SOCIDEMOGRAPHIC AND CLINICAL PREDICTORS OF REMISSION AND RESPONSE IN TREATMENT RESISTANT DEPRESSION

Martina Balestri (a), Raffaella Calati (b), Daniel Souery (c), Siegfried Kasper (d), Stuart Montgomery (e), Joseph Zohar (f), Julien Mendlewicz (g), Alessandro Serretti (a)

a) Department of Biomedical and NeuroMotor Sciences, University of Bologna, Bologna, Italy; b) IRCCS Centro S. Giovanni di Dio, Fatebenefratelli, Brescia, Italy; c) Laboratoire de Psychologie Médicale, Université Libre de Bruxelles, and Centre Européen de Psychologie Médicale-PsyPluriel, Brussels, Belgium; d) Medical University of Vienna, Department of Psychiatry and Psychotherapy, Vienna, Austria; e) University of London, Imperial College, London, United Kingdom; f) Chaim Sheba Medical Center, Chaim Sheba Medical Center, Tel-Hashomer, Israel; g) Université Libre de Bruxelles, Brussels, Belgium

INTRODUCTION

Background: Treatment Resistant Depression (TRD) still characterizes a large portion of Major Depressive Disorder (MDD) patients. However, different TRD definitions have been suggested: from the lack of response to 1 antidepressant (AD), to the lack of response to 2 or more AD of different classes. Several studies attempted to identify predictors of treatment non remission/response to a single AD, but multiple treatment failures in the same episode have been poorly investigated. In a previous retrospective study, we identified some clinical features associated with non response to 2 consecutive adequate ADs: anxiety comorbidity, in particular panic disorder and social phobia, personality disorder, suicidal risk, severity, melancholia, number of hospitalization >1, recurrent episodes, early age at onset, non response to the first AD received lifetime (1).

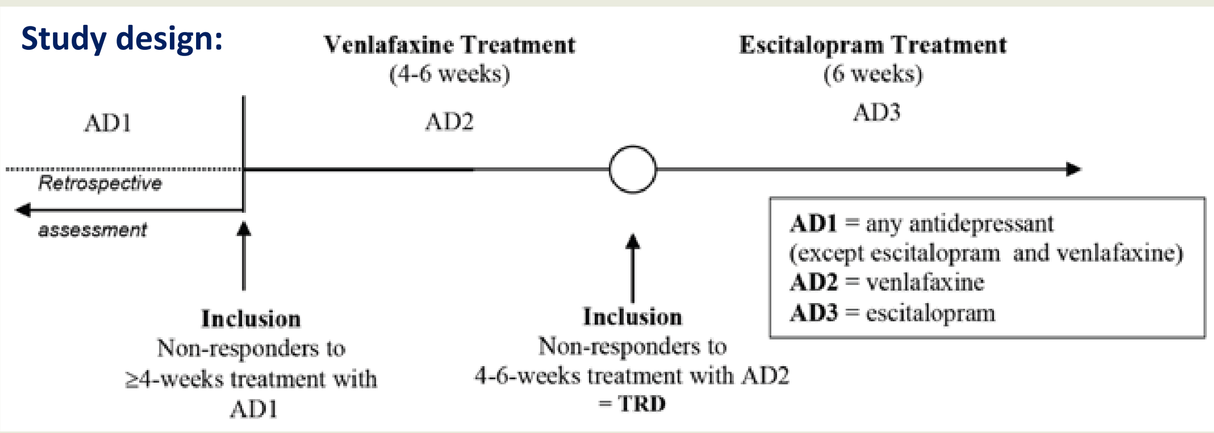
AIMs

Primary aim: to detect sociodemographic and clinical predictors of non remission in a sample of TRD patients who failed to respond to at least two ADs (adequacy in terms of dose and duration).

Secondary aims: to detect: 1) predictors of non response in TRD; 2) predictors of non remission/response in patients who failed to respond to at least one previous adequate AD treatment; 3) differences in socio-demographic and clinical features between early responders and non responders.

METHODS

Study design:



Sample: in the context of a European multicenter project carried out by the Group for the Study of Resistant Depression (GSRD), 407 MDD pts (male: 139, 34.15%, mean age: 45.30±12.67) were prospectively assessed. 170 non responder pts (TRD) (male: 69, 40.59%, mean age: 45.30±12.67) received escitalopram.

Inclusion criteria: 1) Moderate or severe Current Major Depressive Episode (DSM-IV-TR criteria); 2) MADRS total score ≥22

Exclusion criteria: 1) Any current psychiatric disorder other than MDD as a principal diagnosis; 2) not allowed treatments: higher benzodiazepine doses within the last week, antipsychotics, mood stabilizers, ECT within the past 6 months, formal psychotherapies started in the month preceding inclusion.

Evaluation Instruments:

✓ MINI, MADRS, HRSD, CGI-S and CGI-I scales: administered from baseline to week 12.

✓ Other information, such as socio-demographic features, psychiatric antecedents and previous treatments: collected at baseline.

Statistical Analyses: chi-square and t-test to evaluate impact of the investigated variables on remission and response in both TRD and MDD not responding to at least one previous AD trial.

✓ **First step**: all variables were considered (p=0.05).

✓ **Second step**: identification of the correlated variables among the significant ones (correlation matrix).

✓ **Third step**: multiple regression.

