Η Θεραπευτική Πλασμαφαίρεση και Νευρολογικά Νοσήματα: η άποψη του Νευρολόγου

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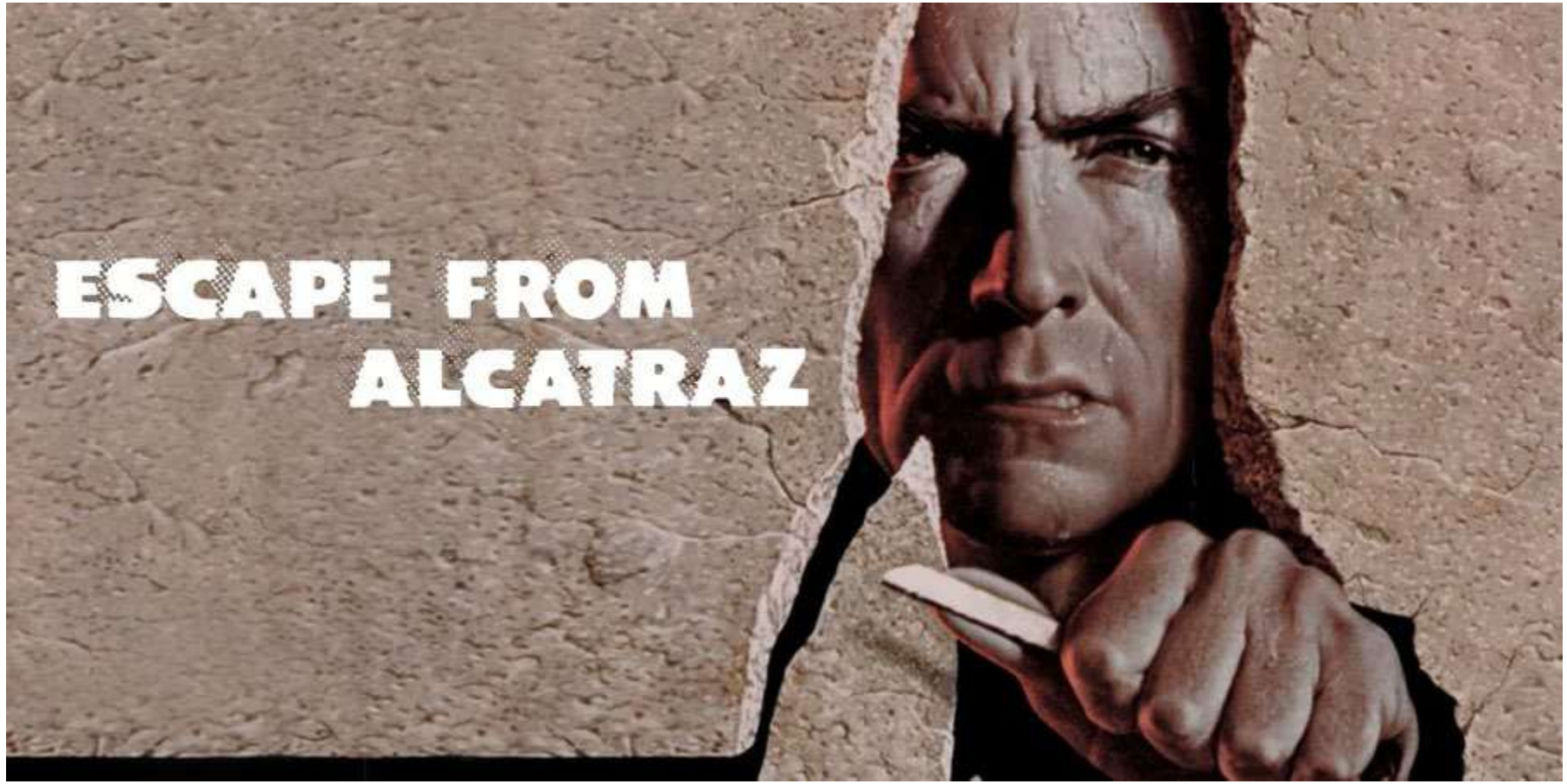


ΘΕΡΑΠΕΙΑ ΑΠΟΔΡΑΣΗΣ-ΔΙΑΦΥΓΗΣ

ΘΕΡΑΠΕΙΑ ΔΙΑΣΩΣΗΣ

Ιστορική αναδρομή

- 1914 Περιγραφή της μεθόδου από τον John Jacob Abel
- 1952: Πρώτη χρησιμοποίηση της πλασμαφαίρεσης για την αντιμετώπιση της υπεργλοιότητας σε ασθενή με πολλαπλό μυέλωμα.
- 1960΄: Ευρεία αποδοχή ως θεραπεία της υπεργλοιότητας
- 1976: αναφορά ως πιθανή θεραπεία για μυασθένεια
- 1978: πρώτη χρησιμοποίηση ως θεραπεία για το σύνδρομο Guillain Barre
- 1980΄- : καθιέρωση της πλασμαφαίρεσης ως αποτελεσματικής θεραπείας για το σύνδρομο Guillain Barre και τη μυασθένεια και σταδιακή προσθήκη και νέων ενδείξεων.

- ΑΥΞΗΜΕΝΟ ΠΟΣΟΣΤΟ ΝΕΥΡΟΑΝΟΣΟΛΟΓΙΚΩΝ ΝΟΣΗΜΑΤΩΝ που μπορούν ταχέως να εξελιχθούν και να προκαλέσουν απειλητικές για τη ζωή κλινικές καταστάσεις.

- ΘΕΡΑΠΕΙΑ ΔΙΑΦΥΓΗΣ-ΔΙΑΣΩΣΗΣ

- ΣΕ ΑΠΟΤΥΧΙΑ ΘΕΡΑΠΕΙΩΝ ΠΡΩΤΗΣ ΓΡΑΜΜΗΣ ή ΜΕΧΡΙ ΝΑ ΔΡΑΣΟΥΝ ΑΛΛΕΣ ΘΕΡΑΠΕΙΕΣ.

- ΔΙΑΘΕΣΙΜΟΤΗΤΑ IVIG και ΑΝΤΕΝΔΕΙΞΕΙΣ ΣΕ ΑΥΤΉ.

TABLE 1 Category and grade recommendations for therapeutic apheresis.

Disease/condition	Indication	Procedure	Category	Grade
Acute disseminated encephalomyelitis	Steroid refractory	TPE	II	2C
Acute inflammatory demyelinating polyradiculoneuropathy	Primary treatment	TPE	I	1A
		IA	I	1B
Chronic acquired demyelinating polyneuropathies	IgG/IgA/IgM related	TPE	I	1B
	Anti-myelin-associated glycoprotein	TPE	III	1C
	CANOMAD/CANDA[a]	TPE	III	2C
Chronic focal encephalitis		TPE/IA	III	2C
Chronic inflammatory demyelinating polyradiculoneuropathy		TPE/IA	I	1B
Multiple sclerosis	Acute attack/relapse	TPE	II	1A
		IA	II	1B
	Chronic primary or secondary progressive	TPE/IA	III	2B
Myasthenia gravis	Acute, short-term treatment	TPE/DFPP/IA	I	1B
	Long-term treatment	TPE/DFPP/IA	II	2B
Neuromyelitis optical spectrum disorder	Acute attack/relapse	TPE	II	1B
		IA	II	1C
	Maintenance	TPE	III	2C
N-methyl-D-aspartate receptor antibody encephalitis		TPE/IA	I	1C

L. Connely-Smith etal. Guidelines on the use of theurapeutic Apheresis in Clinical Practice. The Ninth Special Edition. J Clin Apher.2023;38.77-278

Voltage-gated potassium channel antibody-related diseases		TPE/IA	II	1B
Idiopathic inflammatory myopathies[a]	Anti-synthetase-syndrome	TPE	III	2B
	Clinically amyopathic dermatomyositis	TPE	III	2B
	Immune-mediated necrotizing myopathies	TPE	III	2B
Steroid-responsive encephalopathy associated with autoimmune thyroiditis		TPE	II	2C
Stiff-person syndrome		TPE	III	2C
Immune checkpoint inhibitors, immune-related adverse events[a]		TPE	III	2C
Alzheimer's disease[a]	Mild or moderate	TPE	III	2A
Paraneoplastic neurological syndromes		TPE/IA	III	2C
Pediatric autoimmune neuropsychiatric disorders	PANDAS/PANS, exacerbation	TPE	II	1B
	Sydenham's chorea, severe	TPE	III	2B
Progressive multifocal leukoencephalopathy associated with natalizumab		TPE	III	1C
Lambert-Eaton myasthenic syndrome		TPE	II	2C
Autoimmune dysautonomia[a]		TPE	III	2C

L. Connely-Smith etal. Guidelines on the use of theurapeutic Apheresis in Clinical Practice. The Ninth Special Edition. J Clin Apher.2023;38.77-278

Μηχανισμός Δράσης

ΜΗΧΑΝΙΣΜΟΙ ΔΡΑΣΕΙΣ

Fig 1. Possible mechanisms of plasma exchange. (A) Removal of pathological antibodies. (B) Stimulates the proliferation of B cells and plasma cells, sensitizing them to immunosuppressants. (C) Removal of immune complexes with enhanced macrophage/monocyte function. (D) Replacement of missing plasma components, such as ADAMTS13 (a disintegrin and metalloprotease with thrombospondin type 1 motifs 13). (E) Removal of cytokines. (F) Changes in lymphocyte numbers. (G) Increased T regulatory cells and T suppressor activity. (H) Correction of altered T-helper cell type 1/2 (Th1/Th2) ratio favouring Th1 predominance.

H M. Reeves et al. British Journal of Haematology , 2014, 164, 342–351

ΜΥΑΣΘΕΝΕΙΑ

- Επίπτωση 7-23/1000000
- Παρουσία αντισωμάτων που παρεμβαίνουν στην λειτουργία της νευρομυικής σύναψης (anti-AchR 85%, anti-Musk 8%, anti-LRP4 1%).

