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 response/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).

Primary aims: 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 sociodemographic and clinical features between early responders and non responders.

Methods:

**Study design:**
- Venlafaxine Treatment (4-6 weeks)
- Escitalopram Treatment (AD3)

**Inclusion:**
- Any non responders to treatment in TRD

**Exclusion:**
- Non responders to treatment in TRD

**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.

**Evaluation Instruments:**
- MINI, MADRS, HRSQ, 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.

**RESULTS**

**PREDICTORS OF REMISSION IN TRD**

<table>
<thead>
<tr>
<th>Remiation status</th>
<th>n=39</th>
<th>22.34%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Rem</td>
<td>131</td>
<td>77.66%</td>
<td>1.00</td>
</tr>
<tr>
<td>Total</td>
<td>170</td>
<td></td>
<td></td>
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<tr>
<td>Mean±SD</td>
<td></td>
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</tr>
</tbody>
</table>

**Age last episode (n=124):**
- 36.39±10.32 yrs
- 42.15±12.18 yrs
- 40.63±12.44 yrs
- 2.32 122 0.02

**Severity of current episode (n=165):**
- 77.14±48.57
- 195.66±213.24
- 66.45±193.34
- 0.142 140 0.001

**AIMs**

**METHODS**

**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)

**ESCITALOPRAM**

- Non remission
- Duration current episode
- Age last episode
- Severity current episode
- Current suicidal risk
- Current anxiety disorder (no OCD)
- Panic disorder lifetime and current
- GAD current
- BP 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 suicidal risk
  - Current anxiety disorder (no OCD)
  - Panic disorder

- DIFFERENT FACTORS:
  - Hospitalization
  - Socio 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).