Pediatric-Onset Opsoclonus Myoclonus Ataxia Syndrome (POOMAS): An International Registry

Mark P. Gorman, MD on behalf of POOMAS Steering Committee and Study Team

The Eleventh International Workshop on Opsoclonus Myoclonus Ataxia Syndrome

April 10, 2025

Study timeline

- Concept grew out of International OMAS Workshop meetings
- Steering Committee members developed case report forms
- Funders: OMS Life Foundation, Lauren Mantz Fund for OMS Research
- First patient enrolled May 2018 at Boston Children's Hospital
- Delays in site activation in part related to COVID-19 pandemic
- Additional sites activated between Oct 2020 and Sept 2022

An International Pediatric-Onset Opsoclonus-Myoclonus Ataxia Syndrome Registry and Clinical Research Network: Development, Progress, and Vision Pediatric Neurology 148 (2023) 145–147

Overview

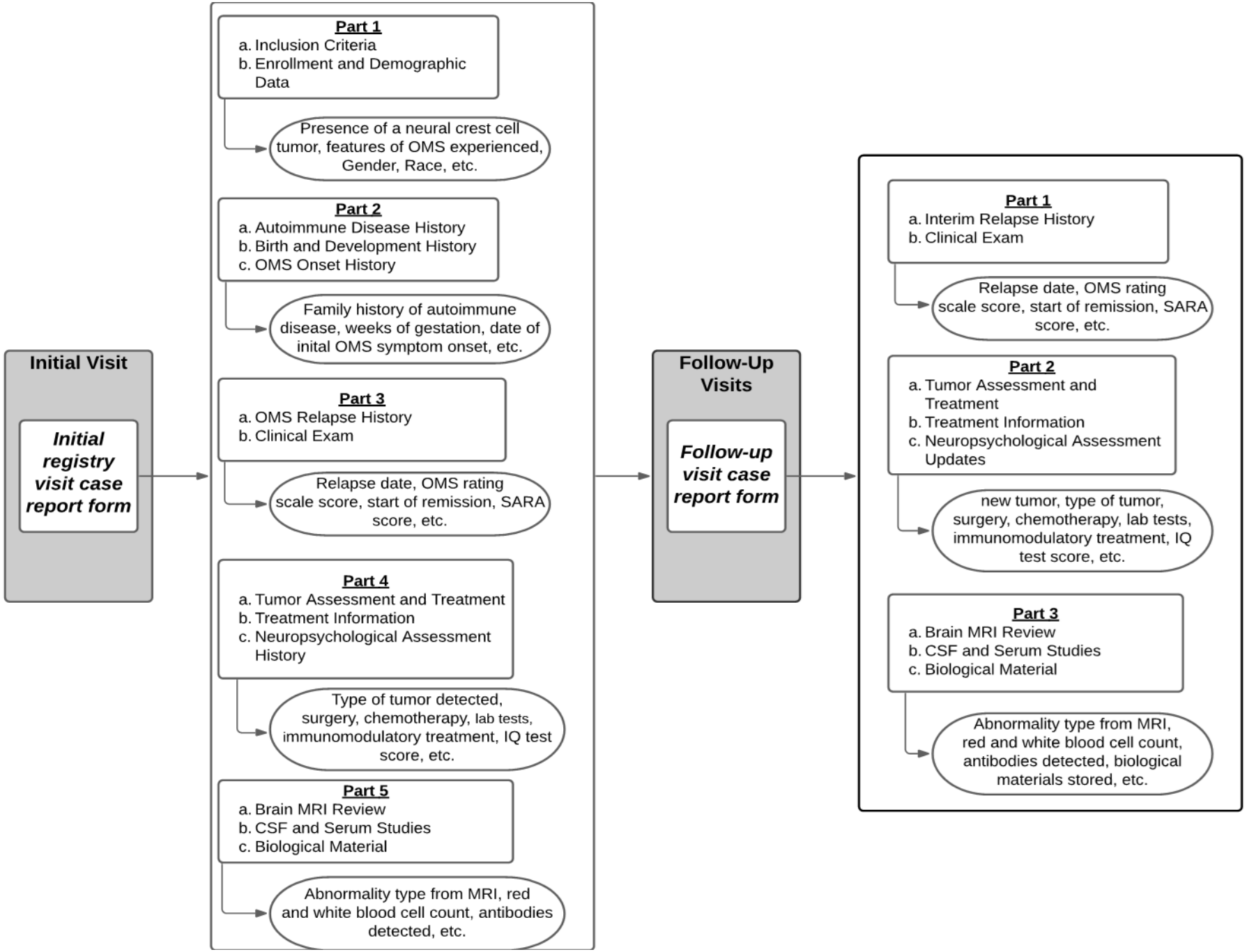
- The POOMAS registry is an observational natural history database and repository of clinical data linked with other information including MRIs
- 8 clinical sites – 6 US, 1 UK, 1 Switzerland
  - **Boston Children's Hospital** – *Mark Gorman, MD, Rebecca MacRae MD, Laura Saucier, MD, Kierstin Hederstedt, BS, Christopher Cortina, MS, Bo Zhang, PhD*
  - **Children's Hospital of Philadelphia** – *Sarah Hopkins, MD*
  - **Children's Hospital of Los Angeles** – *Wendy Mitchell, MD*
  - **Chicago Lurie Children's Hospital** – *Elizabeth Sokol, MD, Angela Waanders, MD, Johanna Blackburn, MD, Kavita Thakkar, MD*
  - **Texas Children's Hospital** – *Tim Lotze, MD, Nikita Shukla, MD*
  - **Memorial Sloan Kettering Cancer Center** – *Yasmin Khakoo, MD*
  - **Evelina London Children's Hospital** – *Ming Lim, MD, Tom Rosser, MD*
  - **University Children's Hospital of Basel** – *Andrea Klein, MD, Cornelia Enzmann, MD*