REFERENCE: 1. Souery, D., et al., Clinical factors associated with treatment resistance in major depressive disorder: results from European multicenter study. J Clin Psychiatry, 2007. 68(7): p. 1062-70

RESULTS

PREDICTORS OF REMISSION IN TRD	Rem n=39, 22.94%	Non Rem n=131, 77.06%	Total n= 170	Statistics		
	Mean±SD/n(%)	Mean±SD/n(%)	Mean±SD/n(%)	t/chi²	d.f.	p
Age last episode (n=124)	36.39±12.32	42.15±12.18	40.62±12.44	2.32	122	**0.02**
Duration current episode (days) (n=142)	77.14±48.57	195.66±213.24	166.45±193.34	0.142	140	**0.001**
Severity of current episode (n=165)						
Severe (with/without psych features)	17 (43.59)	82 (65.08)	99 (60.00)	0.259	1	**0.001**
Moderate	22 (56.41)	44 (34.92)	66 (40.00)			
Suicidal risk (yes/no)	14 (35.90)	72 (54.96)	86 (50.59)	0.192	1	**0.003**
Suicidal risk level (n=86)						
High	6 (42.85)	7 (9.72)	13 (15.12)	0.508	2	**0.002**
Medium	2 (14.29)	37 (51.39)	39 (45.35)			
Low	6 (42.86)	28 (38.89)	34 (39.53)			
CGI severity (baseline) (n=154)	4.41±0.86	4.90±0.83	4.77±0.87	0.132	152	**0.002**
MADRS (baseline)*	25.66±5.92	31.06±7.91	29.82±7.82	0.19	168	**0.0001**
Anxiety disorders (no OCD) *	3 (7.69)	37 (28.24)	40 (23.53)	7.5	1	**0.01**
Panic disorder lifetime	0 (0.00)	17 (12.98)	17 (10.00)	5.62	1	**0.02**
Panic disorder current	0 (0.00)	12 (9.16)	12 (7.06)	3.84	1	**0.05**
GAD current	2 (5.13)	25 (19.08)	27 (15.88)	4.38	1	**0.04**
Psychiatric Antecedents						
BP (2°) (n=113)	2 (6.90)	0 (0.00)	2 (1.11)	5.89	1	**0.01**
Escitalopram doses						
day 56	20.76±2.70	22.60±4.40	22.18±3.14	2.45	168	**0.02**
day 84 (n=157)	24.87±5.06	26.94±4.62	26.43±4.81	2.37	155	**0.02**

Table: Variables associated with non remission in TRD (primary aim). * variables found to be associated with non remission also in multiple regression. Results for secondary aims were resumed below.

PROSPECTIVE STUDY

VENLAFAXINE

Non remission

- ↑ **Current suicidal risk level**
- ↑ MDD 1/2 degree psych antecedents
- ↑ Other psych antecedents
- ↓ BDZ use (Day 0)
- ↑ Side effects (Day 14, 42)
- ↑ **CGI severity (Day 0)**
- ↑ **Dose (Day 14, 28, 42)**

Non response

- ↑ Occupational status
- ↑ **Current suicidal risk level**
- ↑ Other psych antecedents
- ↓ BDZ use (Day 0)
- ↑ **Side effects (Day 14, 42)**
- ↑ Dose (Day 42)

ESCITALOPRAM

Non remission

- ↑ Duration current episode
- ↑ Age last episode
- ↑ **Severity current episode**
- ↑ **Current suicide risk**
- ↑ **Current suicidal risk level**
- ↑ **Current anxiety disorder (no OCD)**
- ↑ **Panic disorder lifetime and current**
- ↑ GAD current
- ↓ BP 2nd degree antecedents
- ↓ Quality of life (work, family)
- ↑ **CGI severity (Day 42)**
- ↑ **MADRS score (Day 42)**
- ↑ **Dose (Day 56, 84)**

Non response

- ↑ Duration current episode
- ↑ **Side effects (Day 84)**

PREVIOUS RETROSPECTIVE STUDY (1)

Treatment resistance SAME FACTORS:

- ↑ **Severity current episode**
- ↑ **Current suicide risk**
- ↑ **Current anxiety disorder (no OCD)**
- ↑ **Panic disorder**

DIFFERENT FACTORS:

- N° hospitalization
- Social phobia
- Recurrent vs single episodes
- Onset before 18 years
- Melancholic features
- Non response to first AD treatment lifetime
- Personality disorder

CONCLUSION

Severity of the current episode (probably associated with higher AD doses and consequently side effects), current suicidal risk and comorbid anxiety disorders (panic disorder, in particular) seemed to predict non remission/non response in two sample of TRD patients, prospectively and retrospectively followed. When present, these predictors could guide clinicians to the choice of more appropriate therapies. The lack of a relationship between anxiety disorders and MDD not responding to at least 1 adequate AD treatment deserve a deeper investigation.

Limitations: design issue (open nature, retrospective assessment of the first AD).

This poster is financially sponsored by Lundbeck A/S and the Belgian National Fund for Scientific Research (FNRS; 3.4.530.07 F). Dr. Serretti is or has been consultant/speaker for: Abbott, Angelini, Astra Zeneca, Clinical Data, Boheringer, Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen, Lundbeck, Pfizer, Sanofi, Servier. Dr. Kasper: Eli Lilly, Lundbeck, Bristol-Myers Squibb, GlaxoSmithKline, Organon, Sepracor, Servier; AstraZeneca, Pfizer, Schwabe, Janssen, Novartis and Pierre Fabre. Professor Montgomery is or has been consultant/speaker for: AstraZeneca, Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Lundbeck, Merck, Merz, Neurim, Pierre Fabre, Pfizer, Sanofi, Servier, Shire, Sepracor, Takeda, Targacept, Wyeth, Bionevia, M's Science, Otsuka, Pharmaneuroboost, Richter, Roche, Theracos, Transcept, UBC and Xytis. Other Authors have no potential conflict of interest.