Frequently Asked Questions
FAQS

NeuroStar TMS Therapies

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NeuroStar TMS Therapy®

ABOUT NEUROSTAR TMS THERAPY

What is NeuroStar TMS Therapy?

The NeuroStar TMS Therapy system is the first and only TMS Therapy® device cleared by the FDA for the treatment of depression.

TMS Therapy is a non-systemic (does not circulate in the bloodstream throughout the body) and non-invasive (does not involve surgery) form of neuromodulation, which stimulates nerve cells in an area of the brain that is linked to depression, by delivering highly focused MRI-strength magnetic pulses.

Patients being treated by NeuroStar TMS Therapy do not require anesthesia or sedation and remain awake and alert.

It is a 40-minute outpatient procedure that is prescribed by a psychiatrist and performed in a psychiatrist's office.

The treatment is typically administered daily for 4-6 weeks.

What happens during TMS Therapy? What's the Mechanism of Action?

During NeuroStar TMS Therapy, pulsed magnetic fields are repetitively transmitted into the left prefrontal cortex, the part of the brain that is thought to regulate mood, in order to stimulate the firing of neurons (nerve cells).

This is believed to trigger a cascade of neurochemical events, including the release of neurotransmitters (such as serotonin, norepinephrine, and dopamine) and to help normalize neurotransmitter function

How long does a patient undergo TMS therapy?

In clinical trials, patients received NeuroStar TMS Therapy 5 times per week for approximately 40 minutes during each session for 4-6 weeks.

Patients should be treated for a minimum of four weeks with additional treatments based on clinical judgment.

What are the benefits of TMS?

• NeuroStar TMS Therapy is the first and only non-systemic and non-invasive depression treatment to be cleared by the FDA

• It is indicated for adult patients who did not achieve satisfactory improvement from prior antidepressant medication

Median of 4 treatment attempts, 1 of which was adequate

• In clinical trials, 1 in 2 patients had significant improvement in symptoms and 1 in 3 had complete symptom resolution

• Since it's non-systemic, it doesn't have side effects such as weight gain, sexual dysfunction, nausea, sedation, dry mouth, etc.

How long does the antidepressant effect last? Do patients need to go back for another session?
During the six-month maintenance of effect study with NeuroStar TMS Therapy, patients were maintained on antidepressant monotherapy and received periodic NeuroStar TMS Therapy for symptom worsening. During this study:

Patients previously treated with NeuroStar TMS Therapy had less than 10% relapse rate at the end of 6 months

~Half of patients experienced symptom breakthrough and required TMS Therapy re-treatment

Is TMS therapy a good alternative for patients who are fearful of the side effects associated with antidepressant medications?

NeuroStar TMS Therapy has been cleared by U.S. FDA for the treatment of patients with depression who have failed to achieve satisfactory improvement from prior antidepressant treatment.

NeuroStar is non-systemic, so it doesn't have side effects such as weight gain, sexual dysfunction, nausea, dry mouth, sedation, etc.

Like any treatment option, patients and clinicians should work together to find the most appropriate treatment option for each patient.

Does NeuroStar TMS hurt?

The most common adverse event related to treatment was scalp pain or discomfort at the treatment area during active treatments, which was transient and mild to moderate in severity. The incidence of this side effect declined markedly after the first week of treatment.

Less than 5% of patients discontinued the study due to adverse events.

Does NeuroStar TMS cause brain tumors?

No, TMS Therapy uses the same type and strength of magnetic fields as MRIs, which have been used in tens of millions of patients around the world and have not been shown to cause tumors. The amount of magnetic field exposure for a full course of TMS Therapy is a small fraction of just one brain scan with an MRI.

What are the long-term consequences of TMS treatment?

TMS is an acute therapy.

With regard to long-term safety, TMS uses the same type and strength of magnetic fields as MRIs, which have been used in tens of millions of patients around the world and have not been shown to cause long-term consequences.

The amount of magnetic field exposure for a full course of TMS Therapy is only a small fraction of one brain scan with an MRI.

If a patient had multiple courses of acute TMS, the magnetic field exposure would be less than exposure from a few MRI sessions.

What is the FDA-cleared indication and what does it mean?
NeuroStar TMS Therapy is indicated for adult patients with major depressive disorder who failed to achieve satisfactory improvement from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode.