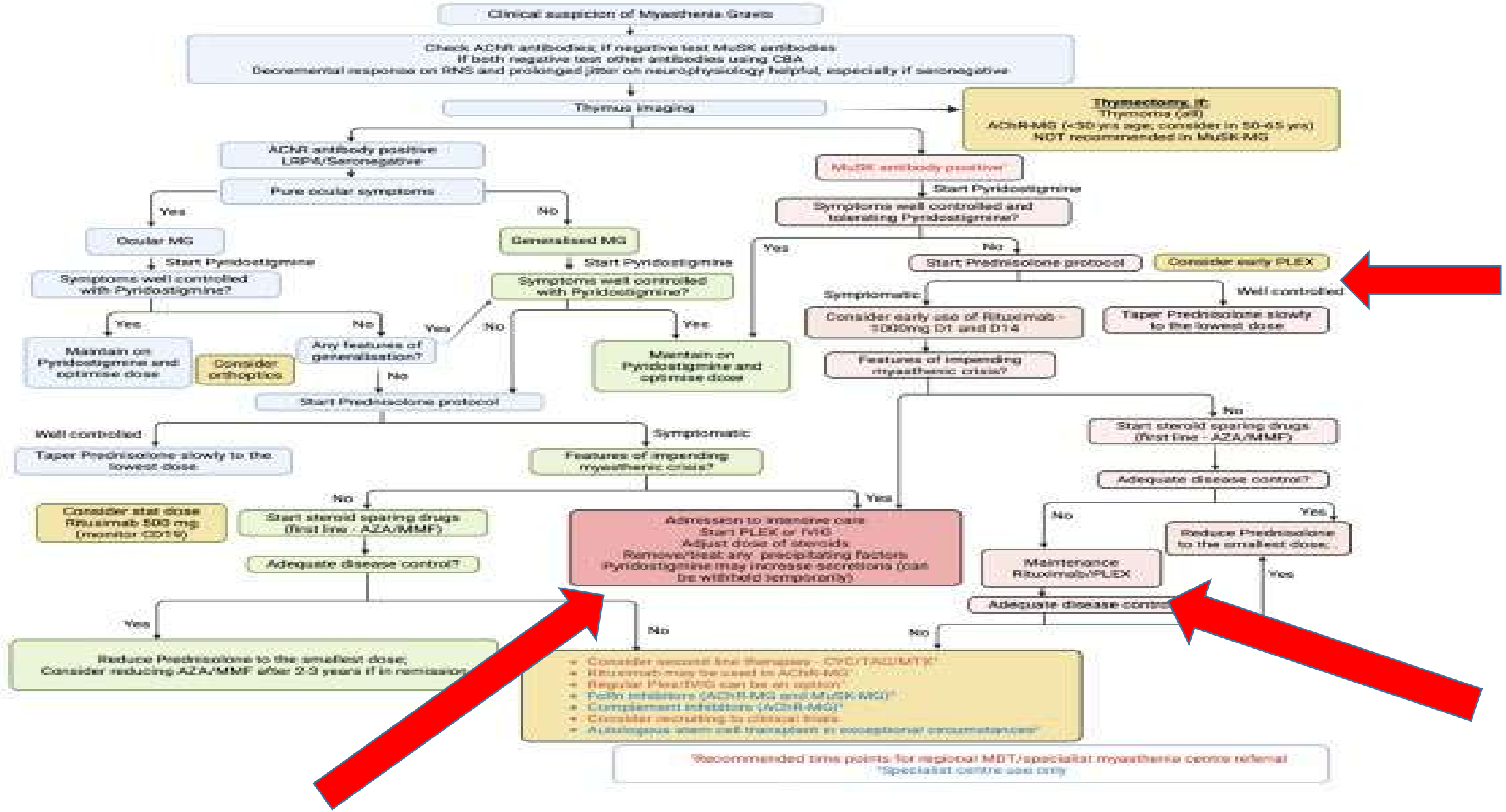
ΜΥΑΣΘΕΝΕΙΑ

- Η ΠΛΑΣΜΑΦΑΙΡΕΣΗ ΕΧΕΙ ΕΝΔΕΙΞΗ ΣΤΗΝ ΜΥΑΣΘΕΝΙΚΗ ΚΡΙΣΗ, ΣΤΗΝ ΥΠΟΤΡΟΠΗ ΜΕ ΓΕΝΙΚΕΥΜΕΝΗ ΑΔΥΝΑΜΙΑ ΚΑΙ ΠΡΟΜΗΚΙΚΗ ΣΥΜΜΕΤΟΧΗ, ΣΕ ΠΡΟΕΓΧΕΙΡΗΤΙΚΗ ΠΡΟΕΤΟΙΜΑΣΙΑ ΓΙΑ ΘΥΜΕΚΤΟΜΗ.

- ΣΥΝΗΘΩΣ 4-6 ΣΥΝΕΔΡΙΕΣ ΠΛΑΣΜΑΦΑΙΡΕΣΗΣ σε 10 με 14 ημέρες

- ΣΥΝΟΛΙΚΑ 1-1,5 TPV

- ΣΠΑΝΙΟΤΕΡΑ ΜΠΟΡΕΙ ΝΑ ΧΡΗΣΙΜΟΠΟΙΗΘΕΙ ΚΑΙ ΣΑΝ ΘΕΡΑΠΕΙΑ ΣΥΝΤΗΡΗΣΗΣ ΣΕ ΑΝΘΕΚΤΙΚΕΣ ΜΟΡΦΕΣ ΠΟΥ ΔΕΝ ΑΝΤΑΠΟΚΡΙΝΟΝΑΙ ΣΕ ΑΛΛΕΣ ΘΕΡΑΠΕΙΕΣ



Jacob S, Farrugia ME, Hewamadduma C, et al. Pract Neurol 2025;25:422–437

Table 1 Summary of the most commonly used medication in myasthenia gravis effective within days

Effective within days					
Medication	**Usual adult dose**	**Common side effects**	**Caution/monitoring**	**Notes**	**Level of evidence**
Pyridostigmine	Start at 30 mg TDS to QDS, slowly titrate up to 360 mg/day	Muscle/abdominal cramps, diarrhoea, increased salivation, bladder urgency	Bradycardia, asthma, heart disease	Propantheline 15 mg TDS to QDS may be used to counteract cholinergic side effects.	Clinical practice
Intravenous immunoglobulin	1 g/kg or 2 g/kg in divided doses over 2–5 days	Headache (aseptic meningitis) and raised blood pressure; rarely skin rash and transaminitis	Venous thromboembolism prophylaxis may be necessary.	May be repeated monthly. Use as maintenance therapy is exceptional.	Clinical practice; RCT
Plasma exchange	Four to five exchanges	Hypocalcaemia symptoms during infusion (due to EDTA use). Haemodynamic instability	Caution in anticoagulation, active sepsis or pregnancy	May be repeated monthly. Use as maintenance therapy is exceptional.	Clinical practice; Case series; RCT
Efgartigimod*	10 mg/kg once weekly if intravenously (max. per dose 1.2 g) for 4 weeks; subcutaneous dose is 1000 mg (for all patients) weekly for 4 weeks. Repeated if necessary as per MG-ADL scores (usually at least 3 weeks after the last dose of previous cycle).	Transient IgG depletion		Not routinely available – specialist initiation only	DBRCT
Zilucoplan*	Daily s/c dose adjusted for body weight. Range 16.6 mg to 32.4 mg daily	Injection site reactions	Need meningococcal vaccination	Not routinely available – specialist initiation only	DBRCT
Rozanolixizumab	280–840 mg (as per body weight) once weekly for 6 weeks, subsequent 6-week treatment cycles to be administered according to clinical evaluation	Angioedema, arthralgia, increased risk of infections		Not routinely available – specialist initiation only	DBRCT

*Some of the potentially effective therapies include calcineurin inhibitors (ciclosporin, tacrolimus), neonatal Fc gamma receptor blockers (eg, efgartigimod, rozanolixizumab), C5 complement inhibitors (eg, eculizumab, ravulizumab, zilucoplan) and alkylating chemotherapy agents (eg, cyclophosphamide). From the newer class of medications, only efgartigimod, rozanolixizumab and zilucoplan are mentioned above since these drugs are most familiar to the authors outside a clinical trial. This does not mean that these are the only drugs available or these are in any way superior to other drugs with similar mechanisms of action. We recommend discussion with an MG specialist in advance of starting these agents.

ADL, activities of daily living; DBRCT, double-blind RCT; MG, myasthenia gravis; OD, once daily; QDS, four times a day; RCT, randomised controlled trial; s/c, subcutaneous; TDS, three times a day.

Jacob S, Farrugia ME, Hewamadduma C, et al. Pract Neurol 2025;25:422–437

Features of impending myasthenic crisis

- Worsening breathlessness
- Progressive drop in FVC
- FVC less than 20ml/kg
- Frequent choking
- Severe dysarthria
- Significant neck drop

- Admit to HDU/ICU
- Monitor - FVC, NIP, PEP
- Identify and treat exacerbating factors

Predictors of Intubation

- VC <15ml/kg
- NIP<30 cm H_2O
- PEP>40 cm H_2O
- Severe bulbar failure
- Inability to manage secretions
- Hypercarbia
- Increasing fatigue
- Evidence of aspiration
- Atelectasis

(Decision to intubate should be a clinical one)

- Start PLEX early (IVIG if PLEX unavailable)
- Increase Prednisolone to 1mg/kg (max 60mg)
- Chest physiotherapy
- High flow nasal oxygen
- NG feeding to maintain calorie intake
- Correction of electrolyte disturbance
- Avoid over correction of magnesium
- Be aware of increased secretions with Pyridostigmine

Factors favouring extubation

- Low secretion volume
- Comfortable with spontaneous breathing trials
- Preserved neck muscle strength
- VC >15ml/kg
- Absence of atelectasis

HFNO and NIV may help with extubation
Physio and SLT crucial after extubation

Myasthenia Gravis (MG)				
Dau et al. 1977	Case series of five patients	5	5	100% (striking clinical improvement observed in all five patients)
Newsom-Davis et al. 1979	Study evaluating long-term effects of PLEX	7	7	100%
Gajdos et al. 1997	Randomized clinical trial evaluating IVIg and PLEX	41	41	63%
Barth et al. 2011	Comparison of IVIg and PLEX in MG	43	43	57%
Makroo et al. 2008	Retrospective study comparing IVIg and PLEX	19	19	84%
Kumar et al. 2015	Retrospective study	35	35	100%

