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Treatment Manual for MDMA-Assisted Psychotherapy for Anxiety Disorder Due to a General Medical Condition in subjects with Advanced-Stage Cancer.

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Goals of this Manual

The goals of this manual are 1) to delineate the core elements of MDMA-assisted psychotherapy in the psychotherapeutic treatment of Anxiety Disorder Due to a General Medical Condition, and, 2) to educate therapists about the phases and steps involved in conducting this therapy. This manual will assist in the process of standardizing and validating this treatment in the context of controlled clinical trials and will provide therapists with appropriate strategies for preparing the patient for MDMA-assisted sessions, conducting the MDMA sessions, and facilitating follow-up sessions designed to expand and integrate the therapeutic process.

The treatment described in this manual involves eight therapy sessions. These include six non-drug sessions each involving one hour of interaction with the co-therapists, and two day-long MDMA-assisted therapy sessions with the co-therapists. The treatment team consists of two co-therapists, one female and one male.

The foundation of this treatment is the theoretical assumption that the medicine, MDMA, is not in itself the therapy. Rather, MDMA is considered a powerful ally for both clinician and patient. The adjunctive position of MDMA in the therapeutic process is based partly on its ability to induce a heightened state of empathic rapport along with its ability to facilitate the therapeutic process (Grob & Poland, 1997). The treatment paradigm rests on hypotheses concerning the benefits of increased rapport combined with the effects of a heightened therapeutic process. These effects are hypothesized to enhance the ability of the advanced-stage cancer patient to deepen his/her understanding of the antecedents that trigger the anxiety and find strength in confronting these issues.

The successful use of MDMA in therapy is dependent on “the sensitivity and talent of the therapist who employs (it)” (Grinspoon & Doblin, 2001, p. 693). With this understanding, the therapist carefully works with the patient to establish a sense of safety, security, trust, and openness, and to delineate the intended goals of the therapy prior to the MDMA-assisted session[s]. As Greer and Tolbert (1998) noted, “The relationship should be oriented toward a general healing for the client, who should feel safe enough in the therapists’

presence to open fully to new and challenging experiences” (p. 372). This requires that the therapist carefully sets the parameters of treatment and prepares the patient for the process prior to and during each MDMA-assisted session. The post-session integrative aspect of the therapy is aimed at bringing the lessons gained in a non-ordinary state of consciousness across the bridge to the ordinary state of mind where these lessons can translate into advances in the patient’s level of functioning. These strategies are introduced at the beginning of therapy and emphasized throughout the process.

Additionally, this manual will outline the inclusion and exclusion criteria, the assessment protocol and other specifics of our current research study of MDMA-assisted therapy for Anxiety Disorder Due to a General Medical Condition in the patient with advanced-stage cancer.

Introduction:

MDMA produces an experience that has been described in terms of “inhibiting the subjective fear response to an emotional threat” (Greer & Tolbert, 1998, p. 371) and increasing the range of positive emotions toward self and others (Adamson, 1985; Grinspoon and Bakalar, 1986). Though promising, reports of the benefits of MDMA-assisted psychotherapy remain anecdotal (Adamson, 1985; d’Otalora, <http://www.maps.org/research/mdma/moaccount.html>; Gasser 1994; Greer and Tolbert 1998; Metzner and Adamson, 1988, 2001; Naranjo, 2001; Styk, 2001; Widmer 1998; Wolfson 1986) or based on an uncontrolled study (Greer and Tolbert 1986). As a result, the Multidisciplinary Association for Psychedelic Studies (MAPS), an IRS-approved non-profit research and educational organization, is sponsoring a series of Phase II clinical trials to explore the potential risks and benefits of MDMA-assisted psychotherapy in treatment-resistant posttraumatic stress disorder (PTSD) patients (Mithoefer 2004). Additionally, MAPS is sponsoring an initial study to evaluate the efficacy of MDMA-assisted psychotherapy for the treatment of Anxiety Disorder Due to a General Medical Condition in advanced-stage cancer patients who are estimated to have one year or less to live. In part, this study is intended to explore whether the therapy will reduce symptoms of anxiety which may allow for meaningful improvements in the quality of life for these patients. This manual will provide researchers with a method of MDMA-assisted psychotherapy to be used in conducting these trials.

Anxiety Disorder due to a General Medical Condition involves symptoms of anxiety severe enough to cause “... clinically significant distress or impairment in social, occupational, or other important areas

of functioning" (DSM-IV, p 437). Anxiety, depression, chronic pain, and unresolved family issues can become serious physical and mental health problems for individuals living with a terminal illness. End-of-life problems, including pain management, are increasingly understood by caregivers and the public as significant public health concerns (Potter et al. 2003; Randall-David et al. 2003; Shvartzman et al. 2003). Efforts to improve the quality of life for these individuals are clearly a public health priority. Recent efforts to devise better medication for protocols for pain control (MacPherson, 2002; Thomas and von Gunten, 2003), improve family communication and support (Wells et al. 2003), and to diagnose and treat psychiatric conditions that may emerge after diagnosis, are all examples of improving care for the terminally ill.

The frustration experienced by the terminally ill with respect to the limited treatment options, inadequate pain control, fears of eventual loss of autonomy, social stigma towards receiving psychological counseling, and resentment about dependence on psychopharmacological agents, has left some these individuals with overwhelming suffering in their remaining days of life. These are some of the problematic issues which underscore the continued drive by the advocates for euthanasia. The assisted suicide law in Oregon (the "Oregon Death with Dignity Act," Oregon Revised Statute § 127.800-897; www.ohd.hr.state.or.us/chs/pas/pas.cfm), a 1994 voter initiative, allowed adult terminally ill to make requests for assistance in their suicide from their physicians, and 171 individuals have followed through since the program commenced. Consequently, there are those terminally ill individuals for which approved treatments and supports (including hospice service) clearly fail to meet their needs. The scientific investigation for more effective treatments and a wider array of treatments is of substantial public health importance.

Developing drugs and psychotherapeutic treatment that can aid the terminally ill in revising their assessment and management of stressors (that promote the expression of anxiety, panic, and other symptoms of an anxiety disorder) may be one of means of broadening the array of treatment options and alleviating some of the suffering of these individuals. Anxiety due to a general medical condition creates a disorienting change in the individual which may promote a spiraling descent into feelings of hopelessness, loss of autonomy over previously manageable activities of daily living, alienation from loved ones and other care givers, panic attacks, and an intense fear over the mystery of the unknown. Pharmacotherapy and psychotherapy are two interventions employed towards reducing the symptoms of anxiety

experienced by those with a medical condition that has a poor prognosis for survival. On the basis of past reports of successful treatment of anxiety associated with having a terminal illness with MDMA-assisted therapy, and on the basis of its reported entactogenic effects (Greer and Tolbert 1998; Holland 2001), we expect that psychotherapy conducted in combination with MDMA should produce symptomatic improvement in patients with advanced-stage cancer.

Anxiety disorders involve prominent fear responses including panic attack. A combined treatment of MDMA and psychotherapy may be ideal for the treatment of anxiety in people with terminal illnesses, because, "the MDMA experience usually involves an almost total attenuation of the usual fear or anxiety reactions" (Metzner, et al 1988, p.14). The qualities that have been associated with MDMA-assisted psychotherapy in anecdotal reports (i.e. decreased defensiveness, decreased stress, and enhanced alliances between subject and therapist or between the subject and other relatives present) may be particularly useful in the treatment of anxiogenic cognitions, behavior and resultant emotion associated with terminal illness. Early clinical experience with MDMA is consistent with the hypothesis that MDMA can increase therapeutic effectiveness of psychotherapy with people with terminal illnesses (Greer and Tolbert 1998).

In a psychotherapeutic context, MDMA was reported to produce a lowering of defenses and greater ability to think about and reflect on distressing thoughts and feelings (Naranjo 2001; Greer and Tolbert 2001; 1998; Metzner and Adamson 2001). Individuals with cancer taking MDMA in unofficial therapeutic settings with significant others present often spent time discussing painful or emotionally sensitive topics, such as the impending death of a loved one in the advanced stages of cancer and concerns about separating from a loved one, or hurting a loved one by separating from them (Stevens 2000; 1999; 1997). Reduction in pain was often reported, also (Greer and Tolbert 1998; Holland 2001; Stevens 2000; 1999; 1997). In a structured psychotherapeutic environment review of anxiogenic issues and fears (including the fear of death) affords the opportunity to reduce or eliminate symptoms of anxiety both during the therapy session as well as outside the therapeutic session.

