ABSTRACT
Late-life depression affects approximately 15% of over 65-years individuals [1]. SSRIs could be responsible of an early exacerbation of anxiety, possibly reduced by a very gradual titration of drugs. The aim of this study is to compare gradual and rapid (standard) titration of paroxetine in an elderly population. 50 elderly (≥ 60 years old) outpatients with Unipolar Mood disorder or Anxiety disorder (HAM-D or HAM-A score ≥ 13) were naturally assigned to abrupt initiation of 10 mg paroxetine or to a gradual increase with 2.5 mg on alternate days up to 10 mg in 7 days. MINI Mental ≤ 20 and/or severe medical illnesses were main exclusion criteria. Outcome were HAM-D ≥ 21, HAM-D symptom subscales (Core, Psychic Anxiety, Somatic Anxiety cluster) and HAM-A change and overall dropouts. All data were recorded weekly for the first 2 months (with one more evaluation after 3 days from the baseline), than after 4 and 6 months from baseline. A significantly greater improvement in depressive and anxious symptoms favored gradual titration both in early and medium-term follow-up (repeated measure ANOVA p=0.026 and p=0.007 respectively for HAM-D ≥ 21, HAM-D Core cluster, HAM-D psychic anxiety subscale, also when controlled for confounders). A higher number of drop out was found in patients managed with abrupt dosage. A gradual titration of paroxetine could lead to better medium-term outcome both in depressive and anxiety symptoms and to less medium-term discontinuations, avoiding the initial treatment anxiety worsening and drop out at the beginning of the treatment.

BACKGROUND AND AIMS
• Late-life depression, often in association with anxiety, affects approximately 15% of over 65-years individuals [1]
• SSRIs are the first line treatment but could be responsible of an early exacerbation of anxiety
• The aim of this study is to compare gradual and rapid (standard) titration of paroxetine in an elderly population

METHODS
• 50 elderly (≥ 60 years old) outpatients with Unipolar Mood disorder or Anxiety disorder were naturally assigned (1:1) to:
  - abrupt initiation of 10 mg paroxetine or
  - a gradual increase with 2.5 mg on alternate days up to 10 mg

• Then dosage could be maintained at 10 mg or increased according to clinical response.

OUTCOMES
HAM-D ≥ 21
HAM-D Core subscale [items: 1 Depressed mood, 2 Feelings of guilt, 3 Work and activities, 8 Retardation, 10 Anxiety (Psychological)], 11 Somatic symptoms
HAM-D Psychic Anxiety subscale [items: 8 Agitation, 10 Anxiety (Psychological)]
HAM-D Somatic Anxiety subscale [items: 21 Anxiety somatic, 12 Somatic symptoms gastrointestinal, 13 Somatic symptoms general]
HAM-A
Drop outs

• All data were recorded weekly for the first 8 weeks of treatment (with one more evaluation after 3 days from the baseline), than after 4 and 6 months from baseline (Fig.1).

RESULTS

<table>
<thead>
<tr>
<th>CLINICAL-DEMOGRAPHIC CHARACTERISTICS</th>
<th>Slow titration (N=26)</th>
<th>Rapid titration* (N=23)</th>
<th>t-test p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years; DS)</td>
<td>70.92 (7.01)</td>
<td>76.04 (6.80)</td>
<td>0.01</td>
</tr>
<tr>
<td>Gender (F/M, %)</td>
<td>73.08/26.92</td>
<td>78.26/21.74</td>
<td>0.67</td>
</tr>
<tr>
<td>HAM-A (mean; DS)</td>
<td>18.12 (7.74)</td>
<td>18.27 (5.43)</td>
<td>0.94</td>
</tr>
<tr>
<td>HAM-D Total ≥ 21</td>
<td>76.04 (6.80)</td>
<td>78.26/21.74</td>
<td>0.01</td>
</tr>
<tr>
<td>Core</td>
<td>7.80 (2.53)</td>
<td>7.50 (2.96)</td>
<td>0.71</td>
</tr>
<tr>
<td>Psychic Anxiety</td>
<td>3.08 (1.66)</td>
<td>2.09 (1.02)</td>
<td>0.02</td>
</tr>
<tr>
<td>Somatic Anxiety</td>
<td>3.48 (1.58)</td>
<td>3.50 (1.77)</td>
<td>0.97</td>
</tr>
</tbody>
</table>

*Out of 50 patients, 1 among rapid arm did not undergo any follow-up evaluation and was excluded from main analysis.

A significantly greater improvement in depressive and anxious symptoms favored gradual titration both in early and medium-term follow-up.

CONCLUSIONS
A gradual titration of paroxetine could lead to better medium-term outcome both in depressive and anxiety symptoms and to less medium-term discontinuations.


No potential conflict of interest