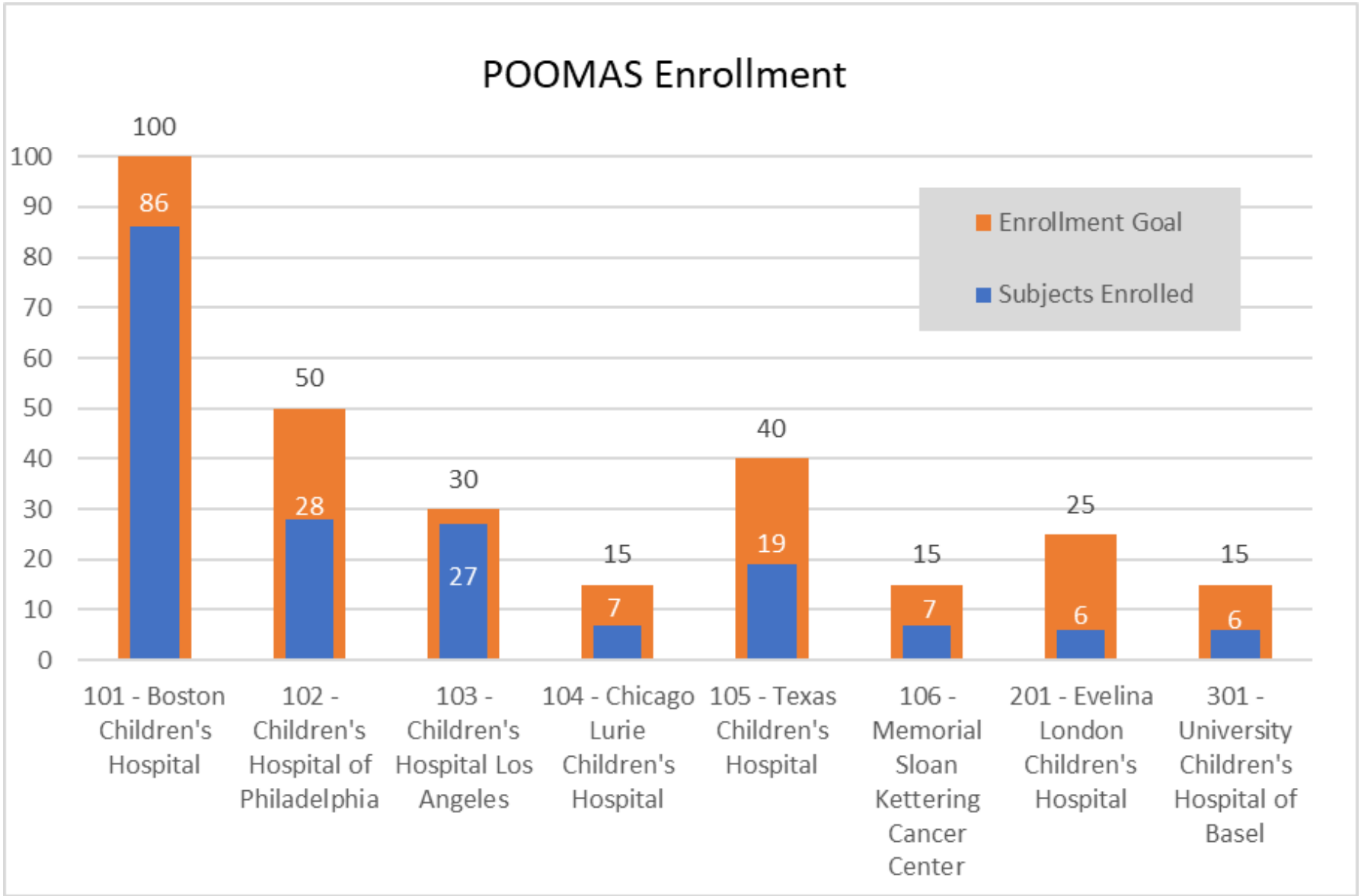
Aims

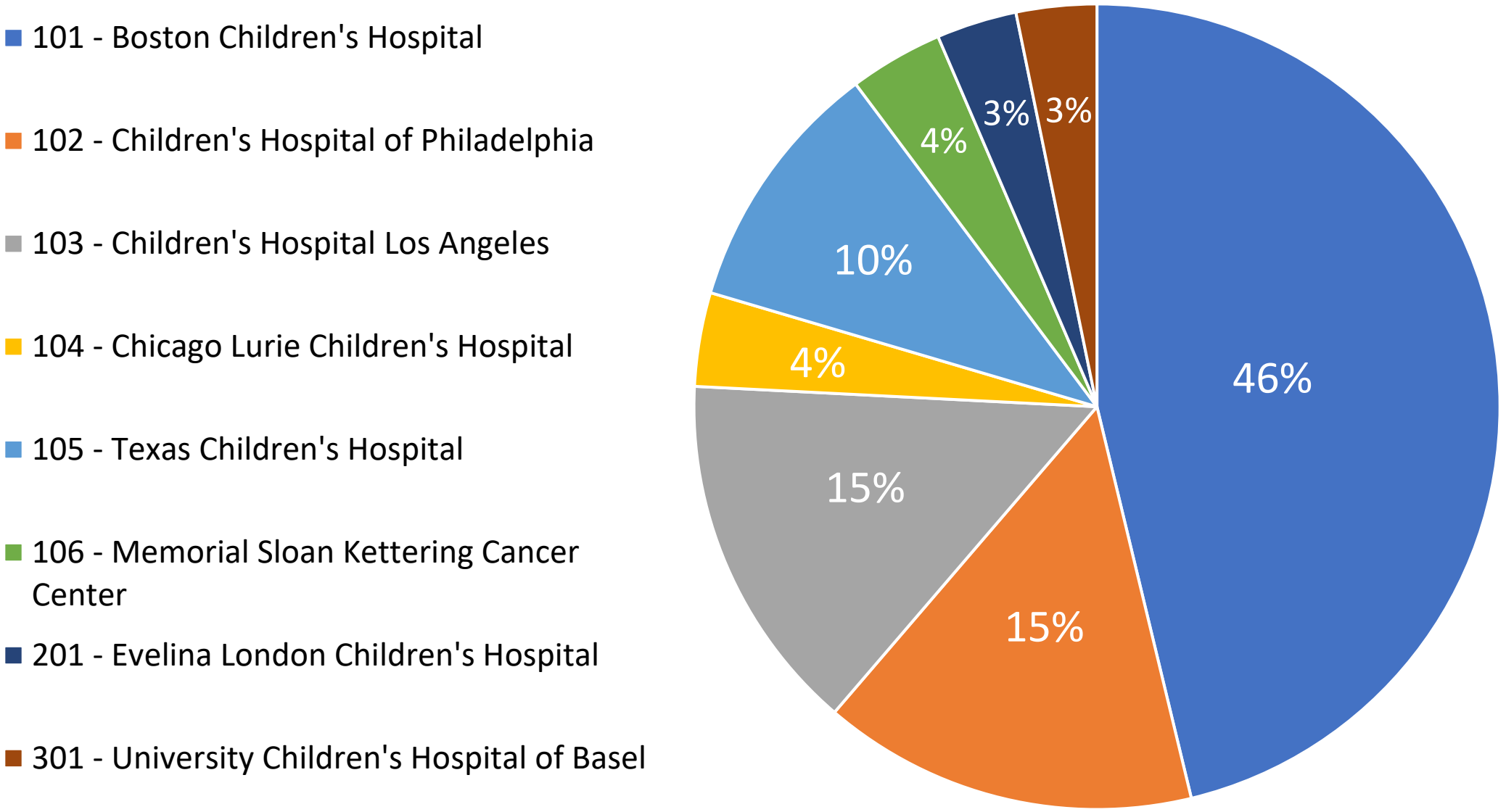
- To determine the course of illness, prognostic factors, and treatment efficacy in an international database of children with OMAS
- To create a registry of clinical information linked with MRI and other key data
- To establish a patient base for future OMAS studies, including clinical trials
- To encourage further academic study, initiative, and publication, accelerating the future of OMAS research

