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…Towards the End of the Year…

As the final months of the year unfold, we find ourselves reflecting on the progress made and the challenges that remain. The evolving landscape of neurological science continues to present us with new opportunities for growth, collaboration, and discovery.

Our journal remains committed to showcasing the latest clinical insights and research contributions that not only advance scientific knowledge but also have a tangible impact on patient care. With each issue, we strive to foster a space where clinical excellence and academic inquiry meet, encouraging dialogue among neurologists, researchers, and healthcare professionals.

This issue brings together a diverse collection of articles that highlight emerging trends, rare clinical cases, and important considerations in the diagnosis and treatment of neurological disorders.

First, Tsianti et al. describe a clinical case of a 27 year old male presenting with bilateral amyotrophic hand weakness who was diagnosed with Hirayama's disease, demonstrating the unique imaging findings of flow voids and ''owl's eyes'' sign in the cervical MRI.

Second, Melanis at al. present their retrospective study which highlights the importance of long term cardiac monitoring (ILR) in patients with cryptogenic ischemic stroke or transient ischemic attack. Detecting atrial fibrillation and the need for anticoagulation in this population is of outmost importance, and Melanis at al. demonstrated that in a population of 352 patients, 17.9% of them were diagnosed with atrial fibrillation after a median of 190.5 days of monitoring, indicating that the investigation and treatment of stroke needs long term follow up, a multidisciplinary team and the adoption of novel techniques.

Finally, Triantafyllou et al. in their review thoroughly describe the available and emerging treatment in myasthenia gravis, proving their point that its treatment is an everchanging field. In the last years a large number of new treatment targeting FcRn and complement inhibition have become available with excellent results in these patients. New treatment options are currently being assessed in randomized-controlled clinical trials and subgroups of myasthenia gravis patients such as seronegative or LRP4 positive patients may also benefit from these novel therapies if the trial results are positive.

We also continue our efforts to increase the journal's visibility and reach, with all articles published in English and in a format that aligns with international indexing standards. These steps bring us closer to our goal of inclusion in PUBMED and similar databases, a milestone that will broaden the journal's impact and accessibility.

As we look ahead, we remain optimistic. The future of neurology is bright, driven by innovation, evidence-based practice, and the unwavering commitment of those who work within this field. We invite you to continue supporting the journal (by contributing, reviewing, and reading) and to remain actively engaged in the collective effort to improve neurological care in our region.

With sincere thanks for your continued support,

Georgios Tsivgoulis
Professor & Chairman of Second Department of Neurology, School of Medicine, National & Kapodistrian University of Athens, "Attikon" University Hospital, Athens, Greece
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Άρθρα...

HIRAYAMA'S DISEASE

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Abstract
We describe an interesting case of a 27-year-old male patient presenting with a 8-year history of amyotrophic hand weakness of obscure etiology. He was diagnosed eventually with Hirayama's disease only after flexion MRI of the cervical spine was performed.

Keywords: Hirayama disease, monomelic amyotrophy, Cervical flexion MRI

ΝΟΣΟΣ ΤΟΥ HIRAYAMA

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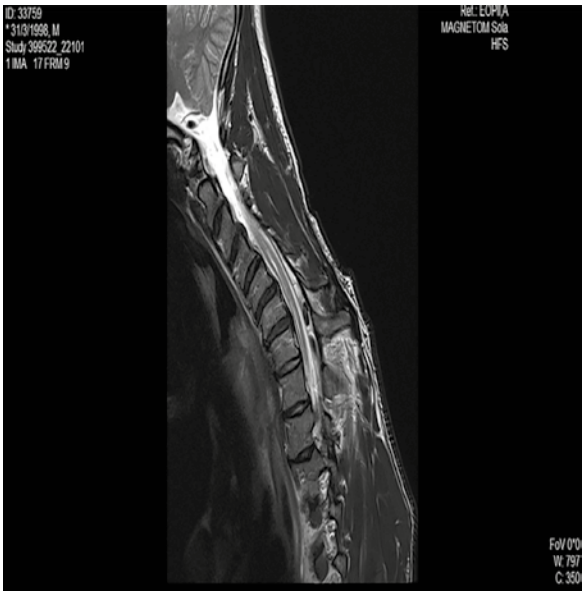
Περίληψη
Περιγράφουμε μια ενδιαφέρουσα περίπτωση άρρενος ασθενούς 27 ετών με ατροφική πάρεση των άκρων χειρών από 8ετίας αγνώστου αιτιολογίας. Ο φαινότυπος αποδόθηκε τελικά στην σπάνια νόσο του Hirayama μόνο κατόπιν διενέργειας μαγνητικής τομογραφίας της ΑΜΣΣ με κάμψη της κεφαλής.

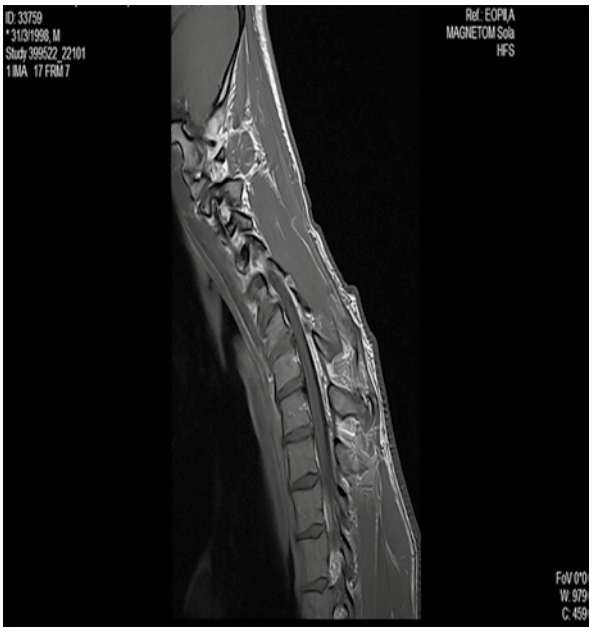
Λέξεις-κλειδιά: Νόσος Hirayama, Μονομελική αμυοτροφία, Μαγνητική τομογραφία ΑΜΣΣ με κάμψη του αυχένα

Άνδρας 27 ετών προσέρχεται με χαλαρή, ατροφική πάρεση σοβαρού βαθμού κατανομής Α8-Θ1 αμφοτεροπλεύρως. Η έναρξη της μυϊκής αδυναμίας τοποθετείται στην ηλικία των 19 ετών από το δεξιό άνω άκρο, ενώ προοδευτικά υπήρξε επέκταση στο αριστερό άνω άκρο και επιβάρυνση του νευρολογικού ελλείμματος. Αναφέρεται, επίσης, επιδείνωση των συμπτωμάτων κατά την έκθεση στο κρύο και άτυπος τρόμος των δακτύλων με χαρακτήρες μινιπολυμυόκλονου. Σε νευροφυσιολογικό έλεγχο καταγράφεται χρόνια μερική απονεύρωση σοβαρού βαθμού κατανομής Α8-Θ1 αμφοτεροπλέυρως, ενώ σε μαγνητική τομογραφία ΑΜΣΣ αναφέρεται πιθανή συριγγο/υδρομυελία. Γενετική εξέταση με επόμενης γενιάς αλληλούχιση δεν κατέδειξε παθογόνες ή πιθανά παθογόνες μεταλλαγές. Ζητείται νέα μαγνητική τομογραφία ΑΜΣΣ με κάμψη του αυχένα υπό γωνία 40°, η οποία αποκάλυψε τα χαρακτηριστικά ακτινολογικά ευρήματα της νόσου του Hirayama (εικ.1).

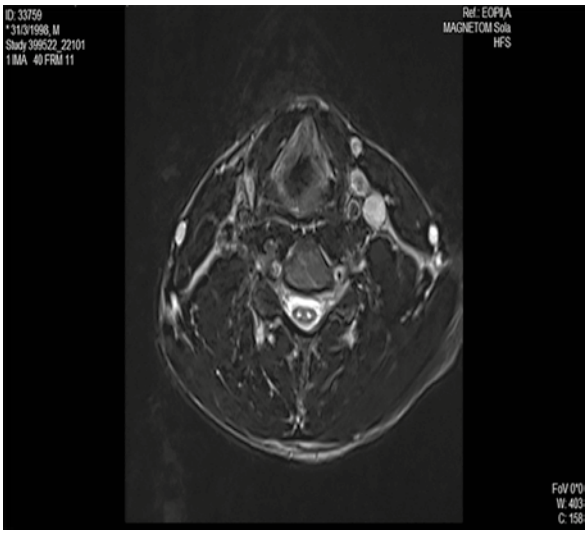


Εικόνα 1 α) Μεγάλου βαθμού μετατόπιση προς τα εμπρός του οπισθίου σκληραίου σάκκου, εμφανή 'κενά ροής'(flow voids) λόγω διεύρυνσης του ραχιαίου επισκληρίδιου φλεβικού πλέγματος. Τ2 οβελιαία τομή (ΑΜΣΣ σε κάμψη 40ο).

Η νόσος του Hirayama αποτελεί μια σπάνια νευρολογική διαταραχή με επιδημιολογική έμφαση σε εφήβους και νέους άνδρες Ασιατικής καταγωγής, που προκαλεί αυτο-περιοριζόμενη απώλεια κινητικών νευρώνων σε ασύμμετρη κατανομή Α7-Θ1.[1] Παθογενετικά θεωρείται ότι η εμπρόσθια μετατόπιση του οπίσθιου σκληραίου σάκκου κατά την κάμψη της κεφαλής προκαλεί συμπίεση του νωτιαίου μυελού με συνέπεια την πρόκληση μικρο-ισχαιμικών αλλοιώσεων στα πρόσθια κέρατα.[2] Στο κατάλληλο κλινικό πλαίσιο, η δυναμική μαγνητική τομογραφία



Εικόνα 1 β) Ημισεληνοειδούς τύπου (crescent like) σκιαγραφική ενίσχυση λόγω συμφόρησης στο επισκληρίδιο φλεβικό πλέγμα.
Τ1 οβελιαία τομή μετά από ενδοφλέβια χορήγηση γαδολινίου (ΑΜΣΣ σε κάμψη 40ο).



Εικόνα 1 γ) 'Οφθαλμοί της κουκουβάγιας' (owl's eyes sign) Τ2 εγκάρσια τομή στο επίπεδο Α6 (ΑΜΣΣ σε ουδέτερη θέση)

σε κάμψη της κεφαλής είναι απαραίτητη και επαρκής για την τεκμηρίωση της διάγνωσης.

ΣΥΓΚΡΟΥΣΗ ΣΥΜΦΕΡΟΝΤΩΝ

Οι συγγραφείς δηλώνουν ότι δεν υπάρχουν θέματα σύγκρουσης συμφερόντων.

Βιβλιογραφία

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DIAGNOSTIC AND PROGNOSTIC ROLE OF IMPLANTABLE LOOP RECORDERS IN PATIENTS WITH CRYPTOGENIC ISCHEMIC STROKE OR TRANSIENT ISCHEMIC ATTACK

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ABSTRACT

Objective: To evaluate the diagnostic yield and clinical impact of implantable loop recorders (ILRs) in patients with cryptogenic ischemic stroke (CS) or transient ischemic attack (TIA) in a real-world, tertiary care setting. **Methods:** We conducted a retrospective observational study of consecutive patients with CS or TIA who underwent ILR implantation between 2019 and 2025 across five cardiology centres in Athens, Greece. Paroxysmal atrial fibrillation (PAF) and other arrhythmias were recorded, and anticoagulation initiation and ischemic stroke recurrence were assessed. **Results:** Among 352 patients, PAF was detected in 63 (17.9%) during ILR monitoring. The median time from stroke onset to PAF detection was 190.5 days (IQR: 64–558.8). Following PAF diagnosis, 60 patients (95.2%) initiated oral anticoagulation, primarily with apixaban (n=28) and rivaroxaban (n=21). Recurrent ischemic stroke was documented in 8 patients (2.2%) of the overall cohort, with no significant differences observed between patients with and without ILR-detected PAF. In addition to AF, ILRs identified clinically significant sinus pauses in 5 patients (1.4%), all of whom subsequently received permanent pacemakers. **Conclusion:** ILRs enabled the detection of PAF and other clinically significant arrhythmias in patients with CS or TIA, facilitating timely therapeutic interventions. The observed high rate of anticoagulation initiation and low stroke recurrence support the clinical utility of ILRs in secondary prevention. These findings reinforce the broader diagnostic role of ILRs beyond PAF detection and underscore their integration into standard post-stroke evaluation pathways.