In their recent report, McClain et al. (2003), support the importance of palliative care developing interventions to improve the well-being of the terminally ill, "... keeping psychological distress of patients who are facing death to a minimum. What is less clear, however, is whether

interventions exist that can help raise a terminally ill individual's sense of spiritual well-being." Patient and therapist reports of MDMA-assisted psychotherapy, conducted prior to the scheduling of MDMA, are suggestive of therapeutic benefits not achievable through other interventions.

Early clinical experience with MDMA is consistent with the hypothesis that MDMA can increase therapeutic effectiveness of psychotherapy with the terminally ill. The combination of anxiolysis (reduction in fear and anxiety), euphoria, feelings of interpersonal closeness, and facilitated recall for past events may maximize or amplify the benefits of psychotherapeutic interventions. Prior to being scheduled as a Schedule I controlled substance, MDMA was used in combination with psychotherapy in the treatment of some individuals with chronic pain (Holland 2001; Greer and Tolbert 1998), and in individuals with advanced cancer (Holland 2001; Stevens 2000; 1999;1997). Case reports and narrative accounts of MDMA-assisted therapy indicate that the treatment was often successful (Adamson 1985; Gasser 1994; Greer and Tolbert 1998; Metzner and Adamson 2001; Stolaroff 1997; Widmer 1997). Hence, the goal of MDMA-assisted psychotherapy for the treatment of Anxiety Disorder Due to a General Medical Condition in patients with advanced-stage cancer is to enable the patient to reorganize his/her issues related to the anxiety and to develop a wider behavioral and emotional repertoire with which to respond to anxiogenic stimuli.

This manual will provide the researcher with a method of MDMA-assisted psychotherapy to be used in conducting a scientific study to investigate the possible risks and benefits of this treatment.

Conditions for the use of MDMA-Assisted Psychotherapy

This section of the manual will address the conditions for the use of MDMA-assisted psychotherapy. MDMA can have profound emotional and physical effects. Its use requires thorough assessment and preparation. The patient must be committed to compliance with dietary and drug restrictions, preparatory therapy and follow-up sessions, and completing evaluation instruments.

The therapists must be committed to providing adequate preparation time during non-drug sessions, to giving careful attention to the set and setting during the MDMA sessions (Metzner, et al, 1988; 2001), and to providing adequate follow-up therapy. The therapists must remain with the patient during MDMA-assisted sessions until the acute emotional and physical effects of the MDMA have worn off. The therapists and patient must all agree that the

patient is in a safe and stable condition at the end of the therapy session. The patient must agree to remain overnight at the treatment facility and participate in a non-drug integrative psychotherapy session the next day.

The initial prerequisites for conducting MDMA-assisted psychotherapy with an individual with a terminal illness such as advanced cancer is that the patient must meet the DSM – IV criteria for Anxiety Disorder Due to a General Medical Condition. Participants in the current study have been diagnosed by an oncologist at the Lahey Clinic Medical Center with advanced-stage cancer, and they must be reasonably predicted to have less than 12 months of life remaining. Participants will have symptoms of anxiety and/or panic associated with the diagnosis of cancer (as opposed to a history of an anxiety disorder distinct from the diagnosis of cancer) that are clinically significant enough that the participant has been offered standard medications and/or psychotherapy for alleviating these symptoms.

The next prerequisite for inclusion is to only include patients who are not taking or who have safely and independently withdrawn from other prescription medications (example, SSRI or MAOI antidepressants) that might present an unreasonable risk of drug-drug interaction or that might confound any findings of therapeutic benefit. Prior to receiving MDMA-assisted therapy, an individual must also have a medical history and physical examination to rule out any medical condition that would require exclusion from this form of therapy.

If a patient is currently taking psychiatric medication (other than non-routine, as-needed anxiolytic medications), then this individual will not be accepted into the study. This potential participant can be re-evaluated for inclusion at a later date if he or she has independently discontinued the medication in coordination with the prescribing physician. In general, it is recommended that the patient be medication-free for at least 5 times a particular drug's half life. Careful clinical judgment must be used to exclude people who could not safely discontinue medication. This issue will be raised with the patient at the baseline interview with the investigators when this potential participant is notified of study exclusion. If the individual is engaged in ongoing psychotherapy, he/she must sign a release for the investigators to communicate directly with the therapist. The patient must also agree to not change therapist, increase the frequency of therapy or commence any new type of therapy until after the evaluation session 2 months following the second MDMA treatment session.

The third prerequisite is that for one week preceding each MDMA session the patient adheres to the following:

- a.) Refrain from taking any herbal supplement (except when judged by the research team to not effect study measures).
- b.) Refrain from taking any nonprescription medications (with the exception of non-steroidal anti-inflammatory drugs or acetaminophen unless with prior approval of the treating therapist).
- c.) Refrain from initiating any new prescription medications (except with prior approval of the research team).

It is also necessary for the participant to refrain from taking anything by mouth except routine medications and water after 12A.M. (midnight) the evening before an MDMA-assisted session. They must refrain from the use of any psychoactive drug, with the exception of caffeine or nicotine, within 24 hours of each MDMA session. They must agree not to use nicotine for at least 2 hours before and 6 hours after each dose of MDMA. They must agree not to ingest caffeinated beverages until at least 6 hours after each MDMA treatment session. They will not take any PRN medications on the morning of the MDMA treatment session prior to arrival to the hospital, although routine daily medications for pain control may be taken provided this use has been reviewed by the research team and is judged not to pose an undue risk to the safety and well-being of the participant. Non-routine PRN medications for treating breakthrough pain that were taken in the 24 hours preceding the MDMA treatment session may result in rescheduling the treatment session to another date.

These restrictions are carefully reviewed with the patient during and after presentation and signing of the Informed Consent.

There are several criteria that, if met, would result in the patient being excluded from this study.

These include the following:

1. Women who are pregnant or nursing, or of child bearing potential and are not practicing an effective means of birth control.
2. Meet DSM-IV criteria for any Dissociative Disorder, Anorexia Nervosa, Bulimia Nervosa, a primary psychotic disorder or affective disorder (other than Anxiety Disorder Due to a General Medical Condition and Simple Phobia).
3. Meeting DSM-IV criteria for abuse of or dependence on any substance (other than caffeine or nicotine) in the past 60 days.

4. Diagnosed with known primary or metastatic cancer of the CNS.
5. Diagnosed with significant, unstable hematological, endocrine, cerebrovascular, cardiovascular, coronary, pulmonary, renal, gastrointestinal, immunocompromising, or neurological disease, including seizure disorder, that in the clinical judgment of the investigators poses too great a potential for side-effects.
6. Diagnosed with significant peripheral vascular disease, hepatic disease, renal insufficiency, or preexisting or past evidence of hyponatremia.
7. Diagnosed with hypertension, even if well-controlled with medication. A systolic blood pressure of 140 or greater and/or a diastolic blood pressure of 90 or greater will exclude the potential participant from this study.
8. Weighing less than 45 kg.
9. Reporting a history of use of "ecstasy" (illicit drug preparations purported to contain MDMA) at any time within the previous 3 months.
10. Reasonably judged to present a serious suicide risk or who are likely to require psychiatric hospitalization during the course of the study.
11. Requiring ongoing concomitant therapy with a psychotropic drug other than PRN as needed anxiolytic medications and pain control medications.
12. Is unable to fully understand the potential risks and benefits of the study and give informed consent.
13. Is enrolled as a participant in any other medical research protocol.

This information is given and obtained during the initial evaluation and introductory sessions. The investigators are required to stringently follow these guidelines and to document compliance with them. Knowing that this context for his/her treatment is reliably in place provides the patient with a sense of safety and comfort. It also establishes a foundation for adequate preparation of the set and setting for therapy. It is an opportunity for the therapists to facilitate development of a therapeutic alliance, identify the patient's concerns, respond to questions and prepare the patient for the nature of the MDMA-assisted treatment sessions.

Individuals who meet the psychiatric criteria and agree to participate in the study will have also received further medical evaluation. The examination involves the following procedures: general medical history and physical exam, electrocardiogram (ECG), metabolic profile, assessment of serum electrolytes, thyroid hormone levels and levels of TSH, HIV serology, urine drug screen, and urine pregnancy test for

females. The co-investigator oncologist, who is not directly involved in the administration of the experimental MDMA treatment session, will perform the medical examination. Results of HIV serology will be kept confidential, and appropriate referral for counseling will be made if necessary. The patient can continue with MDMA-assisted therapy if, after undergoing the medical examination, he or she continues to meet all inclusion criteria without meeting any exclusion criteria.

