



Supplemental Material
BRITE Interim Results Conference Call
May 21, 2007



Safe Harbor Statement

Certain statements in this presentation are forward-looking and may involve risks and uncertainties, including statements with respect to: the expected increase in sales of BIS sensors, the potential impact on market acceptance and demand resulting from the October 2004 Sentinel Event Alert and ASA practice advisory, short term and long term strategies and objectives, and expected profitability in future periods. There are a number of important factors that could cause actual results to differ materially from those indicated by these forward-looking statements including:

- Our ability to achieve widespread market acceptance of our BIS monitoring technology and to compete with new products or alternative techniques that may be developed by others, including third-party anesthesia monitoring products;
- Competitive and regulatory risks relating to our ability to successfully develop and introduce enhancements and new products;
- Risks related to our limited worldwide sales and marketing experience and our ability to develop and implement a successful sales and marketing strategy, including with respect to our own sales force, distributors, OEMs and other sales channels in order to generate meaningful product revenue;
- The risk that we will not remain profitable if hospitals and anesthesia providers do not buy and use our BIS systems and BIS sensors in sufficient quantities;
- The risk that cases of awareness with recall during monitoring with the BIS system and/or significant product liability claims could limit market acceptance; and
- Other factors that could cause our actual results to vary from these forward-looking statements, including without limitation those set forth under the heading "Risk Factors" in our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2007 as filed with the SEC.

In addition, the statements in this presentation represent our views only as of today and should not be relied upon as representing our views as of any subsequent date. While we may elect to update forward-looking statements at some point in the future, we specifically disclaim any obligation to do so, even if our estimates change and, therefore, you should not rely on these forward-looking statements as representing our views as of any date subsequent to today.

This presentation includes non-GAAP financial measures. These non-GAAP measures are not prepared in accordance with U.S. generally accepted accounting principles. A reconciliation of the non-GAAP financial measures to the most directly comparable GAAP measures, and other information regarding these non-GAAP measures, is available in the Investor Relations section of our website at www.aspectmedical.com.

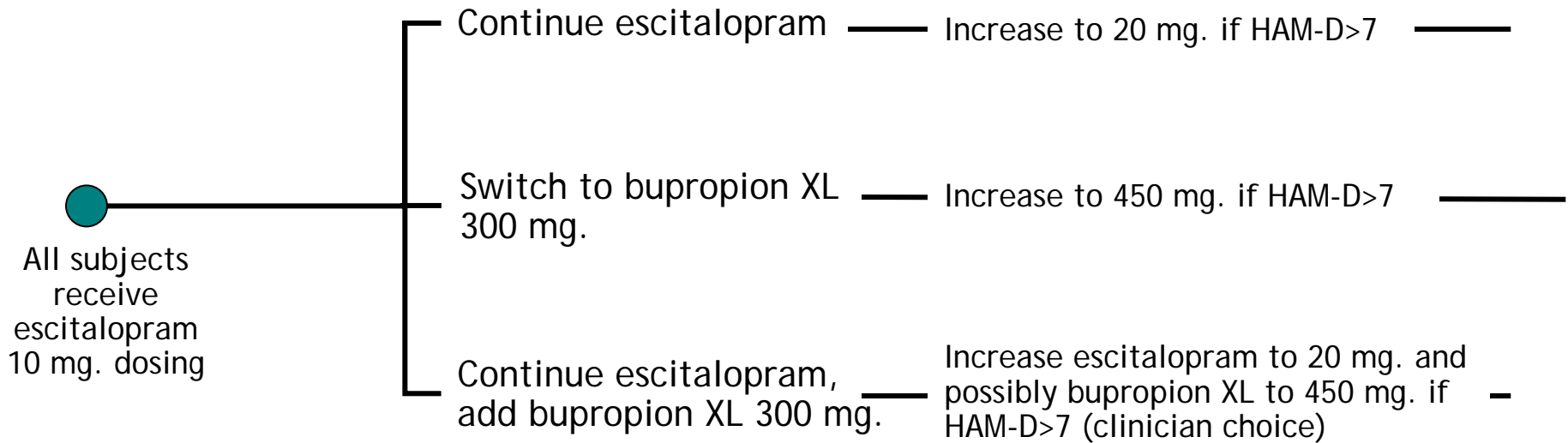
Objectives of the BRITE Trial

- Prospectively validate Aspect's Antidepressant Treatment Response (ATR) indicator as biomarker of clinical response to a SSRI
- Determine the best treatment option for patients who are predicted to be non-responders to a SSRI
- Assess whether the technology can identify worsening of adverse events, e.g. suicidal ideation
- Expand EEG database to allow further refinements of Aspect's algorithms and product offering