Keywords: implantable loop recorder, cryptogenic ischemic stroke, paroxysmal atrial fibrillation, sinus pause

ΔΙΑΓΝΩΣΤΙΚΟΣ ΚΑΙ ΠΡΟΓΝΩΣΤΙΚΟΣ ΡΟΛΟΣ ΤΩΝ ΕΜΦΥΤΕΥΣΙΜΩΝ ΚΑΤΑΓΡΑΦΕΩΝ ΡΥΘΜΟΥ ΣΕ ΑΣΘΕΝΕΙΣ ΜΕ ΚΡΥΠΤΟΓΕΝΕΣ ΙΣΧΑΙΜΙΚΟ ΑΓΓΕΙΑΚΟ ΕΓΚΕΦΑΛΙΚΟ ΕΠΕΙΣΟΔΙΟ Η ΠΑΡΟΔΙΚΟ ΙΣΧΑΙΜΙΚΟ ΕΠΕΙΣΟΔΙΟ

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Περίληψη

Σκοπός: Η αξιολόγηση της διαγνωστικής αξίας και της κλινικής χρησιμότητας των εμφυτεύσιμων καταγραφέων ρυθμού (implantable loop recorders, ILR) σε ασθενείς με κρυπτογενές ισχαιμικό αγγειακό εγκεφαλικό επεισόδιο (ΙΑΕΕ) ή παροδικό ισχαιμικό αγγειακό εγκεφαλικό επεισόδιο (ΠΙΕ) στο πλαίσιο της καθημερινής κλινικής πράξης ενός τριτοβάθμιου νοσοκομείου. **Μέθοδοι:** Διεξήχθη αναδρομική μελέτη παρατήρησης σε διαδοχικούς ασθενείς με κρυπτογενές ΙΑΕΕ ή ΠΙΕ, οι οποίοι υποβλήθηκαν σε εμφύτευση ILR κατά την περίοδο 2019–2025 σε πέντε καρδιολογικά κέντρα στην Αθήνα. Οι ασθενείς παρακολουθήθηκαν για ανίχνευση επεισοδίων παροξυσμικής κολπικής μαρμαρυγής (ΠΚΜ) όπως και άλλων αρρυθμιών, ενώ αξιολογήθηκαν ως προς την έναρξη αντιπηκτικής αγωγής και την εμφάνιση υποτροπιαζόντων ΙΑΕΕ. **Αποτελέσματα:** Μεταξύ των 352 ασθενών, ανιχνεύθηκε ΠΚΜ σε 63 (17,9%) ασθενείς κατά τη διάρκεια παρακολούθησης με ILR. Η διάμεση χρονική περίοδος από την εμφάνιση του ΙΑΕΕ/ΠΙΕ έως την ανίχνευση της ΠΚΜ ήταν 190,5 ημέρες (IQR: 64–558,8). Μετά τη διάγνωση της ΠΚΜ, 60 ασθενείς (95,2%) ξεκίνησαν από του στόματος αντιπηκτική αγωγή. Υποτροπιάζον ΙΑΕΕ σημειώθηκε σε 8 ασθενείς (2,2%) της συνολικής κοορτής χωρίς να διαπιστωθούν σημαντικές διαφορές μεταξύ των υποομάδων με ανιχνευθείσα και μη ανιχνευθείσα ΠΚΜ. Πέραν της ΠΚΜ, οι ILR εντόπισαν κλινικά σημαντικές παύσεις φλεβοκομβικού ρυθμού σε 5 ασθενείς (1,4%), οι οποίοι όλοι υποβλήθηκαν σε εμφύτευση μόνιμου βηματοδότη. **Συμπέρασμα:** Οι ILR επέτρεψαν την ανίχνευση επεισοδίων ΠΚΜ και άλλων κλινικά σημαντικών αρρυθμιών σε ασθενείς με κρυπτογενές ΙΑΕΕ ή ΠΙΕ, διευκολύνοντας την έγκαιρη θεραπευτική παρέμβαση. Τα ευρήματα αυτά ενισχύουν τον ευρύτερο διαγνωστικό ρόλο των ILR πέρα από την ανίχνευση ΠΚΜ, επισημαίνοντας την ένταξή τους σε καθιερωμένα πρωτόκολλα αξιολόγησης μετά από ΙΑΕΕ.

Λέξεις-κλειδιά: εμφυτεύσιμος καταγραφέας ρυθμού, κρυπτογενές ισχαιμικό αγγειακό εγκεφαλικό επεισόδιο, παροξυσμική κολπική μαρμαρυγή, φλεβοκομβική παύση

INTRODUCTION

Implantable loop recorders (ILRs) have emerged as valuable diagnostic tools across a range of clinical scenarios, particularly following the publication of recent European Society of Cardiology (ESC) guidelines on the management of ventricular arrhythmias, sudden cardiac death prevention, and cryptogenic stroke (CS) evaluation.[1,2] Additionally, recent European Stroke Organisation (ESO) guidelines highlight the role of ILRs in the secondary prevention of cryptogenic stroke.[3] Among the most robust indications for ILR use are patients with CS or transient ischemic attack (TIA) in whom initial diagnostic investigations, including 24-hour Holter heart rhythm monitoring, transthoracic and transoesophageal echocardiography and vascular imaging (with the modality left at the discretion of the treating physician) fail to reveal an underlying cause.[4–6]

ILRs enable prolonged cardiac rhythm surveillance, with current devices lasting up to five years.[7] Their early use in patients with unexplained syncope or palpitations is well-established, improving diagnostic precision and guiding therapeutic decisions.[7] In CS populations, ILRs have proven effective in detecting paroxysmal atrial fibrillation (PAF), with reported rates approaching 30% in selected cohorts.(8–11) Timely PAF identification allows for early anticoagulation, a cornerstone of secondary stroke prevention.[12–14]

Beyond PAF detection, ILRs can uncover bradyarrhythmias such as sinus pauses and atrioventricular block.[15,16] These findings may necessitate prompt pacemaker implantation to prevent recurrent syncope or cerebral hypoperfusion.[15,16] Thus, ILRs serve a broader diagnostic role, extending beyond embolic risk stratification to the identification of actionable conduction system disorders.

Despite growing evidence from randomised-controlled clinical trials (RCTs), real-world data on the diagnostic yield and clinical impact of ILRs across diverse healthcare settings remain limited. The present observational study aims to assess the performance of ILRs in a large, unselected cohort of patients with CS or TIA. Specifically, we evaluate the diagnostic contribution of ILRs in arrhythmia detection and their influence on subsequent therapeutic management in routine clinical practice.

Methods

Population

We retrospectively evaluated patients with CS or TIA treated at the "Attikon" University Hospital (Athens, Greece) between 2019 and 2025. All included patients had undergone ILR implantation as part of their diagnostic workup. Cryptogenic stroke was defined using the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria, and after excluding patients with incomplete evaluation, as previously described.[17–22] All patients underwent at least a 12-lead ECG, a transthoracic echocardiogram or transoesophageal echocardiogram and a 24h Holter heart rhythm monitoring prior to ILR implantation.[12–16] All patients received neuroimaging with brain computed tomography (CT) and / or magnetic resonance imaging (MRI) and vascular imaging with the modality left at the discretion of the treating physician (cervical duplex ultrasound, transcranial Doppler, CT angiography and /or magnetic resonance [MR] angiography). All demographics and vascular risk factors were prospectively recorded for all patients using standard definitions, as previously described.[12–16] Stroke severity on admission was assessed with the use of the National Institute of Health Stroke Scale (NIHSS) score by certified neurologists.[12–16]

Procedure of Heart Rhythm Monitoring

In the year 2019, we implemented the use of implantable cardiac monitoring (ICM) devices (Reveal LINQ; Medtronic) for the prolonged outpatient cardiac monitoring of patients with CS or TIAs and at least one negative 24-hour Holter-ECG during hospitalisation. This strategy was applied regardless of baseline risk stratification scores. All devices were implanted subcutaneously under local anaesthesia in the left chest region by experienced cardiologists in our institution and four other cardiac electrophysiology clinics in tertiary care hospitals in the Athens Metropolitan area ("Hippokrateion" University Hospital, "Attikon" University Hospital, 401 General Military Hospital of Athens, Army Equity Fund Hospital of Athens, and General Hospital of Athens "G. Gennimatas"). ICMs were programmed with a validated algorithm for detection of AF episodes lasting at least 2 minutes.[23] Total time in AF was calculated as the sum of each individual AF episode for patients with multiple episodes during monitoring. In addition to PAF, other clinically relevant arrhythmias, namely sinus pauses, were also detected and documented. Experienced cardiologists who were blinded to the clinical outcomes of our patients reviewed all ICM recordings in the five participating cardiac electrophysiology clinics.

Outcomes of Interest

All patients were followed for up to 3 years after hospital discharge at the stroke outpatient clinic of our institution during outpatient or telephone visits, as dictated by their clinical status and at the discretion of the treating vascular neurologist, as previously described.[18,19] PAF was defined by the presence of a confirmatory ECG, Holter, or ICM recording. If PAF was detected, oral anticoagulation with either a new oral anticoagulant (NOAC) or a vitamin K antagonist (VKA) was initiated. Ischemic stroke recurrence was defined as a new neurological event recorded at least 24 hours after hospital discharge and validated by neuroimaging, as previously described.[18,19]

The primary outcome of interest was the rate of PAF detection in patients of the whole cohort receiving ILR implantation. Secondary outcomes of interest included: (1) the percentage of patients with anticoagulation initiation after ILR implantation, (2) percentage of patients with ischemic stroke recurrence after ILR implantation, (3) detection of sinus pauses after ILR implantation.

Statistical analysis

Categorical variables are summarised using counts and percentages, with 95% confidence intervals (CI) calculated for all baseline characteristics and key outcomes. For continuous data, normality was assessed using the Shapiro–Wilk test. Normally distributed variables are reported as mean ± standard deviation (SD), and skewed variables as median and interquartile range (IQR). Group comparisons for categorical variables were performed using chi-square or Fisher's exact test, as appropriate. Continuous variables were compared using the unpaired ***t*** test or Mann–Whitney ***U*** test, as indicated. All tests were two-tailed, and a p value <0.05 was considered statistically significant. Statistical analyses were conducted using R software (version 4.4.2; R Foundation for Statistical Computing, Vienna, Austria).

Ethics Approval

The study followed all national and international principles of good clinical and research practice and was approved by the ethics committee of the coordination institution ("Attikon" University Hospital, National and Kapodistrian University of Athens, Athens, Greece; identification number 2219/23-03-2017). Informed consent for participation in the study was obtained from all patients or guardians of patients. The data sets generated during and analysed during the current study are available from the corresponding author upon reasonable request.

RESULTS

A total of 352 patients underwent ILR placement following an index cerebrovascular event, including CS or TIA. Of these, 320 patients (90.9%) experienced an acute CS, while 32 patients (9.1%) pre-

Table 1. Baseline characteristics.