Study Design

- Tiered enrollment structure
  - “Prospective”: enrolled with 24 months of OMAS onset
  - “Retrospective”: enrolled >24 months after OMAS onset
- Inclusion criteria:
  - Formal diagnosis of OMAS
  - Age of onset < 18 years old


Initial Visit
Initial registry visit case report form
Part 1
a. Inclusion Criteria
b. Enrollment and Demographic Data
Presence of a neural crest cell tumor, features of OMS experienced, Gender, Race, etc.
Part 2
a. Autoimmune Disease History
b. Birth and Development History
c. OMS Onset History
Family history of autoimmune disease, weeks of gestation, date of inital OMS symptom onset, etc.
Part 3
a. OMS Relapse History
b. Clinical Exam
Relapse date, OMS rating scale score, start of remission, SARA score, etc.
Part 4
a. Tumor Assessment and Treatment
b. Treatment Information
c. Neuropsychological Assessment History
Type of tumor detected, surgery, chemotherapy, lab tests, immunomodulatory treatment, IQ test score, etc.
Part 5
a. Brain MRI Review
b. CSF and Serum Studies
c. Biological Material
Abnormality type from MRI, red and white blood cell count, antibodies detected, etc.
Follow-Up Visits
Follow-up visit case report form
Part 1
a. Interim Relapse History
b. Clinical Exam
Relapse date, OMS rating scale score, start of remission, SARA score, etc.
Part 2
a. Tumor Assessment and Treatment
b. Treatment Information
c. Neuropsychological Assessment Updates
new tumor, type of tumor, surgery, chemotherapy, lab tests, immunomodulatory treatment, IQ test score, etc.
Part 3
a. Brain MRI Review
b. CSF and Serum Studies
c. Biological Material
Abnormality type from MRI, red and white blood cell count, antibodies detected, biological materials stored, etc.


POOMAS Enrollment
100
90
80
70
60
50
40
30
20
10
0
Enrollment Goal
Subjects Enrolled
100
86
50
28
30
27
15
7
40
19
15
7
25
6
15
6
101 - Boston Children's Hospital
102 - Children's Hospital of Philadelphia
103 - Children's Hospital Los Angeles
104 - Chicago Lurie Children's Hospital
105 - Texas Children's Hospital
106 - Memorial Sloan Kettering Cancer Center
201 - Evelina London Children's Hospital
301 - University Children's Hospital of Basel


101 - Boston Children's Hospital
102 - Children's Hospital of Philadelphia
103 - Children's Hospital Los Angeles
104 - Chicago Lurie Children's Hospital
105 - Texas Children's Hospital
106 - Memorial Sloan Kettering Cancer Center
201 - Evelina London Children's Hospital
301 - University Children's Hospital of Basel
46%
15%
15%
4%
10%
4%
3%
3%

Demographics

	Total (N=187)
Sex, n (%)	
Male	75 (40.5%)
Female	110 (59.5%)
Missing	2
Age at OMAS Onset	
N	174
Mean (SD)	25.0 (19.33)
Median	20
Range	2.0, 156.0
Disease duration at enrollment (years)	
N	169
Mean (SD)	5.0 (5.32)
Median	3
Range	0.0, 26.0
Prospective or Retrospective Enrollment, n (%)	
Prospective	73 (39.5%)
Retrospective	112 (60.5%)
Missing	2
Tumor detected, n (%)	
No	79 (42.7%)
Yes	106 (57.3%)
Missing	2
Course, n (%)	
Unknown	8 (4.4%)
Monophasic	90 (49.7%)
Multiphasic	83 (45.9%)
Missing	6
Parental History of Autoimmunity, n (%)	
No	134 (79.8%)
Yes	34 (20.2%)
Missing	19

Updates and Future Goals

- Budget extended until end of 2025
- Move towards prospective enrollment
- Explore how to collect remote samples, take a remote history, and perform a remote examination for SARA and OMAS scores
- Begin using the data for analyses
  - Relapses – Dr. Saucier (CHLA)
  - Cerebellar Atrophy – Dr. MacRae (BCH)

Characterizing the frequency, rate, timing and predictors of relapses in POOMAS

Study leads: Laura Saucier, MD and Rebecca MacRae, MD

Background

- Many patients with OMAS relapse but the published studies are limited by lack of relapse definition and limited details on the rate, timing and predictors of relapse
- Combining ten studies published between 1994 – 2020, 455 / 798 (57%) of patients had at least one relapse (variably defined)
- Of five studies which reported details on the number of relapses, the median number ranged between 0.5 and 2 with a total number of relapses between 0 and 15
- Only one small study of six patients reported a median time to relapse of 15.5 weeks
- Annualized relapse rate has not been defined in OMAS to our knowledge

See Appendix for references

Inclusion criteria, time frame and definitions

- Inclusion criteria
  - Diagnosis of OMAS by Genoa criteria with onset ≤ 18 years of age
  - Minimum follow up time of 12 months
  - Sufficient data to determine whether their course was relapsing or monophasic
- Diagnosis onset median: 2018 (range 1998 – 2023)
- Relapse defined as “worsening of OMS symptoms >72 hours after ≥30 days of stability / improvement, or escalation of immunotherapy”
- Prospective = enrolled within 24 months of OMAS onset

	All N = 95 (51%)	Monophasic N = 45 (47%)	Relapsing N = 50 (53%)	
Prospective group, n (%)	44 (46.3%)	22 (48.9%)	22 (44%)	0.6333[1]
Duration of follow-up (months)				**0.0009[2]**
N	95	45 (47%)	50 (53%)	
Mean (SD)	80.5 (64.49)	58.6 (44.72)	100.3 (73.11)	
Median	56	46	76	
Range	14.0, 317.0	14.0, 216.0	24.0, 317.0	
Number of relapses not including onset attack				
N	95	45	50	
Mean (SD)	1.5 (2.00)		2.8 (1.95)	
Median	1		2	
Range	0.0, 8.0		1.0, 8.0	

