# Clinical presentation and outcome of OMAS: A Brazilian perspective

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**Renata Barbosa Paolilo**

| Potential COI | Organization |
|---|---|
| Principal Investigator in clinical trials | Horizon - AMGEN<br>Novartis<br>Roche |
| Speaker / Speakers Boards | Novartis<br>Roche |
| Consultant | Instituto da Criança do Hospital das Clínicas da Faculdade de Medicina da USP<br>Hospital Israelita Albert Einstein |
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# Possible challenges for OMAS care in underdevelopment settings

Under recognized condition
Different triggers
Access to specialized services
Access to treatment

# Brazilian particularities

- Huge dimensions
  - 8.5mi $Km^2$
  - 212mi habitants
- Health service
  - Public (SUS)
  - Private: 51mi
- Social inequality
- Diverse ethnic population

# The patient journey

Girl, 29mo

15mon: ataxia and “nystagmus”

25mon: ataxia


70°O
60°O
50°O
40°O
OCEANO ATLÂNTICO
EQUADOR
0°
Boa Vista
RORAIMA
AMAPÁ
Macapá
Belém
Manaus
AMAZONAS
PARÁ
São Luís
Fortaleza
MARANHÃO
Teresina
CEARÁ
RIO GRANDE DO NORTE
Natal
PARAÍBA
João Pessoa
PIAUÍ
PERNAMBUCO
Recife
ACRE
Porto Velho
Rio Branco
10°S
Palmas
TOCANTINS
ALAGOAS
Maceió
SERGIPE
Aracaju
RONDÔNIA
BAHIA
Salvador
1
MATO GROSSO
Cuiabá
DISTRITO FEDERAL
Brasília
Goiânia
GOIÁS
MINAS GERAIS
ESPÍRITO SANTO
Belo Horizonte
2
Vitória
20°S
Campo Grande
MATO GROSSO DO SUL
SÃO PAULO
3
RIO DE JANEIRO
Rio de Janeiro
São Paulo
TRÓPICO DE CAPRICÓRNIO
PARANÁ
Curitiba
SANTA CATARINA
Florianópolis
RIO GRANDE DO SUL
Porto Alegre
30°S
OCEANO PACÍFICO
OCEANO ATLÂNTICO
N
0
250
500 km

# Briefly about OMAS

Rare condition: recognition and diagnosis
Different treatment regimes
Longterm cognitive impairment

Rossor, T. N2, 2022.

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# OMS in Brazil

## Sindrome opsoclono-mioclonia-ataxia: estudo de aspectos clinicos, etiologicos, terapeuticos e prognosticos em 19 criancas (1990)

Autores:

Kok, Fernando
Franca Netto, Antonio Spina (Orientador)

Autor USP: KOK, FERNANDO - FM

Unidade: FM

Sigla do Departamento: MNE

Assunto: NEUROLOGIA

Idioma: Português

Resumo: A sindrome opsoclono-mioclonia-ataxia (soma) e uma afeccao rara que afeta principalmente criancas e se caracteriza pelo aparecimento subito de movimentos oculares anarquicos (opsoclono), mioclonias parcelares e ataxia cerebelar. Pode ser idiopatica ou estar associada a processos infecciosos do sistema nervoso central ou a neuroblastoma. Acompanhamos por em media tres anos 19 criancas com soma cujo inicio se deu entre 6 meses e 7 anos de idade. Nao se determinou a etiologia em 13 pacientes, detectou-se neoplasia de origem neuroblastica em tres e isolou-se agente infeccioso em tambem tres pacientes (enterovirus 71, coxsackie a21 e agente nao identificado). Quatorze pacientes, incluindo os tres em que se detectou neoplasia, apresentaram sintomas de duracao prolongada e carater recidivante; todos tiveram melhora com corticoterapia e em treze evidenciou-se no seguimento sequela neuro ou psicologica. Quatro criancas, incluindo as tres em que se isolou um agente infeccioso, ficaram assintomaticas em menos de tres meses, nao apresentaram recidiva dos sintomas nem ficaram com sequelas. A evolucao clinica de pacientes com soma associada a neoplasia foi semelhante a de casos idiopaticos com sintomas de duracao prolongada

