# ORIGINAL ARTICLES

# Randomized Controlled Trial of Accelerated Resolution Therapy (ART) for Symptoms of Combat-Related Post-Traumatic Stress Disorder (PTSD)

Kevin E. Kip, PhD*; Laney Rosenzweig, MS*; Diego F. Hernandez, PsyD†; Amy Shuman, MSW‡;
Kelly L. Sullivan, PhD§; Christopher J. Long, MSW*; James Taylor, MSc‖; Stephen McGhee, MSc‖;
Sue Ann Girling, BSAS*; Trudy Wittenberg, BS*; Frances M. Sahebzamani, PhD*;
Cecile A. Lengacher, PhD*; Rajendra Kadel, PhD*; David M. Diamond, PhD¶

**ABSTRACT** Objectives: Therapies for post-traumatic stress disorder (PTSD) endorsed by the Department of Defense and Veterans Administration are relatively lengthy, costly, and yield variable success. We evaluated Accelerated Resolution Therapy (ART) for the treatment of combat-related psychological trauma. Methods: A randomized controlled trial of ART versus an Attention Control (AC) regimen was conducted among 57 U.S. service members/veterans. After random assignment, those assigned to AC were offered crossover to ART, with 3-month follow-up on all participants. Self-report symptoms of PTSD and comorbidities were analyzed among study completers and by the intention-to-treat principle. Results: Mean age was $41 \pm 13$ years with 19% female, 54% Army, and 68% with prior PTSD treatment. The ART was delivered in $3.7 \pm 1.1$ sessions with a 94% completion rate. Mean reductions in symptoms of PTSD, depression, anxiety, and trauma-related guilt were significantly greater ($p < 0.001$) with ART compared to AC. Favorable results for those treated with ART persisted at 3 months, including reduction in aggression ($p < 0.0001$). Adverse treatment-related events were rare and not serious. Conclusions. ART appears to be a safe and effective treatment for symptoms of combat-related PTSD, including refractory PTSD, and is delivered in significantly less time than therapies endorsed by the Department of Defense and Veterans Administration.

## INTRODUCTION

Post-traumatic stress disorder (PTSD) is a disabling trauma and stress-related disorder that may occur after experiencing a traumatic event, and that evokes a combination of intrusion and avoidance symptoms, negative alterations in cognitions and mood, and alterations in arousal and reactivity.[1] Comorbidity rates are often >80%[2] and include sleep disturbance, depression, panic disorder, substance abuse, high somatic

*College of Nursing, University of South Florida, 12901 Bruce B. Downs Boulevard, MDN Room 2010, Tampa, FL 33612.

†Balanced Living Psychology, 13039 West Linebaugh Avenue, Building V, Suite 101, Tampa, FL 33626.

‡Western New England University, 1215 Wilbraham Road, Springfield, MA 01119.

§Department of Neurology, Morsani College of Medicine, University of South Florida, 12901 Bruce B. Downs Boulevard, MDC 55, Tampa, FL 33612.

‖School of Nursing, Midwifery & Health, University of Stirling, FK9 4LA, Room 3T14, Scotland, United Kingdom.

¶Departments of Psychology and Molecular Pharmacology and Physiology, Center for Preclinical/Clinical Research on PTSD, University of South Florida, 4202 East Fowler Avenue, PCD 4118G, Tampa, FL 33620.

symptom severity, decreased role functioning, and an increased risk of suicide.[3-8] From the Operation Iraqi Freedom (OIF)/Operation Enduring Freedom (OEF)/Operation New Dawn (OND) conflicts, prevalence estimates of PTSD vary dramatically from 2% to 31%,[9-12] owing to substantially different sampling methods, combat experiences, PTSD criteria, and treatment versus nontreatment seeking samples. Notwithstanding this variability, the number of military personnel who have served in the OIF/OEF/OND conflicts and are afflicted with PTSD is likely in the hundreds of thousands, and those exposed directly to combat are at significantly higher risk of developing PTSD.[13,14]

Formal guidelines[15-19] provide broad agreement on the use of trauma-focused interventions as first-line treatment for adults with PTSD. These therapies are designed to minimize intrusion, avoidance, and arousal symptoms of PTSD through combinations of reexperiencing and reframing trauma-related memories and emotions, and teaching methods of managing trauma-related stressors.[20] The most frequently endorsed and practiced therapies for the treatment of PTSD among veterans are prolonged exposure (PE) therapy,[21-23] cognitive processing therapy (CPT),[21,24,25] and eye movement desensitization and reprocessing (EMDR).[23,26,27] In this realm, the

Veterans Administration (VA) has mandated that all veterans treated for PTSD have access to either PE or CPT.[28]

Despite the magnitude of the problem, the endorsed first-line treatments for PTSD, which are based on decades of research, have multiple limitations; most notably, they are relatively lengthy, costly, and have variable rates of completion and treatment success. To illustrate, PE consists of 10 sessions approximately 90 minutes each with corresponding homework assignments.[22] The homework assignment is extensive—two major assignments each day, which require 1.5 to 2 hours to complete.[29] This equates to an approximate 30 to 35 hours of actual treatment commitment over several weeks, and treatment success is far from absolute. In clinical trials of PE, dropout rates of up to 50% have been reported,[30–32] along with nonresponse rates between 20% and 67%.[32,33] CPT is delivered over 12 sessions lasting 60 to 90 minutes with additional assigned practice of skills outside of the therapy sessions.[34] Dropout rates up to 29%,[30,32] and nonresponse rates between 4% and 48% have been reported.[32] EMDR consists of 8 to 12 weekly 90-minute sessions,[26] with reported dropout rates of up to 36% and nonresponse rates between 7% and 92%.[32] Exacerbation rates have been reported to range between 13% and 28% for PE and 5% and 10% for cognitive behavioral therapy.[32]

The above limitations of the currently endorsed first-line treatments for PTSD motivated, in part, the development of a new, brief exposure-based therapy in 2008 known as Accelerated Resolution Therapy (ART). This therapy, by protocol, is delivered in 2 to 5 sessions over an approximate 2-week period and requires no homework or skills practice, thereby reducing patient commitment time to approximately one-fifth (−80%) of the time required for PE. Although not developed exclusively for military populations, ART has shown clinically significant reductions in symptoms of psychological trauma in civilians.[35,36] This report describes the results of the first controlled trial of ART conducted among U.S. service members and veterans.

## METHODS

### Study Design

A two-group randomized controlled trial was conducted in which consenting and eligible participants (described below) were randomly assigned to treatment with ART or an Attention Control (AC) regimen. Participants randomly assigned to AC were offered treatment (crossover) with ART upon completion of the AC regimen. Both groups were scheduled for a 3-month follow-up assessment after receipt of ART. Thus, comparisons by random assignment refer to the initial randomly assigned intervention regimen; baseline to 3-month comparisons refer to within-subject analyses. The trial protocol was approved by the institutional review board at the University of South Florida (USF) and the Department of Defense (DoD) Telemedicine and Advanced Technology Research Center (sponsor of the trial). All participants provided written informed consent and the trial was registered with ClinicalTrials.gov (NCT01559688).

### Recruitment

Veterans were recruited from community-based organizations and veteran membership organizations within the Tampa Bay area, as well as through academic programs at the USF. Referrals of veterans for study participation were provided by the James A. Haley VA Hospital (Tampa, Florida), Bay Pines VA Hospital (Bay Pines, Florida), and United States Special Operations Command, Care Coalition, MacDill Air Force Base (Tampa, Florida). Participants recruited from these sources who received ART and/or the AC regimens were evaluated and treated at the USF College of Nursing, Tampa, Florida. Approximately two-thirds through the trial, recruitment was augmented with a one-time screening, enrollment, and treatment effort conducted at the Naval Operational Support Center, Nellis Air Force Base (Las Vegas, Nevada).

### Screening

Clinical evaluation used for trial eligibility consisted of the 17-item PCL-M Checklist, 125-item Psychiatric Diagnostic Screening Questionnaire (PDSQ), Brief Mental Status Examination, and self-developed 9-item ART Intake Questionnaire. The PCL-M (Military) Checklist is a self-report of DSM-IV symptoms of PTSD in response to stressful military experiences[37,38] and is used with service members and veterans. The PDSQ was used to screen for Axis I disorders to serve as a baseline assessment of psychopathology. This instrument has been validated against diagnostic criteria and interview-derived diagnoses over the course of 10 years and more than 3,000 administrations.[39,40] It can be hand scored to obtain a total score which functions as an indicator of psychopathology, plus subscale scores for 13 disorders: major depressive disorder, generalized anxiety disorder, panic disorder, PTSD, drug or alcohol abuse/dependence, psychosis, eating disorder, somatization disorder, obsessive compulsive disorder, social phobia, hypochondriasis, and agoraphobia. The 9-item ART Intake Questionnaire is designed to capture information on traumas impacting the participant including the number of traumatic events, duration of symptoms, self-reported guilt, and prior treatment.