Assessment Protocol – Baseline Measures

Diagnosis will be made by means of structured interviews to enhance the diagnostic reliability and interview validity. The investigators will commence with the baseline evaluation by first administering the SCID (First et al. 1997) to provide a DSM-IV diagnosis of Anxiety Disorder Due to a General Medical Condition and to rule out the presence of exclusionary Axis I diagnoses (i.e., substance dependence, psychotic disorder, dissociative disorder, major affective disorder, or eating disorder). Prospective participants will also complete the STAI again to confirm a score ≥ 40 . Other outcome measures administered at this baseline meeting include observer-rated measures of symptoms of anxiety, depression, hopelessness, and quality of life; subject-rated measures of symptoms and quality of life; and psychiatrist-administered tests of mental status and diagnosis. Participants will also be instructed on keeping the Daily Diary and measures of daily pain. Specifically, the Daily Diary logs daily use of all medications and need for symptom-specific medications for acute symptoms of anxiety and/or pain. The Daily Diary will also ask the participant to rate their prior 24 hours of pain each day using the VAPS. Completing the Daily Diary is expected to take six to eight minutes. A urine sample will also be obtained for drug testing. All study measures described below will be administered during baseline and medical screening assessments.

1. Beck Hopelessness Scale (Beck and Steer 1988; Beck et al. 1974) assesses suicidality along 3 axes of hopelessness: feelings about the future, loss of motivation, and expectations. Extensive normative data has been published on the BHS. The BHS has 20 true/false questions.
2. Daily Diary. Participants will keep a daily log of all medications taken while actively enrolled in the study protocol. The forms provided to participants will also remind them to contact the investigators prior to initiation of any drug or medication not already reviewed during the intake evaluation. The VAPS (see Visual Analog Pain Scale below) will also be completed daily.

3. European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (Aaronson et al. 1993) has satisfactory psychometric properties and currently is one of the most widely accepted measures of quality of life. This instrument has 30 items yielding scores for 5 subscales (physical, role, emotional, social, and cognitive functioning) and 3 symptom subscales (fatigue, pain, and nausea/vomiting). This will be the primary outcome variable for quality of life.
4. Functional Assessment of Chronic Illness Therapy— Spiritual Well-Being Scale (Cella et al. 2002a; Cella et al. 2002b) has two subscales: one measuring sense of meaning and peace, and the other assessing the role of faith in illness. Total combined score offers a measure of spiritual well-being. It has been found to be a psychometrically sound measure of spiritual well-being for individuals with cancer and with other chronic illnesses. Questions do not refer to specific religious beliefs or practices and are not biased for or against any particular religious group. The FACIT-Sp has 12 questions with 5 possible answers, each.
5. Hamilton Anxiety Rating Scale was developed in 1959 (Hamilton 1959) and has since become a widely used and accepted outcome measure for the evaluation of anxiety; it is well-validated and has been administered to a wide population. The HAM-A has 14 items; each is rated on a 5-point scale ranging from 0 (not present) to 4 (severe). A score of 14 or greater is associated with clinically significant symptoms of anxiety.
6. Hamilton Depression Rating Scale, developed in 1960 (Hamilton 1967; Hamilton 1960), is also a widely used and accepted outcome measure for the evaluation of depression and is well-validated, having been administered to patients across hundreds of studies. A score of 10 to 13 indicates mild depression; 14-17—mild to moderate depression; and greater than 17 – moderate to severe depression. We will use the 17-item version of the HAM-D, which, like the HAM-A, is rated on a 5-point scale ranging from 0 (not present) to 4 (severe).
7. Karnofsky Performance Rating Scale is a clinician-rated measurement of quality of life (Karnofsky and Burchenal 1994), scored from 0 to 100: 100 – normal/no complaints/no evidence of disease; 90 – able to carry out normal activity/minor signs or symptoms of disease; 80 – normal activity with effort/some signs or symptoms of disease; 70 – cares for self/unable to carry on normal activity or do active work; 60 – requires occasional assistance but is able to care for most of his/her needs; 50 – requires considerable assistance and frequent medical care; 40 – disabled/requires special care and assistance; 30 – severely

- disabled/hospitalization is indicated although death not imminent; 20 – very sick/hospitalization necessary, active supportive treatment necessary; 10 – moribund/fatal processes progressing rapidly; 0 – dead.
8. Memorial Symptom Assessment Scale (Portenoy et al. 1994) is a self-report inventory of 32 symptoms commonly associated with medical illness. For each symptom present during the prior week, the subject rates on a 4 point scale how often it was experienced, how severe it was usually, and how much the symptom caused distress or bothered the subject. Scoring of the MSAS yields several validated subscale scores: the 10-item MSAS Global Distress Index is considered a measure of overall symptom distress; the 12-item MSAS Physical Symptom Subscale; the 6-item MSAS Psychological Symptom Subscale; and the Total MSAS Score, which is the average of the symptom scores of all 32 symptoms in the MSAS instrument.
 9. Mini-Mental Status Exam is a clinician-administered instrument of 10 items, with a score from 0 to 30. Scores are age- and education-dependent; generally a score equal to or greater than 27 is considered normal (Folstein et al. 1975). A diagnosis of dementia is made when the MMSE score is less than 24, there is evidence of cognitive impairment from subject history, and there is evidence of functional impairments.
 10. Schedule of Attitudes Toward Hastened Death has primarily been administered to individuals with AIDS or with cancer (Breitbart et al. 2000; Rosenfeld et al. 1999). This instrument explores desire for death, including an active desire for death, optimism/pessimism towards one's future quality of life, social and personal factors that may influence willingness to consider assisted suicide or euthanasia, passive hopes for a more expedient death, and behaviors that might reflect a desire for death. The SATHD has 20 true/false questions.
 11. Self-Expansiveness Level Form assesses the transpersonal construct of "self-expansiveness," which is defined as "the amount of True Self which is contained within the boundary demarcating self from not-self through the process of self-conception" (Friedman 1983). It is a paper and pencil test of 18 self-descriptive statements that are rated on a five-point Likert scale by the subject as to how willing he/she identifies with test items. There are three subscales: Personal, Middle, and Transpersonal. Criterion, convergent, discriminant, and factorial validity has been established for this test measure.
 12. Spielberger State-Trait Anxiety Inventory differentiates "state anxiety" (i.e. anxiety dependent on a specific situation or

- stressor) from "trait anxiety" (long-standing anxious affect or disorder) and is considered the definitive instrument for measuring anxiety in adults (Spielberger et al. 1970). Extensive normative group data exists and the STAI has been administered to advanced-stage cancer patients with anxiety, as well. The STAI has 40 questions with 4 possible answers each. A score of 40 or greater is associated with clinically significant symptoms of anxiety. This will be the primary outcome variable for cancer related anxiety.
13. Structured Clinical Interview for the DSM-IV: SCID-IV (First et al, 1994). The SCID is a semi-structured interview that permits accurate diagnosis of lifetime and current psychiatric disorders using DSM-IV criteria.
 14. Symptom Checklist 90-Revised: This is a standardized instrument used to measure subjective, feeling states (Derogatis 1994). Reliability, validity, and utility have been demonstrated across close to 1000 studies and normative data values have been published. The SCL-90-R has subscales along 9 primary symptom dimensions (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism) and 3 global indices (global severity index, positive symptom distress index, and positive symptom total). The SCL-90-R has 90 questions with a 5-point rating scale.
 15. Visual Analog Pain Scale: This is a simple and efficient tool that consists of a drawn 10-cm line labeled at one end "no pain" and at the other end with "worst pain possible." Scoring is accomplished by having the participant mark the line to indicate pain intensity, and the line is then measured to the mark on a 0- to 10-point scale. Extensive prior research indicates that the VAPS is reliable and valid as both a sensitive measure of pain and as a measure of change in pain (Ohnhaus and Adler 1975).

Preparation Phase for MDMA-assisted Therapy Sessions

The Preparation phase of therapy involves three stages. Stage One: Establishing a Therapeutic Alliance; Stage Two: Creating a Safe Psychological and Physical Space; and Stage Three: Therapists' Preparation. While the content and process of each of these stages is woven in each interaction with the patient, the foundation is laid during the sixty (60) minute introductory session with the co-therapists.

