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Antidepressant Treatment Response Questionnaire (ATRQ)

Considerations for Alto Neuroscience
ALTO-300-201 Clinical Trial



ATRQ

- Clinical trial tool developed at MGH to increase the precision associated with MDD diagnosis and course
- Clinician-rated questionnaire examining participant's antidepressant treatment history
- For each antidepressant treatment trial, uses specific anchor points to define:
 1. Adequacy of the dose and duration of the treatment
 2. Degree of symptomatic improvement obtained



ATRQ consists of questions about the participant's:

- Use of a list of antidepressant medications (tricyclics, SSRIs, MAOIs, other specified) taken across a specified timeframe
- Experience with:
 - Electroconvulsive treatment (ECT) during the current episode
 - Vagal nerve stimulation (VNS)
 - Deep brain stimulation (DBS)

ATRQ Form Tools - Save Save & Next

Who administered the ATRQ (first, middle, and last initial)?

Have you received any treatment with medications in the last 24 months? Please select the correct answer. Yes No

Tricyclic Antidepressants

Were any tricyclic antidepressant medications in this section taken? Yes No

Row Tools	Medication Name	Have you taken this medication for at least 6 weeks in the past 24 months?	Have you taken this medication at a dosage equal to or greater than the minimum dosage listed for the medication? The minimum dosage for each medication is listed under the name of the medication.	Did you take this medication with another drug [e.g., buspirone (Buspar), lithium, psychostimulants such as amphetamine (Ritalin), atypical antipsychotics such as olanzapine (Zyprexa)] added to augment or boost the antidepressant effect?	If a rating of 100 is "completely improved" and 0 is "not improved at all," how close to 100 did you get on this medication?
1	<input checked="" type="checkbox"/> doxepin - 150mg/d	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> 75% to 100% <input type="radio"/> 50% to <75% <input type="radio"/> 26% to <50% <input type="radio"/> ≤25%
2	<input checked="" type="checkbox"/> clomipramine - 150mg/d	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> 75% to 100% <input type="radio"/> 50% to <75% <input type="radio"/> 26% to <50% <input type="radio"/> ≤25%
3	<input checked="" type="checkbox"/> amoxapine - 150mg/d	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> 75% to 100% <input type="radio"/> 50% to <75% <input type="radio"/> 26% to <50% <input type="radio"/> ≤25%
4	<input checked="" type="checkbox"/> amitriptyline - 150mg/d	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> 75% to 100% <input type="radio"/> 50% to <75% <input type="radio"/> 26% to <50% <input type="radio"/> ≤25%
5	<input checked="" type="checkbox"/> maprotiline - 150mg/d	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> 75% to 100% <input type="radio"/> 50% to <75% <input type="radio"/> 26% to <50% <input type="radio"/> ≤25%
6	<input checked="" type="checkbox"/> desipramine - 150mg/d	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> 75% to 100% <input type="radio"/> 50% to <75% <input type="radio"/> 26% to <50% <input type="radio"/> ≤25%

ALTO-300-201 Schedule of Assessments: ATRQ

- ATRQ should be administered at Screening 1 Visit (i.e., Visit 1) only
- Participants taking an antidepressant must have an inadequate response (< 50% improvement based on the ATRQ) with an antidepressant treatment of adequate dose and duration
- The ATRQ should be assessed over the past 24 months for adequacy of dose, adequacy of duration (at least 6 weeks), and amount of response utilizing the ATRQ
 - **Note: Adequate dose and duration can be achieved by Visit 2 (e.g., if the participant had 5 weeks duration at Visit 1, they would reach 6 weeks by Visit 2). In this case, the ATRQ will need to be updated at Visit 2**
- The determination of the degree of response on the prior antidepressant(s) is made based on the patient's report and clinician's judgement guided by the ATRQ criteria