BRITE Enrollment Statistics

- Interim Analysis Statistics
 - Interim dataset locked December 2006
 - 156 enrolled subjects
 - 111 total evaluable subjects for interim analysis
 - 40 evaluable subjects in escitalopam arm for testing of primary hypothesis (ATR at 1 week predicts clinical outcome at 7 weeks)
- Current BRITE Status
 - Patient enrollment completed Q1 2007
 - 375 total enrolled subjects
 - Analysis of Final Dataset: Q3 2007
 - Final BRITE analysis to be presented at clinical meetings in Q2 2008

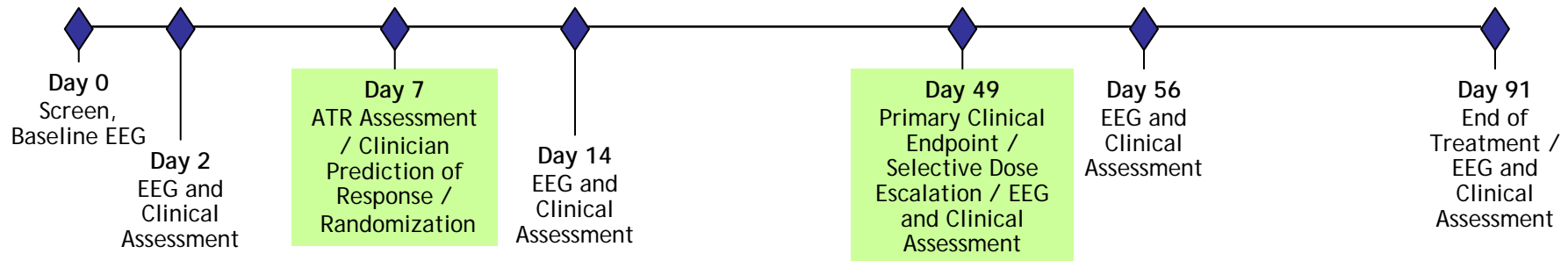
BRITE Trial Protocol Overview



SSRI Challenge

Initial Response Phase

Dose Escalation Phase



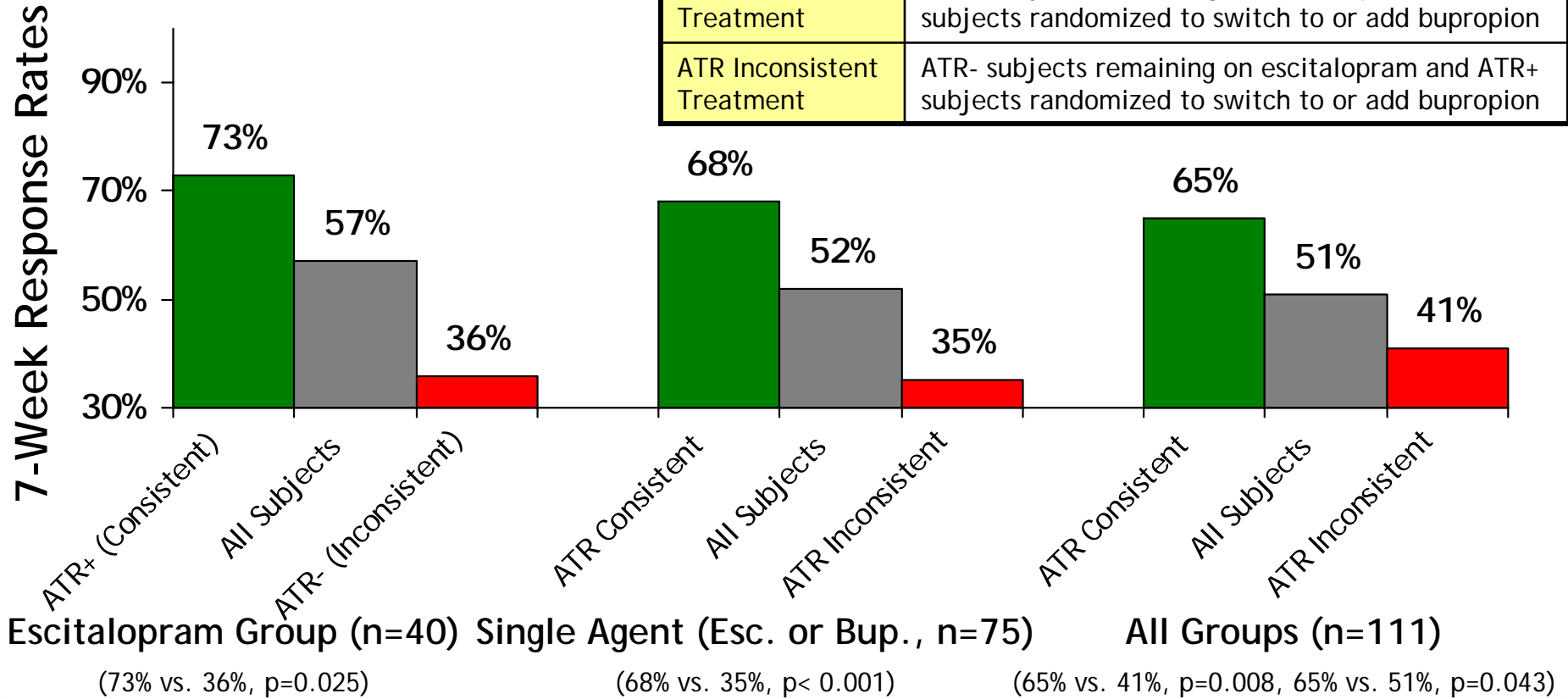
Interim Analysis: ATR Predicts Response

Predictor	BRITE Patient Group	Accuracy of ATR at 1 week in predicting 7 week response
ATR	Patients in escitalopram limb (n=40)	70%, p=0.037
	Melancholic subtype patients (n=22)	81%, p=0.015

Potential Clinical Value of Aspect's ATR

Retrospective Analysis of Response Rates by Consistency of Treatment with ATR Prediction

Definitions	
ATR+	ATR at 1 week predicts subject will respond to escitalopram at 7 weeks
ATR-	ATR at 1 week predicts subject will not respond to escitalopram at 7 weeks