S Jacob et al. Journal of Neuroimmune Pharmacology (2021)16:806–817

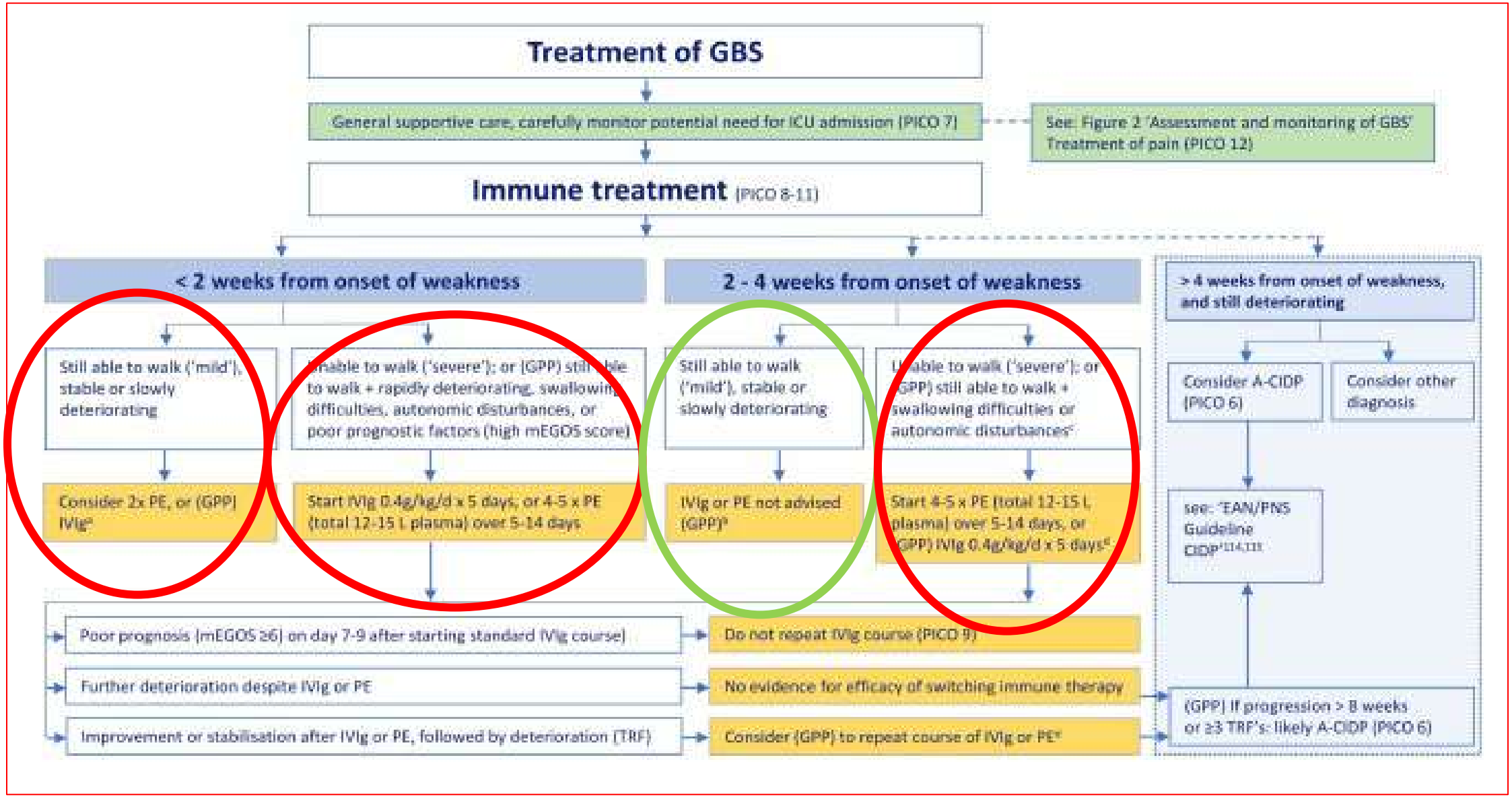
ΣΥΝΔΡΟΜΟ GUILLAIN BARRE

- Επίπτωση 1-2/100000/έτος
- AIDP (acute inflammatory demyelinating polyneuropathy) έως 90%
- AMAN (acute motor axonal neuropathy)
- AMSAM (acute motor sensory axonal neuropathy)
- Miller Fischer
- Acute Autonomic Neuropathy

- Συνήθως προηγείται λοίμωξη ή άλλη ανοσολογική διέγερση-μηχανισμός μοριακής μίμησης
- Εξέλιξη στην μέγιστη αναπηρία από 24 ώρες μέχρι 4 εβδομάδες
- Θνησιμότητα 3-5%

ΣΥΝΔΡΟΜΟ GUILLAIN BARRE

- **ΕΝΔΕΙΞΗ ΩΣ ΕΠΕΙΓΟΥΣΑ ΘΕΡΑΠΕΙΑ ΑΝΤΙΜΕΤΩΠΙΣΗΣ** και θα πρέπει να προσφέρεται ιδανικά στις πρώτες 7 ημέρες από την έναρξη της νόσου (Chevret 2017).
- ΣΥΝΗΘΩΣ 4-6 ΣΥΝΕΔΡΙΕΣ ΠΛΑΣΜΑΦΑΙΡΕΣΗΣ σε 10 με 14 ημέρες (κάποιοι ασθενείς μπορεί να χρειαστούν και επαναληπτικές συνεδρίες)
- ΣΥΝΟΛΙΚΑ 1-1,5 TPV
- Ισοδύναμη με την IVIG (σε μελέτη του 1997 ο μέσος χρόνος ανεξάρτητης βάδισης σε ασθενείς με GB και TPE ήταν 49 ημέρες, με IVIG 51 ημέρες και σε TPE/IVIG 40 ημέρες.
- Στην Ινδία περισσότερο cost effective από την IVIG (Maheshwari 2018).



PA van Doorn et al. Eur J Neurol. 2023;30:3646–3674.

Recommendations

- The TF strongly recommends starting PE as soon as possible inGBS patients unable to walk unaided (GBS- DS grade 3 or more) and within 4 weeks from onset.
- The TF strongly recommends four to five exchanges over 1– 2 weeks with a total exchanged volume of 12– 15 L in patients
- The TF weakly recommends two exchanges in GBS patients still able to walk unaided but who cannot run (GBS- DS grade 2) within the first 2 weeks from onset of weakness.

Good practice points

- The TF advises PE (four to five exchanges over 1– 2 weeks) also in patients who are still ambulatory, but who have a fast rate of deterioration, a risk of requiring ventilatory support, swallowing difficulties or other poor prognostic factors. These patients are considered at high risk of further deterioration, which may potentially be prevented by starting treatment early (PICO 7 and 14).
- The TF does not advise to start PE (a) in very mildly affected patients (GBS- DS grade 1) with stable disease within the first 2 weeks from onset of weakness; (b) in patients still mildly affected (GBS- DS grade 1 or 2) at weeks 2– 4 from onset of weakness. It is considered unlikely that these patients will further deteriorate to a higher GBS- DS grade within the time frame of progression of GBS (max 4 weeks).

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PA van Doorn et al. Eur J Neurol. 2023;30:3646–3674.

CIDP

- Επίπτωση 1-10/100000
- Επίκτητη αυτοάνοση νευροπάθεια. Τυπική εικόνα στο 50-60% των περιπτώσεων με συμμετρική αισθητικοκινητική πολυνευροπάθεια με προοδευτική πορεία ή πορεία με εξάρσεις και υφέσεις.
- Αρχικά δεν διαφέρει από την AIDP.
- Παραλλαγές (MADSAM, DADS, pure motor, pure sensory)
- 3 πρώτης γραμμής θεραπείες: κορτιζόνη, TPE και IVIG
- Μεγάλη ετερογένεια ασθενών και ανοσολογικών μηχανισμών και άρα απαντήσεων στην φα (πχ στις κομβοπάθειες από αντισώματα neurofascin 155,140, 186, contactin 1, caspr 1 –υποκλάση IgG4 – δεν ανταποκρίνονται στην IVIG

CIDP

- Σε μελέτες έχει καταδειχθεί είτε η υπεροχή της πλασμαφαίρεσης έναντι του placebo (Dyck 1986, Hahn 1996) είτε η ισοδυναμία της με την IVIG (Dyck 1994)

Dyck PJ, Daube J, O'Brien P, et al. Plasma exchange in chronic inflammatory demyelinating polyradiculoneuropathy. *N Engl J Med*. 1986; 314:461-465.

Dyck PJ, Litchy WJ, Kratz KM, et al. A plasma exchange versus immune globulin infusion trial in chronic inflammatory demyelinating polyradiculoneuropathy. *Annals Neurol*. 1994;3:838-845.

Hahn AF, Bolton CF, Pillay N, et al. Plasma-exchange therapy in chronic inflammatory demyelinating polyneuropathy. A double-blind, sham-controlled, cross-over study. *Brain*. 1996;119:1055-1066.

CIDP

- ΟΔΗΓΙΕΣ **European Academy Neurology-Peripheral Nerve Society**

- Ισχυρή σύσταση για έναρξη πλασμαφαιρέσεων (5 συνεδρίες 1-1.5 TPV σε 2 εβδομάδες και εν συνέχεια εξατομίκευση).
- Εάν είναι δυνατόν να χρησιμοποιηθούν περιφερικές φλέβες.
- Λόγω των απαιτήσεων σε αγγειακή πρόσβαση την κατατάσσουν στην τρίτη επιλογή για μακρά θεραπεία μετά την κορτιζόνη και την γ-σφαιρίνη.

PYK Van den Bergh etal,Eur J Neurol. 2021 Nov;28(11):3556-3583. doi: 10.1111/ene.14959

Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)				
Mehndiratta et al. 2015	Cochrane literature review, presenting results of two randomized controlled trials	47	47	33–66%
Mahdi-Rogers and Hughes 2014	Cross-sectional study	12	12	42%
Cocito et al. 2010	Retrospective analysis	16	16	56%
Lieker et al. 2017	Prospective study; comparison of PLEX and tryptophan immunoadsorption	9	9	44%

S Jacob et al. Journal of Neuroimmune Pharmacology (2021)16:806–817

Άλλες επίκτητες απομυελινωτικές πολυνευροπάθειες

- Σχετίζονται με αντισώματα IgA, IgM, IgG, anti-MAG,
- CANOMAD (chronic ataxic neuropathy, opthalmoplegia, IgM paraprotein, cold agglutinins and disialosyl antibodies)
- CANDA (chronic ataxic neuropathy with disialosyl antibodies)
- POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonic gammopathy, Skin changes)
- 10% ασθενών με ιδιοπαθείς πολυνευροπάθειες ανιχνεύονται με μονοκλωνικό κλάσμα (η πλειονότητα MGUS)
- Σε λεμφοϋπερπλαστικά σύδνρομα όπως μακροσφαιριναιμία Walderstrom, ανιχνεύεται >50% IgM γαμμοπάθεια.