	All patients (n=352)	PAF patients (n=63)	Non PAF patients (n=289)	p-value
Age, years (median [IQR])	64.0 [57.0–72.0]	67.0 [60.0–76.0]	62.0 [56.0–69.0]	<0.001
Male sex, n (%)	232 (65.9%)	42 (66.6%)	190 (65.9%)	0.91
NIHSS on admission (median [IQR])	3 [1–6]	2 [1–5]	3 [1–6]	0.92
Hypertension, n (%)	251 (71.3%)	54 (85.7%)	198 (68.7%)	0.01
Diabetes mellitus, n (%)	79 (22.4%)	6 (9.5%)	53 (18.3%)	0.008
Dyslipidaemia, n (%)	182 (51.7%)	41 (65.1%)	174 (60.4%)	0.49
CHA_2DS_2-VASc Score (median [IQR])	3.0 [2.0–4.0]	3.0 [2.0–4.0]	3.0 [2.0–4.0]	0.003
HAVOC Score (median [IQR])	4.0 [2.0–4.0]	4.0 [3.0–5.0]	2.0 [2.0–4.0]	0.01
C_2HEST Score (median [IQR])	2.0 [1.0–3.0]	3.0 [2.0–4.0]	1.0 [1.0–2.0]	<0.001
Congestive heart failure, n (%)	10 (2.8%)	4 (6.3%)	6 (2.1%)	0.49
History of stroke/TIA, n (%)	95 (27.0%)	24 (38.1%)	81 (28.1%)	0.11
History of coronary artery disease, n (%)	41 (11.6%)	11 (17.5%)	36 (12.5%)	0.29
History of peripheral vascular disease, n (%)	17 (4.8%)	4 (6.3%)	16 (5.5%)	0.80
Left atrial enlargement, n (%)	80 (22.7%)	22 (34.9%)	60 (20.8%)	0.01
Dilated cardiomyopathy, n (%)	7 (2.0%)	4 (6.3%)	3 (1.2%)	0.06
History of antiplatelet pretreatment, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-

NIHSS: National Institutes of Health Stroke Scale; IQR: interquartile range; TIA: transient ischemic attack.

sented with a TIA. The median age of the cohort was 64 years (IQR: 57–72), with a range of 18 to 87 years (**Table 1**). The majority of patients were male (n = 232; 66%; **Table 1**).

The median NIHSS score among the included patients was 3 (IQR: 1–6), ranging from 0 to 22 (**Table 1**). The median time from stroke onset to ILR implantation was 29.5 days (IQR: 14.8–65.8; **Table 2**). Among all patients in the cohort, the median HAVOC score (hypertension, age ≥75 years, valvular disease, obesity, congestive heart failure, and coronary artery disease) was 4 (IQR: 2–4), the median CHA_2DS_2-VASc score (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or TIA, vascular disease, age 65–74 years, and sex category [female]) was 3 (IQR: 2–4), and the median C_2HEST score (coronary artery disease, chronic obstructive pulmonary disease, hypertension, elderly age ≥75 years, systolic heart failure, and thyroid disease) was 2 (IQR: 1–3), reflecting an overall elevated risk profile for recurrent cardioembolic events.[24–26]

Primary Outcome

PAF was detected in 63 patients (17.9%; 95%CI: 14.0%–21.8%) via ILR monitoring (**Figure 1**). Among these patients, the median number of AF episodes was 1 (IQR: 1–2), with a maximum of 138 episodes recorded (**Table 2**). The median time from stroke onset to AF detection was 190.5 days (IQR: 64–558.8), and the median interval from ILR implantation to PAF detection was 125.5 days (IQR: 23–499.8) (**Table 2**). The median total cumulative duration of AF episodes

Table 2. Outcomes of the Cohort Study.

	All patients (n=352)	**PAF patients (n=63)**	**Non PAF patients (n=289)**	**p-value**
Total follow-up (months, median, range)	15 (0.5–36)	17 (7-32)	12 (6–28)	Not applicable
PAF, n (%)	63 (17.9%)	63 (100%)	0 (0)	Not applicable
Number of PAF episodes (median [IQR])	1 [1–2]	1 [1–2]	Not applicable	Not applicable
Time from stroke to PAF detection, days (median [IQR])	190.5 [64.0–558.8]	190.5 [64.0–558.8]	Not applicable	Not applicable
Time from ILR implantation to PAF detection, days (median [IQR])	125.5 [23.0–499.8]	125.5 [23.0–499.8]	Not applicable	Not applicable
Duration of PAF, seconds (median [IQR])	1200 [360–14010]	1200 [360–14010]	Not applicable	Not applicable
Anticoagulant Initiation	60 (17.1%)	60 (95.2%)	0 (0%)	Not applicable
Recurrent ischemic stroke n (%)	8 (2.2%)	3 (4.8%)	5 (1.7%)	0.14
Sinus pauses, n (%)	5 (1.4%)	3 (4.8%)	2 (0.7%)	0.10
Time from ILR implantation to sinus pause detection, days (median [IQR])	87 [34.0–192.0]	87 (60.0-192.0)	82 (34.0-130.0)	0.60
Permanent pacemaker placement, n (%)	5 (1.4%)	3 (4.8%)	2 (0.7%)	0.10

AF: atrial fibrillation; ILR: implantable loop recorder; IQR: interquartile range; PAF: paroxysmal atrial fibrillation.

per patient was 1,200 seconds (IQR: 360–14,010 seconds), indicating considerable variability in arrhythmic burden across the cohort (**Table 2**). Among patients with documented PAF, the median HAVOC score was 4 (IQR: 3–5), the median CHA_2DS_2-VASc score was 3 (IQR: 2–4), and the median C_2HEST score was 3 (IQR: 2–4), reflecting an overall elevated risk profile for recurrent cardioembolic events.[24–26]

Among the 289 patients (82.1%; 95%CI: 77.7%–85.9%) with no-PAF detection, the median HAVOC score was 2 (IQR: 2–4), the median CHA_2DS_2-VASc score was 3 (IQR: 2–4), and the median C_2HEST score was 1 (IQR: 1–2). These values were lower compared to patients with documented PAF, indicating a comparatively lower estimated risk for cardioembolic events in the non-PAF subgroup (**Table 1**).

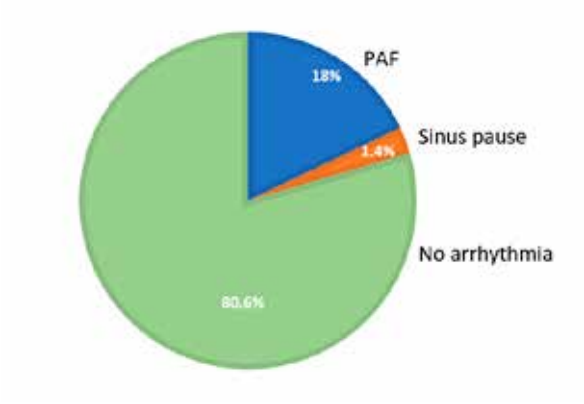
Secondary Outcomes

Following PAF detection, oral anticoagulation was initiated in the majority of patients. The most frequently prescribed agents were apixaban (n=28), rivaroxaban (n=21) and dabigatran (n=7), while acenocoumarol was used in 4 patients. Only three patients declined therapy (**Figure 2**). No oral anticoagulation therapy was initiated in the non-PAF subgroup.

During follow-up, recurrent ischemic stroke was documented in 3 patients (4.8%; 95% CI: 0%–10%) with PAF who had initiated anticoagulation therapy (**Table 2**). Among patients without ILR-detected PAF, recurrent ischemic stroke occurred in 5 of 288 individuals (1.7%; 95% CI: 0.5%–3.9%).

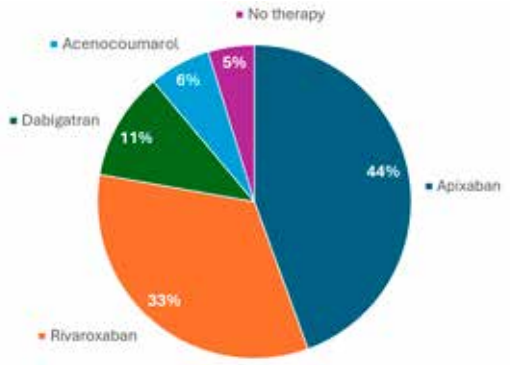
In addition to PAF detection, ILR monitoring identified clinically significant bradyarrhythmias in 5 pa-

Figure 1. Arrhythmias detected in the overall stroke cohort, including atrial fibrillation, sinus pauses, and absence of arrhythmia.



PAF: paroxysmal atrial fibrillation.

Figure 2. Distribution of anticoagulant therapy among patients with ILR-detected atrial fibrillation.



tients of the total cohort (1.4%; 95%CI: 0.5%–3.2%), all of whom exhibited sinus pauses (**Table 2**). The median interval from ILR implantation to sinus pause detection was 87 days (IQR: 34.0–192.0; Table 2) Cardiologic evaluation confirmed symptomatic or high-risk bradyarrhythmias, and all five individuals subsequently underwent permanent pacemaker implantation (**Table 2**).

DISCUSSION

In this cohort of patients with CS or TIA, ILR monitoring identified PAF in 17.9% of cases. The median time from stroke onset to AF detection was 190.5 days, highlighting the limitations of short-term monitoring strategies. In addition to PAF, ILRs revealed other clinically relevant arrhythmias, namely sinus pauses. Most patients diagnosed with PAF were promptly initiated anticoagulation, primarily with NOACs such as apixaban and rivaroxaban. Notably, the overall recurrent ischemic stroke rate in this population was low (4.8%), suggesting a beneficial impact of early rhythm diagnosis and secondary prevention.

Our findings are consistent with major RCTs that have demonstrated the superiority of ILRs over conventional heart rhythm monitoring in detecting PAF. The CRYSTAL-AF trial reported a 12.4% detection rate of PAF at 12 months in the ILR group, compared to 2.0% with standard 24-hour Holter monitoring.[9] Similarly, the PER DIEM trial showed PAF detection rates of 15.3% with ILR versus 4.7% using a 30-day external loop recorder.[27] The LOOP study identified PAF in 31.8% of patients monitored with ILRs, though it did not demonstrate a statistically significant reduction in stroke incidence.[28] In our real-world dataset, the detection rate of 17.9% aligns well with these RCTs.

The majority of patients with ILR-detected PAF in our cohort were initiated anticoagulation shortly after diagnosis, with a preference for NOACs such as rivaroxaban and apixaban. These therapeutic decisions were promptly made following ILR notification and likely contributed to the low observed rate of recurrent ischemic events (4.8%) during follow-up. This is in line with prior studies such as CRYSTAL-AF and ASSERT, as well as our recently published meta-analysis, which demonstrated that the early initiation of anticoagulation following device-detected AF can significantly reduce the risk of stroke.[9,29,30] Importantly, although the LOOP trial did not show a statistically significant reduction in stroke incidence despite a high AF detection rate with ILRs, the study population differed substantially from our cohort.[28] The LOOP trial population included older adults with cardiovascular risk factors, including 262 with prior stroke not limited to CS.[28]

Risk stratification is a cornerstone of both secondary prevention and diagnostic yield optimisation in patients with CS.[31] The CHA_2DS_2-VASc score remains the standard tool for estimating thromboembolic risk and guiding anticoagulation decisions once PAF is diagnosed.[26,32] In our cohort, this score was consistently elevated among patients initiated on anticoagulation, indicating high baseline risk. Beyond treatment guidance, predictive models such as the HAVOC and C_2HEST scores have emerged as valuable tools to estimate the likelihood of incident AF, and may help identify patients who would benefit from prolonged heart rhythm monitoring using ILRs.[24,25] The HAVOC score has been validated in post-stroke populations. In one multicentre study, a HAVOC score ≥4 was associated with a >25% risk of new-onset AF over three years.[24] Similarly, the C_2HEST score has shown strong predictive accuracy in both general and stroke cohorts.[25] A C_2HEST score ≥4 confers a 2–3 fold increased risk of AF development compared to lower-risk patients.[25] These scores can be instrumental not only in selecting individuals for ILR implantation but also in triaging resource allocation in settings with limited device availability. Importantly, both scoring systems incorporate risk factors that are

prevalent in CS patients, allowing their use in routine clinical practice.[24,25]

In addition to detecting PAF, ILRs contributed valuable diagnostic information regarding other cardiac abnormalities within our cohort. Notably, they facilitated the identification of clinically significant bradyarrhythmias, particularly sinus pauses. This underscores the broader diagnostic potential of ILRs in uncovering actionable arrhythmic substrates unrelated to PAF.[33] Prior studies have similarly demonstrated that ILRs can detect other rhythm disturbances, including high-grade atrioventricular block, asystole, and significant sinus pauses, particularly in patients with CS or unexplained syncope.[34] The prevalence of such findings is non-negligible; for instance, the PER DIEM and ASSERT-II trials have documented bradyarrhythmias in 2–5% of ILR-implanted populations.[27,29] The inclusion of ILRs in poststroke workup therefore not only aids in thromboembolic risk assessment, but also enables timely diagnosis and management of bradycardic arrhythmias, including those requiring device-based therapy. These findings advocate for a comprehensive interpretation of ILR recordings that extends beyond AF detection alone.

