



Psilocybin-assisted psychotherapy for cancer-related anxiety and depression

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Women with gynecologic cancers face various physical and psychological challenges throughout their treatment journey. Late stages associated with poor prognosis, along with chronic side effects of treatment, often leave women with existential uncertainty stemming from unpredictable disease trajectory and continuous fear of death.

Recently, a patient in her late 30s (JN) with end-stage ovarian cancer was seen in our center. JN has two children and was diagnosed only a year ago with advanced ovarian cancer, and now has multiple sites of bowel obstruction. Her fear for her future was real and overwhelming. Despite the various successful meaning-based work that has been done to address distress in cancer patients, as well as the more conventional gold standard cognitive behavioral therapy, much of it requires significant time commitment to change old habits, and JN does not have the time or stamina for that kind of work.¹ JN is not alone, as up to a quarter of ovarian cancer patients report depression, anxiety, and death anxiety.² This is not limited to ovarian cancers, as many gynecologic cancers are unfortunately diagnosed in young women where the burden of anxiety and fear is even greater, often related to the fact that young children may lose their mother.

Psychedelics, specifically psilocybin, have shown promise in treating various psychological symptoms including anxiety, depression, post-traumatic stress disorder, and end-of-life distress.³ Although a study focusing on gynecologic cancers has not yet been completed, the studies with mixed cancer diagnosis are encouraging.

Psychedelics modulate brain activity and have been associated with therapeutic effects such as increased neuroplasticity and modulation of reward pathways, not dissimilar to the mechanisms underlying the therapeutic mechanism of conventional anti-depressants.⁴ However, the research with psilocybin-assisted psychotherapy suggests lasting benefits from just one to two sessions, compared with the chronic use that is needed with selective serotonin reuptake inhibitors. A recent study compared psilocybin to escitalopram, a conventional anti-depressant, and found no differences in depression scores between the two groups.⁵ Furthermore, secondary outcomes favored psilocybin

in terms of adverse effects. Concerns regarding psilocybin's potential for recreational abuse or mental illness have not materialized, and data suggests psilocybin use may actually be protective against psychological distress and suicidality.⁶

Clinicaltrials.gov identified 12 trials involving psilocybin and cancer patients, with promising results, including improvements in patient-reported outcomes for cancer-related anxiety and efficacy in treating depression. Importantly, psilocybin might have a lasting effect even after a single dose, which might prove important for patients at end-of-life, when even a single dose of treatment could improve quality of life for the time remaining. For example, McCulloch et al were able to show a long-lasting increase in mindfulness and changes on functional magnetic resonance imaging using a single-dose of psilocybin.⁷ Similarly, a recent meta-analysis pooling the results of 10 trials found that a single-dose or two-dose psilocybin administration had rapid and sustained anti-depressant effects that lasted for up to 6 months.⁸

Considering the prevalence of existential distress among ovarian and other gynecologic cancer patients and the potential benefits and safety of psychedelics, there is a clear need for more well-designed protocols prioritizing safety and exploring psilocybin, and other psychedelics, in this vulnerable population. Our team at the University of Texas MD Anderson Cancer Center will begin a trial in 2024 examining the effects of psilocybin for patients with controlled advanced cancer on maintenance therapy experiencing challenges with mental health.

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