Άλλες επίκτητες απομυελινωτικές πολυνευροπάθειες

- Σε διπλή τυχαιοποιημένη μελέτη (Dyck et al Plasma exchange in polyneuropathy associated with monoclonal gammopathy of undetermined significance. N Engl J Med. 1991;325:1482-1486) η πλασμαφαίρεση (2 συνεδρίες εβδομαδιαίως για 3 εβδομάδες) βελτίωσε την κλίμακα αναπηρίας νευροπάθειας και το συνολικό ύψος των κινητικών δυναμικών (summed CMAP) αλλά όχι και στις ταχύτητες αγωγής και τα ύψη των αισθητικών δυναμικών.

- Μεγαλύτερη αποτελεσματικότητα στις γαμμοπάθειες από IgA και IgG (class I evidence, type A recommendation).

H C. Lehmann et al. ArchNeurol.2006;63:1066-1071

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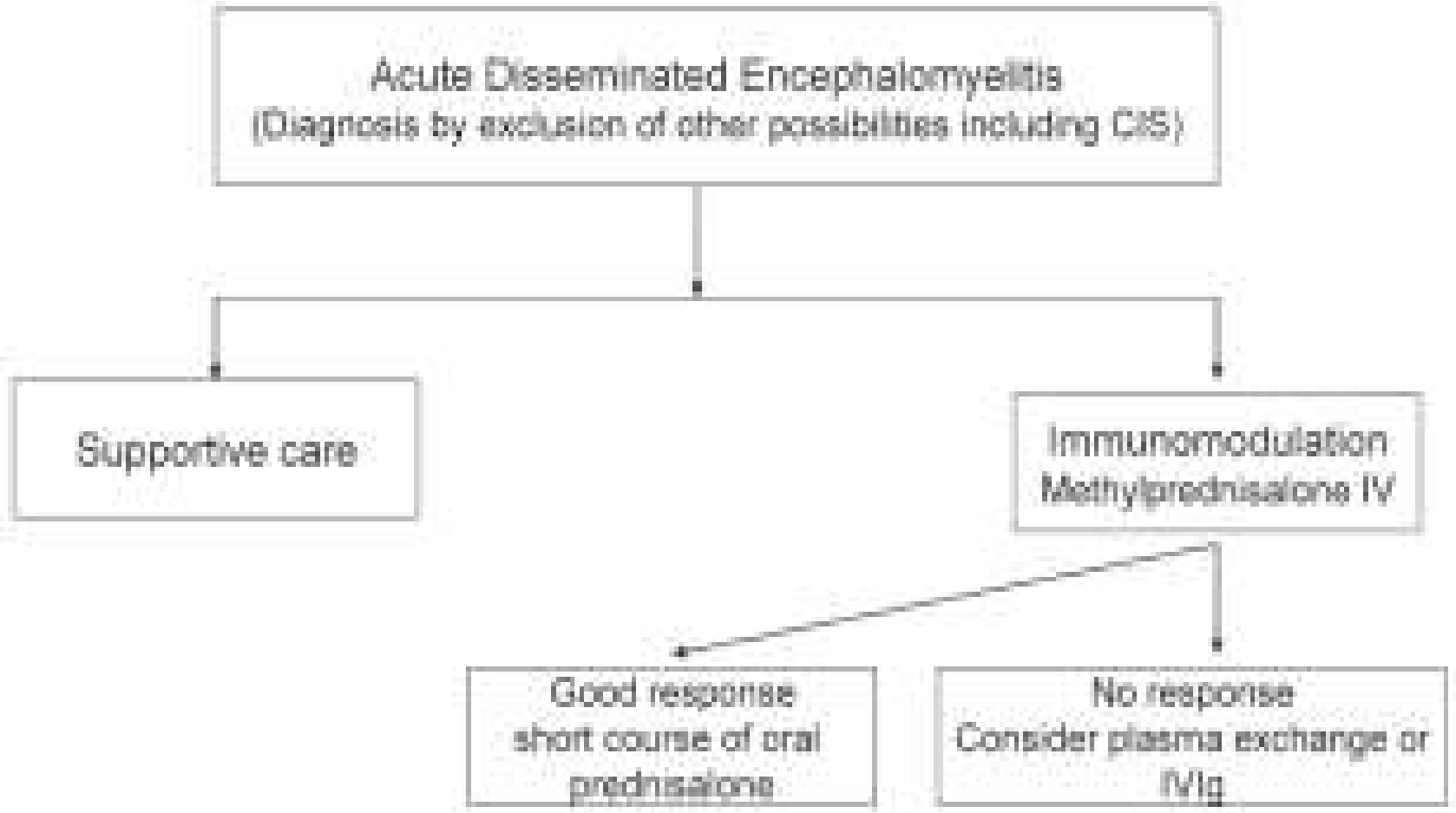
(ΟΞΕΙΑ ΔΙΑΣΠΑΡΤΗ ΕΓΚΕΦΑΛΟΜΥΕΛΙΤΙΔΑ

- Οξεία μονοφασική απομυελινωτική προσβολή του ΚΝΣ.
- Συνήθως προηγείται λοιμώδης προσβολή
- Πιο συχνή σε παιδιά (<1/100.000/έτος)
- Μοριακή μίμηση-επίθεση σε πρωτείνες: MOG (myelin associated protein), MBP (Myelin Basic Protein)
- Έναρξη εντός ημερών ή εβδομάδων από τη λοίμωξη
- Πολυεστιακή σημειολογία και συμπτωματολογία, πυρετός, δυσκαμψία.

Alexander M., J. M. K. Murthy. Annals of Indian Academy of Neurology 2011;14:60-4.

ADEM
(ΟΞΕΙΑ ΔΙΑΣΠΑΡΤΗ ΕΓΚΕΦΑΛΟΜΥΕΛΙΤΙΔΑ

- Η πλασμαφαίρεση απομακρύνει τα αντισώματα.
- Ένδειξη ως δεύτερης γραμμής θεραπεία μετά από αποτυχία των κορτικοστεροειδών ή και της γ-σφαιρίνης.
- Παρημέρα συνεδρίες - τουλάχιστον 5 με 7 σε αρχική φάση.
- Καλοί προγνωστικοί δείκτες: ανδρικό φύλο, διατήρηση των τενόντιων αντανακλάσεων, έγκαιρη έναρξη πλασμαφαιρέσεων.


Acute Disseminated Encephalomyelitis
(Diagnosis by exclusion of other possibilities including CIS)
Supportive care
Immunomodulation
Methylprednisalone IV
Good response
short course of oral
prednisalone
No response
Consider plasma exchange or
IVIg

Σκλήρυνση κατά Πλάκας

- Ένδειξη σε ανθεκτικές στην κορτιζόνη ώσεις ή σε κακοήθεις υποτροπές με σοβαρά ελλείμματα κυρίως στην υποτροπιάζουσα μορφή (RRMS) μετά την αποτυχία των κορτικοστεροειδών.
- Άμεσο όφελος από την απομάκρυνση αντισωμάτων και ανοσοσυμπλεγμάτων, ανακατανομή των ανοσολογικών κυττάρων και της ανοσολογικής απάντησης – καλύτερη ανταπόκριση στις πλάκες τύπου II που χαρακτηρίζονται από έντονη παρουσία ανοσοσφαιρινών και εναπόθεση συμπληρώματος (Stork et al. 2018).
- Πιθανή ένδειξη κατά τη διάρκεια της εγκυμοσύνης όπου οι υψηλές δόσεις κορτιζόνης μπορούν να βλάψουν το έμβρυο.

Multiple Sclerosis (MS)				
Correia et al. 2018	Retrospective cohort study. Patients had relapsing remitting MS (85%) or secondary progressive MS (15%)	46	46	80% responded after mean of 7.8 PLEX sessions (41%: complete recovery, 39%: partial recovery)
Stork et al. 2018	Retrospective cohort study evaluating apheresis in patients with three different histopathological patterns of MS	69	69	39% had moderate or marked therapy response within one month of apheresis
Rodriguez et al. 1993	Uncontrolled study of six cases	6	6	100%
Dau 1995	Study in 10 MS patients	10	10	90%
Ruprecht et al. 2004	Case series	10	10	70%
Keegan et al. 2005	Retrospective study	19	19	53%

