

**Table 1**

**Demographic and Clinical Characteristics of Munich Antidepressant Response Signature Project Sample<sup>a</sup>**

Characteristic	Group						Analysis		
	Treatment-Emergent Suicidal Ideation Subjects		Non- Treatment-Emergent Suicidal Ideation Subjects—A		Non- Treatment-Emergent Suicidal Ideation Subjects—B		2	df	p
	N	%	N	%	N	%			
Total sample	32	8.1	329	82.6	79	19.9			
Gender							0.312	2	0.856
Male		43.8		44.8		49.5			
Female		56.3		55.2		50.5			
Employment status							0.357	4	0.986
Employed	32	62.9	329	63.4	79	61.1			
Retired	32	25.7	329	24.1	79	23.4			
Unemployed	32	11.4	329	12.5	79	15.5			
Living status							2.693	2	0.260
Living with a partner, child, or other person	32	54.3	329	60.9	79	64.5			
Single	32	45.7	329	39.1	79	35.5			
Bipolar features	3	9	52	15	11	13	0.949	2	0.622
Recurrent depression		56.3		58.2		60.4	0.102	2	0.950
Psychotic features		18.8		11.9		13.9	1.253	2	0.534
Family history of depression		46.9		46.6		40.5	1.977	2	0.372
History of attempted suicide		17.9		29.3		20.0	4.846	2	0.089
Medication									
SSRI		37.5		37.8		35.7	1.291	2	0.524
Tricyclic antidepressant		34.4		20.4		22.9	1.141	2	0.565
SNRI		25		19.4		19.2	1.713	2	0.425

Mirtazapine		28		35.7		34	0.776	2	0.679
NRI		12.5		2		4	2.472	2	0.291
Neuroleptic		21.9		17.3		22	1.419	2	0.492
Mood stabilizer		46.9		35.7		29.9	2.173	2	0.337
Benzodiazepine		50		20.4		30	<sup>b,c</sup> 16.094	2	0.001
	Mean	SD	Mean	SD	Mean	SD	t	df	p
Age (years)	47.1	16.1	49.3	14.1	50.8	14.3	1.273		0.206
Age at onset (years)	32.6	16.0	37.3	15.4	40.6	15.6	2.393 <sup>b</sup>		0.018
HAM-D score at inclusion	24.5	7.1	26.6	6.6	22.8	6.5	-0.759		0.45
Previous episodes	3.2	4.0	2.8	5.3	2.7	5.5	-0.218		0.828
Illness duration (years)	13.9	15.4	10.6	10.5	10.3	10.1	-1.507		0.135
Duration of current episode (weeks)	38.0	58.4	39.1	69.3	28.4	21.7	-0.672		0.503
Single nucleotide polymorphism	N	%	N	%	N	%	P	P	OR
GRIK2 gene									
rs2852618									
AA	3	9.4	86	26.3	27	34.6	0.045	0.005	9.0
AG	17	53.1	167	51.1	39	50.0			
GG	12	37.5	74	22.6	12	15.4			
rs954765									
AA	4	12.5	106	32.4	32	41.0	0.06	0.007	7.3
AG	18	56.2	157	47.7	35	44.9			
GG	10	31.2	65	19.9	11	14.1			
rs2782900									
CC	4	12.5	33	10.1	6	7.6	0.042	0.007	4.3
CT	21	65.6	149	45.6	30	38.0			
TT	7	21.9	146	44.3	43	54.4			
rs2518224 <sup>d</sup>									
AA	26	81.2	265	80.5	60	75.9	1	0.86	1.3
AC	6	18.8	60	18.3	18	22.8			
CC	0	0	4	1.2	1	1.3			
GRIA3 gene									

rs4825476									
AA	25	78.1	191	57.9	45	57.0	0.018	0.041	2.7
AG	6	18.8	88	26.8	24	30.4			
GG	1	3.1	50	15.2	10	12.7			

<sup>a</sup>Thirty-two patients (8.1%) developed treatment-emergent suicidal ideation (comparable with 6.2% of patients reported in the STAR\*D study) and were compared with 329 patients (A) without worsening of suicidal thoughts and 79 participants (B) who were completely lacking suicidal ideation, a subgroup of A. Thirty-six patients were excluded from the analysis because their baseline suicidality was greater than zero, and they showed worsening of suicidal ideation and thus did not fit into any of the three groups. Antidepressant treatment is shown for the time frame of the onset of suicidal ideation in the treatment-emergent suicidal ideation group and the respective treatment weeks in the other two groups. Antidepressant monotherapy was administered to 62.5 % of the patients, while 37.5 % received combination therapy. Of patients with treatment-emergent suicidal ideation, 59.3% developed this side effect within the first 2 weeks after admission. Best empiric associations between genetic markers within GRIK2, GRIA3, and treatment-emergent suicidal ideation are shown. P-values are from allelic tests for treatment-emergent suicidal ideation-A versus non-treatment-emergent suicidal ideation-A and treatment-emergent suicidal ideation-B versus non-treatment-emergent suicidal ideation-B. Single nucleotide polymorphisms rs4825476 and rs2518224 were considered for replication of results from the STAR\*D study sample. All GRIK2 single nucleotide polymorphisms are in Hardy-Weinberg equilibrium ( $p > 0.7$ ), and GRIA3 is x-chromosomal. In female comparison subjects, Hardy-Weinberg equilibrium has a  $p$  value of 0.76. Odds ratios refer to allelic tests treatment-emergent suicidal ideation-B versus non-treatment-emergent suicidal ideation-B. Anecdotal evidence from the Munich Antidepressant Response Signature project trial showed that of the three patients who committed suicide under antidepressant treatment, one was homozygote for the risk alleles of both GRIK2 (rs2852618-G) and GRIA3 (rs4825476-A), and the other two patients were heterozygote for these two risk alleles.

<sup>b</sup>Treatment-emergent suicidal ideation-A versus non-treatment-emergent suicidal ideation-A ( $p > 0.05$ ).

<sup>c</sup>Treatment-emergent suicidal ideation-B versus non-treatment-emergent suicidal ideation-B ( $p > 0.05$ ).

<sup>d</sup>STAR\*D study risk allele=G.