Participants were instructed by the study coordinator to complete the PCL-M, PDSQ, and ART Intake Questionnaire in private with no proxy reports allowed. Completion and scoring of the PCL-M and PDSQ was followed by a clinical interview between the participant and an ART clinician to determine study eligibility. This included clinician completion of the Brief Mental Status Examination[41] to assess the participant's current state of mind under 12 domains (e.g., affect, mood, orientation, etc.). Trial inclusion criteria were (i) U.S. service member or veteran with prior deployment(s); (ii) age ≥18 years; (iii) symptoms of psychological trauma including score of ≥40 on the PCL-M Checklist and endorsement of PSTD items on the PDSQ; (iv) ability to read

and speak English to complete survey questions; and (v) denial of suicidal or homicidal ideation, and no evidence of psychotic behavior or psychological crisis. Exclusion criteria consisted of (i) brain injury prohibiting speech, writing, and purposeful actions; (ii) major psychiatric disorder (e.g., bipolar disorder) concomitant to symptoms of psychological trauma (as defined above); (iii) currently undergoing substance abuse treatment; (iv) previous diagnosis of eye movement disorder anticipated by the clinician to interfere with treatment; and (v) any medical condition that, in the judgment of the principal investigator and/ or ART clinician, might place the individual at risk because of a potential reaction (e.g., previous heart attack, seizure disorder).

## Random Assignment

Eligible participants were randomly assigned in a 1:1 ratio using a random number generator and variable blocking scheme (blocks of 4, 6, and 8) to the ART or AC regimen. The first session (ART or AC) was typically scheduled within 1 week (usually sooner) of the date of assignment.

## ART Intervention

The ART intervention, delivered in 2 to 5 sessions approximately 60 to 75 minutes each in duration, consisted of 2 components and use of bilateral eye movements. In the first component, "Imaginal Exposure" (IE) was used whereby participants were asked to recall (verbally or nonverbally) the traumatic event (scene) while focusing on physiological sensations, thoughts, and emotions. During this process, the participant, with coaching from the ART clinician, was composed into a relaxed, alert state of mind, and then exposed to reactivation of the targeted memory for a short 30 to 45 second period of time. This period of exposure to the memory was followed by identification and diminishment (or eradication) of any uncomfortable emotional or somatic symptoms. This occurred by directing the participant to hold his/her awareness of the symptoms while engaging in clinician-directed eye movements. By leading the participant through sets of frequency-regulated eye movements, while "viewing" (recalling) of the memory and self-awareness of physical and emotional sensations, the clinician directed the participant toward two complete phases of exposure to the targeted memory.

In the second component, "Imagery Rescripting" (IR) was used. IR involves the use of techniques in which the participant is instructed to visualize their traumatic scene and imagine changing (replacing) the imagery and sensory components of the scene to anything they choose (like the "director" of a movie). As the new positive scene was then substituted and reviewed, the participant was queried to try to access the original distressing images. Treatment of the traumatic scene was considered complete (successful) when only the replacement scene could be accessed, although, knowledge of the original scene remained in memory. A primary way that each ART session was closed was to ask the participant to envision a bridge and then use a metaphor to elimi-

nate distressing images before crossing the bridge, which represented moving on.

Throughout components and sensation checks of the therapy, the participant was asked to follow the therapists' hand back and forth moving their eyes from left to right, with 40 eye movements per set. During this process, the participant was not speaking, but rather "watching" their original or newly imagined scene. This process of "watching" the scene (during both IE and IR) while performing eye movements was performed multiple times, with the total sets of eye movements determined by the number required to complete the IE and IR components. Additional details on the ART protocol have been published.[35,36] Clinicians were trained in ART over 2 days using the ART manual and supervised practice. This was followed by 2 days of advanced ART training, a 1-day orientation on military culture, terminology, and deployment-related experiences delivered by an Air Force Colonel, and a 14-hour educational credit certification "Certified Clinical Trauma Professional" delivered by a PhD professor in social work and prior infantryman in Vietnam.

## AC Intervention

The AC intervention consisted of two 1-hour sessions of fitness assessment and planning or career assessment and planning, as selected by the participant. The fitness assessment and planning regimen was conducted by a certified health fitness trainer. The assessment included anthropometric measures, determination of body fat percentage, body mass index, a review of previous exercise history, and defining of individualized physical fitness goals. The career assessment and planning regimen was conducted by a professional career counselor. It included completion and review of the Career Planning Scale, which encompasses 6 scales covering knowledge of the world of work, knowledge of occupations, self-knowledge, career decision making, career planning, and career implementation.[42] For both the fitness and career regimens, the first session was devoted to current assessment and the second session was devoted to developing an individualized plan to achieve goals.

The AC intervention was not intended to be equal in contact time compared to treatment with ART. The rationale for providing the two 1-hour AC sessions was to measure the acute effect (on symptoms of PTSD and related comorbidities) of nonpsychotherapeutic interaction with a professional, while at the same time, minimally withholding the amount of time to treatment (crossover) with ART. It was expected that this approach would maximize recruitment and retention in the trial and minimize time of psychological distress.

## Data Collection

After screening and enrollment in the trial, participants completed a demographic and brief medical history questionnaire. In addition, baseline completion of self-reported outcome measures (in addition to the previously completed PCL-M) included the following measures: 20-item Center for

Epidemiologic Studies Depression Scale (CES-D)[43]; 18-item Brief Symptom Inventory (BSI)[44]; 21-item State-Trait Inventory for Cognitive and Somatic Anxiety (STICSA)[45]; Pittsburgh Sleep Quality Index (PSQI)[46]; 32-item Trauma-Related Guilt Inventory (TRGI)[47]; 21-item Post-Traumatic Growth Inventory (PTGI)[48]; 26-item Self-Compassion Scale (SCS)[49]; 29-item Aggression Questionnaire (AQ)[50]; and the 10-item Alcohol Use Disorder Identification Test (AUDIT).[51] These measures were selected to assess a range of psychological treatment response and based on established reliability and validity. They were typically completed in 45 to 60 minutes.

For participants randomly assigned to ART, the outcome measures were completed 3 times; at enrollment, after the final ART session, and at 3 months post-treatment. For participants randomly assigned to AC, the outcome measures were completed 4 times; at enrollment, after the final AC session, after the final ART session (i.e., after crossover to ART), and at 3 months post-treatment. Post-treatment evaluations were completed in person except in rare instances when participants could not come to the study site; in these instances, participants completed and returned assessments via U.S. mail. Occurrence of adverse events was determined by inquiry from the treating clinician before each session including the nature and intensity of each event, subsequent treatment actions, and judgment as to whether the event was related to use of ART. Per requirements of the DoD Office of Research Protections, Human Research Protection Office, a designated Safety Monitor was assigned to the trial. Participants received $50 each time they completed the set of study assessments.

### Statistical Methods

Demographic, military, and clinical characteristics of the study sample are described by means and standard deviations for continuous variables and percentages for categorical variables. Distributions of these characteristics were compared by random assignment by use of student $t$ tests and Fisher's exact test. For the primary outcome of PTSD symptomatology, analysis of covariance was used to compare mean pre-/post-differences on the PCL-M by random assignment, adjusting for the baseline value. The first analysis was conducted on the 50 participants who received and completed their randomly assigned intervention. A second intention-to-treat (ITT) analysis was conducted by imputing mean pre-/post-difference values of 0 on the PCL-M for the 7 participants (ART = 3, AC = 4) without post-intervention assessment. Although this approach is generally expected to reduce the overall effect size, there may be a corresponding increase in statistical power because of a larger sample size and smaller standard of error (i.e., by imputing pre-/post-difference values of zero to represent no treatment effect). To "correct" for the reduced standard errors, a third analysis was conducted using the ITT principle and the original standard errors derived from participants who received and completed their randomly assigned intervention. This latter approach represents the most conservative method for statistical testing in this

analysis. For secondary outcomes of comorbidities measured as continuous variables (e.g., CES-D scale for depression), the same analysis methods were used.

Because different cutpoints suggestive of PTSD exist on the PCL-M and PDSQ used in this study, we classified intervention "responders" (yes/no) based on the concept of reliable change (statistical and clinical), as defined by a reduction of $\geq 10$ points on the PCL-M.[52] This approach avoids the limitation of apparent treatment responders who may be just above the threshold before treatment and then just below the threshold after treatment. The proportion of intervention responders was compared by random assignment by use of Fisher's exact test. Corresponding rate ratios and 95% confidence intervals were calculated. These analyses were conducted among the 50 participants who received and completed their assignment intervention, and based on the ITT principle assigning the 7 noncompleters as nonresponders. The above analyses were repeated stratifying the study sample by entry PTSD symptom scores strongly suggestive of presence versus absence of a formal PTSD diagnosis.