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NMOSD & MOGAD

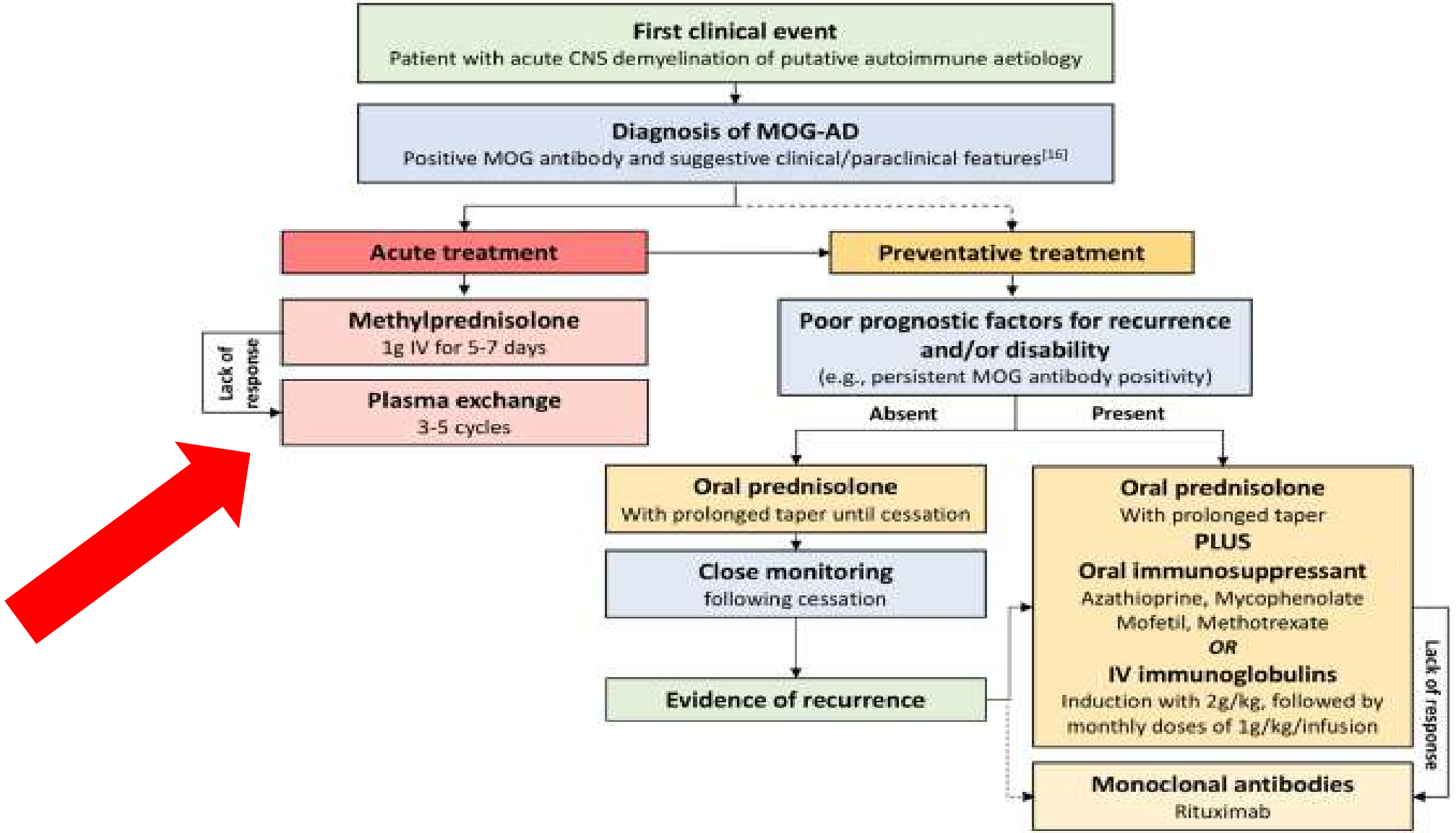
Neuromyelitis Optica Spectrum Disease
Myelin Oligodendrocyte Glycoprotein Antibodies Associated Disease

- Παρουσία αντισωμάτων IgG έναντι AQP4 ή και IgG-MOG.
- IgG-AQP4:προκαλούν κυτταροτοξικότητα εξαρτώμενη από το συμπλήρωμα στα αστροκύτταρα, διήθηση λευκοκυττάρων, απελευθέρωση κυτοκινών και διαταραχή του αιματοεγκεφαλικού φραγμού.Οδηγεί στο θάνατο των ολιγοδενδροκυττάρων, απώλεια μυελίνης και θάνατο νευρώνων.
- IgG-MOG: Απευθείας προσβολή της μυελίνης.
- Συνήθως διαλείπουσα πορεία.
- Θεραπεία 1^{ης} γραμμής: κορτικοστεροειδή +/- πλασμαφαίρεση (5 συνεδρίες σε 10 ημέρες)

Πλασμαφαίρεση σε NMOSD: ΤΟ ΝΩΡΙΤΕΡΟ ΤΟ ΚΑΛΥΤΕΡΟ

- Kleiter I, Gahlen A, Borisow N, et al. Apheresis therapies for NMOSD attacks: a retrospective study of 207 therapeutic interventions. Neurol Neuroimmunol Neuroinflamm 2018; 5:e504. Αναδρομική μελέτη αποτελεσματικοτητας της έγκαιρης πλασμαφαίρεσης στην θεραπεία εξάρσεων NMOSD.

- Bonnan M, Valentino R, Debeugny S, et al. Short delay to initiate plasma exchange is the strongest predictor of outcome in severe attacks of NMO spectrum disorders. J Neurol Neurosurg Psychiatry 2018; 89:346–351. Αναδρομική μελέτη αποτελεσματικοτητας της έγκαιρης πλασμαφαίρεσης στην θεραπεία εξάρσεων NMOSD
- Jiao Y, Cui L, Zhang W, et al. Plasma exchange for neuromyelitis optica spectrum disorders in Chinese patients and factors predictive of short-term outcome. Clin Ther 2018; 40:603–612.



Ray Wynford-Thomas et al. Journal of Neurology (2019) 266:1280–1286

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Miyamoto and Kusunoki 2009	Report of four patients with NMO who underwent plasmapheresis following intensive intravenous corticosteroid therapy	4	4	100%
Kleiter et al. 2016	Analysis of 871 attacks in 185 patients 142 NMO, 43 NMOSD. PE was chosen as first treatment course for 63 NMO attacks in 27 patients	27 patients 63 NMO attacks	27 patients 63 NMO attacks	30% of attacks: complete remission 51% of attacks: partial remission
Watanabe et al. 2007	Report of six patients with NMO who were unresponsive to high-dose intravenous methylprednisolone	6	6	50%
Abboud et al. 2016	Steroids alone versus steroids plus PLEX for the treatment of acute relapses in NMO	43 patients 65 NMO relapses	43 patients 65 NMO relapses	65%
Bonnan et al. 2018	PLEX initiation delay impact on the outcome of severe NMOSD attacks	60 114 NMO attacks	60 114 NMO attacks	50% for complete improvement if PLEX initiated within 1 day after the attack

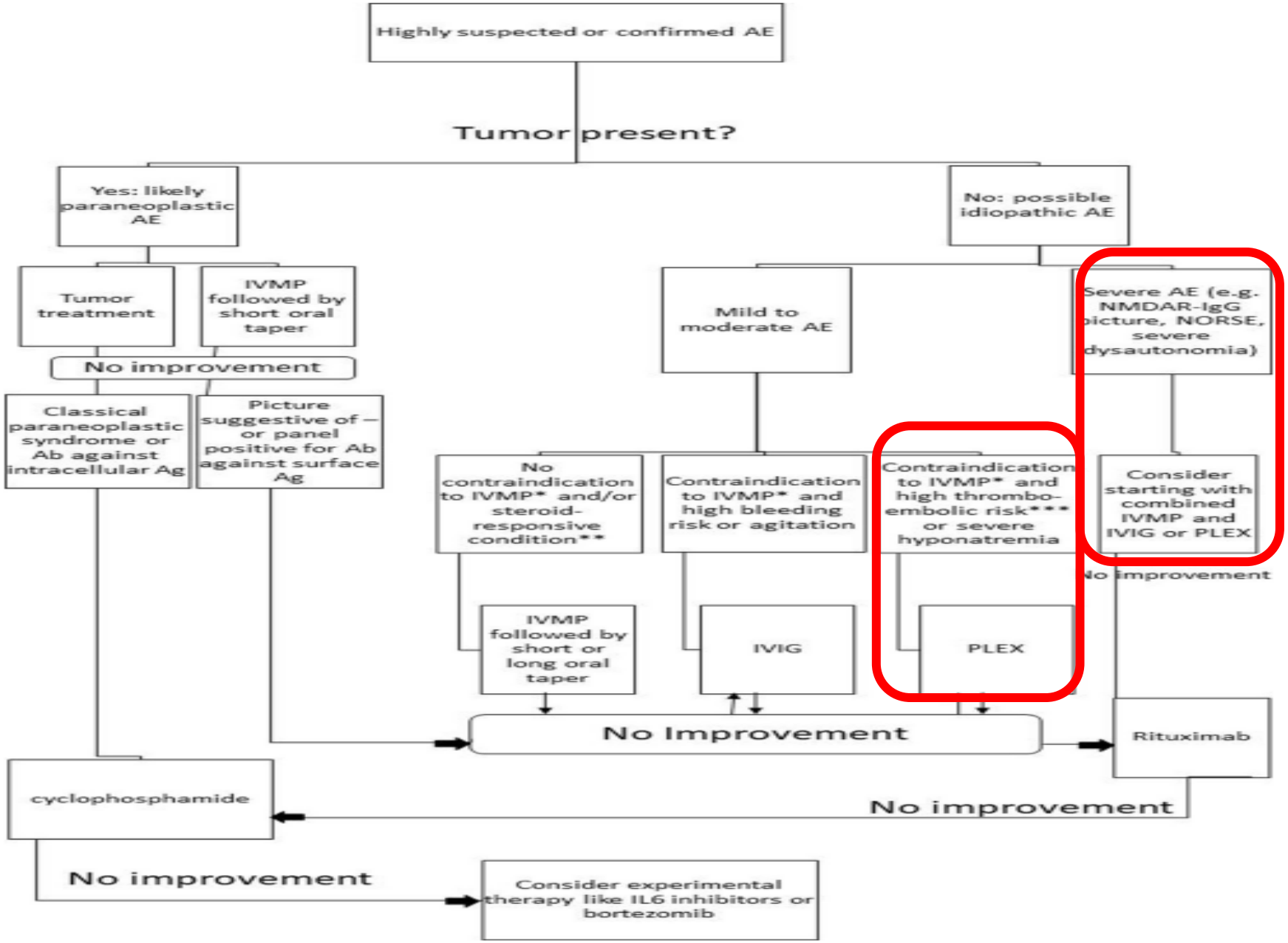
S Jacob et al. Journal of Neuroimmune Pharmacology (2021)16:806–817

ΑΥΤΟΑΝΟΣΗ ΕΓΚΕΦΑΛΙΤΙΔΑ

- Συχνότερη μορφή αυτή με παρουσία αντισωμάτων NMDAR και εμφάνιση σε παιδία ή νέους. Εκδήλωση με αυπνία και ψυχικά συμπτώματα όπως διαταραχές συμπεριφοράς, διέγερση, σπασμούς. Στη συνέχεια εμφανίζονται δυσκινησίες, διαταραχές αυτονόμου.
- Θεραπεία με κορτικοστεροειδή ή και πλασμαφαίρεση (5-12 συνεδρίες σε 3 εβδομάδες).
- Απάντηση στη πλασμαφαίρεση 65% σε αυτοάνοσες εγκεφαλίτιδες σε ανασκόπηση περιπτώσεων 120 ασθενών (Suppiej et al. 2016, DeSena et al. 2015).
- Το ποσοστό των ασθενών που βελτιώθηκαν μετά τη πλασμαφαίρεση ήταν 83% ανάμεσα σε αυτούς με επιφανειακά αντινευρωνικά αντισώματα και 66.7 % ανάμεσα σε αυτούς με αντισώματα σε συναπτικές περιοχές και 0% σε ασθενής με ενδοκυττάρια αντινευρωνικά αντισώματα. (Heine et al. 2016).