The important points are:

NeuroStar TMS Therapy is for patients with MDD only who failed to benefit from prior antidepressant medications

It was only studied in ADULTS (22 years by FDA definition) and was not studied in children (i.e., less than 18 years) or for geriatric use (i.e., older than 70 years)

"One prior antidepressant medication at minimal effective dose and duration" means a previous antidepressant medication that was given at its minimum labeled dose for at least 4 weeks

Patients had only ONE exposure that reached this level of adequacy (patients had also had a median of 4 exposures that did not reach this level of adequacy)

"In the current episode" means all of this applies only to the current depressive episode, however, if the patient had NO treatment in the current episode, then one can look back to the prior episode to see if there was one adequate treatment to which the patient did not benefit

The Antidepressant Treatment Record supplied by Neuronetics and described in the User Manual can be used by the physician to identify the indicated population

Why does it not work/not FDA-cleared in patients who failed to benefit from more than one antidepressant medication? Isn't that where the need is? Why such a narrow indication?

The NeuroStar studies did not include enough patients who failed more than 1 prior adequate medication to determine if NeuroStar is effective in these patients.

Therefore, one can only conclude that efficacy has not been established in these patients.

NeuroStar was safely administered to these patients.

What are the risks of TMS therapy?

NeuroStar TMS Therapy is contraindicated (should not be used) in patients with implanted metallic devices or non-removable metallic objects in or around the head. It also should not be used in patients with implanted devices that are controlled by physiological signals such as pacemakers, etc…

Are there other patients for whom NeuroStar TMS Therapy could pose a risk?

Depression is a lethal disease and, as with all antidepressants, patients treated with NeuroStar TMS Therapy should be monitored for signs or symptoms of worsening depression. The efficacy of NeuroStar TMS Therapy in patients with depression who have failed 2 or more antidepressants has not been proven and it has not been studied in patients who have had no prior antidepressant treatment in the current episode.

How effective is TMS therapy compared with drugs?

- NeuroStar was not compared in head-to-head studies with antidepressant medications.

- It is difficult to compare NeuroStar vs. drugs, because they have been studied in different patient populations

The patients for which NeuroStar has been FDA-cleared had failed multiple treatment attempts, one of which achieved an adequate dose and duration

Almost all antidepressant medications have been studied and approved for 1st-line treatment.

• In the NeuroStar randomized controlled trial, almost 3x the number of NeuroStar-treated patients had a significant improvement in symptoms compared to placebo.

• Finally, it's also important to consider safety and tolerability.

TMS is non-systemic, so it doesn't cause side effects such as weight gain, sexual dysfunction, nausea, dry mouth, sedation, etc.

Is TMS Therapy intended to replace antidepressant medications?

No, there is a significant unmet need in the treatment of depression. Currently there are few options for patients who have had an inadequate response to previous antidepressant treatments. They are often faced with choosing between a complex regimen of multiple drugs or, for more severe cases, more invasive procedures.

While TMS Therapy is a new treatment option, we do not believe it will displace the need for other antidepressants.

Based on its excellent safety profile, NeuroStar TMS Therapy may be used earlier in the treatment algorithm than antidepressant drug classes that carry a significant safety/tolerability burden.

Can TMS patients also take an antidepressant(s)?

NeuroStar TMS Therapy was studied as a monotherapy without additional antidepressants in the controlled clinical trial so the efficacy with additional antidepressants (i.e., as adjunctive therapy) is not known.

NeuroStar TMS Therapy was safety administered in conjunction with medication antidepressants and this replicated what has been shown in the many literature-based single center trials of TMS

In clinical trials, patients were administered antidepressant medications during the taper phase at the end of two of the acute studies.

In the maintenance of effect study, patients who were being treated with antidepressant monotherapy and also had periodic reintroductions of TMS Therapy.

If patients have to go back on drugs anyway, then what's the point?

NeuroStar is used for the acute treatment of patients with depression who have not received satisfactory improvement from prior antidepressant treatment

Most patients who benefited from TMS were able to retain effect for up to 6 months on only one antidepressant medication at a minimal dose.