### Statistical Power

With change in score on the PCL-M before and after conduct of the randomly assigned regimens as the primary outcome, the trial was initially powered for a total sample size of $n = 80$, postulating a "medium-to-large" effect size of 0.67,[53] 2-sided type I error rate of 0.05, and 10% dropout. However, in an interim analysis conducted among the first 30 participants with pre- and post-assessments following ART ($n = 15$) or AC ($n = 15$), a very large between-group effect size of 1.27 was observed on scores from the PCL-M.[54] Therefore, a decision was made to cap recruitment at an estimated 60 consenting and eligible participants.

### RESULTS

#### Sample

A total of 63 service members/veterans were assessed for trial eligibility, of whom, 57 (90.5) were clinically eligible and enrolled (Fig. 1). Of these 57, 50 (87.7%) were from the primary Tampa site and the remaining 7 were from the Las Vegas site. Of the 29 participants assigned to the ART intervention (50.9% of the sample), 28 (96.6%) received treatment and 26 (92.9%) completed treatment. Of the 28 participants assigned to the AC group, 12 (42.9%) selected the fitness assessment and planning regimen and the remaining 16 (57.1%) selected the career assessment and planning regimen. Of these 28 participants, 24 (85.7%) received both sessions (i.e., full compliance). For the 7 participants who did not start treatment, 4 were from the Las Vegas site and withdrew because of scheduling conflicts. After the AC regimen, 22 of the 24 participants (91.7%) crossed over to ART and 21 (95.5%) completed treatment. Considering both groups, 47 of 50 participants (94.0%) who started ART completed the full

## *Accelerated Resolution Therapy (ART) for Psychological Trauma*
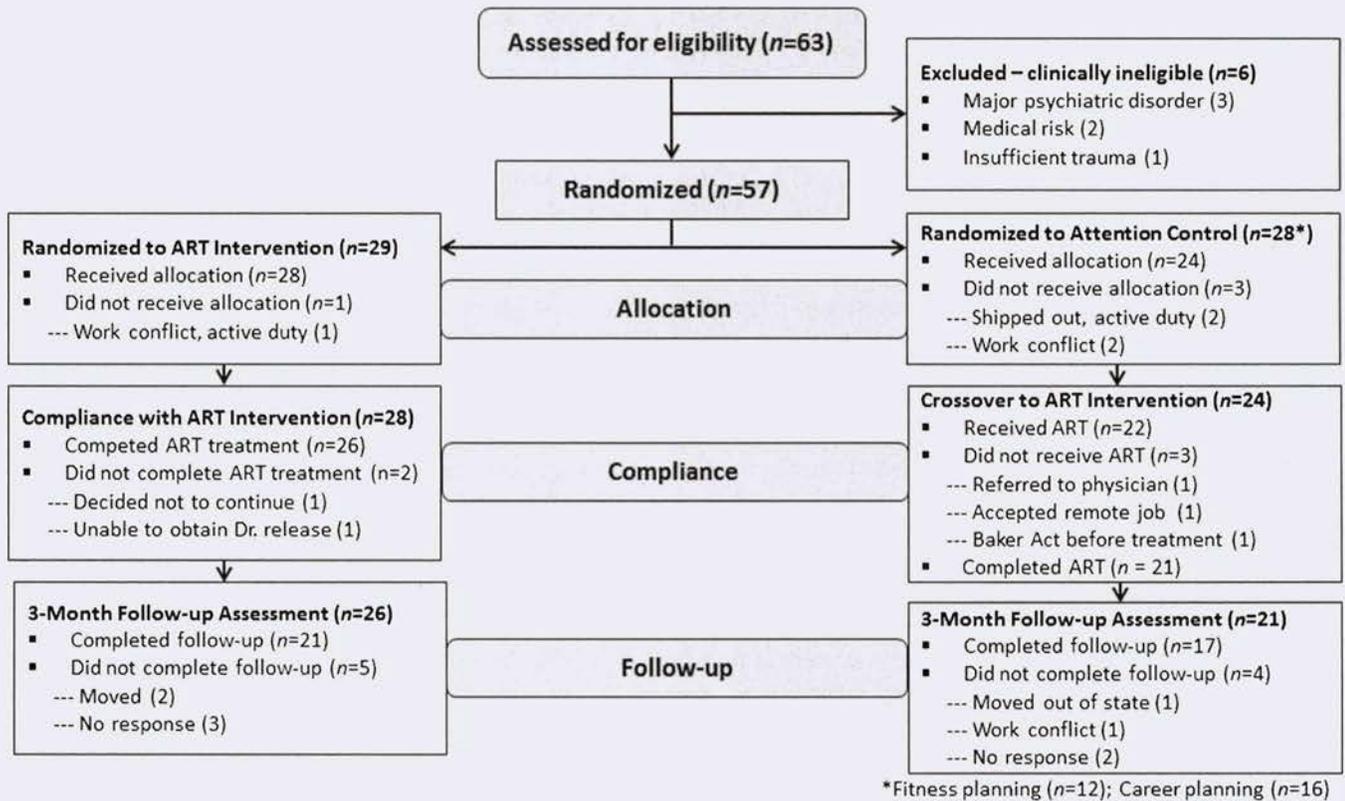### (ClinicalTrials.gov Identifier: NCT01559688)



**FIGURE 1.** Consort diagram of the trial population including those screened, enrolled, randomly assigned, completing treatment, and those who provided 3-month follow-up data.

course of treatment. Of these 47, 38 (80.9%) provided 3-month follow-up data

### *Presenting Characteristics*

The mean age of the study sample was 41.4 ± 12.6 years, 19.3% were female, 84.2% were of Caucasian race, and 10.5% were of Hispanic ethnicity (Table I). The majority of study participants (70.2%) were veterans, 54.4% had prior Army service, and 40.4% had served in Iraq as their principal deployment. Nearly half (42.1%) were receiving disability for PTSD and/or another mental health disorder, approximately half (47.4%) reported 5 or more traumatic memories currently impacting their life, and 68.4% had received prior treatment for PTSD. The principal types of trauma for which treatment was sought included witnessing of death, execution, and/or major injuries (36.8%), or improvised explosive device blast or combat explosion (36.8%). Overall, the 2 groups were well balanced on demographic and military characteristics, although there was a trend for higher Army service representation in the ART group compared to the AC group (65.5% vs. 42.9%; $p = 0.09$).

Clinically (Table II), the mean PCL-M score was 56.9 ± 15.2, 65% had a PCL-M score of ≥50, a suggested cutpoint in VA or civilian specialty mental health clinics locations with a high prevalence of PTSD,[55] and 75% endorsed the requisite

number and type of items on the PCL-M indicative of PTSD.[55] In addition, 89.5% of the sample scored positive on the PTSD subscale of the PDSQ[39,40]; thus, 93% of the sample met at least one of the screening criteria indicative of a diagnosis of PTSD. Comorbid depression was high; 75% of the sample had a screening score of ≥16 on the CES-D, which is indicative of depression.[56] Additional comorbidities that were prevalent, based on subscale scores of the PDSQ, included obsessive compulsive disorder (61%), agoraphobia (61%), generalized anxiety disorder (60%), somatization disorder (56%), social phobia (54%), and hypochondriasis (44%). Although being enrolled in a substance abuse treatment program was an exclusion criterion, 37% and 12% screened positive for alcohol and drug abuse/dependence on the PDSQ, respectively, and 21.8% scored 8 or higher on the AUDIT, which is associated with harmful or hazardous drinking.[51] Given prior PTSD treatment history and presenting status, the majority of the sample was characterized as having symptoms of refractory PTSD and high comorbidities associated with PTSD.

### *Initial Treatment Effect of ART*

The 26 participants assigned to ART who completed treatment underwent a mean of 3.6 ± 1.1 sessions. All 24 participants assigned to the AC group who initiated the intervention