Table 2 Anatomical-clinical syndromes of autoimmune encephalitis

Anatomical classification of autoimmune encephalitis	Corresponding clinical syndromes	Possible associated antibodies
Limbic encephalitis	► Cognitive presentation ► Psychiatric presentation ► Epileptic presentation	Hu, CRMP5/CV2, Ma2, NMDAR, AMPAR, LGI1, CASPR2, GAD65, GABABR, DPPX, mGluR5, AK5, Neurexin-3α antibodies
Cortical/subcortical encephalitis	► Cognitive presentation ► Seizure presentation	PCA-2 (MAP1b), NMDAR, GABA A/B R, DPPX, MOG antibodies
Striatal encephalitis	► Movement disorder presentation	CRMP5/CV2, DR2, NMDAR, LGI1, PD10A antibodies
Diencephalic encephalitis	► Autonomic presentation ► Sleep disorder presentation	Ma 1–2, IgLON5, DPPX, AQP4 antibodies
Brainstem encephalitis	► Cognitive presentation ► Movement disorder presentation ► Cranio-bulbar presentation	Ri, Ma 1–2, KLHL11, IgLON5, DPPX, AQP4, MOG, GQ1b antibodies
Cerebellitis or cerebellar degeneration	► Ataxic presentation	Hu, Ri, Yo, Tr, CASPR2, KLHL11, NIF, mGluR1, GAD65, VGCC antibodies
Meningoencephalitis	► Cognitive presentation ► Seizure presentation ► Meningeal presentation	GFAP antibody or seronegative AE
Encephalomyelitis	► Movement disorder presentation including PERM and SPS ► Spinal presentation ► Opticospinal presentation	GAD65, amphyphysin, glycine receptor, PCA-2 (MAP1B), GABA A/B R, DPPX, CRMP5/CV2, AQP4, MOG antibodies
Possible associated peripheral syndromes		
Neuropathy/neuronopathy	► Ataxic presentation ► Sensoriomotor presentation	Hu, PCA-2 (MAP1B), CRMP5, Amphiphysin, CASPR2, CASPR1, CONTACTIN1, NIF155 antibodies
Autonomic neuropathy/ganglionopathy	► Autonomic presentation	Hu, CRMP5, anti-ganglionic AChR antibodies
Neuromuscular junction dysfunction	► Myasthenic presentation	VGCC, AchR antibodies
Myopathy	► Motor presentation	Striational antibodies



Abboud H, Probasco JC, Irani S, et al. J Neurol Neurosurg Psychiatry 2021;92:757–768.

Table 2 Overview of studies evaluating plasma exchange (PLEX)

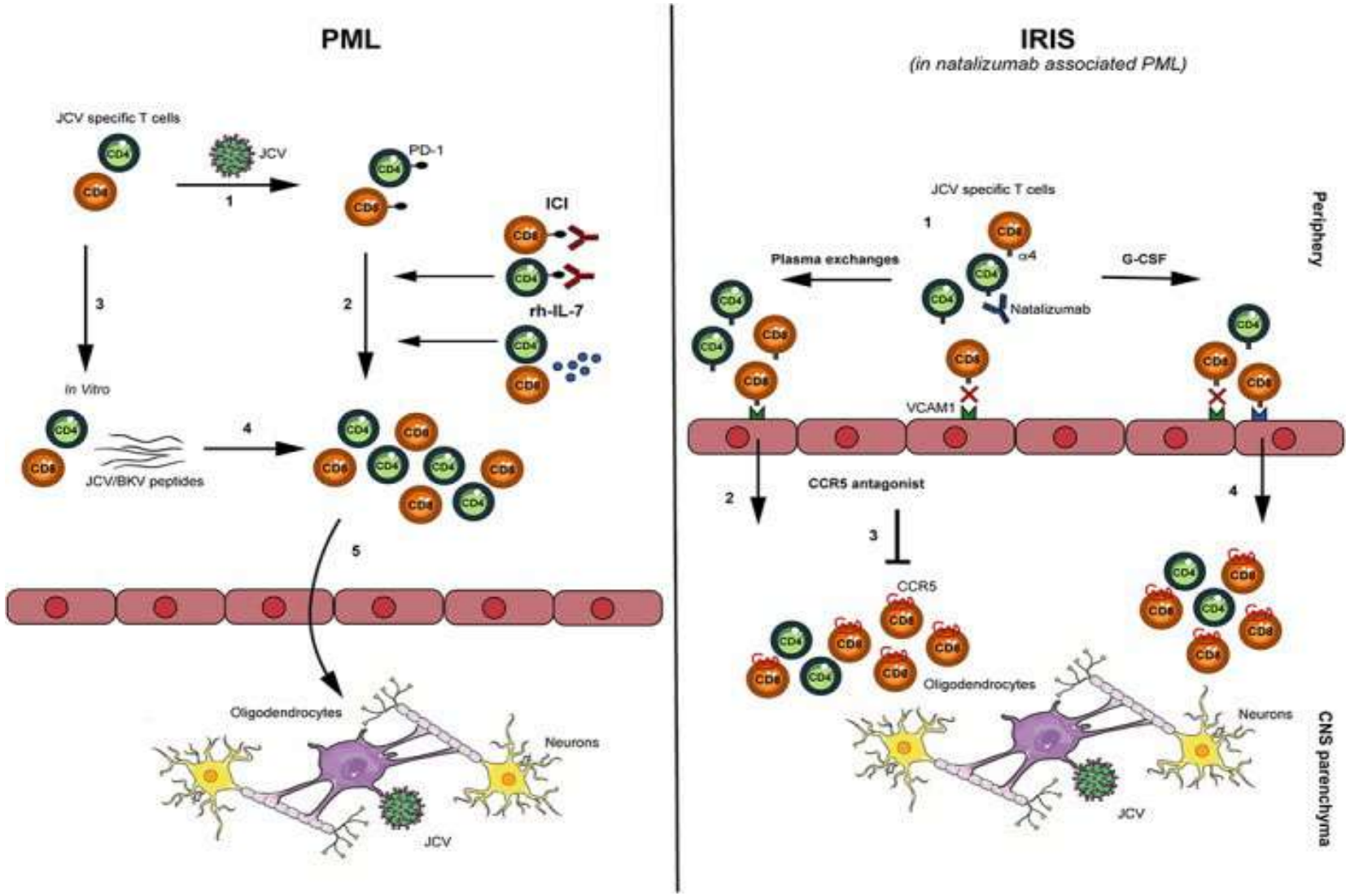
Reference	Study characteristics	N	Diagnosis	% of response
Autoimmune Encephalitis (AE)				
Heine et al. 2016	Pilot study comparing immunoadsorption and PLEX in autoimmune encephalitis	11	11	67%
DeSena et al. 2015	Retrospective study. Intravenous methylprednisolone versus therapeutic PLEX	14	14	64%
Suppiej et al. 2016	Systematic review.	120	120	64%
Moser et al. 2019	Retrospective study comparing the indication, efficacy and safety of PLEX	12	12	75%
Fassbender et al. 2017	Review of immunoadsorption for AE	98	98	Various
Prytula et al. 2015	Case series of PLEX in children with acute autoimmune central nervous system disorders	4	4	100%
Wright et al. 2015	Prospective surveillance study of children with N-methyl-D-aspartate receptor antibody-mediated encephalitis	9	9	89% (full recovery)

S Jacob et al. Journal of Neuroimmune Pharmacology (2021) 16:806–817

PML
Progressive multifocal leukoencephalopathy
(σχετιζόμενη με λήψη natalizumab)

- Σοβαρή επιπλοκή της ΣκΠ υπό θεραπεία με Natalizumab
- Ο ιός είναι παρών στο 50 με 90% του γενικού πληθυσμού.
- Επανενεργοποίηση του ιού JC που προκαλεί λύση των ολιγοδενδροκυττάρων και αστροκυττάρων στο ΚΝΣ
- Natalizumab: μονοκλωνικό αντίσωμα έναντι της υπομονάδας α4 των α4β1 και α4β7 ιντεργκρινών στην επιφάνεια των Τ λεμφοκυττάρων, εμποδίζοντας έτσι την προσκόλληση τους στα ενδοθηλιακά κύτταρα και τους υποδοχείς VCAM 1και την είσοδο στο ΚΝΣ

PML σχετιζόμενη με λήψη ναταλιζουμάμπης



R. Bernard-Valnet etal. Ann Neurol. 2021 Sep 7;90(6):865–873.

PML

- Θεραπεία PML: διακοπή φαρμακευτικής αγωγής (εδώ μπορεί να βοηθήσει η πλασμαφαίρεση στην ταχύτερη απομάκρυνση του φαρμάκου καθώς 5 συνεδρίες πλασμαφαίρεσης ρίχνουν τα επίπεδα της ναταλιζουμαμπης σε <1μg/ml).

- Μεγάλος κίνδυνος εμφάνισης IRIS (Immune Reconstitution Inflammatory Syndrome) νωρίτερα από τους 3 μήνες περίπου που αναμένεται με την διακοπή της natalizumab.

Immune Checkpoint Inhibitors

- Immune checkpoints (ICPs): συνήθως ανασταλτικά μόρια που εκφράζονται στην επιφάνεια των Τ-λεμφοκυττάρων και ρυθμίζουν την ανοσιακή απάντηση και αποτρέπουν την καταστροφή ιστών του οργανισμού από υπερβολική απάντηση σε εξωγενή ή ενδογενή αντιγόνα.
  - Cytotoxic T-lymphocyte – associated protein 4 (CTLA-4),
  - Programmed cell death protein 1 (PD-1)
  - Programmed cell death ligand 1 (PD-L1)
- ***30-79%*** των ασθενών που λαμβάνουν ICIs εμφανίζουν ανοσοσχετιζόμενες ανεπιθύμητες ενέργειες IrAE. (μυασθένεια, μυοκαρδίτιδα, μυοσίτιδα, εγκάρσια μυελίτιδα, TTP).

