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What to Expect When Switching to a Second Antidepressant Medication Following an Ineffective Initial SSRI: A Report From the Randomized Clinical STAR*D Study

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Article Abstract

Objective: An antidepressant medication switch often follows a failed initial trial with selective serotonin reuptake inhibitors (SSRIs). When, for whom, and how often second-step response and remission occur are unclear, as is preferred second-step trial duration. As more treatments are approved for use following 2 failed “adequate” trials, researchers and clinicians require an evidence-based definition of “adequate.”

Methods: Following citalopram in the randomized Sequenced Treatment Alternatives to Relieve Depression (STAR*D) clinical trial (which ran July 2001–September 2006), participants with score ≥ 11 on



SR16 defined response, remission, and no clinically meaningful benefit based on the modified intent-to-treat sample.

Results: About 80% of 438 participants completed ≥ 6 weeks of treatment with the switch medication. All treatments had comparable outcomes. Overall, 21% (91/438) remitted, 9% (40/438) responded without remission, and 58% (255/438) had no meaningful benefit. Half of the responses and two-thirds of remissions occurred after 6 weeks of treatment. Overall, 33% of responses (43/131) occurred after ≥ 9 weeks of treatment. No baseline features differentiated early from later responders or remitters. No early triage point was found, but those with at least 20% reduction from baseline in QIDS-SR16 score around week 2 were 6 times more likely to respond or remit than those without this reduction.

Conclusions: Following nonefficacy with an initial SSRI, only about 20% remit and more than half achieve no meaningful benefit with a second-step switch to another monoaminergic antidepressant. A 12-week trial duration seems necessary to capture as many second-step switch responders as possible.

Trial Registration: ClinicalTrials.gov identifier: [NCT00021528](https://clinicaltrials.gov/ct2/show/study/NCT00021528)

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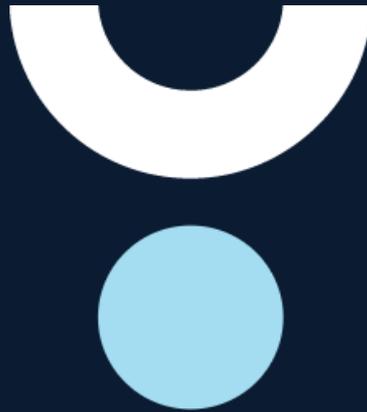
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