**TABLE I.** Demographic and Military Characteristics by Random Assignment

| Characteristic | All ($n = 57$) | ART ($n = 29$) | AC ($n = 28$) | $p$-value |
|---|---|---|---|---|
| Age in Years (Mean ± SD) | 41.4 ± 12.6 | 38.9 ± 11.5 | 44.0 ± 13.4 | 0.13 |
| Female Gender (%) | 19.3 | 17.2 | 21.4 | 0.75 |
| Race (%) | | | | 0.87 |
|   White | 84.2 | 86.2 | 82.1 | |
|   Black or African American | 10.5 | 10.3 | 10.7 | |
|   Other | 5.3 | 3.5 | 7.1 | |
| Hispanic Ethnicity (%) | 10.5 | 17.2 | 3.6 | 0.19 |
| Married (%) | 56.1 | 62.1 | 50.0 | 0.43 |
| Employed—Full or Part Time (%) | 57.9 | 58.6 | 57.1 | 1.0 |
| Education (%) | | | | 0.59 |
|   High School | 17.5 | 13.8 | 21.4 | |
|   Some College | 40.3 | 41.4 | 39.3 | |
|   Bachelors' Degree | 21.1 | 27.6 | 14.3 | |
|   Post-Bachelors' Education | 21.1 | 17.2 | 25.0 | |
| Current Military Status (%) | | | | 1.0 |
|   Active Duty | 12.3 | 13.8 | 10.7 | |
|   Reservist | 17.5 | 17.2 | 17.9 | |
|   Discharged/Veteran | 70.2 | 69.0 | 71.4 | |
| Primary Branch of Military Service (%) | | | | 0.09 |
|   Army | 54.4 | 65.5 | 42.9 | |
|   Navy | 21.0 | 24.1 | 17.9 | |
|   Air Force | 12.3 | 6.9 | 17.9 | |
|   Marines | 12.3 | 3.5 | 21.4 | |
| Four or More Overseas Tours of Duty (%) | 34.0 | 29.6 | 38.5 | 0.57 |
| Principal Location of Deployment(s) (%) | | | | 0.52 |
|   Iraq | 40.4 | 48.3 | 32.1 | |
|   Afghanistan | 10.5 | 10.3 | 10.7 | |
|   Vietnam | 7.0 | 3.5 | 10.7 | |
|   Other | 42.1 | 37.9 | 46.4 | |
| History of Head Trauma (%) | 35.1 | 41.4 | 28.6 | 0.41 |
| On Disability for PTSD/Other Mental Health Disorder (%) | 42.1 | 51.7 | 32.1 | 0.18 |
| Principal Type of Trauma Sought for Treatment (%) | | | | 0.99 |
|   Military Sexual Trauma | 10.5 | 10.3 | 10.7 | |
|   Witness Death, Execution, and/or Major Injuries | 36.8 | 34.5 | 39.3 | |
|   Improvised Explosive Device Blast or Combat Explosion | 36.8 | 37.9 | 35.7 | |
|   Homicide of Civilian | 3.5 | 3.5 | 3.6 | |
|   Multiple Traumas (3 or More) | 12.3 | 13.8 | 10.7 | |
| Five or More Traumatic Memories Currently Impacting Life (%) | 47.4 | 51.7 | 42.9 | 0.60 |
| Lived with Traumatic Memories >10 Years (%) | 49.1 | 44.8 | 53.6 | 0.60 |
| Previous Treatment for PTSD (%) | 68.4 | 65.5 | 71.4 | 0.78 |
|   Individual Therapy | 59.7 | 51.7 | 67.9 | 0.28 |
|   Group Therapy | 19.3 | 17.2 | 21.4 | 0.75 |
|   Pharmacotherapy | 52.6 | 58.6 | 46.4 | 0.43 |

completed 2 sessions (per study protocol). Among the 50 completers of their randomly assigned intervention, the mean pre-/post-change on the PCL-M was $-17.2 \pm 13.4$ in the ART group versus $-2.5 \pm 6.0$ in the AC group (effect size = 1.39; $p < 0.0001$) (Fig. 2). When including the 7 noncompleters in the ITT analysis (defined in methods), the mean pre-/post-change on the PCL-M was $-15.4 \pm 13.7$ in the ART group compared to $-2.1 \pm 5.6$ in the AC group (effect size = 1.25; $p < 0.0001$). Adjusting the standard error for imputed mean differences of zero for the 7 noncompleters did not alter the results (corrected $p < 0.0001$). For the 39 of 50 treatment completers (78% of sample) with evidence of refractory PTSD, the mean pre-/post-change on the PCL-M was $-20.4 \pm 13.6$ in the ART group versus $-1.7 \pm$

5.6 in the AC group (effect size = 1.80; $p < 0.0001$). Results were similar in the ITT analysis (effect size = 1.55, corrected $p$-value <0.0001).

When evaluating PTSD symptom response by the reliable change criterion among the 50 intervention completers (Table III), 65.4% of the ART group experienced a ≥10-point reduction on the PCL-M compared to 12.5% in the AC group (rate ratio = 5.23, 95% confidence interval: 1.80–20.74, $p < 0.0001$). Results were similar in the full ITT analysis (rate ratio = 5.47, 95% confidence interval: 1.83–22.14, $p < 0.0001$), as well as when restricting the analysis to participants who met the different screening criterion cutpoints for PTSD. Among the 17 intervention completers who presented with a PCL-M score <50, there was a slight attenuation of

**TABLE II.**   Clinical Characteristics by Random Assignment

| Characteristic | All (*n* = 57) | ART (*n* = 29) | AC (*n* = 28) | *p*-Value |
|---|---|---|---|---|
| CES-D Score (Mean ± SD) | 26.5 ± 13.6 | 26.2 ± 13.5 | 26.7 ± 14.0 | 0.87 |
| CES-D Score ≥ 16 (%) | 75.4 | 75.9 | 75.0 | 1.0 |
| PCL-M Score (Mean ± SD) | 56.9 ± 15.2 | 57.4 ± 15.0 | 56.4 ± 15.7 | 0.81 |
| PCL-M Score ≥50 (%)[a] | 64.9 | 69.0 | 60.7 | 0.59 |
| PCL-M Critical Items for PTSD (%)[b] | 75.4 | 79.3 | 71.4 | 0.55 |
| PDSQ Score (Mean ± SD) (T-Score) | 54.5 ± 10.4 | 54.6 ± 9.1 | 54.5 ± 11.7 | 0.97 |
| Subscale of PDSQ (% Meeting Cutoff Score)[c] | | | | |
|   PTSD[d] (15/5) | 89.5 | 93.1 | 85.7 | 0.42 |
|   Major Depressive Disorder (21/9) | 56.1 | 55.2 | 57.1 | 1.0 |
|   Bulimia/Binge-Eating Disorder (10/7) | 14.0 | 17.2 | 10.7 | 0.71 |
|   Obsessive Compulsive Disorder (7/1) | 61.4 | 58.6 | 64.3 | 0.79 |
|   Panic Disorder (8/4) | 36.8 | 37.9 | 35.7 | 1.0 |
|   Psychosis (6/2)[e] | 14.0 | 17.2 | 10.7 | 0.71 |
|   Agoraphobia (11/4) | 61.4 | 69.0 | 53.6 | 0.28 |
|   Social Phobia (15/4) | 54.4 | 55.2 | 53.6 | 1.0 |
|   Alcohol Abuse/Dependence (6/1) | 36.8 | 41.1 | 32.1 | 0.59 |
|   Drug Abuse/Dependence (6/1) | 12.3 | 13.8 | 10.7 | 1.0 |
|   Generalized Anxiety Disorder (10/7) | 59.6 | 62.1 | 57.1 | 0.79 |
|   Somatization Disorder (5/2) | 56.1 | 58.6 | 53.6 | 0.79 |
|   Hypochondriasis (5/1) | 43.9 | 41.4 | 46.4 | 0.79 |
| Any PTSD Screening Criteria (%)[e] | 93.0 | 96.6 | 89.3 | 0.35 |

[a]Established screening cutpoint score for probable PTSD. [b]DSM-IV symptom criteria for probable PTSD (at least 1 "B" item [questions 1–5], 3 "C" items [questions 6–12], and at least 2 "D" items [questions 13–17]) rated as "moderately" or above. [c]Parentheses include number of subscale items/number required to meet cutoff score. [d]Screening cutoff score from the 15-item PTSD subscale of the PDSQ. [e]Screening criteria for PTSD from the PCL-M and/or PDSQ.

reliable change (≥10 point reduction) in the ART group (50.0%) compared to the AC group (11.1%) (rate ratio = 4.50, 95% confidence interval: 0.59–103.7, *p* = 0.13).

### *Initial Effect of ART on Comorbidities*

As seen in Table IV among the 50 completers of their randomly assigned intervention, the mean pre-/post-change on the CES-D was −12.3 (95% confidence interval [CI] −17.1 to −7.5) in the ART group compared to 1.3 (95% CI −1.6 to 4.2) in the AC group (effect size = 1.39, *p* < 0.0001). The between-

group effect size of 1.39 on the CES-D was nominally reduced to 1.27 in the ITT analysis (*p* < 0.0001) and remained highly statistically significant (*p* < 0.0001) in the ITT analysis that used the "corrected" standard errors from intervention completers (i.e., the most conservative approach). Large, statistically significant effect sizes associated with ART were observed for cognitive anxiety (effect size = 1.03, ITT corrected *p*-value = 0.002), trauma-related growth–global guilt (effect size = 1.21, ITT corrected *p*-value = 0.0004), and trauma-related growth–distress (effect size = 1.22, ITT
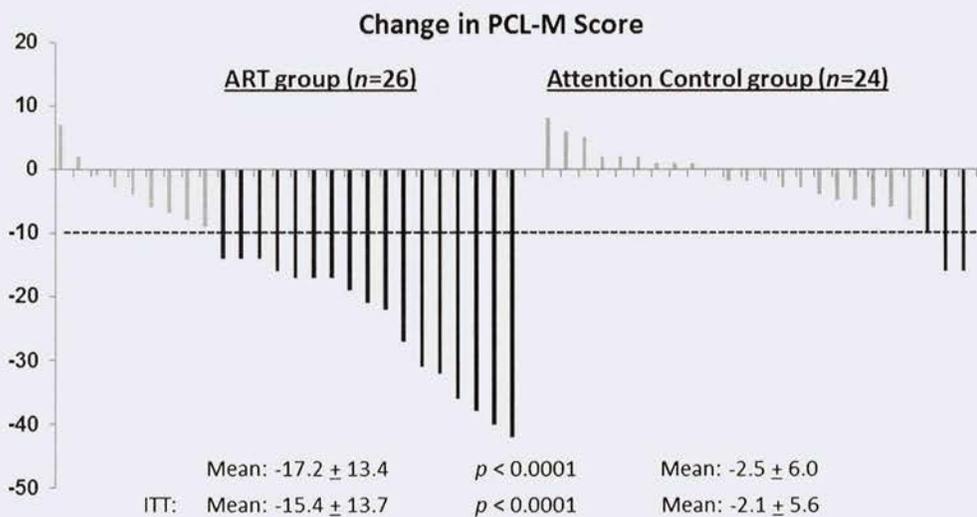