Our findings support the integration of ILRs into standardised stroke care pathways, particularly in patients with CS who remain in sinus rhythm after initial monitoring. Multidisciplinary collaboration between stroke neurologists and cardiac electrophysiologists is essential to interpret ILR findings and implement appropriate treatment. As digital health tools and artificial intelligence evolve, personalized algorithms may help optimise the selection of candidates for ILR implantation and improve long-term outcomes.

This study has several limitations. First, its retrospective and observational design inherently introduces the possibility of selection bias and unmeasured confounders. Furthermore, the absence of a control group receiving conventional cardiac monitoring limits direct comparisons regarding the incremental diagnostic yield and impact on recurrent stroke prevention.

Prospective studies are warranted to validate the prognostic relevance of arrhythmias other than AF, such as sinus pauses, in post-stroke populations. Moreover, defining actionable thresholds for subclinical arrhythmias detected by ILRs will be crucial for guiding therapeutic decisions. In conclusion, our real-world data affirm the diagnostic and therapeutic utility of ILRs in patients with CS or TIA, not only for the detection of occult AF but also for uncovering a broader spectrum of cardiologic complications with implications for individualised care.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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TREATMENT OF MYASTHENIA GRAVIS: AN EVERCHANGING FIELD

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ABSTRACT
Myasthenia gravis (MG) is a chronic autoimmune disorder affecting the neuromuscular junction, characterised by fluctuating muscle weakness. It is primarily mediated by antibodies against acetylcholine receptor (AChR), muscle-specific kinase (MuSK) or low-density lipoprotein-related protein 4 (LRP4). However, seronegative patients may constitute 10-15% of all MG cases. Treatment of MG is traditionally based on corticosteroids and pyridostigmine, with the addition of steroid-sparing immunosuppressive agents such as azathioprine, mycophenolate mofetil or rituximab, depending on the characteristics and the severity of each case. However, these therapies have not been rigorously evaluated in randomised-controlled clinical trials specifically for MG. During the last years, neonatal Fc receptor (FcRn) inhibitors and complement inhibitors have demonstrated a favourable safety and efficacy profile in MG patients within the context of randomised-controlled clinical trials. Therefore, they have been incorporated into daily clinical practice. Emerging agents of these drug classes and other novel therapeutic options, such as anti-CD19 monoclonal antibodies, Bruton's Tyrosine Kinase inhibitors and Chimeric antigen receptor (CAR) T cells are currently being investigated as adjunctive therapies in MG patients. This narrative review aims to provide a comprehensive overview of current pharmacologic treatment strategies for MG, with particular focus on recently approved agents and investigational therapies under clinical development.

Keywords: Myasthenia Gravis, immunotherapy, novel drugs, randomised - controlled clinical trial, adverse events.

Η ΘΕΡΑΠΕΙΑ ΤΗΣ ΒΑΡΕΙΑΣ ΜΥΑΣΘΕΝΕΙΑΣ: ΕΝΑ ΣΥΝΕΧΩΣ ΜΕΤΑΒΑΛΛΟΜΕΝΟ ΠΕΔΙΟ

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Περίληψη
Η βαρεία Μυασθένεια (MG) αποτελεί μία χρόνια αυτοάνοση διαταραχή, η οποία προσβάλλει τη νευρομυική σύναψη και χαρακτηρίζεται από κυμαινόμενη μυϊκή αδυναμία. Προκαλείται από αντισώματα έναντι των υποδοχέων ακετυλοχολίνης (AChR), της ειδικής για τους μυς τυροσινικής κινάσης (MuSK) ή του υποδοχέα LRP4. Ωστόσο, οι οροαρνητικοί ασθενείς αποτελούν το 10-15% των συνολικών περιπτώσεων MG. Η θεραπεία της MG παραδοσιακά στηρίζεται στα κορτικοστεροειδή και την πυριδοστιγμίνη, ενώ συχνά προστίθενται ανοσοκατασταλτικοί παράγοντες, όπως η αζαθειοπρίνη, η μυκοφαινολάτη μοφετίλ ή η ριτουξιμάμπη, ανάλογα με τα χαρακτηριστικά και την σοβαρότητα της νόσου. Παρόλα αυτά, οι παράγοντες αυτοί δεν έχουν ελεγχθεί σε τυχαιοποιημένες-ελεγχόμενες κλινικές δοκιμές. Κατά τη διάρκεια των τελευταίων ετών, οι αναστολείς του νεογνικού υποδοχέα Fc (FcRn) και οι αναστολείς του συμπληρώματος έχουν παρουσιάσει ευνοϊκό προφίλ ασφάλειας και αποτελεσματικότητας στην MG σε τυχαιοποιημένες-ελεγχόμενες κλινικές δοκιμές. Για το λόγο αυτό, οι εν λόγω θεραπείες έχουν ενσωματωθεί στην καθημερινή κλινική πράξη. Νέα φάρμακα των οικογενειών αυτών, καθώς και καινοτόμες θεραπευτικές επιλογές, όπως τα μονοκλωνικά αντισώματα έναντι του CD19 αντιγόνου, οι αναστολείς της τυροσινικής κινάσης του Bruton (BTK) και τα Τ-κύτταρα με χιμαιρικό υπο-

δοχέα αντιγόνου (CAR T cells) δοκιμάζονται σε ασθενείς με MG, ως επιπρόσθετη θεραπεία. Η παρούσα αφηγηματική ανασκόπηση στοχεύει στην αναλυτική παρουσίαση της φαρμακευτικής αντιμετώπισης της MG, με έμφαση στις πρόσφατα εγκεκριμένες θεραπείες, καθώς και στις επιλογές που επί του παρόντος διερευνώνται.

Λέξεις κλειδιά: Βαρεία Μυασθένεια, ανοσοθεραπεία, νέα φάρμακα, τυχαιοποιημένη - ελεγχόμενη κλινική δοκιμή, ανεπιθύμητες ενέργειες.

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disease affecting the neuromuscular junction (NMJ). The clinical presentation is defined by weakness of the skeletal muscles. MG is considered a rare disease affecting approximately 10 – 20 per 100,000 people.[1] The incidence of this disorder may reach up to 30 cases per 1 million person-years.[2]

MG is caused by autoantibodies targeting receptors in the NMJ. Antibodies against acetylcholine receptor (AChR) are found in the serum of up to 80-90% of patients with MG.[3] AChR antibodies lead to NMJ dysfunction via direct binding to the AChRs, cross-linking and internalising AChRs, as well as inducing complement-mediated AChR destruction. The majority of these patients manifest thymic hyperplasia (60-70%), while 10-12% may be diagnosed with thymoma.[4]

Muscle-specific kinase (MuSK) and low-density lipoprotein receptor-related protein 4 (LRP4) are essential for clustering AChRs at the postsynaptic membrane. Antibodies against MuSK and LRP4 are responsible for 1-10% and 1-3% of all MG cases, respectively.[5-7] In contrast to AChR antibodies, MuSK antibodies mostly belong to the IgG4 subtype and thus do not activate complement.[8] Up to 15% of MG patients are seronegative.[4]

The weakness in MG may be generalised or localised, with more proximal than distal distribution.[9] Diplopia and ptosis are the most common symptoms. Apart from extraocular muscles, weakness in MG is usually symmetric. Exercise typically worsens symptoms. The weakness is profound during night hours and may vary from day to day.

The diagnosis is based on the detection of antibodies against AChR, MuSK, or LRP4 in patients with a compatible clinical picture.[10] Repetitive nerve stimulation and single-fibre electromyography may aid in the diagnosis, especially in seronegative cases.

The treatment strategy depends on the severity of the disease, antibody status, age and comorbidities, as it is mainly based on immunosuppression. During recent years, new promising therapeutic regimens have emerged in clinical practice. The aim of the current narrative review is the treatment of MG, with emphasis on substances still under investigation.

METHODS

This narrative review synthesises evidence from randomised-controlled clinical trials (RCTs), observational studies, real-world clinical data, and expert recommendations to provide an integrated overview of current and emerging pharmacologic strategies for the treatment of MG. The review presents both established immunotherapies and newly approved targeted agents, with a focus on their mechanisms of action, regulatory status, clinical efficacy, and safety profiles.

Therapeutic categories discussed include corticosteroids, steroid-sparing immunosuppressants, complement inhibitors, neonatal Fc receptor (FcRn) antagonists, and experimental therapies such as anti-CD19 monoclonal antibodies, Bruton's tyrosine kinase (BTK) inhibitors, telitacicept, and chimeric antigen receptor (CAR) T cells. In addition, the review highlights agents under clinical development and provides insight into the evolving treatment algorithm for MG across patient subgroups, including those with seronegative disease, MuSK or LRP4 antibodies, ocular MG, paediatric patients, and pregnant individuals.

By incorporating data from pivotal trials, ongoing studies, and expert consensus documents, this review aims to guide clinicians and researchers through the expanding therapeutic landscape of MG.

CURRENT TREATMENT OPTIONS

Symptomatic Treatment

Pyridostigmine is the preferred agent for the symptomatic treatment of MG.[11] Its mechanism of action is based on the increase of the acetylcholine amount in the synaptic cleft through inhibition of acetylcholinesterase. Ambenonium chloride is a less effective second-line acetylcholinesterase inhibitor.[12] This drug class is less effective in MuSK-associated MG, with frequent side effects.[5]

Gradual titration of pyridostigmine dosage is required. The typical adult dose is 30-60 mg every 4-6 hours.[13] Muscarinic adverse events may include vomiting, diarrhoea, nausea, muscle cramps, urinary urgency, hyperhidrosis, increased salivation and bronchial secretions, hypotension, and bradycardia. These side effects may be treated with atropine sulfate,

glycopyrronium bromide, or loperamide.[9]

Adjuvant symptomatic treatment with beta-2 adrenergic receptor agonists (salbutamol, tervutaline) may be also considered in selected cases of MG.[14,15]

Corticosteroids

Corticosteroids are the most commonly prescribed immunosuppressive drugs in MG. They exert their action by suppressing complement-mediated reactions at the endplates.[16] They also lead to CD4+ T-cells apoptosis and decrease in the AChR antibody levels, via reduction of B-cells' population.[17]

Prednisolone, rather than prednisone, is more frequently used in Greece.[15] The starting dose is 10-20 mg/day and may be titrated by 5 mg/week up to 60 mg/day. High-starting doses of prednisolone are contraindicated due to possible transient worsening of muscle weakness. The benefit from this treatment is manifested 2–6 weeks after its initiation.[9] Once therapeutic targets have been reached, a slow tapering is advised, due to a plethora of side effects, such as hyperglycaemia, cataract and osteoporosis. However, in most cases a low daily maintenance corticosteroid dose, instead of complete cessation, is advised.[18]

Azathioprine

Azathioprine is a purine synthesis inhibitor, leading to decreased B and T cell proliferation.[4] It is commonly used along with prednisolone as a first-choice treatment for generalised MG. Its effect is delayed and is usually seen after six months to two years.[19] Prednisolone dose may be reduced when the effect of Azathioprine has been reached.

Azathioprine may be started at a dose of 50 mg/day and increased by 50mg every two to four weeks, up to 2-3 mg/kg.[15] Testing for the activity of the enzyme thiopurine methyltransferase is advised before the initiation of azathioprine. Low or absent activity of this enzyme may lead to toxic accumulation of azathioprine. The most common adverse events include cytopenia, hepatotoxicity, and flu-like syndrome, especially during the first months of treatment.[9]

Mycophenolate Mofetil

Mycophenolate Mofetil (MMF) exerts its action by reducing both the T and B cells, via inhibition of the inosine monophosphate dehydrogenase.[20] This enzyme is crucial for the synthesis of guanosine nucleotides. The findings regarding its efficacy in MG are conflicting.[21,22] A slightly faster onset of effect may be shown with MMF compared to azathioprine. MMF, alongside cyclosporine, methotrexate and tacrolimus, are secondary alternatives to azathioprine.[9,14,15]

The starting dose of MMF is 500mg twice daily and may be titrated up to 1 – 1.5g twice daily. The most common side effects include gastrointestinal symptoms and cytopenia.