N=19

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Research Paper

## Characteristics of Opsoclonus-Myoclonus Syndrome in Patients of the Largest Pediatric Hospital in Latin America

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ABSTRACT

*Background:* Opsoclonus-myoclonus syndrome (OMS) is a rare neuroinflammatory disorder characterized by ataxia, opsoclonus, and myoclonus. Clinical diagnosis of OMS has been challenging; therefore, we sought to determine the clinical and treatment profiles of patients with OMS at the largest pediatric hospital in Latin America.
*Methods:* We analyzed the data of patients diagnosed with OMS between 2010 and 2020 at Pequeno Principe Hospital (Brazil) to determine the corresponding clinical profile more accurately.
*Results:* Of the approximately 50,000 visitors to our pediatric neurology department from 2010 to 2020, 10 patients with OMS were observed. Five nontumor cases included three parainfectious and two idiopathic cases. The median time from symptom onset to diagnosis was 34 days. All patients with diagnostic OMS criteria in the idiopathic, nontumor group underwent whole-exome sequencing, with potentially pathogenic mutations identified in two cases. Nine patients were treated with methylprednisolone pulse, followed by oral steroids; eight received one or more intravenous immunoglobulin treatments; and six received azathioprine and cyclophosphamide. Complete symptomatic recovery was observed in only one patient.
*Conclusions:* OMS diagnosis remains challenging. Diagnostic suspicion is necessary to improve the management of these patients and allow early immunosuppressive treatment. Paraneoplastic etiology is the most prevalent. In idiopathic patients who do not respond to immunosuppressive treatment, tests, such as whole-exome sequencing, may reveal a differential diagnosis. Genetic alterations that increase the risk of tumors may be an important clue to the pathophysiology of OMS.


N=10

KOK, F. USP, 1990. Zeny, MS. Pediatric Neurology, 2024.

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# Objective

Describe demographic, clinical, paraclinical and prognostic aspects of OMAS patients in Brazil.

# Methods

Retrospective, nationwide, cross-sectional study
Data collection: January 2021 to June 2023

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# Methods

6 centres:
Hospital das Clínicas HCFMUSP
GRAAC
Hospital Israelita Albert Einstein
Hospital Infantil Albert Sabin
Instituto Nacional do Câncer
Hospital da Criança

5 public services
→ 3 specialized in oncology


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# Methods

RedCap survey with a structured questionnaire:

- Demographic data (age, sex assigned at birth, ethnicity)
- Past health history (neurodevelopment milestones, autoimmune comorbidities)
- Familial health history
- Clinical features (OMAS onset, triggers, relapses, treatment)
- Paraclinic findings
- Neoplastic diagnosis
- Prognostic aspects

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# Methods

## Inclusion criteria:

Patients fulfilling Genoa's diagnostic criteria
≤ 5y of symptom onset
FU > 6 months

## Exclusion criteria:

Other CNS condition
Infection or systemic inflammatory disorder

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# Methods

Disability at last FU:

- Detailed neurologic examination
- OMS score
- Scale of the Assessment and Rating of Ataxia (SARA)
- Sleep disorder
- Social/behavioural disorder
- Educational setting (mainstream school or receiving formal support)
- Formal neuropsychological assessment if available

Remission: normal neurological examination (including behavioural aspects)

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# Methods

Descriptive data of demographic, clinical data and outcome
Association of demographic / clinical data and prognosis
Statistical significance: $p<0.05$.
Statistical analysis: IBM-SPSS (v23).

Approval by the locals and the National Ethical Committee

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# Results

# Results

N= 27

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GRAAC
Hospital Israelita Albert Einstein
Hospital Infantil Albert Sabin
Instituto Nacional do Câncer