These patients had failed a median of 4 antidepressant treatment attempts, one adequate treatment

In the open-label trial, which is most like the real world, among NeuroStar-treated patients, ~1in 2 achieved a significant improvement in symptoms and 1in 3 had complete symptom resolution

Since NeuroStar is non-systemic, these results were achieved without side effects such as weight gain, sexual dysfunction, nausea, dry mouth, sedation, etc.

What is the history of TMS Therapy?

• First used in 1985, TMS has been used by researchers around the world to help understand the function of different parts of the brain. Several hundred manuscripts have been published regarding its use in stimulating select regions of the brain.

• Since the mid 1990s, TMS has been studied as an antidepressant therapy.

• In 2006, the largest randomized, controlled study ever conducted with TMS Therapy was completed. This study was sponsored by Neuronetics and utilized the NeuroStar TMS Therapy system

• Recently, the NeuroStar TMS Therapy system, was cleared by the U.S. Food and Drug Administration for the treatment of adult patients with major depressive disorder who have failed to receive satisfactory improvement from prior medication antidepressant treatment

4 attempts of which 1 was adequate in the current episode

Will treatment be covered by insurance and/or Medicare?

• We certainly hope and expect that it will

• However, the process for unique, new procedures like this to be reimbursed usually takes 1-2 years

• We believe there are compelling reasons for it to be reimbursed:

Target patients have few proven and tolerable options
Rigorously-designed clinical studies
Benefit-risk ratio compares favorably to alternatives
Compelling health economics for payers

Is TMS Therapy like the magnetic bracelets?

No. There are four main differences between the magnet used in NeuroStar TMS Therapy and the regular magnets used in alternative therapies:

Regular magnets are typically weak in field strength, while the magnets used in NeuroStar TMS Therapy are much stronger and the same as those used in MRI machines

Alternative therapy magnets create magnetic fields which do not move in space or time. The magnet used in NeuroStar TMS Therapy is pulsed, which causes the magnetic fields to move rapidly over time. This rapid magnetic field movement is what stimulates brain cells.

No scientific evidence exists to support the therapeutic benefit of regular magnets in the treatment of depression, while rigorous clinical trials have proven the effectiveness of NeuroStar TMS Therapy.

NeuroStar TMS Therapy is cleared by the FDA, while regular magnets are not.

Are there other treatments for depression that rely on magnetic fields?

No

Does NeuroStar cause memory loss?

NeuroStar TMS Therapy was systematically evaluated for its effects on memory.

The clinical trials demonstrated that NeuroStar TMS Therapy does not result in adverse effects on memory or concentration

Does clearance of NeuroStar TMS Therapy mean that all TMS devices are cleared for use in major depression within the United States?

No. NeuroStar TMS Therapy is the first and only TMS device to have been evaluated in a large, multicenter, controlled clinical trial

NeuroStar is the first and only TMS device to be cleared by the U.S. FDA for the treatment of major depression.

Any other TMS Device that is claimed to be "FDA-approved" is not cleared for the treatment of depression and has not been shown to be safe and effective.

ABOUT NEUROSTAR TMS THERAPY – CLINICAL DATA

How were the clinical trials designed and what were the results of the trials?

• NeuroStar TMS Therapy was studied in depressed patients who had failed to receive benefit from prior antidepressant medications.

• A 6-week, randomized, placebo-controlled, double-blind, study was conducted to evaluate the safe and effective use of NeuroStar TMS as a monotherapy.

• An analysis for predictors of response demonstrated that the patients with the best response to NeuroStar TMS Therapy were adults who have failed to achieve satisfactory improvement from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode.

They had received a median of 4 total prior antidepressant treatment attempts in the current episode, one of which achieved treatment adequacy at or above the minimal effective dose and duration.

In these patients, the following efficacy results were observed in the randomized, controlled study:

The primary efficacy measure was statistically significantly superior to placebo (p=0.0006) among NeuroStar-treated patients.

NeuroStar TMS Therapy-treated patients had statistically significant response and remission rates, which were approximately twice the rate of placebo-treated patients.

Patients who did not respond in the randomized, controlled study entered into a 6-week, open-label treatment study. In the open-label study, which is most like real-world clinical practice, the following was observed:

Patients treated for the first time with NeuroStar TMS Therapy achieved a 54% response rate and a 33% remission rate on the HAMD 24-item scale, at the end of 6 weeks

Similar results were observed using the MADRS rating scale.