- Ρόλος της πλασμαφαίρεσης: απομάκρυνση των μονοκλωνικών IgG αντισωμάτων, απομάκρυνση κυτοκινών και αυτοαντισωμάτων
- Χρειάζονται 5-7 συνεδρίες για να απομακρυνθούν οι ICIs.
- Συνήθως σε συνδυασμό με κορτικοστεροειδή λόγω της κλινικής βαρύτητας .

Narayanaswami, Pushpa (2020). International consensus guidance for management of myasthenia gravis [Dataset]. Dryad. https://doi.org/10.5061/dryad.6hdr7sqxx

International Consensus Guidance Recommendations for treatment of Myasthenia Gravis:

MG associated with Immune Checkpoint Inhibitors

1. The risk of MG and other immune-mediated neurologic illnesses should be discussed with patients who are candidates for immune checkpoint inhibitors (ICIs).
2. At this time, there is no evidence to either support or refute the utility of acetylcholine receptor (AChR) antibody testing in patients without MG prior to starting ICIs.
3. MG associated with ICPIs is generally severe, with a high rate of respiratory crises.
4. Pre-existing MG does not constitute an absolute contraindication to the use of ICIs, at least in patients with well-controlled disease (MM status or better). However, in these patients: a. It may be prudent to avoid combined ICPI therapy (anti-CTLA-4 plus anti-PD1/PD-L1 monoclonal antibodies), given the higher potential for severe immune related adverse events. b. Close clinical monitoring, particularly of respiratory and bulbar function, is mandatory. c. Although the therapeutic response to ICIs seems to be less satisfactory in patients receiving immunosuppressants, MG treatment should be maintained and may even be restarted in patients whose MG is in remission prior to treatment with ICIs.
5. Early aggressive treatment with high-dose steroids in combination with plasma exchange or IVIg may be required in patients who develop overt MG while on ICIs. The decision to withdraw ICIs is determined by the oncologic status.

Narayanaswami, Pushpa (2020). International consensus guidance for management of myasthenia gravis [Dataset]. Dryad.ttps://doi.org/10.5061/dryad.6hdr7sqxx

Μυασθενικό σύνδρομο (Lambert-Eaton)

- Αυτοάνοση προσβολή της προσυναπτικής μεμβράνης
- Κλινική τριάδα κεντρομελική αδυναμία – μείωση αντανακλάσεων-διαταραχές αυτονόμου
- Μπορεί να είναι παρανεό εκδήλωση στο 60% (μικροκυτταρικό ca πνεύμονα)
- 85-90% ανίχνευση αντισωμάτων έναντι P/Q type VGCC.
- Θεραπεία συμπτωματική με αμιφαμπριδίνη και ανοσοκαταστολή.
- Η πλασμαφαίρεση έχει θέση σαν συμπληρωματική θεραπεία.
- 5-7 συνεδρίες σε 2 εβδομάδες (μπορεί και περισσότερες).
- Βελτίωση στις 2 εβδομάδες και διάρκεια βελτίωσης έως 6 εβδομάδες.

ΑΛΛΕΣ ΣΥΣΤΑΣΕΙΣ ΓΙΑ ΠΛΑΣΜΑΦΑΙΡΕΣΗ

- **VOLTAGE GATED POTTASIUM CHANNEL ANTIBODY RELATED DISEASE**

  (οι δίαυλοι αυτοί σχετίζονται με την διεγερσιμότητα των κυττάρων στο νευρικό σύστημα).

  Σύνδρομα: επίκτητη νευρομυοτονία, Morvan's σύνδρομο, Isaac's σύνδρομο

  10 συνεδρίες πλασμαφαίρεσης σε 2 εβδομάδες σε συνδυσμό με κορτιζόνη και IVIG

- **ΕΓΚΕΦΑΛΟΠΑΘΕΙΑ HASHIMOTO** (πλέον **SREAT *S***teroid ***R***esponsive ***E***ncephalopathy associated with ***A***utoimmune ***T***hyroiditis)

  επί απουσίας απάντησης στα κορτικοστεροειδή

- ***STIFF PERSON SYNDROME***

  παρουσία αντισωμάτων anti-GAD

  Συνεδρίες πλασμαφαίρεσης επί αποτυχίας άλλων ανοσοθεραπειών για την άμεση αντιμετώπιση καθώς και επιπλέον συνεδρίες συντήρησης.

ΑΛΛΕΣ ΣΥΣΤΑΣΕΙΣ ΓΙΑ ΠΛΑΣΜΑΦΑΙΡΕΣΗ

- ΠΑΡΑΝΕΟΠΛΑΣΜΑΤΙΚΑ ΣΥΝΔΡΟΜΑ με αντισώματα έναντι μεμβρανικών υποδοχέων

Anti-NMDAR	NMDAR (ionotropic Glu receptor)	Extracellular	Ovarian teratoma, testicular germ cell tumors	Limbic encephalitis
Anti-AMPA	AMPA (ionotropic Glu receptor)	Extracellular	Lung, breast, thymus	Limbic encephalitis
Anti-GABA-A	GABA-A (ionotropic inhibitory receptor)	Extracellular	Hodgkin lymphoma	Refractory status epilepticus
Anti-GABA-B	GABA-B (metabotropic inhibitory receptor)	Extracellular	SCLC	Limbic encephalitis with seizures, opsoclonus, ataxia
Anti-mGluR1	mGluR1 (cerebellar metabotropic GluR)	Extracellular	Hodgkin lymphoma, prostate	Cerebellar degeneration
Anti-VGCC	VGCC at NMJ	Extracellular	SCLC	LEMS, cerebellar degeneration
Anti-AChR	AChR at NMJ	Extracellular	Thymoma	Myasthenia gravis, autonomic neuropathy

- Η πλασμαφαίρεση χρησιμοποιείται σε συνδυασμό με άλλες ανοσοθεραπείες. 5-6 συνεδρίες σε 14 ημέρες

Νόσος ALZHEIMER

- Μελέτες με αμφίβολα αποτελέσματα (Boada 2009, 2017.
- Το αμυλοειδές Αβ βρίσκεται σε δυναμική ισορροπία μεταξύ ΕΝΥ και περιφερικούάίματος και συνδέεται με την αλβουμίνη.
- Με την πλασμαφαίρεση αφαιρείται η αλβουμίνη και το αμυλοειδές Αβ και εμμέσως και η συγκέντρωση του στο ΕΝΥ και τον εγκεφαλικό ιστό.
- Μελέτη AMBAR (6 εβδομαδιαίες πλασμαφαιρέσεις μεγάλου όγκου και εν συνεχεία μηνιαίες μικρού όγκου για ένα χρόνο) με μικτά αποτελέσματα.

Acute attacks (severe)

In the following conditions, PLEX is started as soon as practically possible, along with IVMP (especially in NMOSD and MS relapses):

1. Severe encephalopathy, uncontrolled seizures or refractory epilepsy in AE
2. Complete paraplegia, bilateral severe optic neuritis, brain stem events in NMOSD
3. Severe relapse with significant neurological disability in MS, as seen in spinal and brain stem cerebellar relapses
4. Myasthenic crisis or impending bulbar failure in MG
5. Severe muscle weakness in CIDP

Acute attacks (mild)

PLEX is less commonly used in these scenarios:

1. Myelitis with mild sensory and motor symptoms (not affecting walking)
2. Faciobrachial seizures in AE
3. Mild weakness in MG/CIDP/MS

Acute attacks (moderate)

For the majority of the situations between these two extremes, PLEX is usually used after assessing the response to five days of IVMP (that is continued by oral corticosteroids) starting usually by the second week of treatment. In general, the authors prefer to treat early rather than late, bearing in mind the high probability of NMOSD and MS attacks leaving behind permanent damage.

Relapse prevention

PLEX should be an option when conventional and new drugs fail, side effects are too substantial or when they are unavailable or too expensive.

IVMP, IV Methyl Prednisolone; NMOSD, Neuromyelitis Optica Spectrum Disorder; MS, Multiple Sclerosis; AE, Autoimmune Encephalitis; MG, Myasthenia Gravis; CIDP, Chronic Inflammatory Demyelinating Polyneuropathy

S Jacob et al. Journal of Neuroimmune Pharmacology (2021)16:806–817

ΕΥΧΑΡΙΣΤΩ ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ

Classes of recommendations	Definition
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy*
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion*
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful

Grades	Methodological criteria	Recommendation/level of evidence
Grade 1A	Randomized controlled trial with limited bias	Strong recommendation High level of evidence
Grade 1B	Randomized controlled trial with marked bias Observational study producing a high level of evidence	Strong recommendation Moderate level of evidence
Grade 1C	Observational studies or anecdotal case-reports with positive findings	Strong recommendation Low level of evidence
Grade 2A	Randomized controlled trial with limited bias	Weak recommendation High level of evidence
Grade 2B	Randomized controlled trial with marked bias Observational study producing a high level of evidence	Weak recommendation Moderate level of evidence
Grade 2C	Observational studies or anecdotal case-reports with negative findings	Very weak recommendation Low level of evidence