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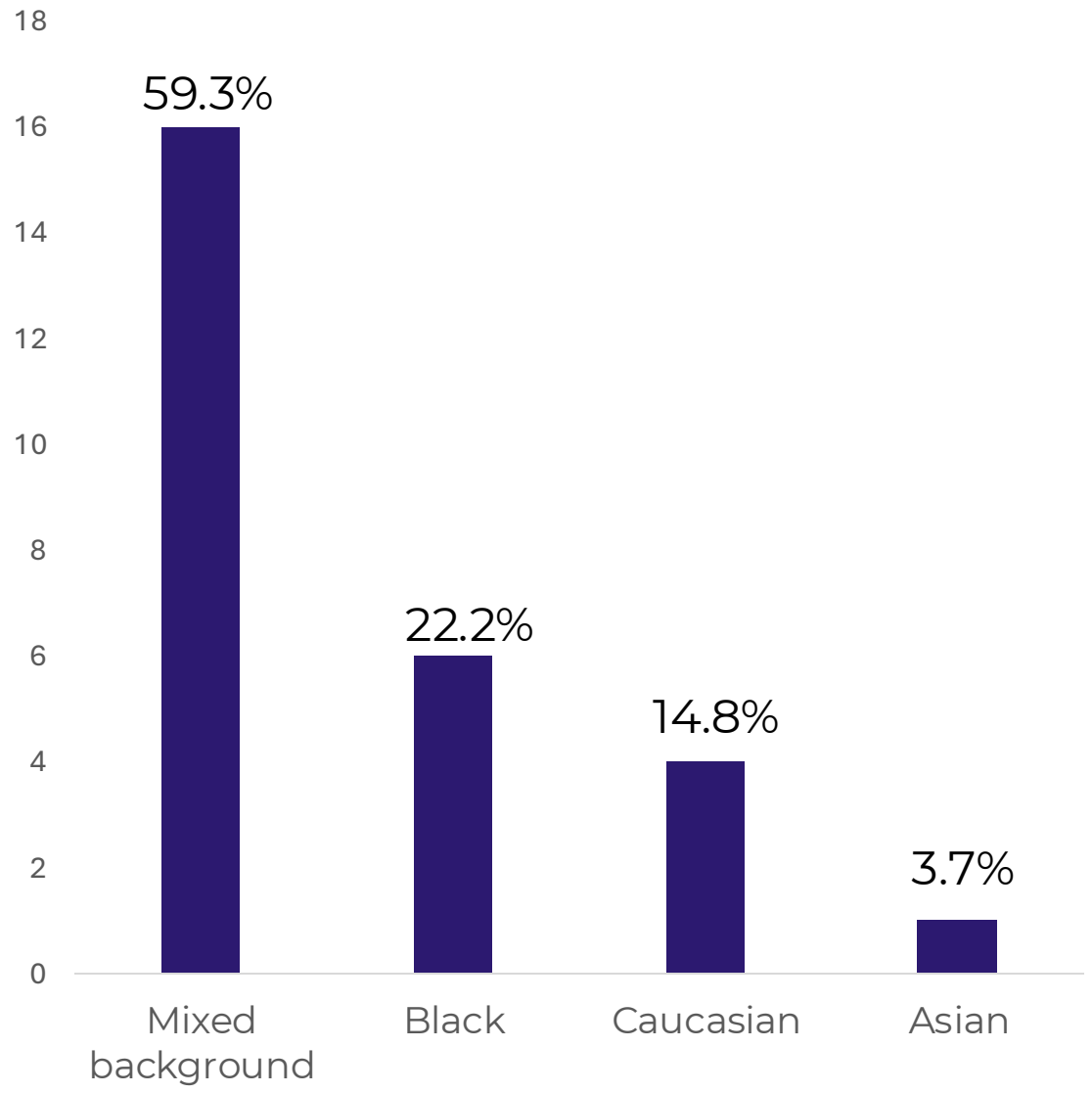
# Results

N= 27

Female: 16 (59.3%)

Non-Caucasian: 85.2%

Tumor: 15 (55.5%)

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# Results - clinical

Abnormal neurodevelopment before onset: 2 (7.4%)
Familial history of AI: 4/23 (17.4%)