**Change in PCL-M Score**

ART group (*n*=26)    Attention Control group (*n*=24)

Mean: -17.2 ± 13.4    *p* < 0.0001    Mean: -2.5 ± 6.0
ITT: Mean: -15.4 ± 13.7    *p* < 0.0001    Mean: -2.1 ± 5.6

**FIGURE 2.**   Plot of change scores on the PCL-M (PTSD) checklist before and after treatment with ART versus before and after an AC regimen. Each vertical line represents the response of an individual service member or veteran. The dashed horizontal line represents a clinically meaningful and reliable reduction of ≥10 points on the PCL-M. ITT: analyzed by the ITT principle.

**TABLE III.** Rate Ratios (RRs) of Reliable Change (%) Treatment Effect by Random Assignment and Based on Presenting PTSD Scores

| Presenting PTSD Score | AC | | ART | | | | |
|---|---|---|---|---|---|---|---|
| | N | % | N | % | RRs | 95% CI | p-Value |
| Full Sample—Completers | 24 | 12.5 | 26 | 65.4 | 5.23 | 1.80–20.74 | <0.0001 |
| Full Sample—ITT[a] | 28 | 10.7 | 29 | 58.6 | 5.47 | 1.83–22.14 | <0.0001 |
| PCL-M Score ≥50 at Entry—Completers | 15 | 13.3 | 18 | 72.2 | 5.42 | 1.56–32.05 | 0.001 |
| PCL-M Score ≥50 at Entry—ITT[a] | 17 | 11.8 | 20 | 65.0 | 5.52 | 1.53–33.54 | 0.002 |
| PCL-M Critical Items for PTSD[b]—Completers | 17 | 11.8 | 21 | 71.4 | 6.07 | 1.75–36.04 | <0.0001 |
| PCL-M Critical Items for PTSD[b]—ITT[a] | 20 | 10.0 | 23 | 65.2 | 6.52 | 1.81–39.41 | <0.0001 |
| PCL-M Score ≥50 and Critical Items for PTSD[b]—Completers | 14 | 14.3 | 18 | 72.2 | 5.06 | 1.47–29.88 | 0.002 |
| PCL-M Score ≥50 and Critical Items for PTSD[b]—ITT[a] | 16 | 12.5 | 21 | 65.0 | 5.20 | 1.45–31.54 | 0.002 |
| PCL-M Score <50 at Entry—Completers | 9 | 11.1 | 8 | 50.0 | 4.50 | 0.59–103.7 | 0.13 |
| PCL-M Score <50 at Entry—ITT[a] | 11 | 9.1 | 9 | 44.4 | 4.89 | 0.62–113.2 | 0.13 |

[a]ITT Method 1: assigning noncompleters as nonresponders. [b]DSM-IV symptom criteria for probable PTSD (at least 1 "B" item [questions 1–5], 3 "C" items [questions 6–12], and at least 2 "D" items [questions 13–17]) rated as "moderately" or above.

**TABLE IV.** Treatment Effect of ART versus AC for Comorbidities of PTSD

| Measure of Comorbidity | AC (n = 24) | | | | ART (n = 26) | | | | Effect Size | | p-Value[a] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Pre | Post | Diff | 95% CI | Pre | Post | Diff | 95% CI | Obs. | ITT | Obs.[a] | ITT[b] | ITT[c] |
| CES-D (Depression) | 26.9 | 28.2 | 1.3 | −1.6–4.2 | 26.7 | 14.3 | −12.3 | −17.1 to −7.5 | 1.39 | 1.27 | <0.0001 | <0.0001 | <0.0001 |
| Brief Symptom Inventory | 28.1 | 24.0 | −3.8 | −9.5–1.9 | 27.1 | 12.9 | −14.2 | −20.1 to −8.3 | 0.75 | 0.72 | 0.006 | 0.004 | 0.02 |
| STICSA (Somatic) | 20.6 | 19.7 | −0.9 | −3.3–1.5 | 18.3 | 15.3 | −3.0 | −4.9 to −1.1 | 0.41 | 0.41 | 0.06 | 0.05 | 0.19 |
| STICSA (Cognitive) | 23.8 | 22.3 | −1.8 | −3.6–0.04 | 23.7 | 16.5 | −7.2 | −9.7 to −4.8 | 1.03 | 0.97 | 0.0006 | 0.0003 | 0.002 |
| Pittsburgh Sleep Quality | 11.7 | 11.7 | −0.1 | −1.0–0.7 | 12.8 | 10.4 | −2.4 | −4.7 to −0.1 | 0.57 | 0.48 | 0.10 | 0.14 | 0.16 |
| Trauma-Related Growth | | | | | | | | | | | | | |
| Global Guilt | 5.8 | 7.2 | 1.4 | 0.1–2.6 | 8.3 | 4.7 | −3.6 | −5.6 to −1.6 | 1.21 | 1.12 | 0.0004 | 0.0004 | 0.0004 |
| Distress | 14.6 | 15.8 | 1.2 | −0.5–3.0 | 16.4 | 10.4 | −6.0 | −8.8 to −3.1 | 1.22 | 1.13 | 0.0002 | 0.0002 | 0.0006 |
| Guilt Cognition | 20.2 | 20.8 | 0.6 | −6.1–7.4 | 26.7 | 15.8 | −10.9 | −19.2 to −2.6 | 0.62 | 0.59 | 0.09 | 0.19 | 0.06 |
| Post-Traumatic Growth | | | | | | | | | | | | | |
| I: Relation to Others | 13.0 | 14.7 | 1.8 | −0.9–4.4 | 11.6 | 14.1 | 2.5 | −2.1–7.0 | 0.08 | 0.08 | 0.92 | 0.89 | 0.79 |
| II: New Possibilities | 11.4 | 11.3 | −0.1 | −2.6–2.5 | 12.9 | 14.4 | 1.5 | −1.0–4.1 | 0.27 | 0.25 | 0.21 | 0.27 | 0.45 |
| III: Personal Strength | 9.8 | 11.3 | 1.5 | −0.6–3.5 | 10.6 | 12.4 | 1.8 | −0.9–4.6 | 0.07 | 0.07 | 0.64 | 0.73 | 0.77 |
| IV: Spiritual Change | 5.2 | 5.0 | −0.2 | −1.2–0.8 | 5.3 | 6.4 | 1.0 | −0.5–2.5 | 0.42 | 0.39 | 0.10 | 0.14 | 0.25 |
| V: Appreciation-Life | 8.9 | 9.5 | 0.6 | −1.1–2.3 | 10.8 | 11.3 | 0.5 | −1.2–2.2 | −0.03 | −0.02 | 0.59 | 0.71 | 0.59 |
| Self-Compassion Scale | 71.8 | 71.6 | −0.2 | −3.6–3.3 | 74.5 | 86.1 | 11.5 | 3.0–20.1 | 0.72 | 0.68 | 0.007 | 0.009 | 0.03 |
| Aggression Questionnaire | 73.4 | 75.5 | 2.1 | −5.3–9.6 | 82.1 | 75.1 | −7.0 | −14.9–0.9 | 0.49 | 0.46 | 0.19 | 0.21 | 0.13 |

[a]p-Value adjusted for baseline measurement. [b]p-Value based on ITT assuming mean difference of zero from baseline to post-intervention assessment and adjusted for baseline value. [c]Based on student t test and ITT assuming mean difference of zero from baseline to postintervention assessment and standard error from completers with nonmissing data.

corrected p-value = 0.0006). Other statistically significant improvements were observed on the BSI and for symptoms of guilt cognition and self-compassion.

### Follow-up Effect of ART

Thirty-eight of the 47 participants (80.9%) who completed treatment with ART provided follow-up data at 3 months. Among these participants, as well as when imputing no treatment response for those lost to follow-up (i.e., ITT analysis), there were strong, sustained reductions in symptoms of PTSD, depression, anxiety, and aggression (p < 0.0001) (Table V). Significant improvements in trauma-related distress and self-compassion were also reported. Among those with follow-up data, 30 of 38 (79.0%) had a sustained reduction of ≥10 points from the baseline assessment of PTSD symptoms (PCL-M).