Throughout the NeuroStar TMS Therapy studies, more than 10,000 active TMS treatments were safely performed. The following were the safety results observed[5]:

No systemic side effects, such as weight gain, sexual dysfunction, sedation, nausea, or dry mouth

The most commonly reported side effect related to treatment was scalp pain or discomfort during the treatment session.

There was a less than 5% discontinuation rate due to adverse events.

Are the rates of response and remission clinically meaningful to patients?

• Yes, particularly in patients who had failed multiple treatment attempts, one of which achieved an adequate dose and duration

• In the RCT, almost 3x the number of NeuroStar-treated patients had a significant improvement in symptoms compared to placebo.

That magnitude of difference is larger than that of most antidepressant medications approved for the treatment of depression, despite the fact that almost all medications have been studied and approved for 1st-line treatment.

In the open-label trial, which is most like the real world, ~1 in 2 patients had a significant improvement and 1in 3 had complete symptom resolution.

• In addition to efficacy, NeuroStar's safety/tolerability profile is also clinically meaningful

It's non-systemic, so it doesn't cause side effects such as weight gain, sexual dysfunction, nausea, dry mouth, sedation, etc.

The most commonly reported side effect related to treatment was scalp pain or discomfort during the treatment session.

What were the patient selection criteria for the study?

- ✓ Adults
- ✓ Unipolar, non-psychotic
- ✓ Had failed at least one, but no more than four, previous medications at an adequate dose and duration.

Do you have data on suicide and violent behaviors in the clinical trials?

There were no incidents of reported suicide or suicide attempts in patients treated with NeuroStar TMS Therapy during the clinical trials.

Patients who were at high risk of suicide were not included in our trial.

Does NeuroStar TMS Therapy work in other disorders? There are lots of studies in the literature suggesting it works in other areas.

NeuroStar has only systematically been evaluated in patients with unipolar, non-psychotic major depression

While there is promising data in a variety of other disorders, these data are preliminary and require systematic evaluation in controlled clinical trials

If you'd like more information on other potential uses for TMS, you can contact our Medical Affairs staff who can provide you with further information.

CYBERONICS VNS THERAPY, ECT QUESTIONS, AND OTHER TMS COMPANIES

How does it compare to Cyberonics' VNS Therapy?

VNS Therapy is approved as an adjunctive treatment to treat depressed patients who have failed at least four previous antidepressant medications. NeuroStar TMS can be used as a monotherapy and is intended to be used earlier in the treatment algorithm

VNS is not approved as an acute treatment, NeuroStar is.

Unlike VNS, TMS Therapy is non-invasive and does not require surgery, anesthesia or sedation. With NeuroStar TMS, patients can return to their normal activities immediately after the 40-minute therapy session.

VNS Therapy requires a surgical procedure, during which the patient is anesthetized and has a device implanted in their neck and chest; NeuroStar is completely non-invasive.

How does it compare to ECT? Is this a replacement?

ECT and TMS both used applied energy to the brain to cause neural stimulation for relieving the symptoms of depression. ECT uses electrical energy applied to the whole brain, while TMS uses magnetic energy applied only to the left prefrontal cortex.

ECT is an effective acute treatment for major depression, but is highly invasive (causing seizure induction and requiring anesthesia) and has significant adverse effects. In contrast, TMS is also effective in patients with Major Depressive Disorder but is non-invasive and has an excellent safety profile.

• TMS will likely be used much earlier in the treatment algorithm, because of its favorable risk/benefit ratio

• ECT will always have an important role for certain depression patients despite safety concerns; however, will be reserved as a "last resort"

Isn't NeuroStar TMS less effective than ECT?

- ✓ NeuroStar TMS Therapy is an outpatient procedure
- ✓ Unlike electroconvulsive therapy, TMS does not require anesthesia, sedation and the production of a convulsion.
- ✓ Also different from ECT, NeuroStar TMS Therapy does not result in adverse effects on memory or concentration.
- ✓ Because of these issues, ECT is often reserved as a last resort.
- ✓ TMS will likely be used much earlier in the treatment algorithm, because of its favorable risk/benefit ratio