Stage One: Establishing a Therapeutic Alliance, Gathering Information, Patient Orientation

Establishing a Therapeutic Alliance

The first stage of the Preparation phase provides adequate time in a non-drug therapy sessions for establishing a safe and positive therapeutic alliance. The therapeutic alliance is a prerequisite for treatment (Johnson, 1996). The development of trust and understanding between the therapists and patient is essential. A safe and positive therapeutic alliance is one in which the patient feels assured that his/her well-being will be attended to with utmost care. The therapists introduce themselves and share how they became interested in this work as well as their experience in treating cancer patients. This may help to assure the patient of the therapists' experience and commitment to support the patient throughout the process. Greer and Tolbert (1998) note that self-disclosure on the part of the therapist created a context for collaboration, intimacy, and trust. Additionally, appropriate self-disclosure from the therapists gives the patient a sense of shared identification with the therapists. This identification may also have the benefit of increasing personal comfort as the patient enters a state of heightened vulnerability.

Gathering Information

The therapists-patient interaction includes sharing mutually relevant information. Starting with the initial interactions with the patient, the co-therapists ask open-ended questions, provide feedback on the participant's test results = and medical evaluation, and encourage the patient to share what he/she believes is personally significant information. The therapists guide these interviews to gather information about the patient's present symptoms, discuss the impairment caused by the anxiety, and assist the patient with identifying the antecedents that trigger episodes of anxiety. The therapists also inquire about and discuss with the patient his/her previous experiences, if any, with MDMA, psychedelic drug use, or other non-ordinary states of consciousness. During this interaction the therapists should ensure that they have gathered sufficient information and established a sound understanding of the patient. This interaction is an opportunity for the therapists to inquire about and address any concerns the patient may have about non-drug therapy sessions or experimental (MDMA-assisted) therapy sessions.

Patient Orientation

In this stage of therapy, the therapists orient the patient to the therapeutic process. The therapists begin a dialogue with the patient about the scope of the MDMA session. They discuss the patient's expectations, motivations, purpose, and intentions for the therapy sessions. The therapists may liken the effect of the MDMA to an opportunity to step inside a safe container in which it will be easier to remain present with his/her intrapsychic material. They will The patient should be encouraged to cultivate an attitude of trust in the

wisdom and timing of their own healing process as is catalyzed by this approach.

During non-drug and experimental sessions, patients will be asked to think about and discuss their thoughts and emotions relating to their medical condition. The patient is advised to include experiencing, understanding, and achieving relief from his/her anxiety symptoms and underlying fears as part of the therapeutic goal. Here the therapists want to clarify the patient's expectations and intentions and encourage an attitude of openness toward the MDMA-facilitated experience in whatever way it unfolds. They may address specific goals or concerns of the patient, such as confronting his or her pain at increasing dependence on others and impending death, or a desire to mend or strengthen social ties that are strained directly or indirectly from the patient's advanced stage cancer, noting how MDMA-assisted therapy will help them to approach their goals. The therapists explain that often the deepest, most effective healing experiences take a course that is quite different from what one's rational mind might have predicted. Patients are encouraged to welcome difficult emotions rather than to suppress them, in order to better resolve deep-seated patterns of fear and powerlessness.

The therapists emphasize their commitment to help the patient cope with and organize all the emotional material that may arise during the experimental (MDMA-assisted) session. This commitment from the therapist is explicitly discussed. They agree to provide support, safety, and guidance for the patient in working with whatever emotions and events arise within the session. It is *sine qua non* for the therapists to use clinical judgment and personal awareness regarding when it is best to facilitate the patient's process and when it is best to silently witness the patient's experience. (This will be discussed at greater length in stage three of this phase of treatment). The patient is encouraged to feel free to ask for support from the therapists during moments of fear, powerlessness, sadness, and other intense emotion. They may ask for reassurance or simply to talk about what they are experiencing. The scope of creating a safe psychological and physical space is discussed in the following section.

Creating a Safe Psychological and Physical Space

Establishing a safe setting for the patient requires that the therapists take an active role in creating an environment that is conducive to the full range of the MDMA therapeutic experience. They must provide a setting in which the patient is able to recline comfortably. In order to minimize any unfavorable distractions, the setting should be free of all objects that would be likely to

have powerful negative or disturbing connotations. The research setting will be made as supportive as possible, yet the patient can be aware of all safety measures in place to respond to the unlikely possibility of a medical complication. The patient is provided with eyeshades and a pre-selected program of music. Music for the drug session is selected on the basis of its ability to elicit emotional responses or to facilitate a sense of passage or transformation. Music is chosen to support emotional experience while minimizing suggestion, with music containing lyrics generally avoided (Bonny and Savary 1990; Grof 2000: pp.186-191; Grof 1980; Unkefer 1990). The therapists will have a limited selection of instrumental music, including classical, jazz and other musical forms, and the patient may request a specific musical style or genre for his or her MDMA-assisted session. The patient is given the opportunity to see the room in which the session is scheduled to take place. The goal is to create a safe, calm, and meditative environment in which the patient is able to experience his/her anxiety and connect with the meaning of life, of death, and move toward an acceptance of the advanced stage of their cancer without concomitant anxiety.

The creation of a safe physical and psychological space is meant to allow and encourage the patient to attend to his/her internal stimuli. The setting as a whole is designed to minimize the impact of external stimuli and to support the patient's attention to his/her intrapsychic process. The patient has the option to request periods of silence and the therapists have the option to forgo sections of the musical program. Patients may also elect to forgo eyeshades.

To maximize the creation of a safe psychological space, the therapists and patient discuss the parameters of each session. Several specific agreements are made. These agreements include the following:

- 1) The patient agrees to remain overnight in the treatment facility. The patient is permitted to have his/her significant-other spend the night unless contraindicated by the clinicians.
- 2) The patient agrees to accept a prearranged ride home the following morning, as opposed to driving him or herself from the hospital.
- 3) At least one of the co-therapists is present at all times during the entire experience.
- 4) The patient's psychological safety also includes establishing the parameters with respect to experiencing and expressing sexual feelings. The role of the therapists' possible physical contact with the patient in the form of nurturing touch will be discussed. The therapists assure the patient that at no time will they engage in any form of sexual contact with the patient. The patient is invited to ask for nurturing touch, (holding of a hand

or being held). The patient is also instructed to use the word “stop” as a specific command if the therapists are doing anything the patient wants them to discontinue. The therapists agree to always respond to this command; the only exception being when the therapists are doing something to the patient that is necessary for the patient’s safety. The patient is reminded that a close personal support person pre-arranged with the investigators may also be present for a portion of the experimental treatment session and so may be available then to serve in this supportive role by holding the participants hand, et cetera, rather than asking this of the therapists.

- 5) The patient agrees to refrain from self-harm, harm to others, and harm to property. If, in the judgment of the therapists, the patient is engaged in any dangerous behavior, the patient complies with the therapists request to stop according to the terms of this agreement. The patient understands that failure to respond to the request may require an appropriate level of intervention.

To further prepare and provide the patient with a safe psychological space, the patient and therapists address difficult emotions of grief, rage, panic, and catastrophic fears. The therapists listen with an empathic ear and collaborate with the patient on strategies that will increase the patient’s feeling of safety. The patient is aware that he/she will be in a heightened state of vulnerability and will likely experience a range of emotions, thoughts, and physical sensations. The therapists discuss the process of helping the patient gain relief from difficult, intense emotions or distressing thoughts and assure the patient that he/she is in a safe environment and under the care of experienced clinicians. The patients are taught diaphragmatic breathing techniques to aid in the relaxation and self-soothing process. They are also taught to use awareness of the breath as a technique for being able to attend to experiences, especially difficult experiences from which they might otherwise attempt to emotionally and cognitively distance themselves.

Another important aspect of developing a psychologically and physically safe space involves a joint exploration of the members of the social support system surrounding the patient. Prior to any MDMA-assisted treatment session, the therapists and patient may consider ways in which the members of his/her social support network can be of help to the patient during the time between therapy sessions. The therapists explain the importance of sharing knowledge about the treatment sessions with selected members of the patient’s social support system. The patient is encouraged to permit the therapists to meet conjointly with the patient and his/her significant other or designated support person to disclose information concerning the nature and expected outcome of

MDMA-assisted therapy. The patient is permitted to invite a selected support person, such as his or her significant other, to part of the introductory session and, with approval of the co-therapists, to the part or all of the MDMA session. With the patient's permission the support person is given information on the process of MDMA-assisted therapy and the nature of the support that is likely to be helpful following the sessions. The participant and significant members of the patient's immediate social network, such as a partner or spouse and including the person the patient selected to remain with them during part or all of the MDMA session, is given emergency contact numbers in the event of a crisis between drug-assisted treatment sessions.