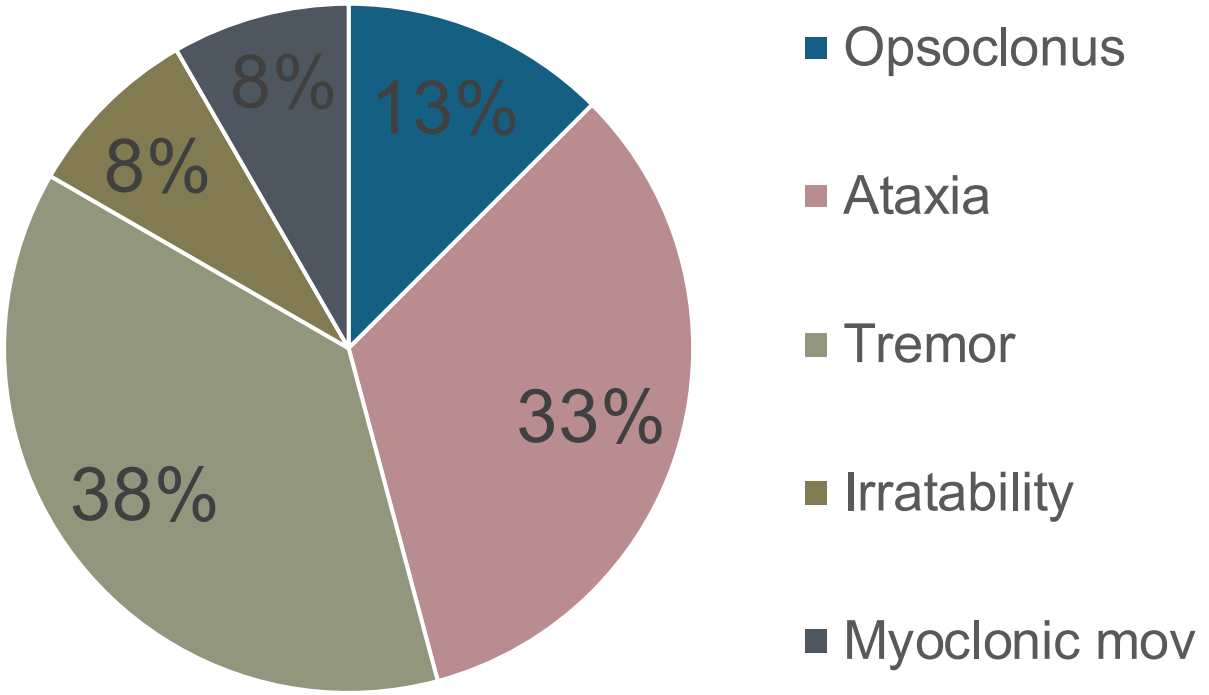
# Results

Median age at first symptom onset: 15.7 (12.2-22.5) mo
Median age at diagnosis: 16.8 (12.7-26.3) mo
Median time to diagnosis:  28 (12-48) days
Median disease duration at the tertiary centre: 147 (28-420) days

Misdiagnosis: 14/26 (53.8%)
Cerebellitis (5), encephalitis (2), ataxia-telangiectasia (1), genetic condition (1), epilepsy (1), Guillain-Barre syndrome (1), intoxication (1), others (2)

# Results - clinical

First symptom:




Triggers:
Vaccination: 4/11 (36.4%)
Fever/infection: 7/11 (63.6%)

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# Results – clinical FU

| **Clinical FU aspects** | |
|---|---|
| Opsoclonus during follow-up, n (%) | 26 (96.3) |
| Time from onset to opsoclonus, days, median (IQR) | 8.5 (3-22.5) |
| Ataxia during follow-up, n (%) | 27 (100) |
| Time from onset to ataxia, days, median (IQR) | 2 (0-7) |
| Tremor/dysmetria during follow-up, n (%) | 25/26 (96.2) |
| Time from onset to tremor/dysmetria, days, median (IQR) | 2 (0-5) |
| Myoclonus during follow-up, n (%) | 21/23 (91.3) |
| Time from onset to myoclonus, days, median (IQR) | 6 (1-42.5) |
| Irritability during follow-up, n (%) | 24 (88.9) |
| Time from onset to irritability, days, median (IQR) | 3 (0-28) |
| Sleep problems during follow-up, n (%) | 16/22 (72.7) |
| Time from onset to sleep disturbances, days, median (IQR) | 3 (1.75-11.25) |
| Speech disturbances during follow-up, n (%) | 21/25 (84) |
| Time from onset to speech disturbances, days, median (IQR) | 7.5 (3-26.25) |
| Drooling during follow-up, n (%) | 8/19 (42.1) |
| Time from onset to drooling, days, median (IQR) | 8.5 (0-56.25) |

# Results – paraclinical aspects

| | |
|---|---|
| Lumber puncture, n (%) | 18/24 (75) |
| OCB positive, n (%) | 2/2 (100) |
| CSF cell count | 4 (3-8.75)<br>range: 2-200 |
| CSF protein count | 23.5 (18.75-31.25)<br>range: 10-52 |
| CSF AB testing, n (%) | 1/24 |
| CSF AB detected, n (%) | 0/1 |
| Serum AB testing, n (%) | 2/24 |
| Serum AB detected, n (%) | ½<br>Anti-GAD (low titer) |