[1] Chi square, [2] Kruskal Wallis

	All (N=95)	Prospective (N=44)	Retrospective (N=51)	p-value
Relapsing course, n (%)	50 (52.6%)	22 (50.0%)	28 (54.9%)	0.63[1]
More than one relapse, n (%)	32 (33.7%)	11 (25.0%)	21 (41.2%)	0.096[1]
Number of relapses (among relapsing subset)				0.046[2]
n	50	22	28	
Mean (SD)	2.84 (1.95)	2.32 (1.91)	3.25 (1.92)	
Median (range)	2 (1-8)	1.5 (1-8)	3 (1-7)	
Disease duration at first relapse (mos)				0.52[2]
n	50	22	28	
Mean (SD)	15.45 (27.23)	9.61 (6.56)	20.25 (35.85)	
Median (range)	9 (0-160)	8 (0-30)	10.5 (2-160)	

[1]Chi square p-value [2] Kruskal Wallis p-value

Univariate factors predictive of relapsing course

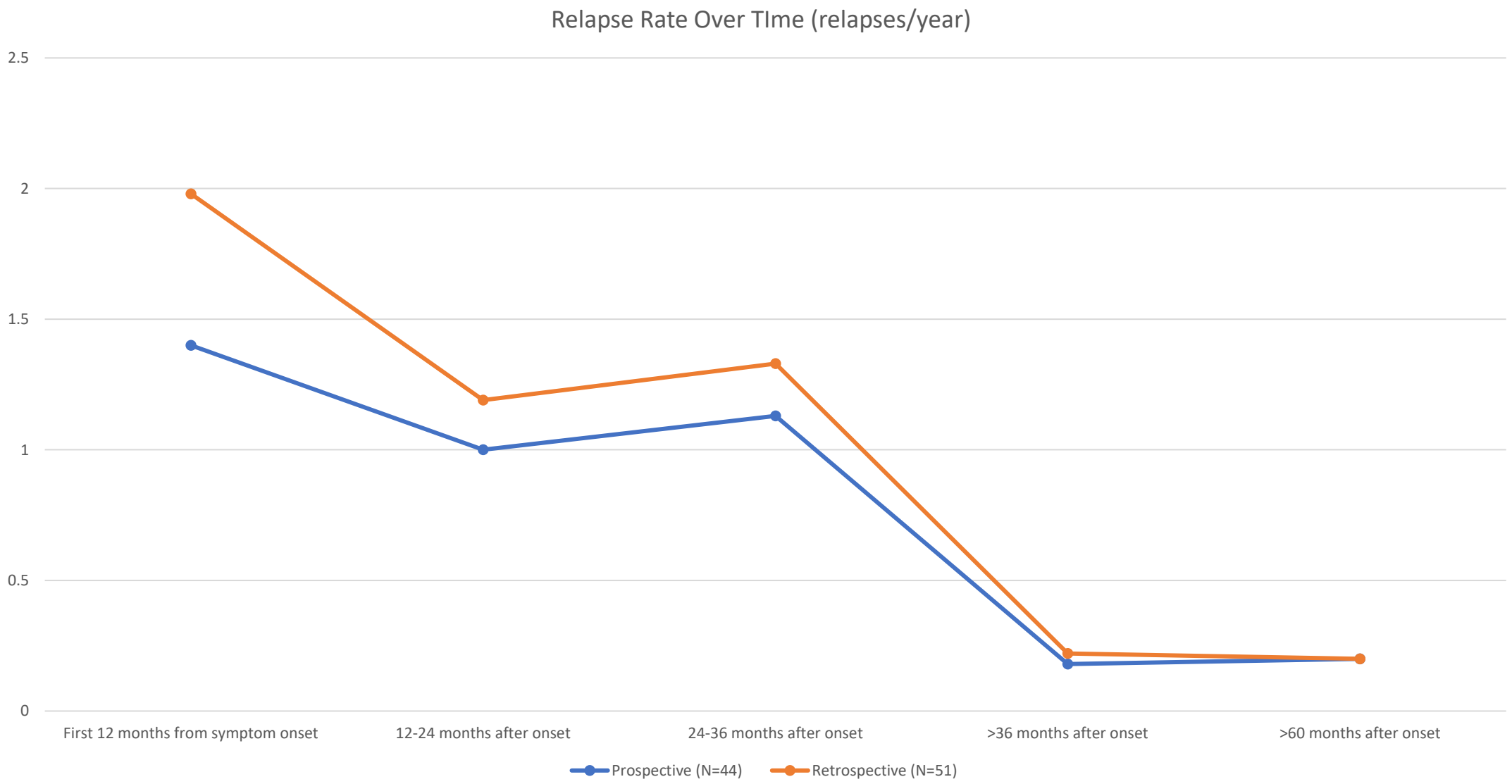
- Earlier year of diagnosis (2019 vs. 2017, p = 0.0098[1])
- Non-Hispanic ethnicity (6% vs. 24%, p = 0.0397[2])
- Higher OMS severity at last follow up (1 vs. 0, p = 0.0453[2])
- Less likely to have FH of autoimmunity (24 vs 42%, p = 0.0586[1])
- Longer time to diagnosis (41 vs. 22 days, p = 0.0614[2])
- Higher SARA score at last follow up (1.7 vs. 1.0, p = 0.0705[1])