Stage Three: Therapist Preparation

In addition to standard training in the psychotherapeutic treatment of Anxiety Associated with a General Medical Condition, therapists would substantially benefit from personal experience with non-ordinary states of consciousness. Preferably, this would include personal experience with MDMA in a clinical setting. If this is not possible for legal or medical reasons, a series of sessions using Holotropic Breathwork (a non-drug method for catalyzing non-ordinary states) would also be beneficial. This personal experience is important for several reasons:

- 1) It will increase the therapist's level of comfort with intense emotional experience and its expression.
- 2) It will provide first hand validation of and trust in the intelligence of the therapeutic process as it arises from an individual's psyche.
- 3) It affords the therapist familiarity with the terrain and flavor of non-ordinary states of consciousness. This can be invaluable to the therapist's effort to understand and empathize with the patient's experience.
- 4) Therapists familiar with non-ordinary states of consciousness would also be familiar with features of the experience that the patient might find most helpful or particularly unsettling. Additionally, the therapist would have an intrapersonal working knowledge of the integration process related to this type of therapeutic genre.
- 5) The patient's sense of security and treatment alliance will be enhanced if the patient is aware the therapist has had a similar kind of experience.

During the introductory non-drug therapy session, the therapists encourage the patient to share his/her purpose and intention for the MDMA sessions and more generally for the course of therapy. During the session the therapists are aware of this intention and may under some circumstances redirect the patient's attention to it. However, the therapists should be guided by and

should follow and support the particular course that the patient's own emotional process takes, rather than trying to impose upon it some predetermined course or outcome. The therapists are charged with maintaining a high level of empathic presence throughout all therapy sessions and especially during each MDMA session. This empathic presence supports the patient in staying with his/her inner process when it is important to do so. Furthermore, this empathic presence allows for the therapists to appropriately respond to the patient's non-verbal gestures, have a dialogue with the patient when necessary, and offer physical touch when indicated.

The therapists enlist the medicine's qualities to enhance the therapeutic experience. The therapists respect the medicine's "apparent facility in inducing heightened states of empathic rapport" (Grob et al, 1996, p. 103) and operate within the previously discussed ethical guidelines and established parameters of treatment. The therapists understand the importance of their own mental set regarding this therapy and have a clear understanding of their own beliefs related to the use of MDMA as an adjunct to therapy.

Therapist Role

A primary role of the therapist is to create and maintain a safe, strong therapeutic alliance with the patient. A key aspect of this therapeutic alliance is the self-awareness of the therapist. The therapists consider the psychological factors influencing the patient, including the patient's expectations of the therapist (Widmer, 1997). They are able to be fully present during the patient's processing of anxiety and fear while at the same time maintaining healthy, appropriate boundaries. This ability on the part of the therapists provides support for the patient in remaining present with his/her inner experience and enhances the patient's willingness to explore new and unexpected perceptions that may arise during the healing process.

The therapeutic experience during the treatment session relies heavily on the therapists' ability, their level of comfort with powerful emotions, and their skill in remaining empathically present and open to a range of emotional experiences the patient may undergo. The therapists are caretakers of the goals that are set prior to the treatment session. As a caretaker of these goals, the therapists maintain an awareness of the patient's intentions for the session while allowing for additional psychic material to emerge. In order to maintain the delicate balance between maintaining focus on the inner experience and providing a safe space for exploring this experience, the therapists must be prepared to respect the natural healing mechanisms of the patient's

own psyche and body and to be prepared to skillfully interweave interaction with the patient and periods of silent witnessing.

During the MDMA-assisted session, the therapists act both as guides and supportive figures. As guides, the therapists facilitate the healing process and encourage the patient to focus on his/her goals when appropriate. This role may require therapists to redirect patient behavior, as when patients are requested to discontinue talking if it is felt that the communication represents either a defensive avoidance of material or a distraction from the opportunity to experience and benefit from the unique effects of the medicine on the patient's inner experience. These MDMA effects can lead to important insights and healing that arise through a non-linear process. This process is enhanced by an attitude of allowing the medicine to bring forth experiences rather than by any intervention and of acceptance rather than analysis. Another aspect of this role may require the therapists to follow the patient as he/she explores new and unexpected perceptions, even if they appear to be leading away from the primary agenda.

As nurturant figures, the therapists provide support and comfort to the patient and assist him/her in facing overwhelming and upsetting thoughts, memories or feelings, and encourage the patient to move toward reaching new perceptions or insights. This is accomplished through empathic listening, the offering and providing of verbal and physical comfort on request, and providing patients with the means to relax and gain a sense of security in the face of intense feelings related to having advanced-stage cancer, such as concerns over mortality or increasing dependence upon others. If the patient has found a support person, the therapists may support the patient when he or she wishes to speak directly with the support person for a limited amount of time, or wishes to share feelings or thoughts with the support person, so long as this interchange does not appear to distract the patient from the therapeutic process.

At other times, patients may describe experiences of exhilaration, joy, resolution, or self-affirmation. The therapists, as guides, provide the patient with room for these expressions and encourage the patient to accept and perhaps further explore these experiences. The therapists may inquire as to how the patient experiences these feelings as part of his/her healing process. These experiences may serve to soften or reduce the intensity of distressing memories, thoughts, or feelings and may provide a life-affirming perspective for the patient.

Agreements concerning appropriate behavior during the MDMA session are integral to the therapeutic and nurturing role of the therapists. Prohibiting any sexual behavior between therapists and patient assures patients that their heightened vulnerability will not be exploited. It simultaneously fosters a safe environment for offering physical comfort during the MDMA-assisted session. Insistence that the patient remain within the confines of the area where the MDMA session has occurred until the completion of the sessions is important for patient safety, and provides assurance to the patient that the therapists will not allow them to leave the safe space until the return of ordinary consciousness.

The therapists provide verbal and physical comfort upon request. This may include reminding the patient of the therapists' presence and reminding the patient that he/she can use breathing exercises to confront or work through periods of anxiety, grief, rage or other intense negative emotions. The therapists also maintain a safe space through the immediate discontinuation of any action, including verbal or physical contact, when the patient says "Stop." Support is also offered through reminding the patient of his or her own strengths and the tools that he or she possesses, such as new insights or self-soothing skills that can be used in the face of intense emotional experience.

In conducting MDMA-assisted sessions, therapists must attend to balancing their responsibilities as facilitators and as noninvasive participant observers. This may prove difficult at times, particularly when it is necessary for the patient to explore and confront his/her inner experience and when it is appropriate for the therapists to facilitate a particular avenue of psychotherapeutic content with the patient.

The therapists may also assist the patient in examining and negotiating ambivalent feelings toward the appropriateness of emotions or thoughts he or she is experiencing during the MDMA session. For example, the patient may experience cognitive dissonance between newfound feelings of self-forgiveness and self-acceptance and habitual thoughts of self-pity and self-loathing. Here the therapists must determine whether or not to intervene. In either case, the therapists seek to maximize the potential benefits of the inner experience facilitated by MDMA while at the same time ensuring that patients are safe. Maintaining this balance requires an intense focus on the verbal and nonverbal communications of the patient and an

understanding of any potential difficulties the patient might be facing as a part of his/her healing process.

Toward the end of the experimental (MDMA-assisted) session as the patient is making the transition from the non-ordinary to the ordinary state of consciousness, the therapists assess the patient's emotional stability, alertness, and presence versus absence of continued alterations in perception. In the event that the patient is experiencing residual emotional distress, the therapists will use clinical judgment to assess the apparent intensity of distress and to gauge what interventions should be employed. In most cases, the proper intervention will be to allow the patient to express his/her feelings and to help him/her understand the importance of these feelings in the overall healing process. The therapists will only depart when they have concluded that the patient is emotionally stable and that most of the MDMA effects have subsided.

The patient should be reassured that, though the acute effects of the MDMA have worn off, the effects of the MDMA session inevitably continue to unfold over the hours and days following the session. The patient is also assured that the therapists will continue to provide support and help in working through and resolving any difficulties. In addition, this would be a good time to review and practice the relaxation and self-soothing techniques that were taught in the introductory sessions.

If severe anxiety persists despite the above measures, a benzodiazepine may be used as a "rescue medication." We anticipate that this will rarely, if ever, be necessary. If a particularly severe panic reaction does occur during or after the first MDMA session, the therapists will make a decision about whether or not the patient is eligible to undergo a second session of MDMA-assisted therapy. This decision should not be made until after assessing the patient during the follow-up session the next day, and should subsequently be thoroughly explained and discussed with the patient at the next follow-up psychotherapy session one week later.

As described above, the principal investigator/therapist is responsible for disqualifying any patient who had an adverse physiological or emotional response to MDMA during the first session sufficiently severe to indicate that he/she would be at risk during a second MDMA session. For all patients who are eligible for a second session, the follow-up visit between MDMA sessions should include a discussion of the patient's thoughts and feelings about undergoing a second session.