Methotrexate

Methotrexate suppresses the proliferation of immune cells via inhibition of dihydrofolate reductase, which is responsible for the conversion of dihydrofolate to tetrahydrofolate.[23] This reaction is vital for the synthesis of purines and pyrimidines. The efficacy and steroid-sparing properties of methotrexate in MG have not been proven in an RCT performed in 2016.[24]

Methotrexate is administered orally, once per week.[15] The initial dose is 7.5mg and may be increased by 2.5mg every one to two weeks, up to 20-25mg once weekly. Daily supplementation with folic acid is advised, except on the day of methotrexate administration.[25] The most important adverse events of methotrexate are suppression of the bone marrow, hepatotoxicity and pulmonary toxicity.

Cyclosporine

Cyclosporine is a calcineurin inhibitor and thus suppresses the synthesis of interleukins (IL), such as IL-2, which is crucial for the activation of T lymphocytes.[26] Cyclosporine's efficacy in MG as an add-on therapy to corticosteroids has been shown in a prospective RCT.[27] Its maximum therapeutic effect may be reached at approximately six to seven months.[28]

The starting dosage of cyclosporine is 2.5mg/kg per day in two divided doses.[15] It is typically increased by 0.5 mg/kg per day every four to eight weeks, up to 5 mg/kg per day. Close monitoring of cyclosporine's levels in the serum is advised due to serious side effects, including hypertension, nephrotoxicity, hepatotoxicity, tremor, and malignancies, such as lymphoma and squamous cell skin cancer.

Tacrolimus

As cyclosporine, tacrolimus is another calcineurin inhibitor. Its efficacy in MG is mainly based on data from observational studies and therefore, is used as an off-label alternative to azathioprine.[29] The onset of clinical response to this treatment may be shown after 6 to 12 months.

The initial dosage of tacrolimus is 1 mg/day and may be titrated up to the usual maintenance dosage of 3 mg/day divided into two doses.[30] Tacrolimus shares common adverse events with cyclosporine, however, with a relatively safer profile.

Cyclophosphamide

Cyclophosphamide is an alkylating agent that acts on DNA and inhibits the proliferation of T and B lymphocytes.[31] It is an off-label option for the treatment of refractory generalised MG, with a possible steroid-sparing effect.[32] Cyclophosphamide is typically administered in monthly pulses of 0.5 – 1.5g/m^2

of body surface area. It is not commonly used due to its unfavourable safety profile, as it may lead to teratogenicity, infertility, alopecia, cytopenia, cystitis and malignancy.[30]

Anti-CD20 monoclonal antibodies

Rituximab is a chimeric anti-CD20 monoclonal antibody which eliminates immature, naive and memory B-cells.[33] This way, rituximab leads to reduction of autoantibodies' levels and thus improvement of muscle strength in patients with MG.[34,35]

In the AChR seropositive MG, rituximab may be used as an alternative option when symptoms are refractory or other therapeutic regimens cannot be tolerated.[14] However, rituximab is considered a first-line treatment option for MuSK-positive MG patients.[36] Furthermore, it may be used in seronegative MG, although RCTs are currently lacking.[37]

Rituximab is administered intravenously, most commonly in two doses of 1g separated by two weeks or in four weekly doses of 375mg/m^2 body surface.[38] It may be administered again, usually after 4-6 months, depending on the disease progression or the CD20+ cell counts in the peripheral blood. Its therapeutic effect may be shown after 1-3 months.[30] The most important side effects include infusion-related reactions, serious infections, such as progressive multifocal encephalopathy (PML), cytopenia and hypogammaglobulinemia.[30]

Intravenous Immunoglobulin (IVIG)

IVIG is a mixture of donated human immunoglobulins, which contains all IgG subclasses. It has several anti-inflammatory and immunomodulatory effects. IVIG inhibits the complement activity and binds to autoantibodies, leading to deactivation of the latter.[39] Furthermore, IVIG blocks Fc receptors in the spleen and liver, leading to inhibition of autoantibodies recirculation in the serum.[40]

IVIG is mainly used in myasthenic crisis or impending crisis.[15,30] Myasthenic crisis is defined by severe weakness of bulbar and/or respiratory muscles with concurrent need for respiratory support. IVIG may be selected as a bridge treatment to corticosteroids or other slow-acting immunosuppressants. Furthermore, it may be rarely used as a maintenance treatment in refractory cases. Finally, IVIG may be administered preoperatively to selected MG cases with increased risk of postoperative deterioration. History of myasthenic crisis, bulbar or respiratory symptoms, and chronic pulmonary disease are risk factors for postoperative clinical worsening.

IVIG has a rapid therapeutic effect occurring approximately after 2-5 days, which may last up to six weeks.[41] The typical dosage of IVIG is 2 g/kg, divided in 2-5 daily doses. Anaphylactic reaction in IgA deficiency is a severe complication of IVIG administration, which may be prevented by routine testing of IgA levels in serum before starting treatment.[42] Other serious but uncommon adverse events include thrombotic events, autoimmune haemolytic anaemia, renal failure, aseptic meningitis and pulmonary oedema.[43]

Plasma exchange (PLEX)

PLEX is a procedure replacing plasma with albumin and saline. Its immunomodulatory function is mainly based on the removal of autoantibodies, immunocomplexes and cytokines, the shift of humoral to cell-mediated immunity and the increase of T-regulatory cells.[44]

The therapeutic benefit of PLEX is similar to IVIG, although PLEX may be more effective in MuSK-associated MG.[45] They share common indications, although PLEX, rather than IVIG, is considered the 1st line treatment option for myasthenic crisis, due to its predictable result.[46]

Three to seven PLEX sessions over 7-14 days are typically required in myasthenic crisis. It is contraindicated in sepsis and may lead to adverse events such as hypotension, hypocalcaemia, thrombosis in the catheter site, and infections.[15]

Immunoadsorption may be an alternative therapeutic option to PLEX for the treatment of severe MG relapses or myasthenic crises. This technique leads to the removal of specific autoantibodies, such as anti-AChR or anti-MuSK, via the use of specific ligands, such as protein A or synthetic peptides (e.g. fragments of AChR).[47] No RCTs regarding its efficacy in MG exist. However, small studies have shown similar benefits to PLEX or IVIG in MG exacerbations.[48,49] Immunoadsorption is not routinely used in clinical practice due to increased cost and limited availability.

Thymectomy

Thymomatous MG is a well-recognised paraneoplastic syndrome. AChR may be expressed in thymic activated epithelial cells and autoreactive T cells against AChR may in turn escape the thymus and activate B cells in the periphery to produce antibodies.[50]

All recently diagnosed MG patients should be examined with thoracic CT or MRI, to identify thymoma or thymic hyperplasia.[14] Patients with thymoma, irrespective of the MG status, should be operated due to oncological indications. In young patients (age < 50 years) with generalised non-thymomatous AChR-associated MG, thymectomy should be performed early on after the diagnosis and as soon as the patient is clinically stable.[14,15] Non-thymomatous thymectomy is currently not indicated for MuSK or LRP4-associated MG. Thymectomy may be a therapeutic option in seronegative MG or ocular AChR-associated MG, when other treatments have failed.[51]

The maximum benefit from thymectomy may be

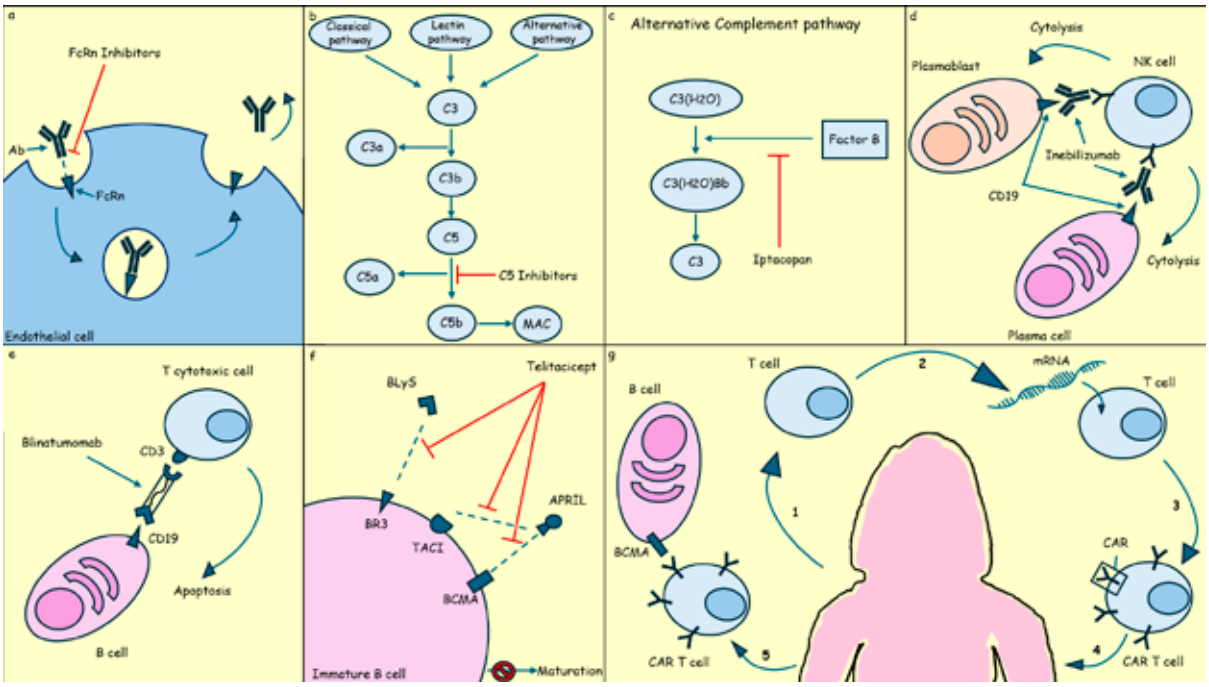

Figure 1. Mechanism of action of emerging therapies for Myasthenia Gravis. (**a**) FcRn Inhibitors. (**b**) Complement C5 Inhibitors. **(c)** Iptacopan - Complement Factor B Inhibitor). (**d**) Inebilizumab – anti-CD19 monoclonal antibody. (**e**) Blinatumomab - bispecific antibody binding to CD3 on T cells and CD19 on B cells. (**f**) Telitacicept - dual BLyS/APRIL inhibitor. (**g**) CAR T cells.

Ab: Antibody; AChR: Acetylcholine Receptor; APRIL: A-Proliferation-Inducing Ligand; BCMA: B Cell Maturation Antigen; BLyS: B-Lymphocyte Stimulator; BR3: BLyS Receptor 3; CAR: Chimeric Antigen Receptor; FcRn: Neonatal Fc receptors; MAC: Membrane Attack Complex; NK cell: Natural Killer cell; TACI: Transmembrane Activator and Calcium Modulator and Cyclophilin Ligand Interactor.

shown up to one year after the operation.[52] In thymomatous MG, thymectomy may lead to complete remission in up to 30% of patients.[53]

FcRn Inhibitors

Neonatal Fc receptors (FcRn) are expressed in multiple cell types, such as endothelial and epithelial cells.[54] FcRn binds to the Fc portion of IgGs and protects them from intracellular degradation, leading to their recirculation in serum and thus increasing their half-life. FcRn inhibitors are a new therapeutic drug class used in MG leading to a decreased half-life of autoantibodies (**Figure 1**).

Efgartigimod is an IgG1 Fc fragment which inhibits FcRn, approved by the U.S. Food and Drug Administration (FDA) in 2021 and by the European Medicines Agency (EMA) in 2022, as an add-on therapeutic option for generalised MG with positive antibodies against AChR. Its approval was based on the phase 3 RCT ADAPT which showed clinical improvement 7 to 14 days after the initiation of each therapeutic cycle.[55] ADAPT-SERON, a multi-centre, phase 3 RCT regarding Efgartigimod's efficacy in seronegative and MuSK-associated generalised MG is currently ongoing (**Table 1**).[56] Interestingly, a phase 3 RCT, called ADAPT oculus, is currently recruiting patients with ocular MG in order to test Efgartigimod's efficacy in this group.[57] ADAPT Jr is a phase 2/3 clinical trial aiming to the study of pharmacokinetics of Efgartigimod in paediatric patients with gMG.[58] Efgartigimod has been off-label used in cases of myasthenic crisis with promising results.[59]

Efgartigimod is administered in cycles of four weekly intravenous doses of 10mg/kg. Each therapeutic cycle must start at least 7 weeks apart from the start of the previous one. Subsequent cycles may be administered according to clinical judgement. A subcutaneous form of Efgartigimod has also been approved for the treatment of MG.