### Adverse Events

The 50 participants who received ART underwent a total of 183 sessions. Seven adverse events were reported and classified as severe (n = 2), moderate (n = 4), or mild (n = 1). The 2 severe events were attributed as "unlikely" or "probably related" to receipt of ART (Table VI). Six of the 7 participants who reported an adverse event completed treatment with ART. The 4 events classified as "possibly" or "probably" related to ART corresponds to a rate of 2.2 adverse events per 100 sessions of ART that may be attributed to receipt of ART.

### DISCUSSION

In this first controlled, unblinded trial of ART and with a central focus on combat-related psychological trauma, we observed clinically and statistically significant reductions

**TABLE V.** Baseline to 3-Month Within-Subject Changes in PTSD and Comorbidity Scores Among Participants Who Completed Treatment with ART and Had Follow-up Data

| Measure | N | Mean Scores | | Diff Scores | | Effect Size | | | p-Value | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Base | 3 Mo. | Mean | 95% CI | Comp. | ITT[a] | ITT[b] | Comp. | ITT[a] | ITT[b] |
| PCL-M | 38 | 53.4 | 32.9 | −20.5 | −25.0 to −16.0 | 1.50 | 1.13 | 1.22 | <0.0001 | <0.0001 | <0.0001 |
| CES-D (Depression) | 38 | 24.8 | 13.0 | −11.8 | −15.5 to −8.0 | 1.03 | 0.85 | 0.84 | <0.0001 | <0.0001 | <0.0001 |
| BSI | 37 | 24.0 | 8.8 | −15.2 | −20.2 to −10.3 | 1.02 | 0.82 | 0.80 | <0.0001 | <0.0001 | <0.0001 |
| STICSA (Somatic) | 37 | 17.2 | 13.6 | −3.6 | −5.1 to −2.2 | 0.83 | 0.64 | 0.65 | <0.0001 | <0.0001 | 0.0003 |
| STICSA (Cognitive) | 37 | 21.2 | 15.5 | −5.7 | −7.8 to −3.6 | 0.90 | 0.69 | 0.71 | <0.0001 | <0.0001 | <0.0001 |
| Pittsburgh Sleep Quality | 30 | 11.6 | 8.8 | −2.8 | −4.4 to −1.3 | 0.69 | 0.51 | 0.44 | 0.0007 | 0.001 | 0.02 |
| Trauma-Related Growth | | | | | | | | | | | |
| Global Guilt | 38 | 7.8 | 4.3 | −3.5 | −5.2 to −1.8 | 0.66 | 0.57 | 0.54 | 0.0002 | 0.0003 | 0.002 |
| Distress | 37 | 15.5 | 9.3 | −6.2 | −8.3 to −4.1 | 0.98 | 0.79 | 0.77 | <0.0001 | <0.0001 | <0.0001 |
| Guilt Cognition | 38 | 23.4 | 15.6 | −7.8 | −13.9 to −1.8 | 0.43 | 0.38 | 0.34 | 0.01 | 0.01 | 0.04 |
| Post-Traumatic Growth | | | | | | | | | | | |
| I: Relation to Others | 30 | 13.5 | 17.4 | 4.0 | 0.3–7.6 | 0.41 | 0.32 | 0.26 | 0.03 | 0.03 | 0.16 |
| II: New Possibilities | 30 | 13.2 | 14.0 | 0.7 | −1.5–3.0 | 0.12 | 0.10 | 0.08 | 0.51 | 0.02 | 0.68 |
| III: Personal Strength | 30 | 10.5 | 12.8 | 2.3 | −0.1–4.8 | 0.36 | 0.28 | 0.23 | 0.06 | 0.06 | 0.22 |
| IV: Spiritual Change | 30 | 5.5 | 5.6 | 0.1 | −1.3–1.5 | 0.03 | 0.02 | 0.02 | 0.89 | 0.90 | 0.93 |
| V: Appreciation-Life | 30 | 10.7 | 10.1 | −0.6 | −2.0–0.8 | −0.15 | −0.12 | −0.10 | 0.42 | 0.41 | 0.60 |
| Self-Compassion Scale | 38 | 76.1 | 87.0 | 10.8 | 5.4–16.3 | 0.65 | 0.56 | 0.53 | 0.0003 | 0.0004 | 0.002 |
| Aggression Questionnaire | 38 | 78.2 | 63.5 | −14.7 | −19.0 to −10.5 | 1.14 | 0.92 | 0.92 | <0.0001 | <0.0001 | <0.0001 |

Comp.: Completers with 3-month follow-up data. [a]p-Value based on ITT assuming mean difference of zero from baseline to 3-month assessment for participant without follow-up data (total $n = 47$). [b]Based on paired $t$ test and ITT assuming mean difference of zero from baseline to 3-month assessment and standard error from completers with nonmissing data.

**TABLE VI.** Adverse Events Reported

| | Event Description | Severity | Attribution to ART | External Treatment[a] | Completed ART |
|---|---|---|---|---|---|
| A | Nightmares related to traumatic events | Mild | Possibly | No | Yes |
| B | Trip to Mexico reminded of trauma from Baghdad | Moderate | Unrelated | No | Yes |
| C | Combat flashback and nightmare after mass shooting in Colorado | Moderate | Unrelated | No | Yes |
| D | Got up abruptly from sleep, passed out and hit head on floor | Moderate | Possibly | No | Yes |
| E | Increase in level of anxiety | Moderate | Probably | No | Yes |
| F | Concern that new medication was causing high anxiety and anger | Severe | Unrelated | Yes[b] | Yes |
| G | Sporadic nightmares consistent with previous history of nightmares | Severe | Probably | No | No |

[a]All events were reported a single time and with subsequent resolution. [b]Referred to James A. Haley Veterans Hospital in Tampa, Florida. Resulted in subsequent medication adjustment.

in symptoms of PTSD and related comorbidities among participants assigned to the ART intervention. No appreciable changes in symptoms were observed among participants randomly assigned to the AC regimen, thereby seemingly negating the explanation of the effect of ART being attributed simply to personal interaction with a professional. Participants assigned to ART completed treatment in a mean of 3.6 sessions, without homework assignments, and a very low incidence of possible treatment-related serious adverse events. This length of treatment time is much shorter (>50%) than current first-line therapies formally endorsed by the DoD and VA.[26,29,34] In addition, favorable treatment results for the ART group and the AC group who crossed over to ART were sustained at 3 months and are consistent with previous treatment results in civilians.[35,36] Collectively, these findings suggest further evaluation of ART as a potential first-line treatment for combat-related PTSD.

## Context of Results

The magnitude of PTSD symptom reduction with the ART intervention indicated that approximately two-thirds of all treated participants were classified as treatment "responders" with a rate of approximately 60% when applying the strict ITT principle (i.e., counting noncompleters as nonresponders). Similarly, the mean reduction of $17.2 \pm 13.4$ points on the PCL-M in the ART group clearly exceeds the concept of statistical and clinically meaningful change, as defined as a reduction of ≥10 points on the PCL-M.[52] Approximately two-thirds of the study population presented with apparent "refractory" PTSD based on their previous treatment history for PTSD and presenting symptomatology, as well as high prevalence of comorbidities. Thus, the study population, in terms of generalizability, included service members and veterans with significantly impaired psychological status, and many with residual symptoms despite previous treatment for PTSD.

Responder rates from this trial cannot be compared directly to previous trials of PE, CPT, and EMDR. Having said this, the majority of published clinical trials on use of PE in the treatment of PTSD have not analyzed results by use of the standard, preferred ITT principle, and instead, have analyzed the data by the subset of treatment completers, which can result in substantial bias.[57,58] Therefore, the approximate 60% responder rate with ART when applying the strict ITT principle would appear to be favorable. This is suggested by an extensive review of outcome studies for PTSD in which Schottenbauer et al[32] stated that a careful review of the treatment literature indicates that currently empirically supported cognitive behavioral therapies have large dropout and nonresponse rates. Similarly, Hoge[59] reported that recovery rates of 60% to 80% among treatment completers (e.g., PE, CPT) decline to about 40% using ITT analyses.

