

## Background and aim

**Refractory myasthenia gravis (rMG)** refers to a subset of MG patients without improvement or with poor tolerance to standard treatments. This condition lacks a universally accepted definition, with varying criteria used across literature. [1,2,3,4]

### Aim of the study:

- ❖ To investigate detailed characteristics of refractory MG patients and factors predicting the chance to have rMG.
- ❖ To study refractory status changes over the time and correlated factors.
- ❖ To compare serum cytokine/chemokine profiles in 18 major rMG patients during refractory and non-refractory periods and with naive patients

## Methods

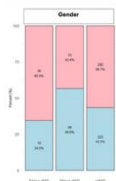
**Retrospective study on 692 patients** treated at the Neuromuscular Centre of Fondazione IRCCS Istituto Neurologico "Carlo Besta" between 2010 and 2021.

### Refractory Classification:

- Major Refractory MG (**major rMG**): no improvement after corticosteroids + 2 immunosuppressants (Sanders' criteria<sup>5</sup>, 2016) for ≥6 months → **7.9%** (55 patients)
- Minor Refractory MG (**minor rMG**): no improvement after corticosteroids + 1 immunosuppressant → **17.6%** (122 patients)
- Non-Refractory MG (**nrMG**): patients not meeting refractory criteria → **74.4%** (515 patients)

## Results

### Results (I): gender



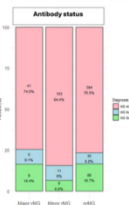
- Females had a significantly higher chance of being in major rMG than in the minor rMG group, compared to males. No significant gender differences were found between the major rMG and the nrMG group nor between the minor and the nrMG group
- Male patients in refractory groups had a later disease onset compared to nrMG (p<0.001): +9 years in major rMG, +13 years in minor rMG

### Results (IV) MGFA-PIS at last visit



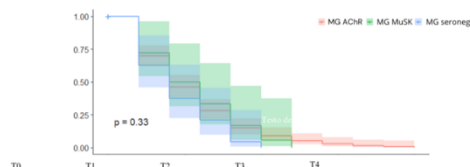
90% of minor rMG patients vs 62% of major rMG vs 86% of NR patients achieved CSR, PR, or MM

### Results (II): Antibody status and histology



- Minor vs nrMG group: anti-AChR (p=0.007) and anti-MuSK (p=0.016) Abs were significantly more frequent in the minor rMG group.
- Minor vs major rMG group: only anti-AChR (p=0.04) Abs were significantly more frequent in the minor rMG group compared to seronegative patients.
- In major and minor rMG rhymosa was significantly more common (p<0.05) when compared to nrMG patients.
- No significant correlation was found between the time from disease onset to rhymotony and the likelihood of developing or remaining refractory

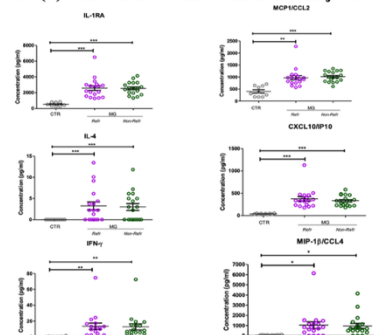
### Results (III): Refractoriness as a dynamic state in major rMG



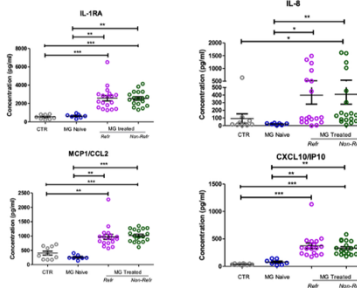
No significant associations were found between gender, antibody status, histology or corticosteroid therapy and the total number of months spent in refractory periods, nor with the resolution or recurrence of refractoriness over time.

### Duration of refractory status in major rMG patients did not correlate with MGFA-PIS at last visit

### Results (V) CYTOKINE & CHEMOKINE in 18 major rMG



### Results (VI) CYTOKINE & CHEMOKINE in 18 major rMG vs 7 NAIVE patients



## Conclusions

- Large rMG cohort analyzed; introduction of "minor rMG" subgroup with distinct features (anti-AChR antibodies, male gender, better outcomes at last follow-up vs major rMG).
- Seronegative MG more frequent in major rMG.
- No correlation between gender, antibody status, histology, MGFA-PIS or corticosteroid therapy and rMG duration or resolution/recurrence.
- No serum cytokine/chemokine profile distinguished refractory from non-refractory phases in major rMG patients, but differences were found compared to healthy controls and naive patients.

1. Manicgazzi R, Amazzini C. When myasthenia gravis is deemed refractory: clinical aspects and treatment strategies. *The Adv Neurol Disord* 2018; 11: 1752-1801/175213.  
 2. Caravacante P, Andreola F, Bonanni S, Yaselli F, et al. Diagnostic refractory myasthenia gravis: Clinical characteristics, treatment, and outcome. *Ann Clin Transl Neurol* 2022; 9: 122-131.  
 3. Rath J, Brunner J, Tomachi M, et al. Frequency and clinical features of treatment-refractory myasthenia gravis. *J Neurol* 2020; 267: 1004-1011.  
 4. Salvi E. Clinical Characteristics of Refractory Myasthenia Gravis Patients.  
 5. Sanders DS, Wolfe GD, Benatar M. International consensus guideline for management of myasthenia gravis.



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