Visit Name	Screening Period		Double Blind (DB) Treatment Period					Open Label (OL) Treatment Period				Follow-up Period
	Screening 1	Screening 2 Biomarker Baseline	Day 1	Week 1	Week 2	Week 4	Week 6 DB EOT	Week 7	Week 8	Week 10	Week 14 OL EOT	Safety Follow-up
Visit Number	1	2	3	4	5	6	7	8	9	10	11	12
Visit Window	-7 days	-7 days		± 3 days	±3 days	±4 days	±4 days	±3 days	±4 days	±5 days	-5 days	±3 days
ATRQ	X											

ALTO-300-201 inclusion criteria relevant to ATRQ:

Type of Participant and Disease Characteristics

At **Visit 2**, all of the following:

1. Taking a stable dose of a single antidepressant, which may be an SSRI (other than fluvoxamine), SNRI, or bupropion,
2. Have been on that antidepressant for ≥ 6 weeks at an adequate dosage defined by the Antidepressant Treatment Response Questionnaire (ATRQ), and with no modification to dosage for ≥ 2 weeks prior to Visit 2, AND
3. Have a response to their currently prescribed antidepressant of $< 50\%$ improvement as defined by the ATRQ



ALTO-300-201 inclusion criteria relevant to ATRQ:

Based on clinical assessment have either:

- had a period of remission of at least 2 consecutive months (not meeting DSM-5 criteria for MDD) in the past 26 months, regardless of the number of failed antidepressants

OR

- did not have a period of remission of at least 2 consecutive months in the past 26 months and within the past 24 months have not failed > 3 antidepressants (including current antidepressant) at an adequate dosage and duration (≥ 6 weeks) as defined by the ATRQ





1

Have you received any treatment with medications within the last 24 months?
YES NO



2

Were any [tricyclic, SSRI, MAOI, other] antidepressant medications in this section taken? YES NO

Move on to last 2 items (ECT and VNS/DBS)



3

[For each medication] Have you taken this medication for at least 6 weeks in the past 24 months? YES NO



4

[For each medication] Have you taken this medication at a dosage equal to or greater than the minimum dosage listed for the medication? YES NO



5

[For each medication] Did you take this medication with another drug (e.g., buspirone (Buspar), lithium, psychostimulants such as methylphenidate (Ritalin), atypical antipsychotics such as olanzapine (Zyprexa)) added to augment or boost the antidepressant effect? YES NO



ATRQ Items 1-5

Sample List of Antidepressant Medications

List of Antidepressant Medications.