The issue of treatment dropout is particularly germane given that OEF/OIF veterans have been reported to dropout from treatment twice more frequently than Vietnam veterans.[60] In the present trial, the treatment completion rate in the ART assigned group was 90%, with 3 of 29 participants classified as dropouts, one of which was due to active duty assignment. This completion rate appears to be much higher than that experienced with PE, whereby a significant proportion of Iraq and Afghanistan war veterans who fail to complete such treatment appear to drop out before even initiating therapy.[61] This is consistent with 59% of psychologists in clinical practice who reported harboring a belief that using exposure therapy is likely to increase the patients' desire to drop out of treatment,[62] as well as low reported use of IE to treat PTSD by both U.S.[62] and European clinicians.[63] As the current DoD/VA mental health system is substantially challenged now and in the coming decades to meet the very high current PTSD treatment need,[64] there exists a premium on delivering therapy with approaches that maximize successful treatment initiation and completion.[65]

### Clinical Comparison to Other Therapies

Clinically, major distinctions between ART and PE, CPT, and EMDR can be briefly summarized into 4 areas. First, ART is delivered in a much shorter period of time, 2 to 5 sessions approximately 1 hour in length and without additional homework or practice assignments. Second, ART uses IR to "replace" negative imagery (and other sensations) with positive imagery, whereas PE aims to extinguish the conditioned emotional "response" to the traumatic stimuli; CPT focuses on challenging and "modifying" maladaptive beliefs related to the trauma; and EMDR focuses on "desensitization," as opposed to actual replacement of negative images. Third, ART can be "silent" in that the participant need not verbalize any details of the traumatic experience; CPT, PE, and EMDR typically involve verbal and/or written recall of the trauma. Finally, ART uses eye movements to help process traumatic material, but differs from EMDR by performing a "sensation check" after each set, using a standard number of

40 eye movements, and being highly directive (in changing images) without free association.

### Impact on Comorbidities

The substantial reductions in symptoms of both PTSD and depression with use of ART among service members and veterans is consistent with results published among civilians,[36] and the high prevalence and symptom overlap of these two disorders.[66,67] At the 3-month post-treatment follow-up, we observed substantial reductions in self-reported aggression. This is of considerable societal interest because of the relationship between PTSD-mediated aggression and violence in domestic relationships.[68] Similarly, our findings of greater self-compassion reported 3 months after completing ART suggest the potential for improved family relations with this therapy, an area encouraged for future research.

### Treatment Costs

For U.S. military members who served in the wars in Iraq and Afghanistan since 2001 and are afflicted with PTSD, the U.S. Congressional Budget Office estimates an average annual treatment cost per member of $8,400 within the VA system, a cost that is 4 times higher than those treated without PTSD or traumatic brain injury.[69] For completers of ART in this study, a mean of 3.7 sessions were delivered. Estimating a clinician cost of $100 per session with ART, plus allowing for an initial intake evaluation session and two post-treatment visits, aggregate costs per person with ART remain under $1,000 within a clinical setting. Thus, the potential cost savings of treatment of PTSD with ART are substantial.

### Strengths and Limitations

Strengths of the study include use of a highly standardized treatment protocol (ART); wide range of therapists with different backgrounds, which enhances the generalizability of treatment delivery; analysis of results using strict application of the ITT principle to report response rates in the most conservative manner; and not having the founder (L.R.) or lead ART trainer (A.S.) have any involvement with outcome assessment to eliminate potential ascertainment bias. A limitation is that the ART intervention was not compared to an active psychotherapy regimen, such as PE. Thus, no direct comparison of treatment efficacy of ART versus current first-line treatments (PE, CPT, and EMDR) can be made. Second, by design, the AC group was not parallel in contact hours to the ART intervention. Although not methodologically ideal, the AC group showed essentially no improvement in overall psychological status, a finding we believe would have likely continued had additional control sessions been offered. Third, formal diagnoses of PTSD were not used; however, a large percentage of participants had previously received treatment for PTSD, 93% of the sample met at least one of the screening criteria indicative of a diagnosis of PTSD, and we analyzed the data using multiple measures and approaches that

are indicative of a diagnosis of PTSD, and results were similar throughout. Finally, the 3-month post-treatment follow-up period is relatively brief and 19% of treatment completers did not provide follow-up data; hence, long-term sustainability of results cannot be concluded from this analysis. However, the robust findings at 3-month post-treatment, which included the ITT analysis, support the need to investigate the approach further and for longer periods of time.

## Conclusions

In this first controlled trial, ART appears to be a brief, effective, and safe method of exposure therapy for veterans with symptoms of combat-related PTSD. Given the military population that was studied in this trial, results suggest that ART be considered as a treatment option for refractory PTSD, meaning those who have experienced suboptimal response from existing first-line therapies endorsed for PTSD. Future comparative effectiveness studies of ART versus first-line therapies appear warranted, along with mechanistic studies to examine how the IE and IR components of ART may use the reconsolidation window to change traumatic images and sensations, and subsequently lead to resolution of symptoms of PTSD.

## REFERENCES

1. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Ed 5. Washington, DC, American Psychiatric Association, 2013. Section 309.81 (F43.10). Available at http:// dsm.psychiatryonline.org.ezproxy.hsc.usf.edu/book.aspx?bookid=556; accessed August 5, 2013.
2. Kessler RC, Berglund P, Delmer O, Jin R, Merikangas KR, Walters EE: Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005; 62: 593–602.
3. Bisson J: Post-traumatic stress disorder. BMJ 2007; 334: 789–93.
4. Brady KT, Killeen TK, Brewerton T, Lucerini S: Comorbidity of psychiatric disorders and posttraumatic stress disorder. J Clin Psychiatry 2000; 61: 22–32.
5. Hoge CW, Terhakopian A, Castro CA, Messer SC, Engel CC: Association of posttraumatic stress disorder with somatic symptoms, health care visits, and absenteeism among Iraq war veterans. Am J Psychiatry 2007; 164: 150–3.
6. Kessler RC: Posttraumatic stress disorder: the burden to the individual and to society. J Clin Psychiatry 2000; 61(Suppl 5): 4–12.
7. Krysinska K, Lester D: Post-traumatic stress disorder and suicide risk: a systematic review. Arch Suicide Res 2010; 14: 1–23.
8. Oquendo MA, Friend JM, Halberstam B, et al: Association of comorbid posttraumatic stress disorder and major depression with greater risk for suicidal behavior. Am J Psychiatry 2003; 160: 580–2.
9. Thomas JL, Wilk JE, Riviere LA, McGurk D, Castro CA, Hoge CW: Prevalence of mental health problems and functional impairment among active component and National Guard soldiers 3 and 12 months following combat in Iraq. Arch Gen Psychiatry 2010; 67: 614–23.
10. Kok BC, Herrell RK, Thomas JL, Hoge CW: Posttraumatic stress disorder associated with combat service in Iraq or Afghanistan. J Nerv Ment Dis 2012; 200: 444–50.
11. Ramchard R, Schell TL, Karney BR, Osilla KC, Burns RM, Caldarone LH: Disparate prevalence estimates of PTSD among service members who served in Iraq and Afghanistan: possible explanations. J Trauma Stress 2010; 23: 59–68.
12. Richardson LK, Frueh BC, Acierno R: Prevalence estimates of combat-related PTSD: a critical review. Aust N Z J Psychiatry 2010; 44: 4–19.
13. LeardMann CA, Smith TC, Smith B, Wells TS, Ryan MA: Baseline self-repotred functional health and vulnerability to PTSD after combat deployment: prospective US military cohort study. BMJ 2009; 338: 1–9.
14. Smith TC, Ryan MA, Wingard DL, Slymen DL, Sallis JF, Kritz-Silverstein D: New onset and persistent symptoms of post-traumatic stress disorder self-reported after deployment and combat exposures: prospective population-based US military cohort study. BMJ 2008; 336: 366–71.
15. Foa EB, Keane TM, Friedman MJ: Effective Treatments for PTSD: Practice Guidelines from the International Society for Traumatic Stress Studies. New York, Guilford, 2008.
16. Forbes D, Creamer M, Bisson JI, et al: A guide to guidelines for the treatment of PTSD and related conditions. J Trauma Stress 2010; 23: 537–52.
17. Management of post-traumatic stress. Department of Veterans Affairs, 2004. Available at http://www.healthquality.va.gov/ptsd/ptsd_full.pdf; accessed February 22, 2013.
18. American Psychiatric Association: Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder. Arlington, VA, American Psychiatric Association, 2004.
19. National Institute for Health and Clinical Excellence: Post-traumatic stress disorder: the treatment of PTSD in adults and children. NICE Clinical Guidelines, No. 26. London, 2005. Available at http://www.nice .org.uk/nicemedia/pdf/CG026publicinfo.pdf; accessed March 16, 2013.
20. Institute of Medicine: Treatment of posttraumatic stress disorder: an assessment of the evidence. Washington, DC, National Academies Press, 2008. Available at http://www.nap.edu/openbook.php?record_id=11955; accessed April 14, 2013.
21. Ballenger JC, Davidson JR, Lecrubier Y, et al: Consensus statement update on posttraumatic stress disorder from the international consensus group on depression and anxiety. J Clin Psychiatry 2004; 65(Suppl 1): 55–62.
22. Foa EB, Hembree EA, Rothbaum BO: Prolonged Exposure Therapy for PTSD. Emotional Processing of Traumatic Experiences. Therapist Guide. New York, Oxford University Press, 2007.
23. Nemeroff CB, Bremner JD, Foa EB, Mayberg HS, North CS, Stein MB: Posttraumatic stress disorder: a state-of-the-science review. J Psychiatr Res 2006; 40: 1–21.
24. Resick PA, Schnicke MK: Cognitive processing therapy for sexual assault victims. J Consult Clin Psychol 1992; 60: 748–56.
25. Resick PA, Williams LF, Suvak MK, Monson CM, Gradus JL: Long-term outcomes of cognitive-behavioral treatments for posttraumatic stress disorder among female rape survivors. J Clin Consult Psychol 2012; 80: 201–10.
26. Friedman MJ: Post Traumatic Stress Disorder: The Latest Assessment and Treatment Strategies, Ed 3. Kansas City, KA, Compact Clinicals, 2003.
27. Shapiro F: Eye Movement Desensitization and Reprocessing: Basic Principles, Protocols and Procedures, Ed 2. New York, Guilford, 2001.
28. VA Office of Inspector General: VHA Handbook 1160.01: Uniformed mental health services in VA medical centers and clinics, 2008.