ATR Consistent Treatment	ATR+ subjects remaining on escitalopram and ATR- subjects randomized to switch to or add bupropion
ATR Inconsistent Treatment	ATR- subjects remaining on escitalopram and ATR+ subjects randomized to switch to or add bupropion



Key Takeaways - BRITE Interim Analysis

- ATR is a significant predictor of response to escitalopram after 1 week of treatment based on analysis of interim BRITE data
- ATR-predicted non-responders to escitalopram experienced increased response rates if randomized to the switch or augment study arm, suggesting that a 1-week biomarker of treatment response could have important clinical benefits

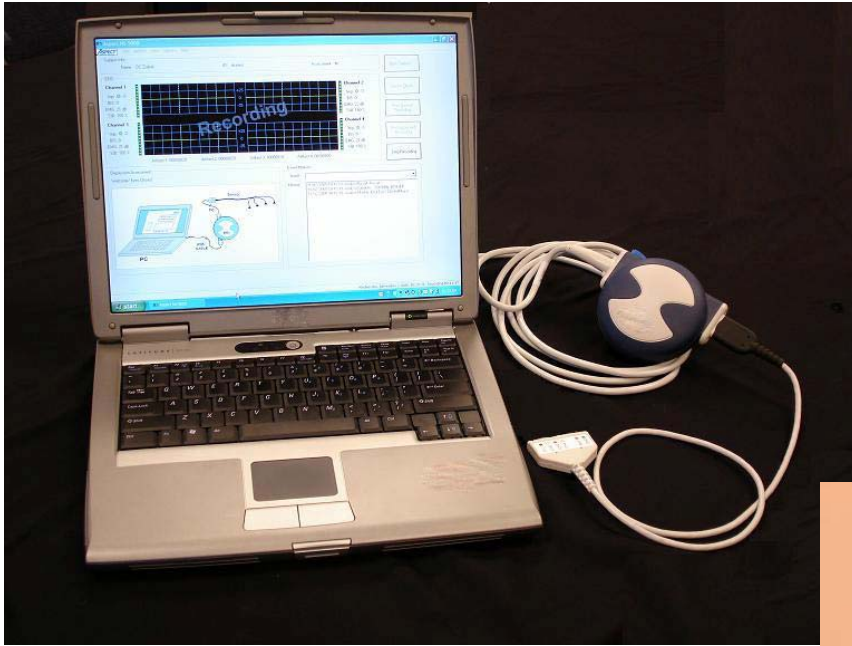
BRITE Research Sites

- Harbor-UCLA Medical Center, Los Angeles, CA
- Semel Institute for Neuroscience and Human Behavior at UCLA, Los Angeles, CA
- Massachusetts General Hospital, Boston MA
- Northwestern University, Chicago IL
- Baylor College of Medicine, Houston TX
- Cedars-Sinai Medical Center, Los Angeles, CA
- University of Pittsburgh, Pittsburgh, PA
- UT Southwestern Medical School, Dallas, TX
- UCSD, San Diego, CA
- R/D Clinical Research, Lake Jackson, TX