[1] Chi square, [2] Kruskal Wallis

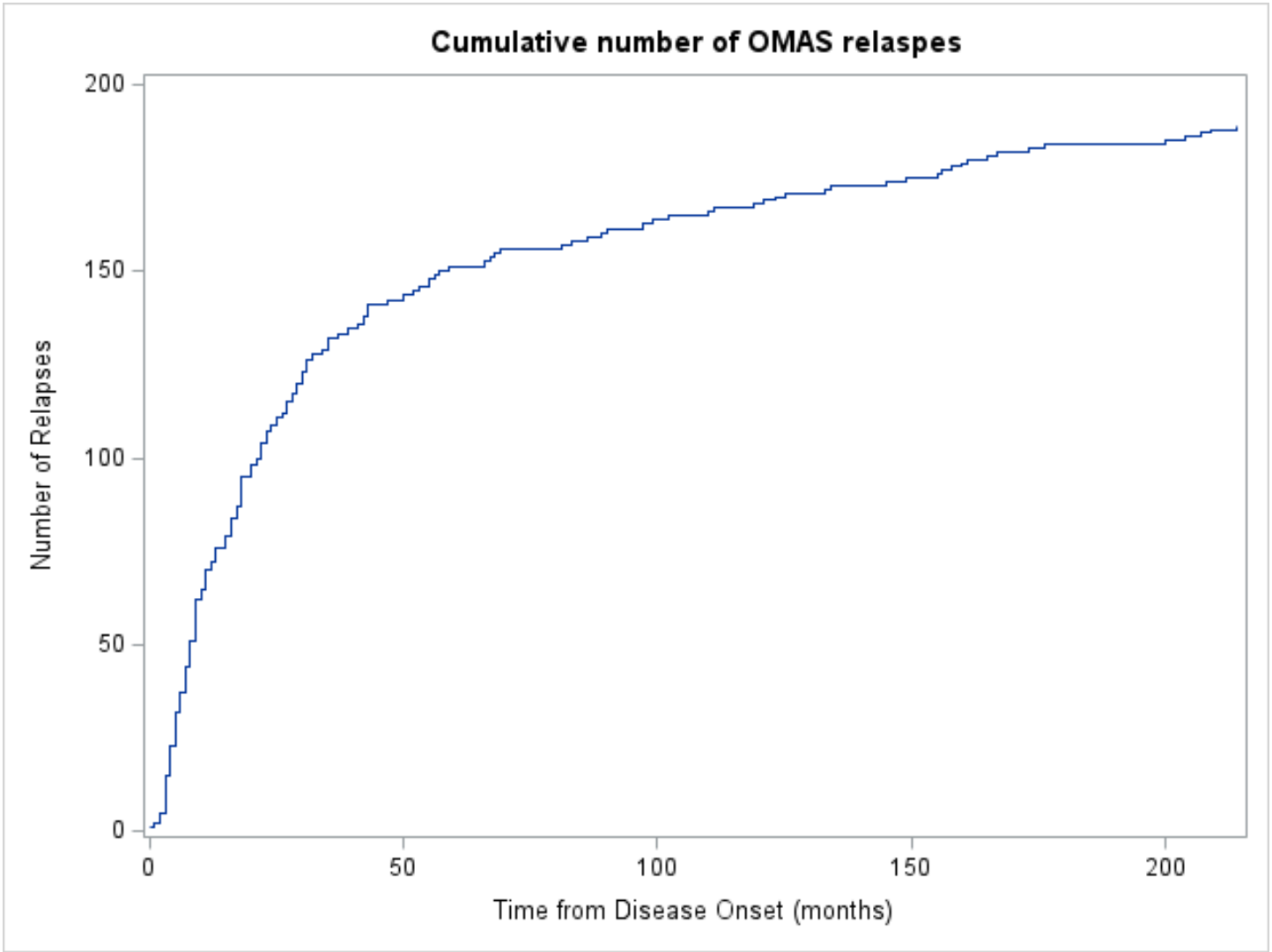
Univariate factors not predictive of relapsing course

- Prospective versus retrospective cohort
- Age at diagnosis
- Sex
- Race
- Presence of neuroblastoma
- Degree of tumor resection
- Initial OMS Severity Score
- Abnormal CSF

Annualized relapse rates decrease over time



Majority of relapses occur within 4 years



Limitations and strengths

- Limitations
  - Retrospective assessment of relapses may have under- or over-estimated relapses but the lack of significant differences between the prospective and retrospective mitigates this concern
  - Definition of relapse is somewhat arbitrary, but is expert opinion based and has been correlated with IQ outcomes in a prior study suggesting face validity
    - Could consider varying lengths of time of increased symptoms and/or more quantitatively assessed symptoms to define relapses but will require large prospective cohorts and very detailed data collection
- Strengths
  - A priori definition of relapse
  - Relatively large sample size
  - Novel assessment of annualized relapse rate in OMAS

Conclusions

- In this cohort of 95 patients with POOMAS with ≥ 12 months of follow up with a median follow-up duration of 56 months, 53% had ≥ 1 OMAS relapse and 34% had ≥ 2 relapses with no significant difference between the retrospective and prospectively followed subsets

Conclusions

- The median number of relapses in the overall group was 1 and in the relapsing group was 2
- Of potential predictors available at OMAS onset, only non-Hispanic ethnicity, lack of FH of autoimmunity, and longer time to diagnosis were predictive of relapsing course
  - In other pediatric neuro-inflammatory disorders such as multiple sclerosis, Hispanic ethnicity generally predictive of more severe disease; unclear if this is a spurious finding in our cohort, related to site of enrollment or other
  - Lack of FH of autoimmunity is counter-intuitive
  - Longer time to diagnosis emphasizes need for rapid diagnosis
  - Overall, consistent with prior literature that it is difficult to impossible to separate patients into lower and higher risk groups at OMAS onset

Conclusions

- The annualized relapse rate decreases over time with very low rates after 36 months from OMAS onset
  - Confirms clinical observations
  - May inform decisions around type and duration of treatment
  - Potential outcome measure in clinical trials
- The median disease duration at first relapse was 9 months
  - Potential outcome measure in clinical trials

Next steps

- Assessment of treatment (type, timing) as potential predictor of relapsing course
- Multivariate analyses of predictors of relapsing course
- Univariate and multivariate analyses using annualized relapse rate as dependent variable

Characterizing the frequency and predictors of cerebellar atrophy in POOMAS

Study lead: Rebecca MacRae, MD

Background

- Over 50% OMAS patients have long-term neurologic sequelae, with language, sleep, and cognitive deficits often as the most impactful symptoms.
- The cerebellum's role in cognitive and neuropsychological functioning has been established through studies of disorders of posterior fossa malformation, cerebellar tumor, posterior circulation stroke, and acquired cerebellar atrophy from causes such as prematurity or fetal alcohol exposure.
- Cerebellar atrophy has been described in pediatric OMAS patients, but little is yet known about the frequency or clinical significance of this finding.
  - Thus far, studies identifying and describing cerebellar atrophy in pediatric OMAS patients are small studies of less than 15 subjects.