The consequences of continuing MDMA-assisted therapy and the consequences of discontinuation are both frankly discussed, and the patient's decision about what he or she would prefer is respected.

The therapists may offer the patient specific suggestions to write about his/her thoughts, feelings, and experiences of the day, and to bring this writing to the follow-up session. The patient will also be encouraged to pay close attention to his/her dreams. The patient will also be encouraged to review the videotapes of the MDMA session or sessions (if the second MDMA session).

Phase II: MDMA Sessions

The overarching goal of an MDMA-assisted session in this patient population is to manage the anxiety through acceptance of the advanced stage of his/her cancer and appreciation for the moments of life remaining. This is accomplished through gaining new perspectives on the meaning of his or her life, identifying the antecedents to the anxiety, and encouraging the patient to experience the full range of his/her emotional and cognitive reactions. Reducing anxiety may involve working through difficult thoughts and feelings about life choices, social relationships, and alterations in life path caused by the cancer diagnosis. The therapeutic benefit of MDMA that allows the patient to openly look at the self with acceptance also serves to help the patient become comfortable with the "mystery of not knowing."

The MDMA-assisted sessions are discussed below in three steps. As the therapists prepare the patient for ingesting the substance, they take time to talk with the patient and familiarize him/her with the MDMA-experience. The next step involves working with the acute and sub-acute effects of the substance and the final step addresses the therapists' role throughout the MDMA-assisted session.

Step 1: Initiating therapy

The MDMA-assisted session begins with the therapists and patient reviewing the patient's goals for the session, the range of experiences that can occur during the session, and any concerns the patient might have as he or she prepares for the MDMA-assisted therapy session. This review allows the patient to disclose his/her feelings about the process and provides the therapists with the opportunity to encourage, reassure, and guide the patient towards maintaining a therapeutic intention. Once this review is completed, the subject takes the medication.

The therapists explain to the patient that MDMA is known to increase feelings of intimacy or closeness to others and reduce fear when confronting emotionally threatening material (Adamson 1985; Cami et al. 2000; Downing 1985; Greer and Tolbert 1998; 1986; Grinspoon and Bakalar 1986; Grob et al. 1996; Harris et al. 2002; Tancer et al. 2001; Vollenweider et al. 1998). They remind the patient that in the context of psychotherapy, a combination of drug effects may all serve to facilitate the therapeutic process and bring the patient closer to his/her goals for the course of the therapy. These effects include enhanced positive mood, changed thoughts about meaning, increased access to distressing thoughts and memories, reduced anxiety and increased feelings of empathy or closeness to others, and decreased self-blame and judgment. This combination of drug effects should allow the patient to examine and organize his/her anxiety in the face of death, and to open fully to feelings of fear, anger, or grief. The therapists will also address some of the unwanted subjective effects of MDMA, particularly anxiety often experienced in the context of feeling as if one is losing control. The patient will be reminded that he or she will be working through negative emotions, and that the therapists will maintain a safe space throughout the MDMA session. In preparation for the effects of MDMA, the patient is guided towards a relaxed state, encouraged to focus his/her attention on abdominal breathing and to set aside any expectations about what will or should happen during the session.

Step 2: MDMA Session

Onset of subjective and physiological effects begins 30 to 60 minutes after oral administration. During this period of the MDMA-assisted session, the patient is in a comfortable position and may find it helpful to focus on his/her breathing. The patient will have the option to use eyeshades and have music playing. At the beginning of the session patients will have been reminded of their intentions, including

intentions regarding working with psychological issues related to their episodes of anxiety for which they may have taken PRN anxiolytic medications. During this stage of the session it is important that neither the patient nor the therapists be forceful about directing attention toward these goals. It is more useful for all involved to take a stance of openness to whatever unfolds, knowing that the patient's psyche is capable of discovering a route to self-acceptance that is apt to be more effective and ingenious than the rational mind could have devised. The patient may talk to the therapists at any time.

After the session begins, participants will recline in a comfortable position with eyes closed or wearing eyeshades if preferred. They will listen to a program of music designed to support their experience by initially aiding relaxation and later evoking and supporting deep emotions and the emergence of unconscious material, as described earlier in "Creating a Safe Psychological and Physical Space" of this manual (Bonny and Savary, 1990; Grof, 2000, pp.186-191; Grof 1980; Unkefer, 1990).

In some cases the patient may become anxious as they feel the early effects of the MDMA. If they tell the therapists this or if they appear restless during the first hour an interaction with the therapists might be as follows:

Patient: "I'm feeling scared, my heart's beating fast."

Therapist: "You're in a safe place and we're paying close attention to how your body is reacting. Let us be in charge of keeping you safe. What you're experiencing is a normal reaction to the MDMA effect starting. When people feel anxious at first it usually passes quickly. Would you like one of us to hold your hand to remind you we're here with you?"

Patient: "Yes, that would be nice."

Therapist: "Take some slow, deep breaths from your diaphragm the way we talked about before. Let your breath help you relax and open to the experience. The medicine will help you do that."

Peak effects are expected to occur 70 to 90 minutes after drug administration (Harris et al, 2002; Liechti & Vollenweider, 2001; Tancer and Johanson 2003), and to persist for 1 to 1.5 hours. The therapists will check-in with the patient after 60 minutes if the patient has not talked since the administration of the medication. This check-in reminds the patient of the therapists' presence and provides the therapists with a cue as to the patient's inner status. This is a brief

interaction that is followed by the therapist guiding the patient to return to an inner focus.

To check in with the patient at 60 minutes, one of the therapists may put a hand gently on the patient's shoulder (if the patient has given permission to be touched in this way before the session began) and ask softly,

Therapist: "It's been an hour and we're just checking in to see how you're doing."

Patient: "I feel good. My body is kind of tingly with a lot of energy, and the music is really beautiful."

Therapist: "Good, would you like a drink of juice?"

Patient: "Sure, I guess that would be a good idea."

Therapist: "Then you can put your eye shades back on and go back inside if you want to, and we'll check with you again in awhile. Tell us if you need anything or if you want to talk."

The majority of the MDMA session consists of the patient attending to his/her intrapsychic experience and the therapists maintaining a clear empathic presence in order to attend to the process of the MDMA session. As the session progresses the patient is likely to experience a positive mood and a sense of trust for both self and others, along with embracing the difficult and painful emotions associated with advanced-stage cancer. Ideally the effects of the MDMA and the therapeutic set and setting will lead to catharsis and improvement.

The effects of MDMA-assisted psychotherapy are expected to assist the patient to face anxiogenic issues, which may include loss of autonomy, loss of physical strength, the impending loss of relationships, and fear of death. Enhanced self-acceptance and an increased sense of self-efficacy provide the opening for the patient to examine his or her anxiety and implement skills which improve the quality of life and overall sense of spiritual well-being. A sense inner of calm, rather than extreme arousal, on unfolding anxiogenic material is expected to help the patient examine emotions and thoughts more closely and objectively. The sense of safety and the facilitated recall may work in concert to allow for a deeper or more intense exploration of the anxiety as the patient faces his/her own near-term mortality and the effects this has on relationships and other aspects of the patient's life.

An MDMA-induced increased sense of closeness to others, trust, and intimacy may foster feelings of empathy and forgiveness for the self and others that may lead the patient to feel worthy as he/she faces

death. In addition, changes in feelings of closeness to others may allow for enhanced rapport between therapists and patient. If a support person is present during at least part of the MDMA session, the patient may also experience increased empathy and rapport with the support person as well. While patients are directed to focus on their inner experience during much of the MDMA session, enhanced interpersonal trust and feelings of closeness to others may make it easier to convey his/her inner experience to the therapists. Greater rapport during the MDMA-assisted session may also increase compliance with instructions provided by the therapists that are intended to improve the therapeutic experience or to reduce avoidance of fully experiencing a particular element of the experience, such as a memory, insight or feeling.

The therapists will engage in listening and talking with the patient. Additionally, the therapists make judgments about when verbal interaction with the patient is indicated and when verbal interaction is an attempt by the patient to defend against difficult or painful emotional material. The therapists listen for cues that alert them to the patient's intellectualizing which may indicate that the patient needs to allow his/her experience additional time to unfold within. This is sometimes referred to as the patient "getting ahead of the internal emotional experience." In this situation, it is necessary for the therapists to intervene and guide the patient back to his/her internal experience. The therapists are also sensitive to the patient's need to share strong feelings of bliss and joy. The therapists recognize that these feelings may also be a significant aspect of the healing process.