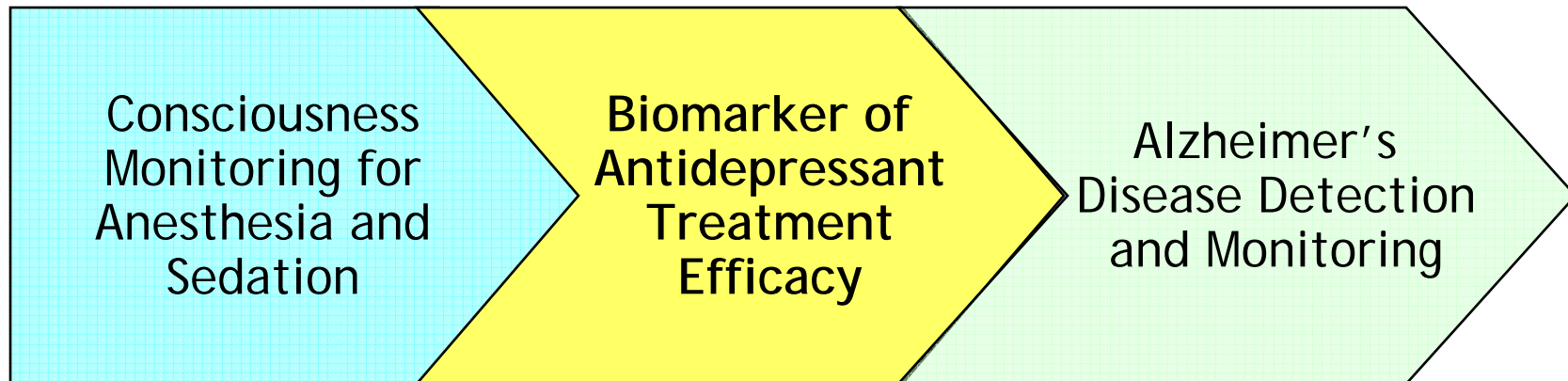
Brite Study Public Information

- Biomarkers for Rapid Identification of Treatment Efficacy in Major Depression
- Website
 - www.brite-md.org
- ClinicalTrials.gov
 - <http://www.clinicaltrials.gov/ct/show/NCT00289523;jsessionid=BE95477D0F1891E6401F27A499276ACE?order=1>