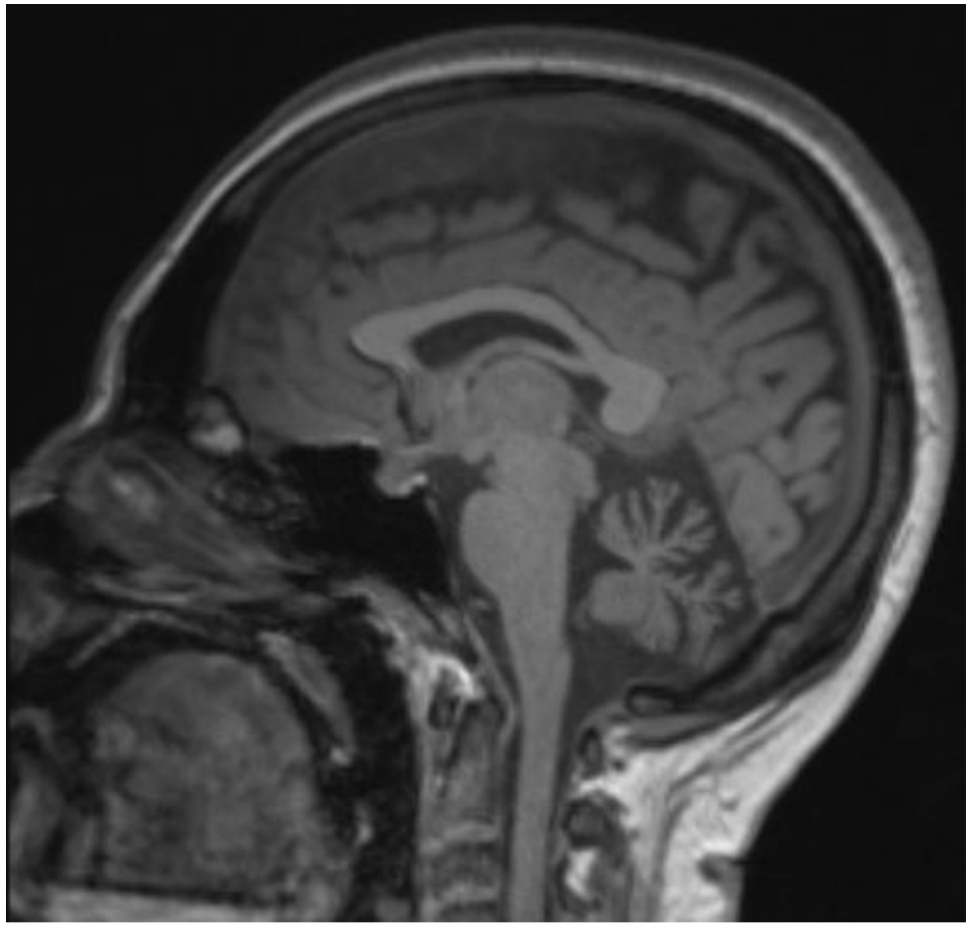
Almudhry et al 2024. Anand et al, 2015. DeGrandis et al, 2009. Hayward et al, 2001

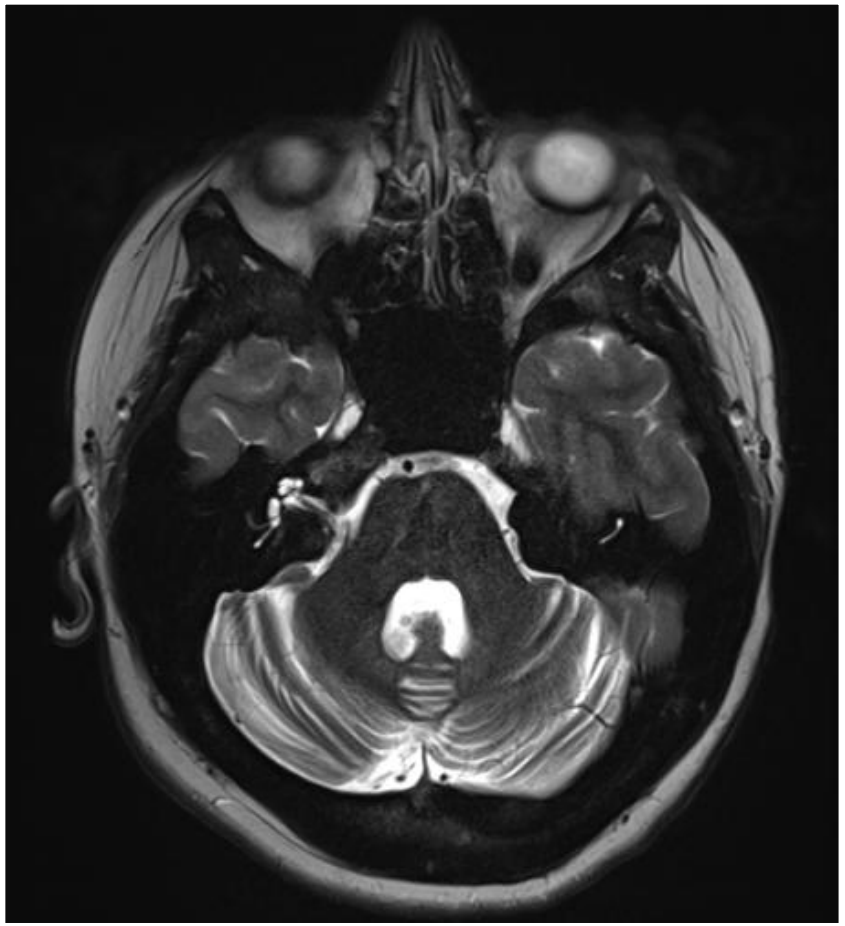
Inclusion criteria and atrophy definition

- At least 1 MRI ever obtained during the clinical course
- Sufficient clinical, treatment, and disease severity evaluation data

- Atrophy was defined with formal neuroradiology report (qualitative)