<u>Drug Class</u>	<u>Brand Name</u>	<u>Generic Name</u>	<u>At least</u> <u>6 Weeks</u>	<u>Minimum</u> <u>Dose</u>	<u>Equal or</u> <u>greater to</u>	<u>Maximum</u> <u>Dose</u>	<u>Equal or</u> <u>greater to</u>	<u>Drug was added</u> <u>augment or boost c</u>
Tricyclic Antidepressants								
	Adapin	doxepin	_____	150mg/d	_____	250mg/d	_____	_____
	Anafranil	clomipramine	_____	150mg/d	_____	250mg/d	_____	_____
	Asendin	amoxapine	_____	150mg/d	_____	250mg/d	_____	_____
	Endep/Elavil	amitriptyline	_____	150mg/d	_____	250mg/d	_____	_____
	Ludiomil	maprotiline	_____	150mg/d	_____	250mg/d	_____	_____
	Norpramin	desipramine	_____	150mg/d	_____	250mg/d	_____	_____
	Pamelor	nortriptyline	_____	75mg/d	_____	125mg/d	_____	_____
	Sinequan	doxepin	_____	150mg/d	_____	250mg/d	_____	_____
	Surmontil	trimipramine	_____	150mg/d	_____	250mg/d	_____	_____
	Tofranil	imipramine	_____	150mg/d	_____	250mg/d	_____	_____
	Vivactil	protriptyline	_____	30mg/d	_____	60mg/d	_____	_____
	Azafen	pipofezine	_____	150mg/d	_____	300mg/d	_____	_____
	Agedal/Elronon	noxiptiline	_____	100mg/d	_____	250mg/d	_____	_____
Monoamine Oxidase Inhibitors (MAOIs)								
	Marplan	isocarboxazid	_____	30mg/d	_____	60mg/d	_____	_____
	Nardil	phenelzine	_____	45mg/d	_____	90mg/d	_____	_____
	Parnate	tranylcypromine	_____	30mg/d	_____	60mg/d	_____	_____
	Emsam	selegiline patch	_____	6 mg/24 hrs	_____	12 mg/hrs	_____	_____
	Aurorix	moclobemide	_____	300 mg/d	_____	600 mg/d	_____	_____
	Pirazidol	pirindole	_____	200 mg/d	_____	300 mg/d	_____	_____
Selective Serotonin Reuptake Inhibitors (SSRIs)								
	Luvox	fluvoxamine	_____	50mg/d	_____	150mg/d	_____	_____
	Paxil	paroxetine	_____	20/25mg/d	_____	60/75mg/d	_____	_____
	Prozac	fluoxetine	_____	20mg/d	_____	60mg/d	_____	_____
	Zoloft	sertraline	_____	50mg/d	_____	150mg/d	_____	_____
	Celexa	citalopram	_____	20mg/d	_____	60mg/d	_____	_____
	Lexapro	escitalopram	_____	10ma/d	_____	30mg/d	_____	_____
Serotonin-Norepinephrine Reuptake Inhibitors (SNR)								
	Effexor	venlafaxine	_____	75mg/d	_____	250mg/d	_____	_____
	Cymbalta	duloxetine	_____	60mg/d	_____	120mg/d	_____	_____
	Pristiq	desvenlafaxin	_____	50mg/d	_____	100mg/d	_____	_____
	Savella	milnacipram	_____	100mg/d	_____	200mg/d	_____	_____
Other Antidepressants								
	Viibryd	vilazodone	_____	40 mg/d	_____	80mg/d	_____	_____
	Desyrel	trazodone	_____	300mg/d	_____	600mg/d	_____	_____
	Serzone	nefazodone	_____	300mg/d	_____	600mg/d	_____	_____
	Wellbutrin	bupropion	_____	300mg/d	_____	450mg/d	_____	_____
	Remeron	mirtazapine	_____	15mg/d	_____	45mg/d	_____	_____
	Valdoxan	agomelatine	_____	25mg/d	_____	50mg/d	_____	_____
	Stablon	tianeptine	_____	37.5mg/d	_____	75mg/d	_____	_____
	Edronax	reboxetine	_____	4 mg/d	_____	8mg/d	_____	_____
	Bolvidon/Depnon,		_____		_____		_____	_____
	Norval/Tolvon	mianserin	_____	30 mg/d	_____	90mg/d	_____	_____
	Insidon	opipramol	_____	150 mg/d	_____	300mg/d	_____	_____

- Antidepressants used in the past 2 years (24 months) are captured on the ATRQ
- All medications and therapies (including psychotherapies) used in the 30 days prior to signing the ICF through the end of the study should be captured in the concomitant therapy section of the eCRF



ATRQ Item 6

Degree of Improvement

If a rating of 100 is “completely improved” and 0 is “not improved at all,” how close to the 100 did you get on this medication?

- a. 75% to 100%
- b. 50% to < 75%
- c. 26% to < 50%
- d. \leq 25%

- ATRQ assesses the degree of improvement (in the most efficacious treatment trial or in all treatment trials during the current episode) on a scale of 0% to 100%
- Rater should guide the participant to think about their improvement within the past week including the day of the visit
- For participants on an adequately dosed antidepressant as determined by the ATRQ, their current response to the antidepressant needs to be < 50% improvement based on clinical assessment



Thank you!

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