Research Equipment Used in BRITE Trial

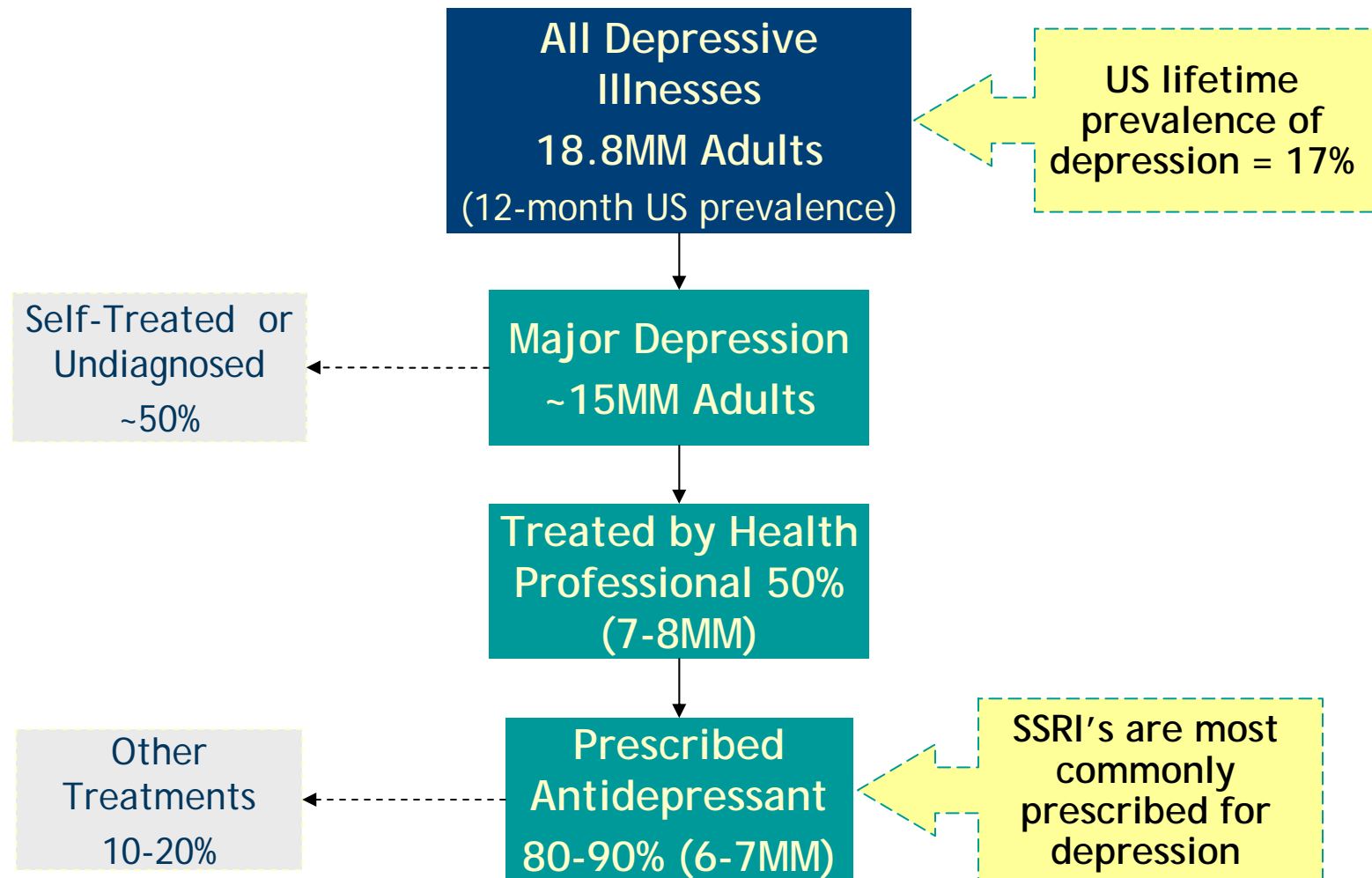


Building the Aspect Portfolio



- Leveraging 18 years of experience in brain monitoring
- Addressing clinical unmet needs to improve patient care
- Supporting novel applications with rigorous scientific investigation

US Depression Population



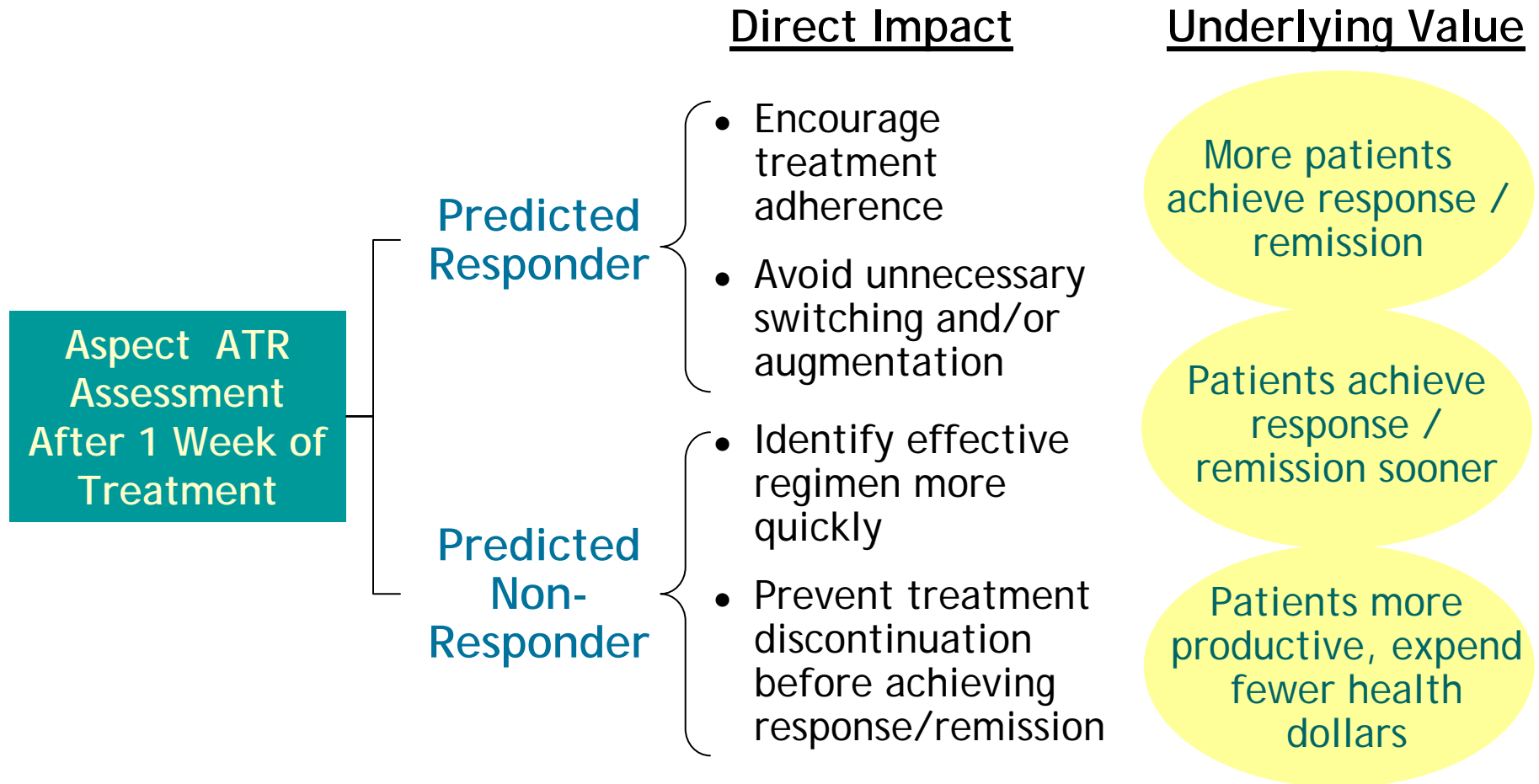
Source: The Epidemiology of Major Depressive Disorder: Results from the National Comorbidity Survey Replication, JAMA, 06-18-2003. Advance Data: National Ambulatory Medical Care Survey, 2003 Summary, CDC, October 4, 2005. National Trends in the Outpatient Treatment of Depression, JAMA, 01-09-2002.