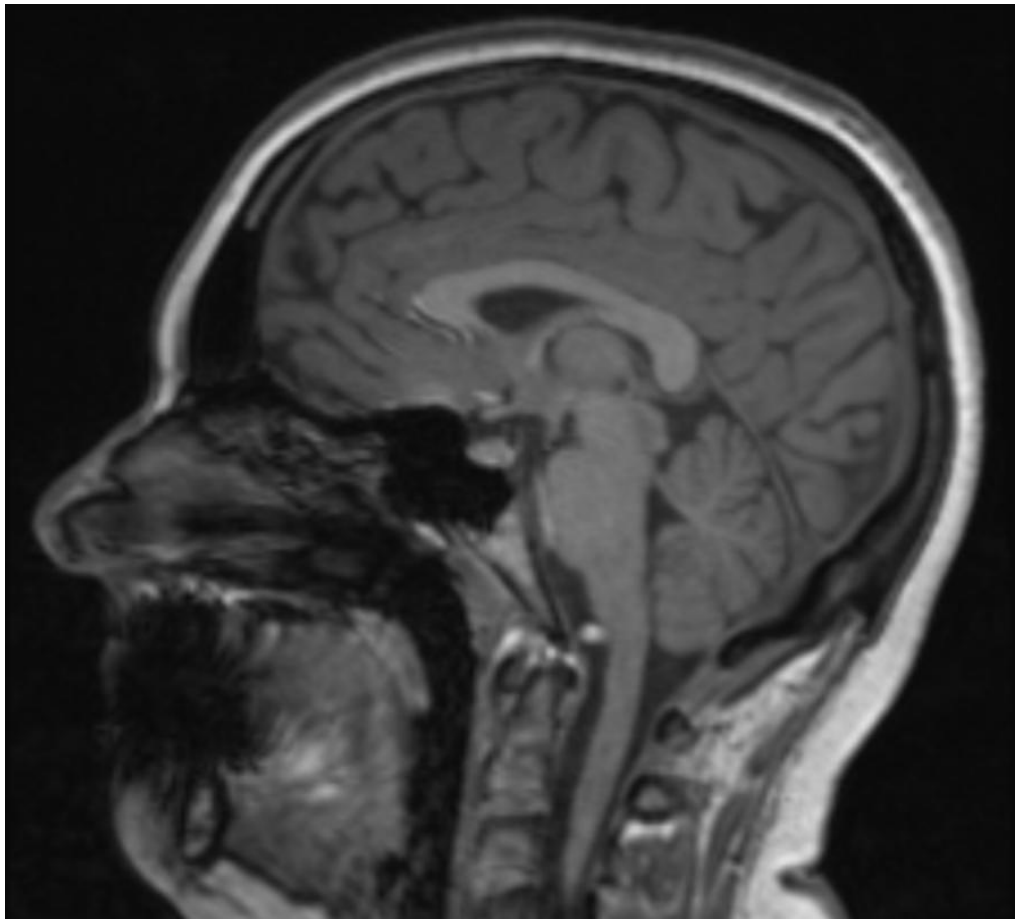
Severe OMAS cerebellar atrophy example

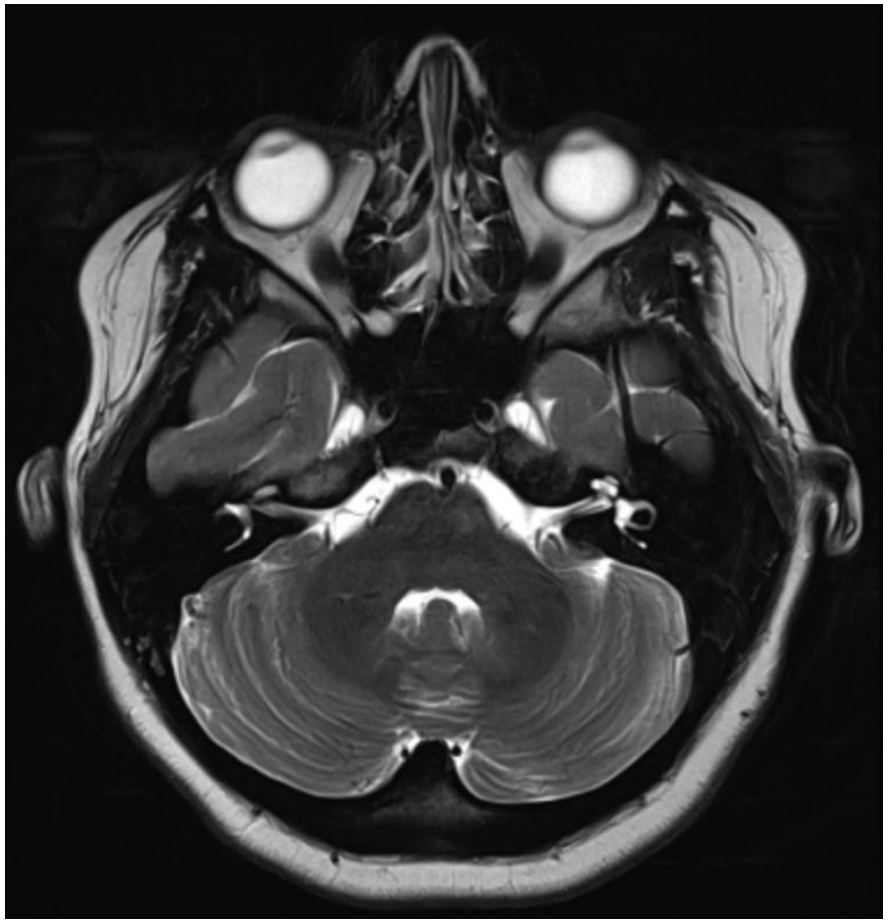




T1 sagittal and T2 axial MR Brain of 22yo woman with history of severe paraneoplastic OMAS as child

Mild OMAS cerebellar atrophy example





T1 sagittal and T2 axial MR Brain of 17yo woman with history of severe paraneoplastic OMAS as child

POOMAS cerebellar atrophy data overview

- Total cohort: 165 participants, mean 77mo follow-up (SD 65mo), 23mo from disease onset to atrophy/last MRI (SD 49mo)
  - Atrophy group: 8 participants
  - Non-atrophy group: 157 participants

- Cerebellar atrophy occurred in 5% of the total cohort

Univariate factors predictive of atrophy

- Older age at diagnosis (43 vs 27 months, p = 0.035[2])
- Presence of neural crest cell tumor (100% vs 53%, p = 0.0089[1])
- Longer time between symptom onset and diagnosis (median 172 vs 30 days, p = 0.046[2])
- Non-monophasic clinical course (25% vs 52%, p = 0.017[1])
- Educational setting with formal supports (100% vs 33%, p = 0.011[1])

- Duration of follow-up (median 178 vs 52 months, p = 0.0096[2])
- Time from symptom onset to atrophy/last MRI (median 40 vs 2 months, p = 0.0083[2])