It is essential for the therapists to recognize and work with both the patient's underlying psychological processes and the experience produced by MDMA. Working with both of these components of the treatment involves supporting the patient in experiencing painful feelings of alienation, grief, rage, fear, or panic and experiencing the softening effects of MDMA simultaneously. The therapists' presence and the effects of the medicine provide a feeling of safety as the patient's barriers to perception open to allow increased access to finding meaning, experiencing the mind-body connection and witness the stages of bereavement. The therapists continually create a safe space for the patient as he or she experiences increased anxiety. MDMA may also produce in some patients a feeling of loss of control. The therapists must be prepared to work with the patient to embrace these feelings and move through them as the patient is encouraged to surrender control and open to inner emotions which may previously have been too fearful to encounter.

The increase in sensitivity to interpersonal relationships and intimacy issues may draw patients to consider ways in which their symptoms have altered or impaired their relationships with others. These MDMA effects may better equip patients to view their interpersonal relationships, including relationship difficulties, without judging themselves or others too harshly. The increased focus on interpersonal relationships may assist patients who have distanced themselves from others as a way of coping with his/her mortality. Feelings of interpersonal trust may also assist patients with acceptance of unresolved relationship issues. The therapists and patient might explicitly seek to explore these areas during part of the MDMA session.

During the MDMA session the patient may experience strong negative emotional reactions, including a feeling of loss of control. When the therapists become aware of the patient's distress, they intervene to encourage the patient to stay with deeper levels of emotion, to trust that it is safe to face the experience. This may take the form of introducing the previously practiced breathing exercises, (e.g., "use your breath to stay with the experience, breathe into it"), verbal statements assuring the patient that he/she is in a safe place, orienting the patient to the "here and now", encouraging the patient to talk about his/her emotions, holding the patient's hand, or providing other nurturing touch. In this way, the therapists help the patient stays with and move through his/her emotional experience, (i.e., the patient stays with the fear, anxiety, shame, guilt, etc), and acknowledge this as a natural progression of the therapeutic process.

An example of helping the patient with a difficult experience:

Patient: (looking agitated) "I just keep having images of dying, I try to think of something else but I can't make it stop!"

Therapist: "We're right here with you. (Perhaps with some nurturing touch) I know this part is hard, but it's coming up now for healing. If you can use your breath to stay with the experience instead of trying to make it stop that will help you move through it. Use your breath, just breathe into it and stay as present as you can with your experience. And express it in any way you need to, crying, making sounds, letting your body move, talking to us about it, however you can express it. We're right here, and the medicine will help you with this too."

There are specific measures for the therapists to take in the event that the patient is experiencing emotional distress that they are not able to

process and move through spontaneously. In most cases, these steps should be taken sequentially, proceeding to the next step only if necessary:

- 1) Ask, "What are you aware of in your body?" This will help the patient become conscious of the link between distressing emotions and any somatic manifestations. Making this link and making the suggestion to, "Breathe into that area and allow your experience to unfold", may be the only intervention that is needed at that point.
- 2) Encourage the patient to "Use your breath to help you stay as present as you can with this experience. Go inside to allow your inner healing intelligence to work with this." If it is during the MDMA session add, "The medicine will help that to happen."
- 3) If the patient is quite anxious (anxious affect, restlessness, opening eyes) it may be helpful to hold his or her hand or for the therapist to lightly touch the subjects arm or shoulder as a gentle reminder that the therapists are present to be supportive and assist the patient through difficult emotional content. This can be reassuring and help refocus attention on inner experience. This should only be done with the patient's permission.
- 4) If this does not lead to resolution of the distress, ask, "Is there content (specific images, memories or thoughts) that's coming up with these feelings?" If so it may be helpful to talk about it. The opportunity to put the experience into words may in itself be therapeutic, especially in this safe setting and with the tendency of the MDMA to decrease critical self-statements, fear and to increase trust. This will also be an opportunity for the therapists to help the patient explore connections between symptoms and past traumatic experiences, and to put these experiences into perspective in his/her current lives.
- 5) After this period of talking, and periodically throughout the session, encourage the patient to "go back inside", to focus on his/her own inner experience.

As the patient makes the transition from the non-ordinary state of consciousness into an ordinary state of consciousness, the therapists may communicate with the patient more extensively about what she or he experienced. The therapists ask the patient for detailed feedback on his/her emotional and psychosomatic status (Grof, 2001). The therapist will encourage the patient to reflect upon and accept the experience, and to consider any newly experienced insights. If the patient indicates awareness of physical pain, tension, anxiety, or other

manifestations of distress, the therapist would encourage the patients to fully explore those feelings.

Two and a half hours after the initial dose, the co-therapists will assess the patient's physiological and psychological reaction to the MDMA. If, in their determination, a supplemental dose of half the initial dose can be safely administered, they will offer this dose to the patient in order to prolong the plateau of the MDMA state for several more hours. They will discuss with the patient any issues that this offer generates. The subject may decline to take this dose.

During the MDMA session, the patient has the option of inviting his/her significant other into the consultation room to join the patient in his/her emotional process, subject to the approval of the co-therapists. The patient and therapists share with this individual information about the patient's present condition as well as encourage the support person to share any concerns or questions he/she may have. The therapists may educate the support person about the after-effects of the MDMA experience and together the group may discuss what might be expected over the course of time as the healing process unfolds. The patient remains in the hospital overnight and is given the option of having his or her support person stay at the hospital as well, again subject to the approval of the co-therapists. A follow-up session is scheduled for the following morning. The patient and/or the support person are instructed to contact the covering psychiatry resident who has been hired expressly to remain overnight to be available for the study in the event the patient may need something throughout the night. The principal investigator may also be paged and can return to the hospital within 10 minutes, if warranted.

The Second MDMA-Assisted Therapy Session

The second MDMA-assisted therapy session will be conducted in a manner identical to that described for the first MDMA-assisted therapy session. The second MDMA therapy session will be scheduled to occur two to three weeks after the first session. The patient and therapists will review the patient's goals at the outset of the session, and the patient will be encouraged to follow his or her inner experience throughout the session. As previously described, the therapists will guide and support the patient throughout this process.

The second MDMA session has the potential for facilitating a deeper emotional experience. In part this is due to the therapeutic alliance that has been established, familiarity with the effects of MDMA, and an increased openness to further exploration. In the current study, the

increased potential for facilitating a deep emotional experience may also arise as a result of the larger dose that eight subjects will receive on the second MDMA session. The psychic material that has revealed itself from the first MDMA session and the therapeutic work that occurs in the follow-up sessions may afford the patient an increased sense of safety and security with the process. Feeling a stronger sense of trust and familiarity with the substance, the patient is likely to move even further beyond his/her defenses during the second session. The patient and therapists integrate the progress and experience from the previous sessions to set intentions for the second MDMA session.

Phase III: Integrative Follow-up Sessions

The integrative follow-up sessions occurs the day after each MDMA session, each week between the two MDMA sessions and the week after the second and final MDMA session. The following section describes three steps involved in conducting the integrative follow-up sessions. The first step involves implementing a “safety net;” step two addresses the structure, nature, and goals of the follow-up sessions; and step three considers the therapists’ role during the integrative follow-up therapy sessions.

Safety Net

The therapists provide a sixty-minute follow-up session the day after each MDMA session. There are several aspects of the integrative follow-up session that contribute to the patient’s felt sense of safety after his/her experimental (MDMA) session. These include, but are not limited to, the following:

- 1.) Knowing that he/she has access to the therapists at any time through their pager as well as during the scheduled appointment the day after the experience may reduce any anxiogenic thoughts the patient may have about his/her experience.
- 2.) Knowing that he/she will participate in a non-drug therapy session less than 24 hours after each MDMA session for an opportunity to debrief and understand the intensity of his/her experience.
- 3.) Strengthening of the therapeutic alliance.
- 4.) Knowing that the therapists may have had an opportunity to work with or speak with members of the patient’s support system, including the support person, if one was present.
- 5.) Knowing that the therapists may have had the opportunity to dialogue with patient’s primary therapist if the patient is in therapy.

- 6.) Knowing it is an opportunity to connect with the therapists and process any experience they may have of a heightened state of vulnerability.

In the Safety Net stage of treatment the patient is reminded that he/she has the commitment of the therapists to provide support throughout the study. The therapists review the procedure by which they can be contacted at any time should the patient or his/her designated support team need to talk with them about any difficulties or concerns.

