The Afterglow: Reflections on Phase 2 & 3 MDMA-Assisted Psychotherapy for PTSD Trials

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In April 2017, I made the decision to open my home-based private practice and turn it into a Phase 2 study for MDMA-assisted psychotherapy for posttraumatic stress disorder (PTSD) sponsored by the Multidisciplinary Association for Psychedelic Studies (MAPS). To do this, I founded the San Francisco Insight and Integration Center (SFIIC). Over two years later, SFIIC is now a Phase 3 study site and we are looking ahead to being one of the first legal psychedelic therapy centers in the world. During this time, we have also begun offering ketamine-assisted psychotherapy (KAP), based on some elements of the MAPS MDMA treatment protocol. Writing this article has encouraged me to reflect back on the incredible experience of working on a large scale U.S. Food and Drug Administration (FDA)-regulated study of an Investigational New Drug.

I serve in the roles of co-principal investigator, along with Sylver Quevedo, M.D., a co-therapist at our site. I am responsible, along with Dr. Quevedo, for executing the contract we have with MAPS to implement the study according to the FDA protocol and to maintain accurate data collection. Dr. Quevedo and I could not do any of this important work without the invaluable support of our study coordinator, Rachel Bacigalupi. In addition, our team consists of eight licensed therapists trained by MAPS to deliver MDMA-assisted psychotherapy in clinical trials for PTSD, including: myself, Julane Andries, LMFT, Harvey Schwartz, Ph.D., Veronika Gold, LMFT, Eric Sienknecht, Psy.D., Genesee Herzberg, Psy.D., Evan Sola, Psy.D., and Emily Williams, M.D. We also have two study physicians, Kristi Panik, M.D., and Dr. Williams.

In addition, we have a team of wonderful night attendants who stay with study participants at the clinic during the required overnight stay following MDMA sessions. The night attendants continue the care and support of participants by delivering or preparing dinner and breakfast, setting up their sleeping arrangements, and remaining available throughout the night should participants need anything at all. During this time, the therapy team and study physician remain on call should there be any problems or concerns. To date, we have had no serious adverse events associated with the study.

Once deciding to become a study site, we had many meetings, phone calls, and discussions spread out over the next year along with mountains of paperwork. After much work meeting FDA and Drug Enforcement Administration (DEA) requirements to get our site ready, we enrolled our very first participant in the preparatory Phase 2 open-label MDMA-assisted psychotherapy for PTSD study in April 2018 (referred to as MP16).

We had four study participants across four therapy teams in MP16 with very positive results. The Clinician Administered PTSD Scale-5 (CAPS-5) is our primary outcome measure. All participants had severe PTSD as measured by the CAPS-5 at the time of enrollment. After three MDMA-assisted psychotherapy sessions, with accompanying non-drug preparatory and integrative sessions, all four participants had large improvements in PTSD symptoms as measured by the CAPS-5. Anecdotally, we observed reductions in suicidal ideation, reductions in depressed mood and anxiety, improvements in sleep, improvements in interpersonal relationships, improvements in educational and career functioning, and increased hope for the future. While we are certainly excited about this outcome, we must be cautious about making any assumptions regarding this type of outcome in Phase 3. Phase 3 is a very different study design, most importantly being a double-blind placebo study.

Now, 18 months later, we have enrolled five participants as part of the Phase 3 study and we have an additional 3 in active screening. We plan to enroll 7 participants in total as part of the first study of Phase 3 (referred to as MAPP1) and an additional 8 in the second study of Phase 3 (referred to as MAPP2).

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As awareness of the study has grown, we have received a lot more interest from people with PTSD and their families than we ever expected. We believe this is a testament to the integrity and power of the treatment and how well it has been received by the media and the general public. Due to the popularity of the trial and people's desire for effective treatment, it can be challenging to exclude those who are looking for an end to their suffering. Similar to any Phase 3 trial, the specificity of the inclusion and exclusion criteria can be limiting, disappointing, and confusing for those wanting to be in the study. This is not unique to this particular study, but is often a necessary part of pharmaceutical research so that findings can be interpreted and are generalizable to a larger population of patients.

Another challenge is the general public's misunderstanding of the Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnostic criteria for PTSD. We hear a lot about trauma in the general discourse today. People can experience a range of traumas in their lifetimes, which can result in deep suffering and many symptoms that look like PTSD, yet these traumas may not meet the strict criteria for inclusion in this particular study. One of the many challenges of being a researcher is telling people they do not qualify for the study. Needless to say, a lot of thought, care, and concern goes into how we deliver this news.

We want to acknowledge the significant sacrifices our therapist teams have made to be part of this study given the many other responsibilities we have in our professional lives. Most of us have private practices, relationships, children, and a myriad of other commitments we are juggling simultaneously. None of us work full-time for MAPS-sponsored trials. Working on a study of this size requires an incredible amount of dedication, coordination, and sacrifice to execute it with scientific rigor. Our site is blessed to have a highly cohesive and dedicated team and we very much consider ourselves a family. We are all extremely grateful to be part of such exciting and groundbreaking research and we continue to make the necessary sacrifices to see this study through to its completion. It is a very exciting time of growth in the field of psychedelic therapy. Ketamine-assisted psychotherapy (KAP), led by Phil Wolfson, Raquel Bennett, and others, has exploded with the treatment being offered at a growing number of clinics nationwide. KAP has become an alternative treatment for some who do not meet criteria for inclusion in the study.

Finally, we could not do any of this work without the ongoing support of MAPS and MAPS Public Benefit Corporation (MAPS PBC) staff. We are deeply grateful to our trainers and mentors, Annie and Michael Mithoefer, Marcela Ot'alora, and Bruce Poulter; to Shannon Clare Carlin, to Alia Lilienstein, and to all of the people who keep this incredible endeavor up and running. We all look forward to the day when this potentially life-saving therapy is legally available to all who seek it.

Gregory Wells, PhD, *has been a licensed psychologist in San Francisco for the past 10 years. Prior to that, he practiced in New Orleans where his trauma related work focused on post-Katrina relief and recovery. He currently serves as co-principal investigator and co-therapist on the Phase 3 MDMA study at San Francisco Insight and Integration Center. Gregory is also co-founder of Polaris Insight Center offering Ketamine Assisted Psychotherapy.*

Sylver Quevedo, MD, *has been in continuous practice of medicine for 40 years and practices nephrology, family, internal, and integrative medicine. He serves as Assistant Professor at Stanford and UCSF. He has played pivotal roles in several global health projects, including planning and development of medical and nursing school in Africa. He is currently co-principal investigator of the Phase 3 MDMA study at San Francisco Insight and Integration Center and he is co-therapist at the Phase 3 site at UCSF. Sylver is also co-founder of Polaris Insight Center offering Ketamine Assisted Psychotherapy.*

Rachel Bacigalupi, MA, *is a clinical trials coordinator at San Francisco Insight and Integration Center who began working with MAPS in 2017 on MP16, a phase 2 open label trial of MDMA-assisted psychotherapy for PTSD and has continued in this role into phase 3 trials. A native New Orleanian, Rachel earned her BS in Psychology from the University of New Orleans where she began a career in research. After graduating, she went on to work as a clinical trials coordinator at New Orleans Children's Hospital. She has since earned her master's degree in Clinical Psychology from Palo Alto University, where she is currently a PhD doctoral candidate researching suicidality and culturally informed treatment and assessment. Rachel is passionate about her work with MAPS and the opportunity to integrate her knowledge of research and clinical work in order to contribute to forms of treatment which innovate the field of psychology.*