IgG class medicinal products, such as IVIG or monoclonal antibodies, should not be administered concurrently with Efgartigimod, as it may decrease their half-life. They should be administered at least two weeks after the last dose of Efgartigimod.[15] All vaccinations should be administered at least two weeks after the last dose or four weeks before the initiation of a therapeutic cycle. IgG levels in serum should be measured before initiation of this agent. The most common adverse events include headache and nasopharyngitis.[55]

Rozanolixizumab is a humanised IgG4 monoclonal

Table 1. Emerging treatment options for Myasthenia Gravis.

Drug Class	Therapeutic agent	Clinical Trial	Phase	MG Subtypes	Number of patients	Time frame	Status	Primary Outcomes
FcRn inhibitors	Nipocalimab	Vivacity-MG3[64]	3	Adult / gMG	196	6 months	Completed	Decrease in MG-ADL
	Efgartigimod IV	ADAPT SERON[56]	3	Adult / gMG, MuSK+, seronegative	119	29 days	Active	MG-ADL
	Efgartigimod SC	ADAPT oculus[57]	3	Adult / ocular MG	124	29 days	Recruiting	MGII
	Efgartigimod SC / IV	ADAPT Jr SC[58] / ADAPT Jr[124]	2/3	2 – 17y / gMG, AChR+	12	24-26 months	Recruiting	Pharmacokinetics, IgG levels, AChR-Ab levels
	Batoclimab	FLEX[81]	3	Adult / gMG	240	3 months	Active	MG-ADL (AChR+)
	Rozanolixizumab	roMyG[62]	2/3	2-17y / gMG, AChR+, MuSK+	12	18 weeks	Recruiting	Adverse events
	IMVT-1402	NCT07039916[82]	3	Adult / gMG	231	3 months	Recruiting	MG-ADL
Complement C5 inhibitors	Zilucoplan	ziMyG[79]	2/3	2-17y / gMG, AChR+	8	29 days	Recruiting	Pharmacokinetics, C5 serum levels
	Pozelimab + Cemdisiran	NIMBLE[85]	3	Adult / MG, AChR+, LRP4+	335	6 months	Recruiting	MG-ADL
	Gefurulimab	PREVAIL[88]	3	Adult / gMG, AChR+	260	26 weeks	Active	MG-ADL
Factor B Complement inhibitor	Iptacopan	NCT06517758[91]	3	Adult / gMG, AChR+	146	6 months	Recruiting	MG-ADL
Anti-CD20 monoclonal Ab	B007	NCT06447597[92]	2/3	Adult / gMG, AChR+, MuSK+	104	16 weeks	Recruiting	MG-ADL
Anti-CD19 monoclonal Ab	Inebilizumab	MINT[97]	3	Adult / AChR+, MuSK+	238	26 weeks	Active	MG-ADL
Anti-CD19 BiTE	Blinatumomab	NCT06836973[98]	2/3	Adult / Refractory, AChR+, MuSK+, LRP4+	2	6 months	Not yet recruiting	Efficacy, Safety, Autoantibodies status
IL-6 receptor inhibitor	Satralizumab	LUMINESCE[102]	3	Over 12 y / gMG, AChR+, MuSK+, LRP4+	188	6 months	Completed	Decrease in MG-ADL

BlyS / APRIL inhibitor	Telitacicept	NCT05737160[106,107]	3	Adult / gMG, AChR+, MuSK+	114	24 weeks	Completed	Decrease in both MG-ADL + QMG / IgG, IgA, IgM decrease
BTK inhibitor	Remibrutinib	RELIEVE[110]	3	Adult / gMG, AChR+, MuSK+, seronegative	180	6 months	Recruiting	MG-ADL
Purine analog	Cladribine	MyClad[112]	3	Adult / gMG, AChR+, MuSK+, LRP4+, seronegative	240	6 months	Recruiting	MG-ADL
mRNA anti-BCMA CAR T cell therapy	Descartes-08	AURORA[119]	3	Adult / Generalized AChR+	100	4 months	Recruiting	MG-ADL

Ab: Antibody; APRIL: A-proliferation – inducing ligand; BCMA: B Cell Maturation Antigen; BiTE: Bispecific T-cell engager; BlyS: B-lymphocyte stimulator; BTK: Bruton's tyrosine kinase; CAR: Chimeric Antigen Receptor; FcRn: Neonatal Fc receptors; gMG: generalized Myasthenia Gravis; IL-6: Interleukin-6 IV: intravenous; LRP4: Lipoprotein Receptor-related Protein 4; MG-ADL: Myasthenia Gravis Activities of Daily Living scale; MGII: Myasthenia gravis impairment index; MuSK: Muscle-specific Tyrosine Kinase; QMG: Quantitative Myasthenia Gravis scale; SC: subcutaneous.

antibody targeting and inhibiting the FcRn. It was approved by the FDA in 2023 and by the EMA in 2024, as an add-on treatment for generalised MG with positive antibodies against AChR or MuSK, based on the multi-centre, phase 3 RCT Mycarin G.[60] Its therapeutic benefit may be apparent as soon as day 8 after its administration.[61] Rozanolixizumab is given via subcutaneous infusion in six weekly doses. Further therapeutic cycles may be initiated based on clinical assessment. A phase 2/3 clinical trial is currently recruiting paediatric patients with AchR or MuSK-positive generalised MG, in order to assess the efficacy and potential adverse effects of rozanolixizumab in this patient group (**Table 1**).[62]

The most common adverse events include headache, diarrhoea, and fever.[61] Rozanolixizumab should not be offered to patients with hyperprolinaemia, as it contains 29mg of proline per ml. Further precautions regarding vaccinations, IgG class medications and hyperglobulinemia resemble those of Efgartigimod alfa.

Nipocalimab is another monoclonal antibody which inhibits FcRn.[63] It has been approved by the FDA on April 2025 for the treatment of AChR or MuSK-associated generalised MG in adult and paediatric patients ≥12 years of age and has been submitted for approval to the EMA. The phase 3 RCT Vivacity-MG3 showed a statistically significant reduction of MG-ADL in the nipocalimab group against the placebo group (**Table 1**).[64] A statistically significant decrease of quantitative Myasthenia Gravis scale (QMG) score was observed in the nipocalimab group, compared to the placebo group, within 8 weeks of treatment initiation.[65] The most commonly observed adverse events were infections and headache. Nipocalimab is administered intravenously every two weeks based on the patient's body weight.

Complement Inhibitors

Complement activation is one of the main pathophysiologic mechanisms of AChR-associated MG. Complement inhibitors have been recently approved by the FDA and the EMA for generalised anti-AChR MG cases, including eculizumab, ravulizumab and zilucoplan.[14,15,30]

Eculizumab is a humanised monoclonal antibody that binds to the complement protein C5 and thus inhibits the formation of the membrane attack complex (**Figure 1**).[66] It was the first complement inhibitor to be approved for MG by the FDA and EMA in 2017.[30] In Greece, it is indicated as an add-on therapy for refractory cases. It has also been approved for children ≥ 6 years of age in 2025.[67]

Eculizumab is administered intravenously at a starting weekly dose of 900mg for the first four weeks, followed by 1200mg for the fifth dose one week later and thereafter 1200mg every two weeks.[67] Clinical improvement is usually shown within two weeks after the first infusion, while the maximal effect is reached after three months.[68] Eculizumab has been used off-label in a handful of cases of myasthenic crisis with good results.[69-71]

Complement inhibition poses an increased risk of meningococcal infections.[30] Therefore, before initiating complement inhibitors, patients should be vaccinated with both the quadrivalent and group B Neisseria meningitidis vaccines. Other infections, including respiratory or urinary tract infections may be seen as well. In case of urgent need for initiation of this class of drugs without vaccination completion, chemoprophylaxis with antibiotics is advised.[15]

Ravulizumab is a modified version of eculizumab with a longer half-life.[30] It is indicated as an add-on treatment in AChR-associated generalised MG. Ravulizumab is administered intravenously, once per eight weeks, starting 2 weeks after the loading dose. Its efficacy in MG has been proven in a multi-centre, phase 3 RCT leading to its approval by the FDA and EMA in 2022.[72] The median time to clinical improvement is similar to eculizumab.[73] Ravulizumab has also been used effectively in case reports of myasthenic crisis.[74,75] However, further research is needed for the establishment of complement inhibitors' efficacy in this clinical scenario.

Zilucoplan is a synthetic peptide which binds to the C5 complement protein, preventing its cleavage to C5a and C5b by C5 convertase.[76] It also inhibits the binding between C5b and C6. The binding site of zilucoplan in C5 is different from eculizumab, thereby rendering it as a possible alternative if eculizumab or ravulizumab fail.[77]

Zilucoplan was approved as an add-on therapy in AChR-positive generalised MG, by the FDA and the EMA in 2023. As shown in the RCT RAISE, zilucoplan may benefit patients from the first week of its administration.[78] The maximum effect is seen during the fourth week and may remain at least until the 12th week. Zilucoplan is given as a subcutaneous injection once daily. It shares a common safety profile with other complement inhibitors, and thus vaccination against Neisseria meningitidis is necessary. A phase 2/3 clinical trial regarding the pharmacokinetics of zilucoplan in paediatric patients with AChR-positive generalised MG is currently recruiting participants (**Table 1**).[79]

EMERGING TREATMENT OPTIONS

Novel FcRn Inhibitors

Other FcRn inhibitors are currently being tested in MG. Batoclimab is a fully human monoclonal antibody targeting the IgG-binding site on FcRn.[80] It has been tested in thyroid eye disease, with favourable results.[80] However, this study was terminated due to cholesterol increase. The efficacy of batoclimab in generalised MG is currently being investigated in a phase 3 RCT called FLEX (Table).[81] No restrictions regarding the antibody status apply in this study. However, the primary outcome concerns patients with positive antibodies against AChR. Finally, IMVT-1402, a monoclonal antibody which blocks the FcRn, is under investigation for the treatment of generalised MG in a phase 3 RCT (**Table 1**).[82] The main outcome refers to the potential decrease in MG-ADL. This study is currently recruiting patients.

Novel Complement Inhibitors

Emerging complement inhibitors are currently being investigated for the treatment of MG. Pozelimab is a human IgG4 human monoclonal antibody which binds to C5 and prevents its cleavage to C5a and C5b.[83] It is currently approved for the treatment of CD55-deficient protein-losing enteropathy. Cemdisiran is an N-acetylgalactosamine conjugated siRNA which suppresses liver production of C5 protein.[84] Pozelimab and cemdisiran are currently being investigated as monotherapies and as a combination for the treatment of AChR or LRP4-postive MG in the multi-centre, phase 3 RCT NIMBLE trial (**Table 1**).[85] Approximately 335 patients are estimated to participate in this study. These agents are administered subcutaneously. Besides infections, adverse events of pozelimab may include hypertension, alopecia, bone fractures, increased uric acid and liver enzymes.[86]

Gefurulimab is a bispecific antibody which inhibits the cleavage of C5 to C5a and C5b. It also binds to albumin which may prolong its circulatory half-life and thereby lead to extended intervals between each dose.[87] A multi-centre, phase 3 RCT, called PREVAIL, regarding the efficacy of the subcutaneous form of Gefurulimab in adult patients with AChR-positive generalised MG is currently ongoing (**Table 1**).[88]

Iptacopan is a complement factor B inhibitor which has been approved for the treatment of paroxysmal nocturnal haemoglobinuria, complement 3 glomerulopathy, and immunoglobulin A nephropathy. Iptacopan is a small molecule which inhibits the alternative complement pathway, leaving the classical and lectin pathways intact (Figure).[89] This may lead to adequate immune responses against pathogens. Another benefit of this agent is the oral form. The most common side effects include headache, diarrhoea, nasopharyngitis, and nausea.[90] A phase 3 RCT is currently recruiting adult patients with AChR-positive generalised MG, in order to test the efficacy of iptacopan in this group (**Table 1**).[91]

A novel anti-CD20 monoclonal antibody

B007 is an experimental recombinant anti-CD20 humanised monoclonal antibody currently tested for the treatment of adult patients with AChR or MuSK-associated generalised MG (Table).[92] This study is a multi-centre phase 2/3 RCT with a primary outcome of Myasthenia Gravis – Activities of Daily Living (MG-ADL) scale reduction by two or more points. B007 is

administered subcutaneously. This agent is currently being investigated in other autoimmune disorders such as primary membranous nephropathy and pemphigus.[93,94]

Anti-CD19 agents

Plasmablasts and plasma cells contribute immensely to the pathophysiology of MG and other autoimmune diseases by the production of autoantibodies. The majority of these cells do not express CD20, but rather CD19 on their surface.[95] Anti-CD20 therapies may not effectively deplete these cell populations. Therefore, anti-CD19 agents have been designed and are currently being investigated in MG and other autoantibody-related diseases (**Figure 1**).