Follow-up and Integration Sessions

The initial Follow-up session is scheduled for the day after the first MDMA session and is designed to begin the integration process. The therapists and patient begin the process of understanding the lessons and experiences of the previous day. These sessions are designed to assist the patient with integrating the events of the MDMA session through exploring the patient's psychological and physical response and to prepare him/her for the second MDMA session. The therapists engage in an active dialogue and elicit detailed disclosure as a means to accomplish the following:

- 1.) To examine the events of the MDMA-assisted treatment session and explore what is occurring for the patient on a psychological and physical level.
- 2.) To ensure that the patient understands that the experience catalyzed by MDMA-assisted therapy will likely unfold and resolve over days or even weeks following the MDMA session.
- 3.) To assess how the patient tolerated the MDMA session and process content of the MDMA session. Based on this process, the therapists discuss effects on anxiety symptoms, re-evaluate goals and discuss integration of insight and new perceptions gained from the MDMA session.
- 4.) To assess any possible contraindications for the second MDMA-assisted therapy session.

In response to distress or upsetting thoughts, memories or feelings lingering after the MDMA session and those that may unfold over the course of time, the patient is reminded to perform the relaxation and centering techniques such as diaphragmatic breathing. These exercises may be especially important immediately after each MDMA session, as the anxiolytic effects of MDMA decline while some upsetting memories, thoughts or feelings brought forth during the session may remain. Information on the utility of breathing exercises can be reinforced in this session in preparation for the next MDMA session. Review of the

videotaped treatment session may also similarly aide the patient in the days following the MDMA session, and patients will be encouraged to view their copy of the videotape.

The primary goal of MDMA-assisted psychotherapy is the elimination of symptoms of anxiety and a return to an improved level of functioning and quality of life. This is accomplished by the patient's weaving all aspects of therapy into a new relationship with self, others, and with his/her anxiety related to having advanced stage cancer. The integration phase of treatment brings these elements together, in a cohesive, harmonious way. Integration involves the ability to access and apply to daily life the lessons, insights, changes in perception, awareness of bodily sensations, and whatever else was revealed to the patient during his/her treatment experiences.

The therapists and patient use several strategies to bring the lessons gleaned from the non-ordinary state of consciousness over the bridge to the ordinary state of consciousness. This is done during the integrative follow-up sessions as the patient works with the therapists to understand and accept the changes he/she has undergone. It involves giving meaning to the memories, thoughts, feelings, and insights experienced during the MDMA and integrative follow-up sessions and determining how this new meaning will be manifested in daily living.

The therapists encourage the patient to record and examine MDMA session material, refer to the music listened to during the sessions, watch and listen to the videotape recording of the MDMA session, practice breathing techniques, or drawing, singing, dance, exercise, painting, or other forms of creative expression. The use of creative endeavors in recalling and retaining MDMA-session related memories, thoughts, feelings or insights may provide the patient with a new set of coping skills with which to restructure anxiogenic cognitions. The therapists skillfully support these activities that allow the restructuring to emerge from the patient's own thinking and exploration.

Each integrative follow-up session should begin with an invitation for the patient to talk about whatever is on his/her mind. This is so the session will be directed primarily by the patient's experience rather than the agenda of the therapists. After allowing sufficient time for this open-ended discussion and exploration, the therapists should consider directing the session into other potentially useful areas. The therapists may use a variation of the following comments always in the spirit of offering something for the patient to consider, and with respect for the fact that it may or may not apply to any given individual:

- “Sometimes one of the challenges of this kind of therapy is that the MDMA experience may cause significant changes in a person’s point of view or belief systems. It can sometimes be hard to reconcile these changes in thinking with old beliefs or with the attitudes of other people in your life or with the society in general. Is this something you’ve noticed?”
- “Since the MDMA experience is quite unique it can be hard to explain to other people, and it can be painful if such an important experience is misunderstood or judged by other people in your life. It may be important to exercise judgment about how and when you talk about your experience.”
- “Often people have very valuable insights and corrective emotional experiences with the help of MDMA which aids in decreasing fear and judgmental thinking. Sometimes the next day the judging mind can get active again and start doubting the truth of these experiences, or sometimes people can have emotional reactions the next day that are different from those they had during the MDMA session. This can sometimes be confusing or upsetting. It’s really helpful to acknowledge and talk about it if you’re having any experiences like this.”
- “It is very common for the MDMA experience to continue to unfold for days after the session. Often it unfolds in an easy, reassuring way, but sometimes it can be more difficult. Sometimes working with anxiety in any therapy, including MDMA assisted therapy, can stir things up so that symptoms may temporarily get worse. This may come in waves of emotion or memories. When this happens it is part of the healing process and we’re here to help you work with anything that comes up for you after the MDMA sessions. It’s important to let us, (“and your other therapist” if they have one) know about it if you have any difficulties like this.
- “It may be helpful to write about your MDMA experience and your thoughts and feelings since then. It’s best to write this for yourself without the thought doing it for anyone else, but if you want to bring it in to share with us that could be useful. It may also be helpful you to listen to the videotape of the session in connection with this assignment.”

- “It can be helpful to write down your dreams and bring them in to discuss with us. For some people MDMA makes dreams more vivid and meaningful.”
- “There are some books we can recommend that address some of the experiences you’ve been talking about.”
- “Drawing, painting, collage, working with clay can all be helpful, nonverbal, ways of expressing and further exploring your experience.”
- “If a lot of feelings or images are coming up for you after the MDMA session it’s good to allow them to unfold and explore them when you have time and energy to do so, but it can also be important to set them aside when you have other obligations or when you need a break. It may be helpful to write a sentence or two about what you are setting aside and acknowledge that you will attend to it later, either in the therapy or when you have the time and energy. Hot baths, walks in nature, physical exercise, working in a garden, cleaning the house, nourishing food, playing with a pet are all activities that can help to ground you in the present.”
- “If there are tensions left over in the body, yoga or a massage can be helpful.”

During the integrative follow-up therapy sessions, the patient continues the process of accessing and interpreting the other levels of consciousness experienced during the MDMA sessions. This expansion in consciousness may lead to a personal paradigm shift. The shift in self and other-related cognition and emotion is then applied to subsequent experiences that trigger unwanted and habitual patterns of thought or emotion.

With the therapists’ help, the patient develops a bridge between ordinary consciousness and his/her experiences in non-ordinary states of consciousness, so that these states are experienced more as a continuum than as separate realms. For example, the patient is able to readily access two of the most noted therapeutic aspects of the MDMA experience, “inhibiting the subjective fear response to an emotional threat” (Greer & Tolbert, 1998, p. 371) and increasing the range of positive emotions toward self and others (Adamson, 1985; Came et al, 2000; Grinspoon & Bakalar, 1986) at times when he/she may be confronted with cues and realities of reduced ability to perform everyday functions, increased pain, and impending death. This allows

the patient to maintain a sense of calm security in the face of these anxiogenic stimuli. The ability to expand consciousness assists the patient with restoring a sense of intrapersonal safety while gaining mastery over the debilitating symptoms of anxiety.

The therapists recognize that the information revealed during the MDMA and integrative follow-up sessions serves as a starting point for enhancing the patient's emotional, behavioral, and spiritual well-being. As the days between the MDMA sessions and integrative follow-up sessions unfold, the patient is instructed to be mindful of any changes in his/her perceptions thoughts, feelings, interactions, and other experiences. When confronting emotionally threatening material he/she is encouraged to return to or reactivate the feelings of intimacy and closeness to others and the reduced fear originally experienced during the MDMA-assisted therapy sessions. Teaching the patient to do this between sessions involves cueing him/her to recall the accepting attitude experienced during the MDMA session and to ask him/herself, "How can I best use my new knowledge in this situation?" The therapists validate the patient's use of this technique.

MDMA-assisted psychotherapy utilizes the effects of MDMA administered within a therapeutic setting to help patients gain insights into their symptoms and adopt new, more effective means of coping with these symptoms. The MDMA-assisted treatment sessions provide the basis for constructing new meanings about self, others and his/her world. In turn, these newly constructed meanings can serve as a template for coping with the variety of ways in which the anxiety may manifest. The patient should feel less fearful, with a greater sense of self-control or insight when confronted with anxiogenic situations. Strengthened interpersonal trust will allow the patient to further develop his or her social network. Greater insight into the whole range of thoughts and feelings about having advanced-stage cancer give the patient confidence in confronting his or her emotions and reduce the likelihood of continued or increasing anxiety. Maintaining and nurturing the social network may also be made easier when an individual has gained a sense of mastery over feelings of anxiety and fear and when he or she is better acquainted with these feelings. Relying on the new perspectives gained from the MDMA sessions, the patient can confront anxiety-producing situations with more confidence and may be more comfortable with asking for assistance from his/her supportive network.

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