Unmet Needs in Depression

- Only one-third of patients being treated with SSRIs for depression achieve remission on the first drug tried
 - 25-30% of non-responders to first-line treatment can achieve remission by switching or adding of a second medication
- Finding an efficacious regimen for an individual patient is a trial and error process taking several weeks to months
 - Clinical improvement generally requires 4-12 weeks
- Over 40% of patients prescribed antidepressants discontinue treatment in the first 30 days on medication
 - Side effects combined with delay in clinical response contribute to early treatment disruption
 - Many patients who receive inadequate treatment for depression continue to suffer, costing the economy and health care system

Sources: Medication Augmentation after the failure of SSRIs for Depression, New England Journal of Medicine 354;12, March 23, 2006, pp. 1243-1252. Bupropion-SR, Sertraline, or Venlafaxin-XR after Failure of SSRIs for Depression, New England Journal of Medicine 354;12, March 23, 2006, pp. 1231-1242.

Aspect Technology Clinical Relevance



Biomarkers for Rapid Identification of Treatment Effectiveness in Major Depression (BRITE-MD): Prospective Evaluation of an EEG Biomarker



Andrew F. Leuchter, M.D.¹, Lauren B. Marangell, M.D.², Karl S. Burgoyne, M.D.³,
Jeff Sigl, Ph.D.⁴, Rakesh Jain, M.D., M.P.H.⁵, Sidney Zisook, M.D.⁶, Maurizio Fava, M.D.⁷



¹UCLA Laboratory of Brain, Behavior, and Pharmacology, Semel Institute, Los Angeles, CA, ²Psychiatry, Baylor College of Medicine, Houston, TX,
³Psychiatry, Harbor-UCLA Medical Center, Los Angeles, CA, ⁴Neuroscience, Aspect Medical Systems, Norwood, MA,
⁵Psychiatry, RD Clinical Research, Houston, TX, ⁶Psychiatry, UCSD, San Diego, CA, ⁷Psychiatry, Massachusetts General Hospital, Boston, MA

ABSTRACT*

Objective: To prospectively evaluate the role of frontal quantitative electroencephalography (fqEEG) as an early predictor of subsequent clinical response in major depressive disorder (MDD).

Method: 40 subjects (age: 42 ± 11 ; 62% female) meeting DSM-IV criteria for MDD entered prospective treatment with a fixed dose of escitalopram (10 mg/day) for 7 weeks in one limb of an ongoing study (www.BRITE-MD.org). At each study visit we assessed severity of depression with the Hamilton Depression Rating Scale (HAM-D-17), and we recorded 4-channel fqEEG (At1-Fpz, At2-Fpz, A1-Fpz, A2-Fpz). An EEG index (Antidepressant Treatment Response [ATR, rev 0.4]) previously developed to predict clinical response (0 to 100, low to high probability of response) was tested prospectively using fqEEG assessed at baseline and week 1. Clinicians were also asked to predict likelihood of response or remission based on overall clinical judgment at the week 1 assessment. Response to treatment was defined as a reduction from baseline symptom burden at week 7 of $\geq 50\%$ (i.e., predicted HAM-D change of $<50\%$ vs. $> 50\%$).

Results: 57% of subjects responded to ESC treatment. ATR was higher in responders than non-responders (52 ± 13 vs. 43 ± 12 , $p=0.045$) and correlated with % change in HAM-D from baseline to week 7 ($r=-0.312$, $p=0.05$). ATR correctly predicted response in 28 subjects ($p=0.041$). Clinician's prediction of response was not significantly better than chance.

Discussion: EEG response to initial dosing was predictive of clinical response and numerically more accurate than clinician prediction.

Conclusions: This prospective evaluation confirmed that an EEG biomarker can be used to predict treatment efficacy after one week of escitalopram treatment. Future studies are needed to evaluate the utility of this EEG predictor in helping to guide antidepressant treatment decisions.

Source of Funding:

This research was supported by Aspect Medical Systems, Inc.

*Updated since submission.