EEG: 10/19 (52.6%)
Abnormal: 5/10 (50%)

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# Results – Brain MRI

Abnormal: 1/18

Median time to brain MRI: 29 (15.5-118.5) days

12 brain MRI performed within 60 days: all normal

“slight global atrophy” – performed 6mo after onset

# Results – oncology aspects

15 patients

| | |
|---|---|
| Time from onset to tumor detection, days, median (IQR) | 40 (21-372) |
| Time from OMS diagnosis to tumor detection, days, median (IQR) | 10 (2-161) |
| Tumor location, n (%) | |
| Thoracic | 3/14 (21.4) |
| Adrenal | 5/14 (35.7) |
| Other abdominal | 4/14 (28.6) |
| Pelvic | 2 (14.3) |
| Tumor type, n (%) | |
| Neuroblastoma | 7/10 (70) |
| Ganglioneuroblastoma | 3/10 (30) |
| Tumor ressection, n (%) | 15/15 (100) |
| Time from diagnosis to tumor resection, days, median (IQR) | 128.9 (13.25-195.75) |
| Chemotherapy, n (%) | 6/14 (42.8) |
| Radiotherapy, n (%) | 0 |

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# Results - Immunotherapy

First scheme:
- Monotherapy: 14 (51.9%)
- Combined*: 13 (48.1%)

Time to first immunotherapy:
- Median time from disease onset: 27.5 (15.5-65) days
- Median time from OMAS diagnosis: 1.5 (0-11)

*combined: > 1 different drug within 2 mo

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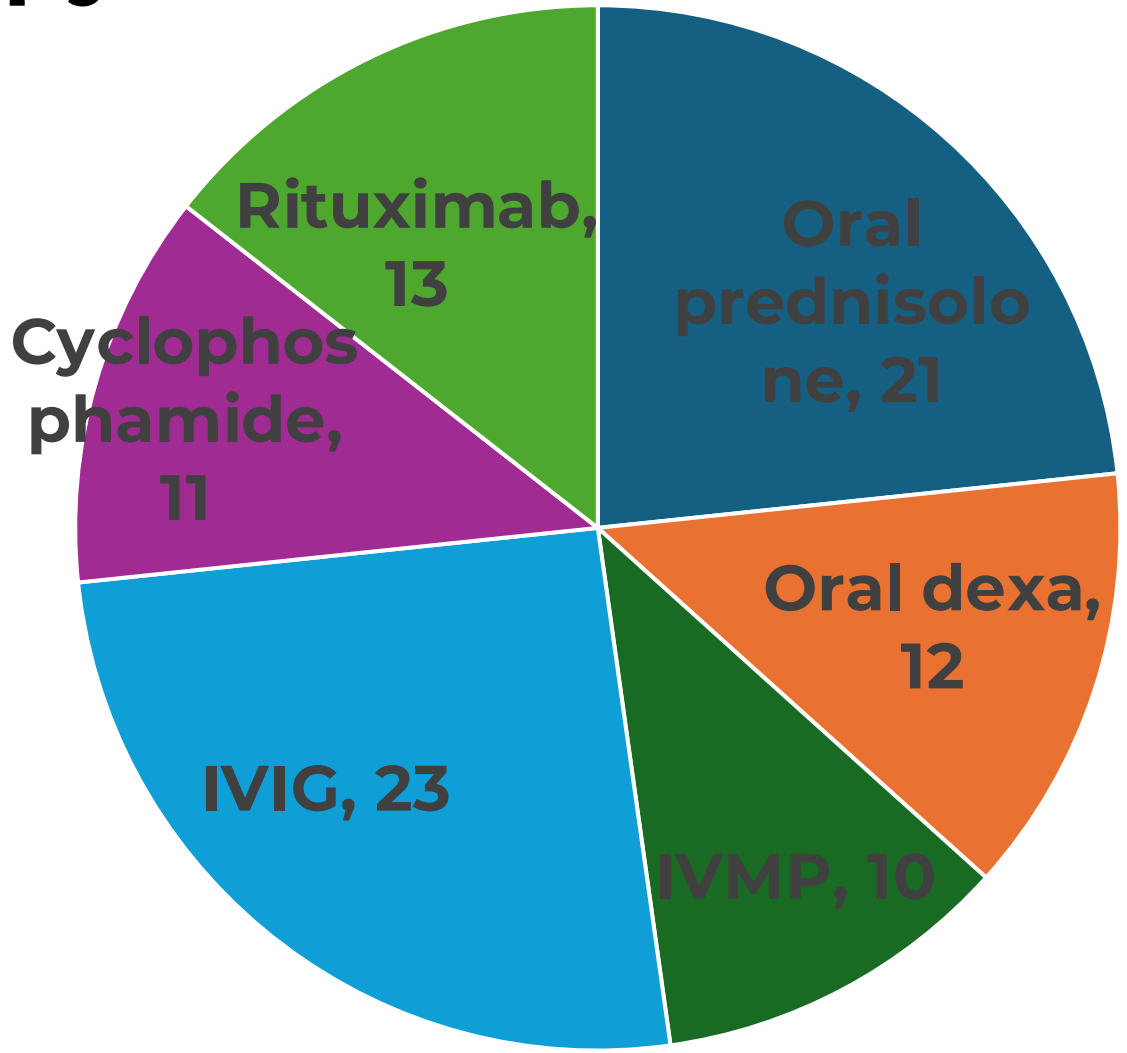
# Results - Immunotherapy

