

ATR-guided Antidepressant Selection May Improve Response and Remission Rates: Insights from the BRITE-MD Trial



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ABSTRACT

Objective: The BRITE-MD study assessed the accuracy of a frontal quantitative EEG (fqEEG) biomarker in predicting treatment outcome with escitalopram (ESC). This analysis compares response and remission rates between subjects receiving treatment consistent with the biomarker prediction vs. other subjects.

Methods: Adults with DSM-IV-defined MDD began treatment with ESC (10 mg/day) and after 1 week were randomized either to: 1) continue ESC (10 mg/d; n=73) for 7 more weeks; 2) switch to bupropion XL (BUP; 300 mg/d; n=73) for 7 weeks; or, 3) augment with bupropion XL (AUG; 300 mg/d; n=74). Symptom severity was assessed with the Hamilton Depression Rating Scale (HAM-D-17) and 4-channel fqEEG was recorded. Outcomes were response ($\geq 50\%$ decrease in HAM-D) and remission (final HAM-D ≤ 7). A composite EEG index (Antidepressant Treatment Response, ATR rev 4.1) was developed to predict clinical response using fqEEG from baseline to week 1.

Results: 220 subjects (age 43 ± 13 ; 62% female) were evaluated after excluding protocol violators and subjects with EEG artifact. For subjects remaining on ESC, the response rate was significantly higher in ATR-predicted responders than for ATR-predicted non-responders (68% vs. 28%, $p=0.001$). Similarly, for subjects remaining on ESC, the remission rate was significantly higher in the ATR-predicted remitters than the ATR-predicted non-remitters (50% vs. 21%, $p=0.010$). ATR-predicted non-responders who were randomized to BUP had a significantly higher response rate compared to those remaining on ESC (53% vs. 28%, $p=0.034$). ATR-predicted non-responders who were augmented had a modestly higher response rate compared to those remaining on ESC treatment (33% vs. 28%, $p=ns$).

Conclusions: The use of a fqEEG biomarker at week 1 of ESC treatment may help guide antidepressant selection. Subjects whose ATR predicts response or remission do better when continued on ESC, while subjects whose ATR predicts poorer outcomes may benefit from alternate regimens.

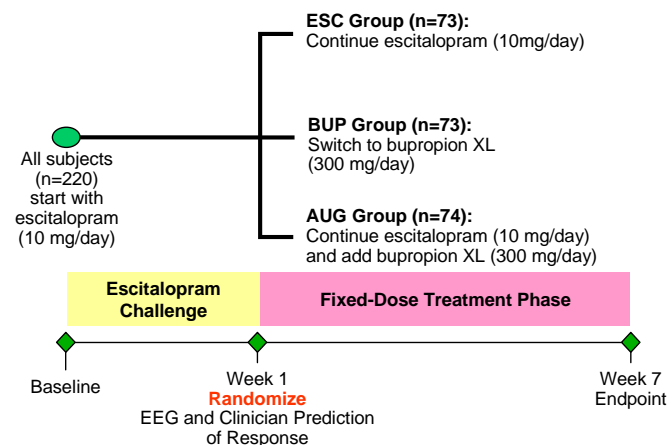
INTRODUCTION

- ◆ Prior work demonstrated that a simple-to-use frontal quantitative EEG (fqEEG) biomarker (ATR) predicted response to antidepressant treatment in MDD [1][2]
- ◆ This work compares response rates between subjects randomized to treatment consistent with biomarker prediction vs. other subjects in an analysis of the BRITE-MD trial (www.BRITE-MD.org)

METHODS

- ◆ MDD subjects (DSM-IV criteria; baseline IDS-SR ≥ 12) began treatment with escitalopram and were randomly assigned after 1 week to either: 1) continuation of escitalopram (ESC; 10mg/day), 2) augment with bupropion XL (AUG; 300 mg/day), or 3) switch to bupropion XL (BUP; 300mg/day) for a total of 7 weeks
- ◆ At each study visit, 4-channel fqEEG was recorded and HAM-D-17 was assessed. Clinical response was defined as a reduction in HAM-D-17 $\geq 50\%$ at week 7 from baseline

METHODS (Continued)



- ◆ ATR, an index (0 to 100) of EEG features from baseline and week1 recordings, was evaluated to estimate the probability of clinical response
- ◆ Subjects treated consistently with ATR prediction were those who continued on ESC when $ATR \geq THRESHOLD$ and those switched to alternate treatment when $ATR < THRESHOLD$. All others subjects received treatment inconsistent with ATR.

RESULTS

- ◆ 220 subjects completed 7 weeks of treatment (age: 43 yrs (13 sd); 62% female)
- ◆ For subjects remaining on the initial treatment (ESC):
 - > the response rate was higher for ATR-predicted responders than the ATR-predicted non-responders (68% vs. 28%, $p=0.001$)
 - > the remission rate was higher for the ATR-predicted remitters than the ATR-predicted non-remitters (50% vs. 21%, $p=0.010$)
- ◆ ATR-predicted non-responders who were randomized to BUP had a higher response rate compared to those remaining on ESC (53% vs. 28%, $p=0.034$)
- ◆ ATR-predicted non-responders who were augmented had a modestly higher response rate than those remaining on ESC (33% vs. 28%, $p=n.s.$)

RESULTS (Continued)

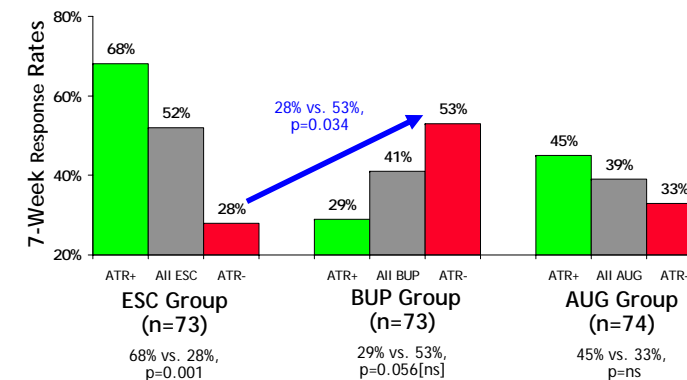


Figure 1. Response rates of subjects predicted by ATR (rev 4.1) to respond to ESC treatment (ATR+, green), predicted by ATR not to respond to ESC (ATR-, red), and average response rate (grey) for each study limb.

CONCLUSIONS

- ◆ Antidepressant Treatment Response (ATR) Index at week 1 of ESC treatment may help guide antidepressant selection
 - > Subjects whose ATR predicts response do better when continued on ESC, while subjects whose ATR predicts non-response may benefit from alternate regimens
 - > When ATR predicts non-response, switching to BUP, rather than augmenting with BUP, may be the preferred alternate regimen
- > Clinical implication: Early identification of positive or negative EEG prediction of response to treatment may aid in decisions regarding medication adjustments, potentially leading to improved outcomes of antidepressant therapy

REFERENCES

- [1] Leuchter AF, Cook IA, Gilmer WS, Greenwald SD, Howland RH, Trivedi MH. **Can EEG-guided Antidepressant Selection Improve Response Rates? Insights from the BRITE-MD Trial.** Poster presented at the New Research session, American Psychiatric Association Annual Meeting. San Diego, CA. May 21, 2007
- [2] Cook IA, Leuchter AF, Morgan M, Witte E, Stubbeman WF, Abrams M, Rosenberg S, Uijtdehaage SH. **Early changes in prefrontal activity characterize clinical responders to antidepressants.** *Neuropsychopharmacology* 27:120-131, 2002