Inebilizumab is a humanised anti-CD19 monoclonal antibody, approved for the treatment of IgG4-related disease and neuromyelitis optica spectrum disorder (NMOSD). It is administered intravenously every 6 months besides the first month, at which time two doses are given with a gap of two weeks between them. Premedication with antihistamine, acetaminophen, and corticosteroids is advised.[96]

The most common adverse events include urinary tract infection, lymphopenia and arthralgia. Patients should be screened for hepatitis B and tuberculosis before the initiation of inebilizumab. Although no confirmed cases of PML have been observed in clinical trials, treating physicians should be aware of this risk, as PML has been described during treatment with other B-cell depleting therapies. MINT study is an active multi-centre, phase 3 RCT, investigating the efficacy of inebilizumab in adult patients with AChR or MuSK-positive MG (**Table 1**).[97]

Another anti-CD19 therapeutic option, currently being tested in MG is blinatumomab (**Table 1**).[98] This is a bispecific antibody which binds simultaneously to CD3 on T cells and CD19 on B cells (**Figure 1**). This concurrent binding leads to the release of cytotoxic substances, such as perforins and granzymes, directly into the B cells, triggering apoptosis of the latter.[99] Blinatumomab has been approved for the treatment of relapsed or refractory B cell precursor acute lymphoblastic leukaemia. It is administered intravenously. The most common side effects of blinatumomab include infections, headache, pyrexia, infusion-related reactions, and cytopenia. Cytokine release syndrome (CRS), which may be life-threatening or fatal, has been reported in patients receiving blinatumomab.

Interleukin-6 (IL-6) receptor inhibitors

IL-6 is a proinflammatory cytokine that is implicated in immunologic responses during inflammatory disease, infection, haematopoiesis, and oncogenesis.[100] IL-6 coordinates the proliferation and the differentiation of T cells, as well as the terminal differentiation of B cells. IL-6 may also be implicated in antibody production. IL-6 receptor inhibitors have been used in many autoimmune diseases such as rheumatoid arthritis (RA), giant cell arteritis and scleroderma. Serum IL-6 levels are higher in MG patients compared to healthy controls.[101]

Satralizumab is a humanised monoclonal antibody which inhibits IL-6 receptors. It is approved for the treatment of NMOSD. This agent has been tested in seropositive (AChR, MuSK, LRP4) generalised MG, in a multi-centre, placebo-controlled, phase 3 RCT, called LUMINESCE (**Table 1**).[102] Eligible patients were over 12 years old, with MG-ADL score of 5 or more and use of stable background therapy. The primary outcome was a change in MG-ADL scale at 6 months of treatment with satralizumab. One-hundred and eighty-eight patients participated in this study. A statistically significant, yet small, reduction of MG-ADL score was noticed between satralizumab and placebo groups with positive anti-AChR antibodies. Three patients showed a serious adverse event in the satralizumab group, including pneumonia, pyelonephritis and increased lipase. The open-label extension of this study was terminated early, due to the halt of further development of satralizumab for the treatment of MG by the sponsor.

Telitacicept

Telitacicept is a fusion protein which binds to and neutralises the activity of B-lymphocyte stimulator (BLyS) and A-proliferation-inducing ligand (APRIL) (**Figure 1**).[103] BLyS is an important molecule for the differentiation, maturation, function and survival of B cells. Increased serum levels of BLyS have been reported in patients with autoimmune disorders, such as systematic lupus erythematosus (SLE).[104] APRIL, as well, regulates the differentiation and maturation of B lymphocytes.[105]

Telitacicept is currently being tested in multiple autoimmune diseases, such as RA, ANCA-associated vasculitis, SLE, and multiple sclerosis (MS). It has also been tested recently in 114 adult patients with AChR or MuSK-positive generalised MG, in a multi-center placebo-controlled phase 3 RCT (Table).[106,107] The treatment group received weekly subcutaneous doses of telitacicept for 6 months. MG-ADL and QMG scores were significantly decreased in the treatment group compared to the placebo group. This also applied to the IgG, IgA and IgM serum levels of the patients treated with telitacicept compared to placebo. The most frequently reported side effect was IgM decrease.

Bruton's Tyrosine Kinase (BTK) inhibitors

BTK inhibitors have been used in multiple hematologic disorders for almost 15 years. Among numerous functions, BTK is a crucial component of the B cell receptor (BCR) signalling pathway, which is activated

when a B cell encounters an antigen.[108] This leads to B cell proliferation, differentiation, and antibody production. BTK inhibitors may block these processes and thus lead to potential remission of autoimmune diseases.

Remibrutinib is a new oral, highly selective BTK inhibitor which has been tested in chronic spontaneous urticaria with success and a favourable safety profile.[109] RELIEVE is a multi-centre, placebo-controlled phase 3 RCT, currently investigating the efficacy of remibrutinib in 180 adult patients with AChR or MuSK-associated or seronegative generalised MG (**Table 1**).[110] The primary outcome of this study is a potential reduction of MG-ADL score at 6 months. Researchers are currently recruiting patients.

Cladribine

Cladribine is a chlorinated deoxyadenosine analog. It induces B and T lymphocyte apoptosis, via increasing the expression of deoxycytidine kinase, disrupting intracellular processes and inhibiting DNA synthesis / repair.[111] It has been approved for the treatment of various haematologic cancers and MS as well. It is administered orally. The adverse events of cladribine may include anaemia, thrombocytopenia, lymphopenia, headache, serious infections, fever, and neurotoxicity. Cases of PML have been reported in patients receiving cladribine. Screening for human immunodeficiency virus, tuberculosis, hepatitis B, and hepatitis C is advised before each treatment cycle. Varicella zoster virus antibody status should be evaluated as well.

Cladribine is currently being investigated in adult patients with generalised MG, in a multi-centre, placebo-controlled, phase 3 RCT, called MyClad (**Table 1**).[112] Two-hundred and forty patients are estimated to participate in this study. Patients will be divided into three groups. Participants of the first group will receive placebo in two courses separated by four weeks. A low dose of oral cladribine will be administered to the patients of the second group, in two courses separated by four weeks. Participants of the third group will receive a high dose of oral cladribine, following the same schedule as the previous groups. The primary outcome is a change of MG-ADL score at 6 months.

Chimeric antigen receptor (CAR) T cells

CAR T cells are genetically engineered immune cells designed to recognise and destroy specific cells in the body. The CAR molecule combines the extracellular target binding domain of an antibody directed toward the desired target with the intracellular T-cell activation protein domains.[113] This treatment has been used in cancer and, more recently, in autoimmune diseases, such as SLE.[114]

CAR T cell therapy has been tested in refractory generalised MG in a prospective, non-randomised phase 1b/2a study.[115] In this study, the researchers used autologous RNA CAR T cells, targeting B-cell maturation antigen (BCMA), which is expressed on the surface of mature plasma cells. Eleven patients with anti-AChR antibodies, two with anti-MuSK antibodies and one seronegative patient participated in this study. The main outcome of this study was safety and tolerability, whereas the secondary outcomes concerned efficacy. The adverse events were mild, with the most common ones being headache, nausea and vomiting. Significant clinical improvement was shown in a follow-up period of up to 9 months.

Case reports regarding the treatment of refractory generalised MG with CAR T cells have been published as well. Haghikia et al. have treated one patient with anti-AChR-positive refractory generalised MG with an anti-CD19 CAR T construct, with minimal side effects, subsequent elimination of anti-CD19 B cells and a significant decrease of autoantibodies up until day 62 after the infusion.[116] Significant improvement of muscle strength was noted as well. Similar results were reported by two other studies using anti-BCMA CAR T cells and bispecific anti-CD19/BCMA CAR T cells respectively, in anti-AChR and anti-MuSK-positive refractory generalised MG patients.[117,118] The AURORA study, which is a double-blind, placebo-controlled phase 3 RCT evaluating the tolerability, safety and efficacy of anti-BCMA CAR T cell therapy in generalised MG with positive antibodies against AChR, is currently recruiting patients (**Table 1**, **Figure 1**).[119]

Potentially dangerous side effects of CAR T cell therapy include CRS and immune effector cell-associated neurotoxicity syndrome (ICANS).[120] CRS is characterised by fever, hypotension, hypoxia and multiorgan system toxicities. It usually occurs during the first week after CAR T cells infusion, whereas ICANS occurs during the second week. ICANS is characterised by headache, encephalopathy, focal neurological deficits, seizures and brain oedema. Both adverse events may be life-threatening. However, none of these have been reported in studies regarding MG treatment with CAR T cells.[115-118] Nevertheless, further research regarding the efficacy and safety of this treatment in MG is required.

Special Myasthenia Gravis populations

The therapeutic landscape of MG has widened through the last decade, especially due to the approval of FcRn inhibitors and complement inhibitors. However, the treatment options in specific populations, such as non-AChR-associated MG, ophthalmic MG and pregnant patients remain limited.

Anti-MuSK MG is currently treated with corticosteroids and rituximab, although the latter is an off-label treatment. If rituximab is not available, aza-

thioprine or MMF may be used.[15] Rozanolixizumab and nipocalimab, two FcRn inhibitors, have been approved as add-on therapies for anti-MuSK MG. Real world data regarding their efficacy and safety profile in this population is awaited. Multiple active RCTs are currently recruiting anti-MuSK-associated MG patients.[56,81,82] However, they are commonly outnumbered by the anti-AChR-associated MG subgroup.

Anti-LRP4 MG patients are even more underrepresented in clinical trials compared to the anti-MuSK subgroup. Their treatment is currently based on corticosteroids and older off-label immunotherapies.[15] Refractory cases may benefit by the off-label addition of a complement inhibitor or an FcRn inhibitor. Studies focused on this population are needed.

Seronegative MG is not rare as it may constitute up to 15% of all MG patients.[4] Nevertheless, treatment options resemble those of Anti-LRP4 MG patients. Seronegative MG patients are not usually included in RCTs. However, ADAPT SERON is currently investigating the efficacy of efgartigimod in seronegative patients.[56] Furthermore, seronegative patients are included in the RCTs currently testing remibrutinib and cladribine, respectively.[110,112]

Ocular MG is treated with corticosteroids. Other immunomodulatory agents, such as azathioprine and MMF may be used in refractory cases or patients who do not tolerate corticosteroids. Efgartigimod may be an additional option for ocular MG, depending on the results of the currently active RCT ADAPT oculus (**Table 1**).[57]

Pregnant MG patients pose a therapeutic challenge. Pyridostigmine and daily doses of prednisolone under 20mg are considered safe during pregnancy and lactation.[15] However, corticosteroids increase the risk of gestational diabetes mellitus, hypertension and infections. Alternative options to steroids are azathioprine and cyclosporine. Rituximab may be administered at least 3 months before pregnancy.[121] MMF, methotrexate and cyclophosphamide should not be administered to women of reproductive age, due to their teratogenic effects. IVIG and PLEX may be used to treat exacerbations of MG during pregnancy. Data regarding safety and efficacy of new MG therapeutic options, such as FcRn inhibitors and complement inhibitors, are currently lacking. However, eculizumab has been used in case reports of pregnant MG patients without safety-concerning issues.[122]

The first-line therapeutic option for paediatric MG is pyridostigmine. Steroids are avoided in children if symptoms are well-controlled, due to their side effects. Azathioprine, MMF and cyclosporine have been used effectively in juvenile MG.[123] New therapeutic agents, such as eculizumab (over 5 years of age) and nipocalimab (over 11 years of age) have been approved for the treatment of paediatric MG. Phase 2/3 studies regarding the safety and efficacy of efgartigimod, rozanolixizumab and zilucoplan in children suffering from MG are currently active (**Table 1**).[58,62,79]

CONCLUSION

The treatment of MG has reached an unprecedented level of variety with the addition of FcRn inhibitors and complement inhibitors. These drug classes have shown their safety and efficacy through well-designed RCTs, in contrast to older regimens, most of which have never been tested in such studies. Furthermore, new members of these classes are currently being tested and may be soon added to the therapeutic arsenal against MG. Novel drug families, such as anti-CD19 monoclonal antibodies, BlyS / APRIL inhibitors and BTK inhibitors are currently being investigated. Finally, personalised treatment with CAR T cell therapy is quite promising in multiple diseases, such as MG, and may change the whole therapeutic strategy of these patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Ενημερωτικές Σελίδες...

