	Partial
Hawaii	2000	Certify Dx and benefit	Yes	No	Yes
Illinois	2013	Certify Dx and benefit	Yes	No	Yes
Louisiana	2015	Prescribe	No[3]	No	No
Maine	1998	Certify Dx and benefit	Yes	Yes	Yes
Maryland	2003	Certify Dx and benefit	Yes	Yes	Yes
Massachusetts	2012	Certify Dx and benefit	Yes	No	Yes
Michigan	2008	Certify Dx and benefit	Yes	Yes	No
Minnesota	2014	Certify Dx	No[3]	No	Yes
Montana	2004	Certify Dx and recommend	Yes	No	No
Nevada	2000	Certify Dx	Yes	Yes	Yes
New Hampshire	2013	Certify Dx	No[3]	Yes	Yes
New Jersy	2010	Certify Dx and authorize amount	No[3]	No	Yes
New Mexico	2007	Certify Dx and benefit	Yes	No	Yes
New York	2014	Certify Dx, authorize brand, amount	No[3]	No	Yes
Oregon	1998	Certify Dx and benefit	Yes	Yes	Yes
Rhode Island	2006	Certify Dx and benefit	Yes	No	No
Vermont	2004	Certify Dx	Yes	No	Partial
Washington	1998	Certify Dx and benefit	No[3]	No	Yes
CBD only laws					
Alabama	2014	May prescribe[1]	No[2]	No	No
Florida	2014	Certify Dx and order	Yes	No	Yes
Georgia	2015	Certify Dx and authorize	No[3]	No	No
Iowa	2014	Certify Dx and recommend	No[2]	No	No
KY, MS	2014	Written order[1]	No[2]	No	No
MO, UT, WI, WY	2014	Certify Dx and benefit	No[2]	No	No
NC, OK, SC, TN	2014	Research only	No[2]	No	No
Texas	2015	Certify Dx and benefit	No[2]	No	Partial
Virginia	2015	Written certification	No[2]	No	No

Physicians should be aware that this is a rapidly changing area of the law, and would be well advised to seek legal counsel regarding the current status of medical marijuana laws in their state and local jurisdiction.

[1] Further specific state restrictions exist

[2] Intractible epilepsy or seizures only

[3] Varies, but typically limited to intractible nausea/vomiting or pain or terminal illness or inability to function

Federal prosecutors were instructed to "not focus federal resources in your States on individuals whose actions are in clear and unambiguous compliance with existing state laws providing for the medical use of marijuana" [26].

The US Department of Justice updated its official marijuana enforcement policy on August 29, 2013 in response to the Colorado and Washington State ballot initiatives which legalized production, processing, sales, and possession of small amounts of marijuana for non-medical use [27]. In general, the 2009 and 2013 changes to enforcement policy have resulted in removing the persistent risk previously existing for cancer patients using medical marijuana that, even though legal in

their home state, marijuana possession violated federal law, rendering them susceptible to arrest and prosecution under federal statutes.

Nevertheless, there remain aspects of the federal law which are particularly problematic. First is the issue that because marijuana and its derivatives, potentially including CBD, are listed as schedule I substances, they cannot legally be prescribed by physicians. Most states have circumvented this issue with a two-step process, enacting specific lists of diagnoses which can qualify a patient for medical marijuana usage and creating registries of patients whose physician has certified that the patient has been diagnosed with a qualifying condition, and that the potential benefits of marijuana outweigh the risks of use. This approach effectively avoids the "prescription" problem. However, the current laws in some states, such as Alabama and Louisiana, only authorize physicians to prescribe medical marijuana, creating a conflict with federal law and a potential legal risk for physicians.

Second, several states have enacted laws which do not allow for the manufacture, distribution, or sale of medical marijuana within the state. As a result, patients who have a physician certification of a qualifying condition and who are appropriately registered with the state can only obtain marijuana via illegal purchase "on the street," or by crossing state lines and purchasing marijuana in a state where it is legal, as long as that state recognizes out-of-state registration cards. However, in that case, transportation of marijuana across state lines back to their home state represents a violation of federal law, due to the inter-state transportation of a schedule I substance.

Medical Marijuana Quality Issues

Products used to treat serious medical conditions such as cancer need to provide at least a basic level of consistency from batch to batch, clear labeling regarding ingredients and potency, and a significant degree of freedom from contaminants. Since medical marijuana is a plant-based product, it may also be susceptible to significant variability due to varying species and strains, differences in growing conditions and harvesting, and inconsistency in producing the final dosage form. While guidelines and standards are firmly in place for pharmaceuticals, via the Food, Drug, and Cosmetic Act, and dietary supplements, via the Dietary Supplement Health and Education Act, and their respective regulations, because of the schedule I status of *Cannabis*, no similar federal regulations apply. Therefore, the degree to which the quality of medical marijuana is regulated is at the discretion of each state, and there is considerable variability, as demonstrated in Table 2.