Washington, DC, VA Office of Inspector General. Available at http://www.mirecc.va.gov/VISN16/docs/UMHS_Handbook_1160.pdf; accessed May 20, 2013.

29. Resick PA, Nishith P, Weaver TL, Astin MC, Feuer CA: A comparison of cognitive-processing therapy with prolonged exposure and a waiting condition for the treatment of chronic posttraumatic stress disorder in female rape victims. J Consult Clin Psychol 2002; 70: 867–79.

30. Hembree EA, Foa EB, Dorfan NM, Street GP, Kowalski J, Tu X: Do patients drop out prematurely from exposure therapy for PTSD? J Trauma Stress 2003; 16: 555–62.

31. Schnurr PP, Friedman MJ, Engel CC, et al: Cognitive behavioral therapy for posttraumatic stress disorder in women: a randomized controlled trial. JAMA 2007; 297: 820–30.

32. Schottenbauer MA, Glass CR, Arnkoff DB, Tendick V, Gray SH: Nonresponse and dropout rates in outcome studies on PTSD: review and methodological considerations. Psychiatry 2008; 71: 134–69.

33. Minnen AV, Hagenaars M: Fear activation and habituation patterns as early process predictors for response to prolonged exposure treatment in PTSD. J Trauma Stress 2002; 15: 359–67.

34. Resick PA, Schnicke MK: Cognitive Processing Therapy for Rape Victims: A Treatment Manual. Newbury Park, CA, Sage, 1993.

35. Kip KE, Elk CA, Sullivan KL, et al: Brief treatment of symptoms of post-traumatic stress disorder (PTSD) by use of Accelerated Resolution Therapy (ART). Behav Sci 2012; 2: 115–34.

36. Kip KE, Sullivan KL, Lengacher CA, et al: Brief treatment of co-occurring post-traumatic stress and depressive symptoms by use of accelerated resolution therapy. Front Psychiatry 2013; 4: 1–12.

37. Blanchard EB, Jones-Alexander J, Buckley TC, Forneris CA: Psychometric properties of the PTSD checklist (PCL). Behav Res Ther 1996; 34: 669–73.

38. Weathers F: PTSD Checklist (PCL). United States Department of Veterans Affairs, National Center for PTSD. Available at http://www.ptsd.va.gov/professional/pages/assessments/ptsd-checklist.asp; accessed February 22, 2013.

39. Zimmerman M, Chelminski I: A scale to screen for DSM-IV Axis I disorders in psychiatric out-patients: performance of the Psychiatric Diagnostic Screening Questionnaire. Psychol Med 2006; 36: 1601–11.

40. Zimmerman M, Mattia JI: A self-report scale to help make psychiatric diagnoses: the Psychiatric Diagnostic Screening Questionnaire. Arch Gen Psychiatry 2001; 58: 787–94.

41. Trzepacz PT, Baker RW: The Psychiatric Mental Status Examination. Oxford, UK: Oxford University Press, 1993.

42. Liptak JJ: Treatment Planning in Career Counseling. Belmont, CA, Thomson Brooks/Cole, 2001.

43. Radloff LS: The CES-D scale: A self-report depression scale for research in the general population. Appl Psycholo Measurement 1977; 1: 385–401.

44. Derogatis LR: Brief Symptom Inventory (BSI)-18. Administration, Scoring And Procedures Manual. Minneapolis, MN, National Computer Systems, 2001.

45. Ree MJ, French D, MacLeod C, Locke V: Distinguishing cognitive and somatic dimesions of state and trait anxiety: development and validation of the state-trait inventory for cognitive and somatic anxiety (STICSA). Behav Cogn Psychother 2008; 36: 313–32.

46. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatric Residency 1989; 28: 193–213.

47. Kubany ES: Development and validation of the Trauma-Related Guilt Inventory (TRGI). Psychol Assess 1996; 8: 428–44.

48. Tedeschi RG, Calhoun LG: The Posttraumatic Growth Inventory: measuring the positive legacy of trauma. J Trauma Stress 1996; 9: 455–71.

49. Neff KD: The development and validation of a scale to measure self-compassion. Self Identity 2003; 2: 223–50.

50. Buss AH, Perry M: The aggression questionnaire. J Pers Soc Psychol 1992; 63: 452–9.

51. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M: Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption. II. Addiction 1993; 88: 791–804.

52. Monson CM, Gradus JL, Young-Xu Y, Schnurr PP, Price JL, Schumm JA: Change in posttraumatic stress disorder symptoms: do clinicians and patients agree? Psychol Assess 2008; 20: 131–8.

53. Cohen J: "A power primer." Psychol Bull 1992; 112: 155–9.

54. Kip KE, Sullivan KL, Kadel R, et al: Accelerated Resolution Therapy (ART) for brief treatment of combat-related psychological trauma (Abstract). Presented at the 2012 Military Health System Research Symposium, Fort Lauderdale, FL, August 15, 2012. Available at http://www.acceleratedresolutiontherapy.com/MHSRS%20ART%20Poster%20Presentation%208-15-2012.pdf; accessed February 22, 2013.

55. National Center for PTSD: Using the PTSD Checklist (PCL). Available at http://www.ptsd.va.gov/professional/pages/assessments/assessment-pdf/pcl-handout.pdf; accessed June 2, 2013.

56. McDowell I, Newell C: Measuring Health, A Guide to Rating Scales and Questionnaires, Ed 2. New York, Oxford University Press, 1996.

57. Bisson JI, Ehlers A, Matthews R, Pilling S, Richards D, Turner S: Psychological treatments for chronic post-traumatic stress disorder: systematic review and meta-analysis. Br J Psychiatry 2007; 190: 97–104.

58. Schnurr PP: Treatments for PTSD: understanding the evidence. PTSD Res Qtly 2008; 19: 1–11.

59. Hoge CW: Iinterventions for war-related posttraumatic stress disorder. Meeting veterans where they are. JAMA 2011; 306: 549–51.

60. Erbes CR, Curry KT, Leskela J: Treatment presentation and adherence of Iraq/Afghanistan era veterans in outpatient care for posttraumatic stress disorder. Psychol Serv 2009; 6: 175–83.

61. Garcia HA, Kelley LP, Rentz TO, Shuko L: Pretreatment predictors of dropout from cognitive behavioral therapy for PTSD in Iraq and Afghanistan war veterans. Psychol Serv 2011; 8: 1–11.

62. Becker CB, Zayfert C, Anderson E: A survey of psychologists' attitudes towards and utilization of exposure therapy for PTSD. Behav Res Ther 2004; 42: 277–92.

63. Van Minnen A, Hendriks L, Olff M: When do trauma professionals choose exposure therapy for PTSD-patients? A controlled study about the influence of therapist and patient factors. Behav Res Ther 2010; 48: 312–20.

64. American Psychological Association: The psychological needs of U.S. military service members and their families: a preliminary report. Washington, DC, American Psychological Association, 2007. Available at http://www.ptsd.ne.gov/publications/military-deployment-task-force-report.pdf; accessed February 22, 2013.

65. Jakupcak M, Varra EM: Treating Iraq and Afghanistan war veterans with PTSD who are at high risk for suicide. Cogn Behav Pract 2011; 18: 85–97.

66. Hankin CS, Spiro A III, Miller DR, Kazis L: Mental disorders and mental health treatment among U.S. Department of Veterans Affairs outpatients: the Veterans Health Study. Am J Psychiatry 1999; 156: 1924–30.

67. O'Donnell ML, Creamer M, Pattison P: Posttraumatic stress disorder and depression following trauma: understanding comorbidity. Am J Psychiatry 2004; 161: 1390–6.

68. Byrne CA, Riggs DS: The cycle of trauma; relationship aggression in male Vietnam veterans with symptoms of posttraumatic stress disorder. Violence Victims 1996; 11: 213–25.

69. Congress of the United States: The veterans health administration's treatment of PTSD and traumatic brain injury among recent combat veterans, 2012. Available at http://www.cbo.gov/sites/default/files/cbofiles/attachments/02-09-PTSD.pdf; accessed June 4, 2013.