Συνέδρια - Ημερίδες - Συμπόσια - Επιστημονικές εκδηλώσεις

2025 - 2026

- **12-15 Οκτωβρίου 2025: 27th World Congress of Neurology,** *Seoul, South Korea*
- **31 Οκτωβρίου-2 Νοεμβρίου 2025: Ημέρες Νευρολογίας 2025,** *Λάρισα*
- **6-8 Νοεμβρίου 2025: 28th CONFERENCE OF THE WORLD ORGANIZATION OF NEUROSONOLOGY (WON),** *Athens*
- **11-13 Νοεμβρίου 2025: The 2nd International Electronic Conference on Medicine,** *Online*
- **20-23 Νοεμβρίου 2025: 13ο Πανελλήνιο Συνέδριο Αγγειακών Εγκεφαλικών Νόσων,** *Θεσσαλονίκη*
- **11-14 Δεκεμβρίου 2025: 12ο Πανελλήνιο Συνέδριο Ελληνικής Ακαδημίας Νευροανοσολογίας,** *Θεσσαλονίκη*
- **6-8 Μαΐου 2026: European Stroke Organization Conference,** *Maastricht, the Netherlands*
- **15-17 Μαΐου 2026: 14ο ΔΙΕΘΝΕΣ ΣΥΜΠΟΣΙΟ ΤΗΣ ΕΤΑΙΡΕΙΑΣ ΓΙΑ ΤΗΝ ΕΡΕΥΝΑ ΤΗΣ ΠΑΡΕΓΚΕΦΑΛΙΔΑΣ ΚΑΙ ΤΩΝ ΑΤΑΞΙΩΝ,** *Λευκωσία*
- **4-7 Ιουνίου 2026: 37ο Πανελλήνιο Συνέδριο Νευρολογίας,** *Καλαμάτα*

Αρχεία Κλινικής Νευρολογίας

Για λόγους ενημέρωσης αρχείου, παρακαλούμε συμπληρώστε τα στοιχεία αλληλογραφίας σας και στείλτε το απόκομμα με fax στο: **210 7247556** ή αποστείλετε τα στοιχεία στο e-mail: **info@jneurology.gr**

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ΤΟΠΟΣ ΑΠΟΣΤΟΛΗΣ:

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- *Εάν επιθυμείτε να λαμβάνετε το περιοδικό «Αρχεία Κλινικής Νευρολογίας» και σε ηλεκτρονική έκδοση συμπληρώστε την ηλεκτρονική σας διεύθυνση:*

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Σημειώσεις

Σημειώσεις

Σημειώσεις

Οδηγίες προς τους συγγραφείς

Το περιοδικό *ΑΡΧΕΙΑ ΚΛΙΝΙΚΗΣ ΝΕΥΡΟΛΟΓΙΑΣ* κυκλοφορεί κάθε δύο μήνες και αποτελεί το επίσημο όργανο της Ελληνικής Νευρολογικής Εταιρείας. Με την Υπουργική Απόφαση ΔΥ2α/Γ.Π.οικ. 66198/1/6/2006, που δημοσιεύθηκε στο Φ.Ε.Κ. 1034/Β/1-08-2006, προστέθηκε στον κατάλογο των περιοδικών με Εθνική Αναγνώριση.

Ύλη του Περιοδικού

1. Ανασκοπικά Άρθρα: Η έκτασή τους δεν πρέπει να υπερβαίνει τις 6.000 λέξεις.
2. Εργασίες: Κλινικές ή εργαστηριακές μελέτες. Δεν πρέπει να υπερβαίνουν τις 4.000 λέξεις (συμπεριλαμβανομένων έως 6 πινάκων και εικόνων). Δεν πρέπει να έχει προηγηθεί δημοσίευσή τους σε άλλο έντυπο. Περιλαμβάνουν σελίδα τίτλου, δομημένη περίληψη, εισαγωγή, μέθοδο, αποτελέσματα, συζήτηση και βιβλιογραφία.
3. Σύντομες ανακοινώσεις και Γράμματα προς τη σύνταξη: Σχόλια για εργασίες που έχουν δημοσιευθεί ή σύντομες αναφορές σε ένα θέμα. Δεν πρέπει να υπερβαίνουν τις 1.500 λέξεις και περιλαμβάνουν έως 2 πίνακες ή εικόνες.
4. Ενδιαφέροντα περιστατικά: Όριο λέξεων 1.500, με τη σελίδα τίτλου, περίληψη και τις βιβλιογραφικές αναφορές. Επιτρέπονται μέχρι 2 εικόνες ή πίνακες.
5. Νευρολογικές Εικόνες με εκπαιδευτικό ενδιαφέρον: Όριο 4 εικόνες για το ίδιο θέμα και 200 λέξεις.
6. Επιλογές και σχολιασμός της βιβλιογραφίας.
7. Νευρολογικά Νέα - Ειδήσεις - Ενημερωτικές Σελίδες, όπως νέα της Ελληνικής Νευρολογικής Εταιρείας και συγγενών εταιρειών, ανακοινώσει συνεδρίων και άλλων εκπαιδευτικών δραστηριοτήτων.

Δομή της ύλης

Γίνονται δεκτές εργασίες στα ελληνικά ή αγγλικά.
Υποβάλλεται πάντοτε ο τίτλος, τα ονόματα των συγγραφέων και η περίληψη και στα αγγλικά.
Τα κείμενα θα πρέπει να αποστέλλονται σε μορφή Microsoft Word document.
Σελίδα τίτλου: Περιέχει τον τίτλο, τα πλήρη ονόματα των συγγραφέων, το ίδρυμα προέλευσης, τη διεύθυνση και το τηλέφωνο του υπευθύνου για την αλληλογραφία και τον καταμετρημένο αριθμό λέξεων.
Περίληψη: Παρουσιάζει τα κυριότερα σημεία της εργασίας. Δεν πρέπει να υπερβαίνει τις 250 λέξεις. Στο τέλος της παρατίθενται 3-10 λέξεις ευρετηρίου.
Αγγλική περίληψη: Παρουσιάζει σε συντομία την εργασία. Η έκτασή της είναι ως 400 λέξεις. Στην αρχή της γράφονται τα ονόματα των συγγραφέων και ο τίτλος της εργασίας στα αγγλικά.
Λέξεις-κλειδιά: έως 6 λέξεις κλειδιά.
Βιβλιογραφία: Οι βιβλιογραφικές παραπομπές αριθμούνται με αύξοντα αριθμό ανάλογα με τη σειρά εμφάνισής τους στο κείμενο (Vancouver). Όλες οι βιβλιογραφικές παραπομπές να αναφέρονται μέσα σε αγκύλες. Π.χ. Ο Smith [1] ανέφερε ότι ... και τα ευρήματα αυτά επιβεβαιώθηκαν από τον Adams και συν [2]. Αναγράφονται έως και οι 6 πρώτοι συγγραφείς. Στον πίνακα της βιβλιογραφίας περιλαμβάνονται μόνο εκείνες οι βιβλιογραφικές παραπομπές που αναφέρονται στο κείμενο και ο πίνακας συντάσσεται με αύξοντα αριθμό που αντιστοιχεί στη σειρά εμφάνισης των βιβλιογραφικών παραπομπών στο κείμενο π.χ.
Πίνακες: Γράφονται σε ξεχωριστή σελίδα, μετά το τέλος των βιβλιογραφικών αναφορών. Αριθμούνται με τη σειρά εμφάνισής τους στο κείμενο και συνοδεύονται από σύντομη επεξήγηση.
Εικόνες: Αποστέλλονται τα πρωτότυπα σχέδια ή φωτογραφίες καλής ποιότητας. Να υποβάλλονται σαν αρχεία εικόνας ξεχωριστά από το κείμενο του MS Word. Αριθμούνται με τη σειρά εμφάνισης στο κείμενο. Στο κείμενο θα πρέπει να υπάρχει σαφής παραπομπή στον τίτλο των ηλεκτρονικών αρχείων. Σε ξεχωριστή σελίδα αναγράφονται οι τίτλοι των εικόνων και οι τυχόν επεξηγήσεις.
Ιατρική Δεοντολογία: Σε περιπτώσεις ερευνών που αφορούν ανθρώπους, η έρευνα πρέπει να έχει γίνει με βάση τη διακήρυξη του Ελσίνκι (1975). Σε περιπτώσεις φωτογραφιών ασθενών, θα πρέπει να υπάρχει έγγραφη συγκατάθεση.

Συνοδευτικό έντυπο υποβαλλόμενης εργασίας

Θα πρέπει να συμπληρωθούν ΟΛΑ τα σημεία του εντύπου. Άλλη συνοδευτική επιστολή δεν είναι απαραίτητη.

Είδος άρθρου (σημειώστε μόνο ένα)

❑ Ερευνητική εργασία ❑ Βραχεία εργασία - ενδιαφέρον περιστατικό ❑ Ανασκόπηση

❑ Βραχεία ανασκόπηση ❑ Ειδικό άρθρο ❑ Γράμμα στη σύνταξη ❑ Νευρο-εικόνες

Τίτλος:

Υπεύθυνος για την αλληλογραφία συγγραφέας:

Διεύθυνση:

Τηλέφωνο: FAX: e-mail:

Επιβεβαιώστε την πληρότητα της υποβολής του χειρογράφου σας, σημειώνοντας ΟΛΑ τα παρακάτω σημεία

- ❑ Τίτλος του άρθρου στα Ελληνικά και στα Αγγλικά με μικρά γράμματα
- ❑ Ονόματα συγγραφέων στα Ελληνικά και στα Αγγλικά *(πλήρη ονόματα π.χ. Νικόλαος Παπαδόπουλος)*
- ❑ Κέντρο προέλευσης της εργασίας στα Ελληνικά και στα Αγγλικά
- ❑ Δομημένη περίληψη στα Ελληνικά και στα Αγγλικά
- ❑ Έως πέντε λέξεις ευρετηριασμού *(κατά προτίμηση από το MeSH Hellas-Βιοϊατρική Ορολογία)* στα Ελληνικά και στα Αγγλικά
- ❑ Όλα τα ονόματα των συγγραφέων στις βιβλιογραφικές παραπομπές (*μέχρι 6 και στη συνέχεια* «*και συν.*» *ή* «*et al*»)
- ❑ Η βιβλιογραφία στις τελευταίες σελίδες των άρθρων

Δήλωση

Δηλώνω υπεύθυνα ότι:

1. Όλοι οι συγγραφείς της εργασίας συμφωνούν με το περιεχόμενό της και με την υποβολή της στο περιοδικό: *Αρχεία Κλινικής Νευρολογίας.*
2. Το ίδιο κείμενο ή τα αποτελέσματα της εργασίας δεν έχουν υποβληθεί για δημοσίευση σε άλλο Ελληνικό ή ξένο περιοδικό.
3. Δηλώνω υπεύθυνα ότι δεν υπάρχει θέμα υποκλοπής πνευματικής ιδιοκτησίας (σε περίπτωση εικόνων, πινάκων ή υλικού από άλλες δημοσιεύσει έχει ζητηθεί και ληφθεί η νόμιμη άδεια η οποία και συνυποβάλλεται).
4. Δεν υπάρχουν θέματα σύγκρουσης συμφερόντων – σε περίπτωση εξωτερικής χρηματοδότησης αυτό θα πρέπει να αναφέρεται στο τέλος της εργασίας.

Ο υπεύθυνος για την αλληλογραφία συγγραφέας

(υπογραφή)