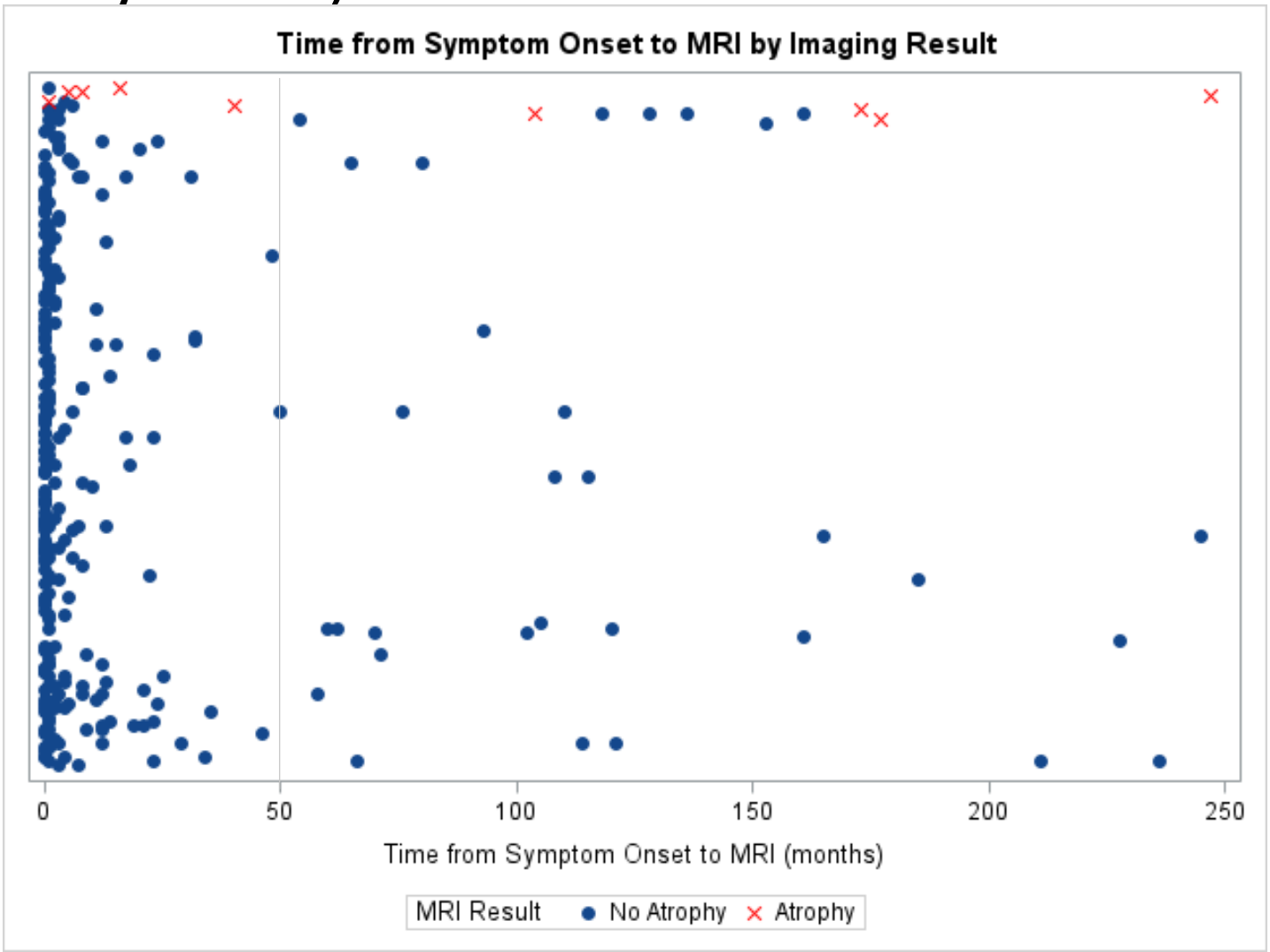
[1] Chi square, [2] Kruskal Wallis

Univariate factors not predictive of atrophy

- Sex
- Race / Ethnicity
- Gestational age at birth
- Pre-OMAS development
- Peak disease severity (OMS Severity Score)
- Abnormal CSF
- Treatment with tumor-directed therapy
- Treatment without rituximab
- Last follow-up disease severity (OMS Severity Score, SARA score)

- *FSIQ testing could not be assessed because only 1 patient with cerebellar atrophy had sufficient neuropsych testing data*

Atrophy occurs in early phase (<4yrs) and late phase (>4 years)



Strengths and limitations

- Limitations
  - Possible underestimation of true cerebellar atrophy frequency given lack of standardized long-term follow-up MRI acquisition
  - Selection bias with more severely affected patients more likely to be imaged
    - School setting with formal support had association with atrophy suggestive of worse cognitive outcomes, however follow-up OMAS severity & SARA scores were not more severe
- Strengths
  - First study evaluating the frequency of cerebellar atrophy
  - Relatively large sample size

Conclusions

- In this cohort of 165 patients with POOMAS with at least one MRI obtained over their clinical course, the overall frequency of cerebellar atrophy is estimated to be 5%
- Association with older age suggests possible difference in cerebellar plasticity over time
- Association with longer time to diagnosis intuitively follows with more severe disease brain parenchyma sequalae
  - Emphasizes need for rapid diagnosis
  - Although motor/coordination scores are not more severe in patients with cerebellar atrophy, unfortunately we did not have enough data to investigate cognitive outcomes
- Association with the presence of neuroblastoma suggests possible biological differences between paraneoplastic (vs non-paraneoplastic) OMAS
  - ?Different antibodies associated with paraneoplastic vs non-paraneoplastic OMAS
- Association with longer follow-up MRI supports the need for long-term MRI surveillance
  - Standardized MRI surveillance 4? 8+? years after disease onset

Next steps

- Multivariate analyses of predictors of cerebellar atrophy
- Quantitative imaging analysis to identify more subtle cerebellar atrophy / regional cerebellar atrophy
- Prospective investigation with standardized imaging acquisition times and FSIQ testing

Questions & Discussion

Appendix

Publication	N	% relapsing	Median # relapses	Median time to relapse	Relapsing cases with >1 relapse	Treatment	Median follow-up, months	Definition of relapse
Sheridan et al, 2020 [1]	71	70%	2 (0-10)	NR	NR	Various treatments	68	Worsening of OMS symptoms >72 hrs after 30+ days of stability / improvement, or escalation of immunotherapy
Wilbur et al, 2019 [2]	6	33% ***	NR	15.5 wks	NR	IVMP, oral steroids, IVIG or PLEX, and Rituximab	15.5 (12-34)	Not defined
Galstyan et al, 2017[3]	12	50%	0.5 (NR)	NR	66%	Various treatments	36 (6-127)	Not defined
Pranzatelli & Tate, 2017 [4]	9	56%	1 (0-2)	NR	40%	Pulse dexamethasone, IVIG, and Rituximab	NR	Not defined
Tate et al, 2014 [5]	389	41%	?	?	47%	?	?	?
Brunklaus et al, 2011 [6]	101	93% *	NR	NR	34%	Treated (various treatments) and untreated	88 (36-384)	Worsening of OMS symptoms >24 hrs
Pranzatelli et al, 2010 [7]	12	25%	0	NR	NR	Combination ACTH, IVIG, and rituximab	12	Worsening or reappearance of OMS symptoms >72 hrs
Tate et al, 2005 [8]	105	52%	?	?	?	?	?	?
Mitchell et al 2005 [9]	19	74%	NR	NR	NR	ACTH and/or steroids	NR	Not defined
Pohl et al, 1996 [10]	54	91% **	?	NR	?	Treated (ACTH or prednisone) and untreated	?	?
Hammer et al, 1995 [11]	10	90%	2 (0-15)	NR	67%	ACTH	NR (12-115)	Not defined
Koh et al, 1994 [12]	10	90%	1.5 (0-7)	NR	56%	ACTH	53.5 (8-111)	Not defined
Mitchell et al 1990 [13]	?	?	?	?	?	?	?	?

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