The American Herbal Products Association (AHPA) has produced a set of "Recommendations for Regulators – Cannabis Operations" designed to provide an outline of appropriate quality requirements which could reasonably be included in legislation or regulations [28]. These recommendations cover the following: Cultivation and Processing Operations, Manufacturing and Related Operations, Laboratory Operations, and Dispensing Operations. We believe the most critical are those requiring laboratory testing to verify active ingredients and potency, accurate labeling of the final product with this information, laboratory testing for contaminants, and appropriate guidelines on the use of pesticides when growing *Cannabis*.

Of the 41 jurisdictions which have passed some form of a medical marijuana law, only 18 appear to have comprehensive quality requirements, with an additional 4 having enacted partial quality requirements. The other 10 states with medical marijuana laws have either very weak or non-existent quality requirements.

Future Directions and Perspectives

The legal status of marijuana presents obstacles researchers must navigate to perform clinical trials. In order to perform any clinical studies on a schedule I drug, researchers must apply for a license from the DEA. These licenses are issued only if several strict eligibility requirements are met by the applicant. In addition, securing funding can pose a challenge as the National Institute on Drug Abuse (NIDA), which provides the majority of money for research involving schedule I drugs, has focused mainly on studies that target the dangers of marijuana and treating abuse. Given the legal landscape researchers are confronted with in the USA, at this time, most of the human studies evaluating the effects of cannabis are taking place in other countries such as Canada and Israel, where the medicinal use has already been legalized.

At the current time, there are more than 15 trials evaluating clinical outcomes in cancer patients using cannabis or cannabis analogues [29]. Our search revealed two studies examining the safety and pharmacokinetics of various cannabis products [30]. These studies will help to bolster the safety profile of cannabis as well as establish maximum tolerated dose and potential herb-drug interactions. One of these studies, taking place in Israel and currently recruiting patients, is aiming to determine the potential effects cannabis has on cognitive impairment in cancer patients undergoing chemotherapy [31]. This study represents the first time these effects have been tested in a cancer population.

Seven clinical trials are aiming to evaluate cannabis' effects on pain in cancer patients [32]. One of these studies is taking place in the USA at the New York State Psychiatric Institute, which has published previous research on marijuana addiction. The study is not yet recruiting but the stated outcome is to evaluate the efficacy of smoked cannabis for pain relief in patients undergoing radiation therapy for lung cancer [33]. This is notable as it is the first study the authors are aware of taking place solely inside the USA with an outcome of pain

relief in cancer patients. It is also unique from all of the other active trials in that the intervention is smoking marijuana versus the more common oral cannabis products now available. One of these oral products, Sativex (nabiximols), which is an oral spray, is the intervention being used in the other three current trials for pain relief in cancer patients. Sativex has been patented and approved for cancer-related pain in Canada and several European countries. GW pharmaceuticals, the company behind Sativex, has had similar trials published recently through an ongoing series known as SPRAY [34–36].

One of the more established benefits of cannabis is stimulating appetite. One study is focusing on dronabinol's effects on appetite stimulation in addition to effects on chemosensory abnormalities (i.e., taste and smell alterations) [37]. Until now, all human studies investigating cannabis' effects on appetite have used THC analogues only; however, one current study is employing a newly formulated oral capsule (Cannabics®) containing both CBD and THC in varying ratios [38].

We now are beginning to see human trials underway investigating the anticancer effects of cannabis. In one of these studies, mentioned earlier, cannabis will be combined with temozolomide for treating patients with highly aggressive brain tumors (GBM). This study aims to build on the preclinical data supporting the pro-apoptotic effects of cannabis on glial cells in animal models as well as similar effects on temozolomide-resistant tumors [39]. In addition, there is a phase 1b, multicenter study combining cannabis with several chemotherapy agents aiming to determine MTD as well as any tumor response in patients with pancreatic and hepatocellular cancer [40]. These findings will help to lay a foundation for future research using cannabis as an adjunct to other chemotherapy agents.

Perhaps the most anticipated study in this category is a phase 2 Israeli study investigating the anticancer effects of pure CBD on patients with advanced cancers that have progressed through all standard treatments [41]. This is the only study to date to evaluate a cannabis product as a single anticancer agent in humans. The results of these current studies will drive future research.

Conclusion

Medical marijuana has potential for therapeutic applications in oncology, yet the available evidence and legal status pose a challenge for physicians and oncology providers. There is moderate level evidence for the use of cannabis in pain management. Some patients subjectively report benefit from cannabis for nausea, appetite, sleep, and anxiety, yet the level of published evidence remains low. Clinical trials are underway, but the legal status in the USA presents challenges to research. It is critical that oncology professionals are able to at least address the known risks and adverse effects of marijuana when questions arise from patients. Current available evidence is conflicting in terms of cancer risk. Since marijuana is smoked less frequently and in smaller amounts, as well as administered via oral and mucosal routes, the risk for carcinogenesis may not be as significant as for tobacco. In addition, there is preliminary research on anticancer effects of cannabis as well that may somewhat balance out the risk. Overall, medical marijuana may have use in cancer care, but more research is needed to better inform physicians and patients.

Compliance with Ethical Standards

Conflict of Interest Shauna M. Birdsall, Timothy C. Birdsall, and Lucas A. Tims declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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