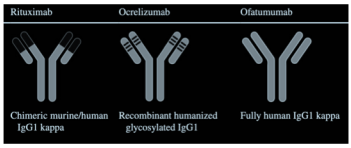
# Neutropenia in patients treated with anti-CD20 monoclonal antibodies for central nervous system inflammatory diseases: a single-center retrospective analysis

**Irene Gattuso*[1], Leonardo Palazzo[1], Giorgio Guido[1], Angela Genchi[1], Simone Guerrieri[1], Chiara Zanetta[1], Vittorio Viti[1], Maria Assunta Rocca[1, 2, 3], Massimo Filippi[1, 2, 3, 4, 5], Lucia Moiola[1]**

[1]*Neurology Unit, Multiple Sclerosis Center, IRCCS San Raffaele Scientific Institute, Milan, Italy,*
[2]*Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy,*
[3]*Vita-Salute San Raffaele University, Milan, Italy,*
[4]*Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy,*
[5]*Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy*

## Introduction and Aims:

Use of **anti-CD20 monoclonal antibodies (anti-CD20s)** in inflammatory Central Nervous System (CNS) diseases has widely increased in the past few years, bringing to the discovery of previously unknown adverse events.




*Krajnc et al., 2022*

Among these, **grade 3 or 4 neutropenia** is a rare but potentially severe event, whose mechanisms and clinical course remain elusive.

**Aim** of this work is to report our single-center experience of grade 3 or 4 neutropenia in patients with inflammatory CNS diseases treated with anti-CD20s.

## Methods:

We retrospectively identified patients with **Multiple Sclerosis (MS)** or **Neuromyelitis Optica Spectrum Disorder (NMOSD)**:

- Under treatment with anti-CD20s
- Developing grade 3 or 4 neutropenia* not better explained by other medical conditions

Grade 3: Absolute Neutrophil Count <1000/uL
Grade 4: Absolute Neutrophil Count <500/uL

*Given the absence of clinical relevance, grade 1 or 2 neutropenia were not considered.

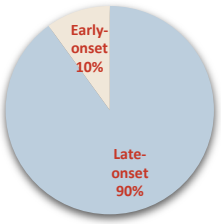
## Results:

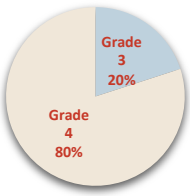
Baseline characteristics of patients are summarized in the table below.

| Baseline characteristics | Study population |
|---|---|
| No. of patients | 10 |
| Type of disease (MS/NMOSD) | 9/1 |
| Type of anti-CD20 (OCR/OFA/RTX) | 8/3/1 |
| Female sex, % | 90 |
| Median age (IQR), years | 39.7 (13.9) |
| Median disease duration (IQR), years | 9.6 (11.3) |
| Median FU from neutropenia onset (IQR), years | 1.4 (1.9) |

8/10 patients experienced grade 4 neutropenia, with a **median ANC at nadir of 255/uL (IQR 365).**
9/10 were late-onset neutropenia, i.e., occurred >4 weeks after last drug administration [median (IQR): 116.5 (92.2) days] and after a median (IQR) of 7.5 (4.2) anti-CD20 cycles.

**Neutropenia severity**

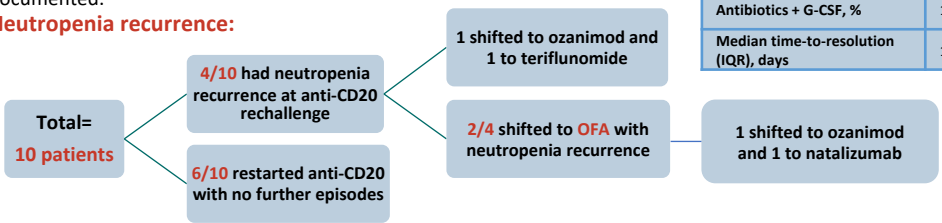



| Clinical characteristics | Study population |
|---|---|
| Fever, % | 60 |
| Oral aphthae, % | 30 |
| Antibiotics administration, % | 40 |
| G-CSF administration, % | 20 |
| Antibiotics + G-CSF, % | 10 |
| Median time-to-resolution (IQR), days | 15 (20) |

6/10 patients developed fever and 3/10 also had oral aphthae, 4/10 received antibiotics, 2/10 received Granulocyte Colony Stimulating Factor (G-CSF), and 1/10 received both, with **median time-to-resolution of 15 (IQR 20) days**.
ANC at nadir was not associated with presence of symptoms (p=0.353) or with need for G-CSF administration (p=0.428). No disease activity after G-CSF was documented.

## Neutropenia recurrence:




## Discussion and conclusions:

Grade 3 or 4 neutropenia can be a complication of all anti-CD20s, ranging from asymptomatic episodes with spontaneous resolution to **febrile neutropenia requiring G-CSF treatment**. It can be either monophasic or relapsing and in this case shift to another anti-CD20 equally exposes to recurrence risk, due to a **possible class-effect**.