INTRODUCTION

- ◆ Prior work demonstrated that frontal EEG activity predicted response to antidepressant treatment [1][2]
- ◆ This work prospectively evaluated a simple-to-use frontal quantitative EEG (fqEEG) biomarker of efficacy of antidepressant treatment response (ATR)

METHODS

- ◆ MDD subjects (DSM-IV criteria; baseline IDS-C ≥ 12) entered a longitudinal, 7-week prospective treatment study with escitalopram (10mg/day)
- ◆ Clinical response was defined as a $\geq 50\%$ reduction in HAM-D-17 from baseline to week 7
- ◆ At each study visit (baseline, 48hrs, week 1, 2 and 7), 4-channel fqEEGs were recorded (At1-Fpz, At2-Fpz, A1-Fpz, A2-Fpz) and HAM-D-17 was assessed
- ◆ Power spectra of the EEG were estimated for each consecutive 2-sec EEG epoch collected during a resting period with closed eyes
- ◆ ATR (rev 0.4), a composite index previously derived to predict clinical response from EEG features, was tested prospectively using fqEEG assessed at baseline and week1
 - ATR ranges from 0 (low probability of response) to 100 (high probability of response)

RESULTS

- ◆ Interim results: 40 subjects (62% female, age 42 ± 11 y.o.) completed 7 weeks of treatment and had fqEEG and clinical data available for this interim analysis
- ◆ 57% were antidepressant treatment responders
- ◆ At week1, ATR was significantly higher in treatment responders than in non-responders (52 ± 13 vs. 43 ± 12 , $p=0.045$) and correlated with % change in HAM-D at baseline to week 7 ($R=-0.312$, $p=0.05$).
- ◆ ATR correctly predicted response in 28 subjects and achieved 70% Area Under the Receiver Operating Curve (AUC) ($p=0.037$)
- ◆ ATR prediction (70% accuracy) was numerically better than clinician prediction (57% accuracy)
 - ◆ Response prediction by ATR was better in the 22 subjects (54%) with Melancholic subtype of MDD compared to all subjects (i.e., 81% vs. 70%)

RESULTS (Continued)

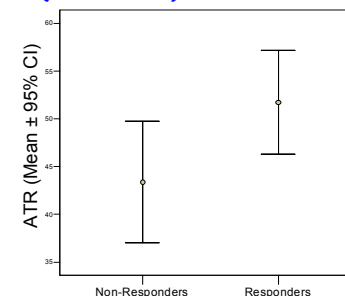


Figure 1. Distribution of ATR values (mean \pm 95% CI) for Responders (right) and Non-Responders (left). ATR was higher in Responders than Non-Responders (52 ± 13 vs. 43 ± 12 , $p=0.045$)

CONCLUSIONS

- ◆ Antidepressant Treatment Response (ATR) Index measured after 1 week of medication predicts clinical response at 7 weeks to fixed-dosed treatment with escitalopram (10mg/day) in MDD in an ongoing study (www.brite-md.org)
 - The predictive accuracy was best in subjects with Melancholic subtype of MDD
- ◆ Clinical implication: Early identification of positive or negative EEG response to treatment may aid in decisions regarding medication adjustments, potentially leading to improved compliance and efficacy of antidepressant therapy

REFERENCES

- [1] Cook IA, Leuchter AF, Witte EA, Stubbeman WF, Abrams M, Rosenberg S. Early Changes in Prefrontal Activity Characterize Clinical Responders to Antidepressants. *Neuropsychopharmacology* 2002; 27:130-131.
- [2] Iosifescu D, Greenwald S, Smith C, Devlin P, Alpert J, Hamill S, Fava M. Frontal EEG at 1 Week Predicts Clinical Response to SSRI Treatment in Major Depressive Disorder. Presented at the 2006 Annual Meeting of the American Psychiatric Association, Toronto, CA (#231).

Can EEG-guided Antidepressant Selection Improve Response Rates? Insights from the BRITE-MD Trial



Andrew F. Leuchter, M.D.¹, Ian A. Cook, M.D.¹, William S. Gilmer, M.D.²,
Scott D. Greenwald, Ph.D.³, Robert H. Howland, M.D.⁴, Madhukar H. Trivedi, M.D.⁵



¹UCLA Laboratory of Brain, Behavior, and Pharmacology, Semel Institute, Los Angeles, CA,
²Psychiatry, Northwestern University, Chicago, IL, ³Neuroscience, Aspect Medical Systems, Norwood, MA,
⁴Western Psychiatric Institute and Clinic, University of Pittsburgh, Pittsburgh, PA, ⁵Psychiatry, University of Texas Southwestern Medical School, Dallas, TX

ABSTRACT

Objective: The BRITE-MD study (www.BRITE-MD.org) was designed to assess the accuracy of a frontal quantitative electroencephalographic (fqEEG) biomarker in predicting response to escitalopram (ESC) treatment. This analysis compares the response rate between subjects who received treatment consistent with the biomarker prediction vs. other subjects.