Drugs used anytime in FU




Median time to 1st use (days):

- Oral prednisolone: 40 (27-91)
- Dexamethasone: 167 (64-443)
- IVMP: 52.5 (21.5-210.2)
- IVIG: 66 (22.7-304.5)
- **Cyclo: 302.5 (83.5-594)**
- **RTX: 516 (186.5-684.5)**

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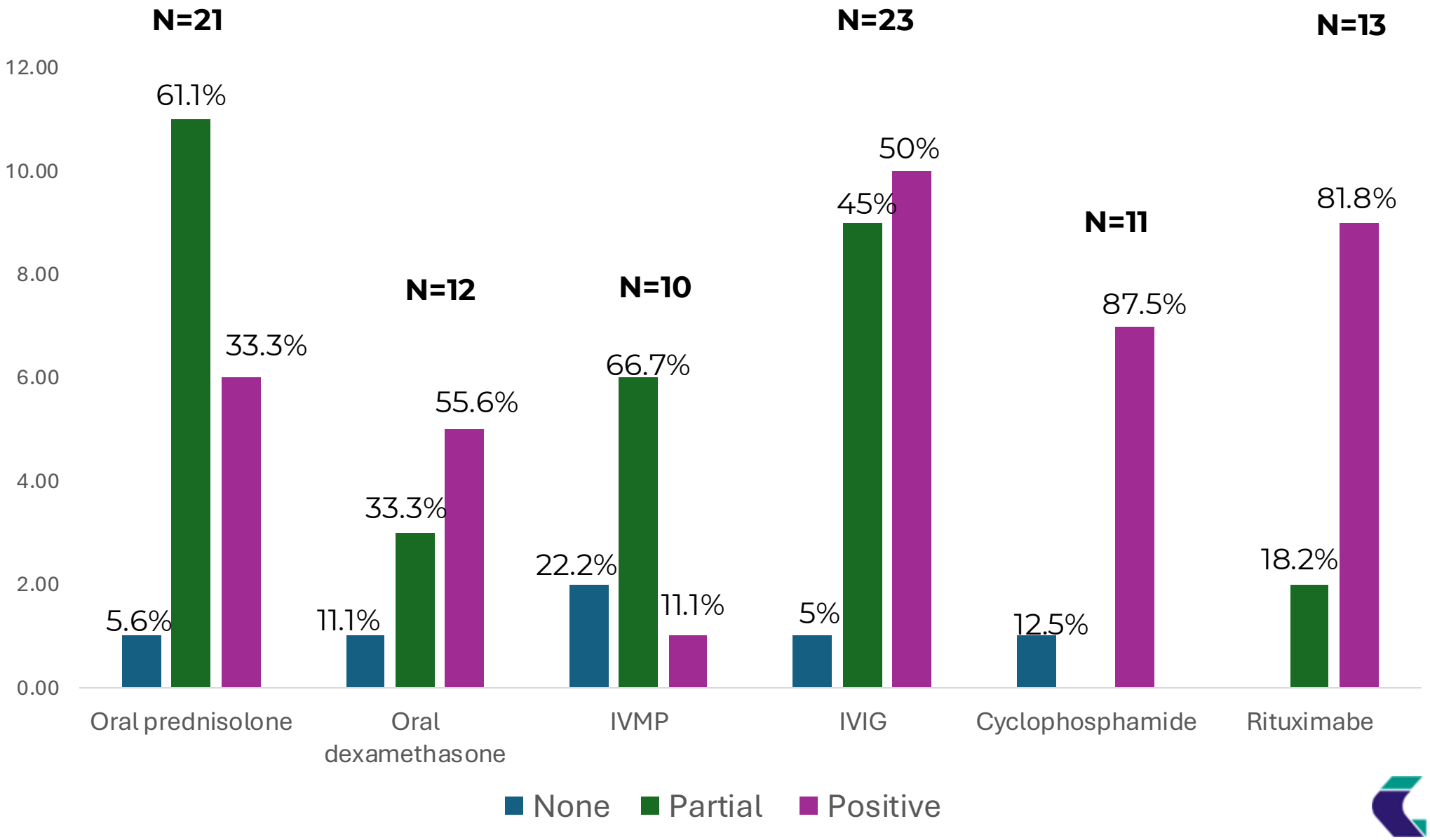


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# Results - relapses

Relapses: 19/25 (76%)
Median relapses: 2 (range 1-6)

Triggers: 28/45 relapses
- Medication withdraw: 57.1%
- Fever/Infection: 39.3%
- Other: 3.6%
- Vaccination: 0

# Results – outcome at last visit

Median FU: 2 (1-3), range 0-5
Median age at last FU: 50.35 (32.32-64.35) mo
1 death

| **Neurological examination at the last FU, n (%)** | |
|---|---|
| Normal | 5 (19.2) |
| Limb ataxia | 10/26 (38.5) |
| Gait ataxia | 5/26 (19.2) |
| Opsoclonus | 0 |
| Myoclonic movements | 1/26 (3.8) |
| Speech abnormality | 16/26 (61.5) |
| Irritability | 9/26 (34.6) |

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# Results – outcome at last visit

N=26
Social/adaptative/behavioural disorders*: 42.3%
Learning disability*: 30.4%

| | |
|---|---|
| Sleep abnormality, n (%) | 5/25 (20) |
| Social or behavioural concerns, n (%) | 11/26 (42.3) |
| Learning disability, n (%) | 7/23 (30.4) |
| Educational setting, n (%); N=15 | |
| Mainstream school | 11/15 (73.3) |
| Formal support | 4/15 (26.7) |
| Not at school yet | 10 |
| Formal neuropsychological assessment, n (%) | 0/26 |

*not formally evaluated

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# Results – outcome at last visit

N=26

| | |
|---|---|
| OMS clinical scale, median (IQR) | 2 (1-3) range: 0-8 |
| Abnormalities in OMS Scale, n (%) | |
| Stance | 7 (26.9) |
| Gait | 6 (23.1) |
| Arm/hand | 12 (46.1) |
| Opsoclonus | 1 (3.8) |
| Mood/behavior | 7 (26.9) |
| Speech | 19 (73) |
| SARA, median (IQR); N=12 | 6 (2-13.37) |

# Results – Comparative analysis

N=26

Disease remission
OMS score
SARA
Behavioural/social problems
Learning disabilities
Sleep disorder

Age at onset
Ethnicity
Neoplastic etiology
Time to diagnosis
Time to treatment
Time to initiate FU at institution
Combined therapy
Early vs late treatment

*early steroids: < 30 days from onset; early IVIG, CCF, RTX: < 60 days from onset

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# Results – Comparative analysis

N=26

Sleep disorders:

- Initial monotherapy (0/5 vs 12/20; p=0.039)
- Late IVIG initiation (0/5 vs 15/17; p=0,001)

Learning disabilities:

- Longer time to diagnosis: 9.5 vs 28 days; p=0.022
- Longer time to initiate treatment: 14 vs 60 days; p=0.007
- Higher OMS scale (3 vs 1; p=0.018)
- Higher SARA (13.5 vs 3; p=0.038)

# Discussion

First multicentre study in Brazil
Demographic and clinical data are similar to other cohorts
Insightful prognostic aspects regarding treatment initiation

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# Discussion - limitations

Cross-section and retrospective design
Absence of formal cognitive evaluation
Treatment was not standardized through the cohort
Symptomatic treatment and rehabilitation were not evaluated
Poor characterization of relapses

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