Method: 111 subjects (age: 42 ± 14 ; 59% female) meeting DSM-IV criteria for MDD began treatment with escitalopram (ESC; 10 mg/day) and were randomly assigned after 1 week to either: 1) continue ESC (10 mg/day; n=40); 2) augment with bupropion XL (AUG; 300 mg/day; n=36); or, 3) switch to bupropion XL (BUP; 300 mg/day; n=35) for 7 weeks of treatment. At each visit severity of depression was assessed with the Hamilton Depression Rating Scale (HAM-D-17) and 4-channel fqEEG was recorded. Clinical response was defined as a reduction in HAM-D at week 7 $\geq 50\%$ from baseline. A previously developed index to predict probability of clinical response (0 to 100) using baseline and week 1 EEGs (Antidepressant Treatment Response (ATR) rev 0.4) was evaluated. Treatment consistent with ATR included subjects continued on ESC when $ATR \geq THRESHOLD$ or switched to alternate treatment when $ATR < THRESHOLD$. All other subjects received treatment inconsistent with ATR.

Discussion: For subjects remaining on the initial treatment (ESC), the response rate was higher with ATR-consistent treatment vs. ATR-inconsistent treatment (73% vs. 36%, $p=0.025$). For all subjects, the response rate was higher with ATR-consistent treatment than with ATR-inconsistent treatment (65% vs. 41%, $p=0.008$), and higher than the pooled response rate (65% vs. 51%, $p=0.043$).

Conclusions: Using a fqEEG biomarker 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.

Funding: This research was supported by Aspect Medical Systems, Inc.

INTRODUCTION

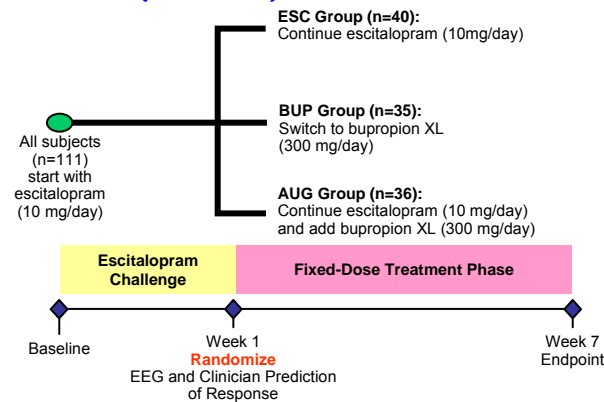
◆ Prior work demonstrated that a simple-to-use frontal quantitative EEG (fqEEG) biomarker (ATR) predicted response to antidepressant treatment in MDD [1][2]

◆ This work compares response rates between subjects treated consistent with biomarker prediction vs. other subjects in an interim analysis of the BRITE-MD trial (www.BRITE-MD.org)

◆ 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 prospectively evaluate 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 other subjects received treatment inconsistent with ATR.

◆ 111 subjects completed 7 weeks of treatment (age: 42 ± 14 ; 59% female)

◆ For all subjects, the response rate was higher with ATR-consistent treatment than with ATR-inconsistent treatment (65% vs. 41%, $p=0.008$) and higher than the pooled response rate (65% vs 51%, $p=0.043$)

◆ For subjects remaining on the initial treatment (ESC), the response rate was higher for ATR-consistent treatment vs. ATR-inconsistent treatment (73% vs. 36%, $p=0.025$)

◆ For subjects receiving alternate treatment and whose ATR predicted non-response, those receiving BUP trended towards a higher response rate than those with augmentation (AUG) (58% vs. 50%, $p=n.s.$)

RESULTS (Continued)

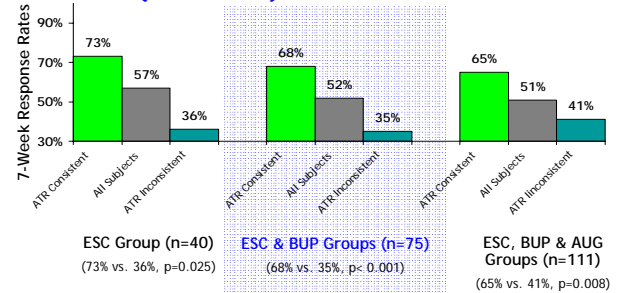


Figure 1. Potential Clinical Impact: Retrospective analysis of response rates by consistency of treatment with ATR prediction demonstrated higher response rates in subjects whose treatment was consistent with ATR prediction.

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 response to treatment may aid in decisions regarding medication adjustments, potentially leading to improved outcomes of antidepressant therapy

REFERENCES

[1] Iosifescu D, Greenwald S, Smith C, Devlin P, Alpert J, Hamill S, Fava M. Frontal EEG at 1 Week Predicts Clinical Response to SSRI Treatment in Major Depressive Disorder. Presented at the 2006 Annual Meeting of the American Psychiatric Association, Toronto, CA (#231).

[2] Poland R, Greenwald S, Smith C, Kustak C, Schulz J, Rowe S, Gertsik L. Frontal EEG at 1 Week Predicts Response to Treatment with Citalopram in MDD. Presented at the 2006 Annual Meeting of the American Psychiatric Association, Toronto, CA (#269).