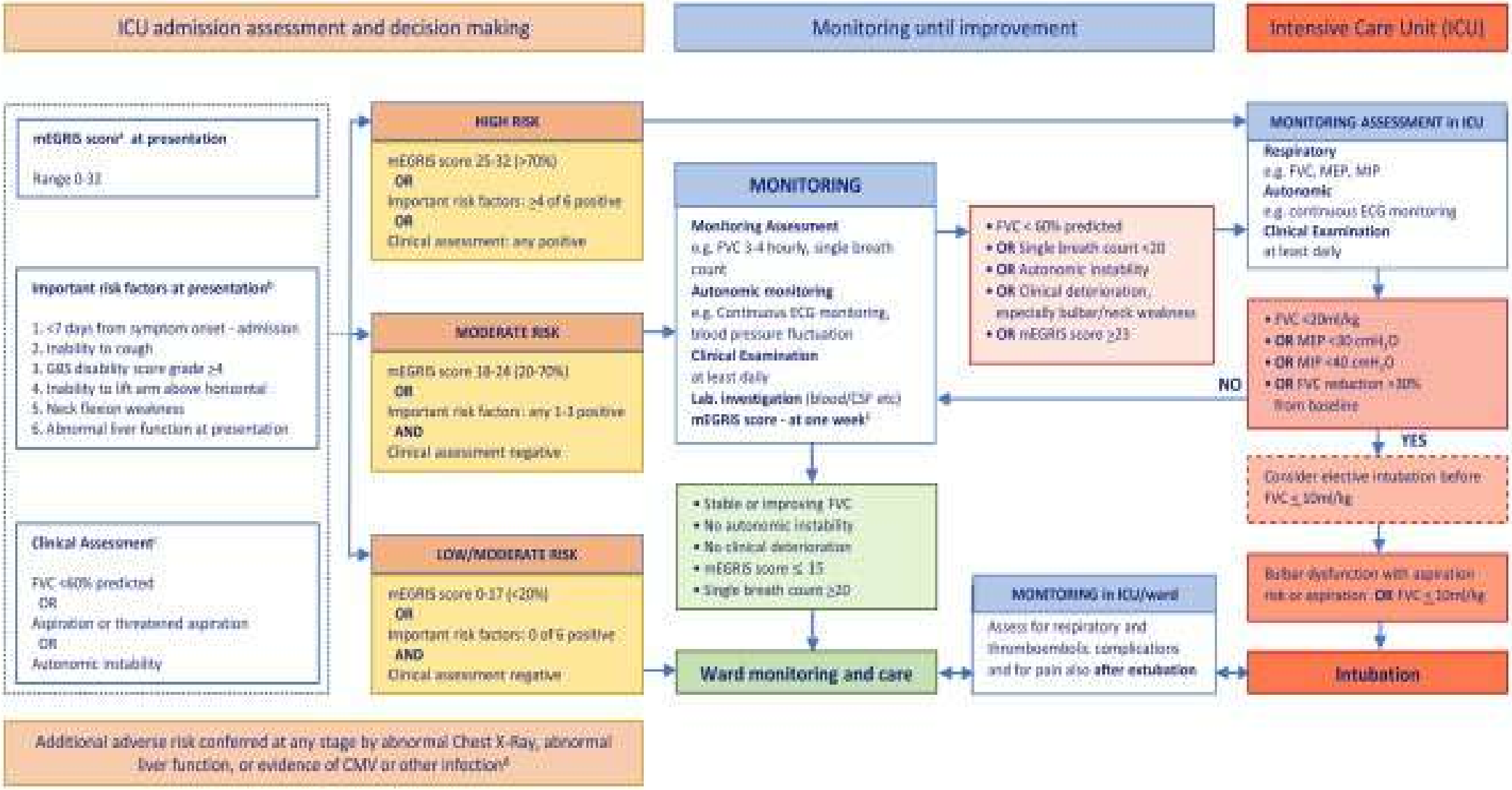
Plasma exchange

► Plasma exchange is now considered as effective and safe as IVIg if the facilities are available. Where possible, plasma exchange should be performed via peripheral vein access with centrifugal machines which minimises the requirement for central venous access and significantly reduces the morbidity of the procedure. Each session should aim to exchange up to 1.5 plasma volumes and a typical schedule is five sessions over 5–10 days, as per local guidelines.

► Plasma exchange is best avoided in sepsis.

Jacob S, Farrugia ME, Hewamadduma C, et al. Pract Neurol 2025;25:422–437

Assessment and monitoring of GBS



Management of Guillain-Barré Syndrome: A Systematic Review of Clinical Practice Guidelines

Ankita Sood[1], Gagandeep Kaur[1], Barinder Singh[2]
[1]Pharmacoevidence, Mohali, India; [2]Pharmacoevidence, London, UK

HSD4

Pharmaco Evidence

CONCLUSIONS

In the current review, IVIg and TPE emerged as the most effective and endorsed therapies for the management of GBS worldwide. Whilst IVIg and TPE were considered equally effective, there seemed to be a lack of globally recommended treatment alternatives for patients with poor outcomes to these therapies. Addressing these research gaps will aid in the development of informed decision-making and optimizing patient care strategies

INTRODUCTION

- Guillain-Barré syndrome (GBS) is a rare, potentially fatal, immune-mediated neuropathy, usually triggered by infections that results in autoimmune destruction of the peripheral nerves[1]
- With a global incidence of approximately 1-2 per 100,000 people per year, GBS can affect people of any age with incidence increasing linearly with age[2]
- The management of GBS is complicated due to the heterogeneity in clinical presentation, the absence of highly sensitive diagnostic tools, and the variability in the course of disease progression[3]
- The outbreak of infectious illnesses can lead to an increased incidence of GBS emphasising the importance of devising globally applicable clinical guidelines for managing GBS[1]

OBJECTIVE

- This systematic literature review (SLR) aimed to identify treatment recommendations based on clinical practice guidelines (CPGs) for GBS

METHODS

- This review followed the standard methodology for conducting an SLR as per the guidelines provided by the National Institute for Health and Care Excellence
- A systematic search was performed across key biomedical databases (EMBASE® and MEDLINE®) from database inception until June 2024 to identify relevant English language publications providing CPGs for GBS patients. The prespecified eligibility criteria are presented in Figure 1
- Each publication was reviewed by two independent reviewers, and disagreements were arbitrated by a third reviewer

Figure 1: Prespecified PICOS eligibility criteria for the selection of evidence

RESULTS

- Of the 458 publications retrieved, the SLR identified nine CPGs from 16 publications offering valuable information on the management of GBS (Figure 2)
- The majority of the studies (n=8) were published in peer-reviewed journals. Three CPGs each were identified from the USA and Europe followed by one each for Australia, Canada, and Southeast Asia (Figure 3). A list of the recommending bodies is provided in Figure 4
- Across all the CPGs, intravenous immunoglobulin (IVIg) at 0.4 g/kg/day for 5 days and therapeutic plasma exchange (TPE) emerged as effective first-line treatments, with IVIg often preferred due to its lower side effect profile
- Sequential therapy with TPE followed by IVIg was generally not recommended, whereas, for treating relapse, a second course of IVIg treatment was preferred
- Corticosteroids were largely discouraged in managing GBS; however, the European Federation of Neurological Societies guidance suggested that high-dose intravenous methylprednisolone (MP) combined with IVIg might have a minor short-term benefit
- The European Academy of Neurology/Peripheral Nerve Society (EAN/PNS) Guidelines provided a weak recommendation to use gabapentin or carbamazepine for pain
- The EAN/PNS do not recommended use of therapies such as immunoadsorption, eculizumab, amantadine, and IVMP either alone or in combination with IVIg

Figure 3: Country-wise CPGs that provided recommendations for the treatment of GBS

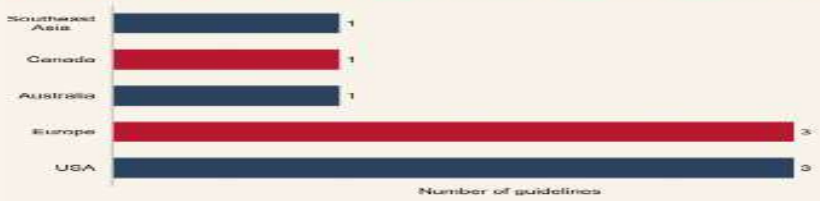
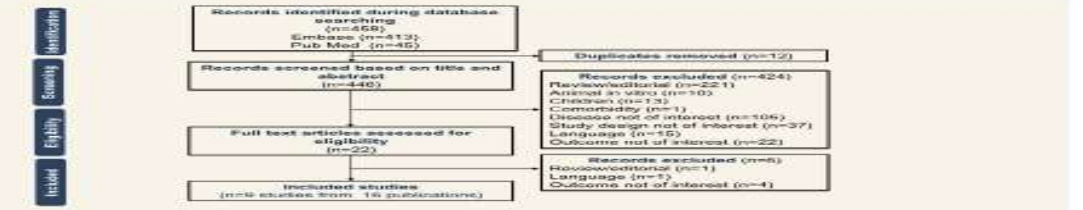


Figure 2: PRISMA diagram for the screening process



Embase: Excerpta Medica database; PRISMA: Preferred Reporting Items for Systematic Reviews

Figure 4: List of recommending bodies that provided treatment guidance for GBS

AAN: American Academy of Neurology; AANEM: American Association of Neuromuscular & Electrodiagnostic Medicine; ASFA: American Society for Apheresis; EAN: European Academy of Neurology; EFNS: The European Federation of Neurological Societies; EU: European Union; GBS: Guillain-Barré syndrome; NAC: National Advisory Committee on Blood and Blood Products; NBA: National Blood Authority; PNS: Peripheral Nerve Society; SEATPEC: Southeast Asia Therapeutic Plasma Exchange Consortium; USA: United States of America; ZikaPLAN: Zika Preparedness Latin American Network

Table 1: Country-wise treatment recommendations for treatment of GBS

Treatment								Recommending body
IVIg	TPE	CS	High dose IV MP with IVIg	Gabapentin or carbamazepine	IA	TPE followed by IVIg or IA followed by IVIg	Others[A]	
USA								
✓	✓	–	–	–	–	–	–	AANEM[3]
–	✓	–	–	–	✓	–	–	ASFA[4]
✓	✓	✗	–	–	✗	✗	–	AAN[5]
Europe								
✓	✓	–	✓*	–	–	–	–	EFNS[6]
✓	✓	✗	✗	–	–	✗	–	The EU-funded ZikaPLAN[1]
✓	✓	✗	✗	✓*	✗	✗	✗	EAN/PNS[2]
Canada								
✓	–	–	–	–	–	–	–	The NAC and Canadian Blood Services[7]
Australia								
✓	–	–	–	–	–	–	–	The NBA of Australia[8]
Asia-Pacific								
✓	✓	✗	✗	–	–	–	–	SEATPEC[9]

*: Weak recommendation; ^Others: Alemtuzumab, eculizumab, brain-derived neurotrophic factor, CSF filtration, cyclophosphamide, IFNβ-1a, muronomab-CD3, mycophenolate mofetil or tripterygium polyglycoside-AAN: American Academy of Neurology; AANEM: American Association of Neuromuscular & Electrodiagnostic Medicine; ASFA: American Society for Apheresis; CS: Corticosteroids; EAN: European Academy of Neurology; EFNS: The European Federation of Neurological Societies; EU: European Union; GBS: Guillain-Barré syndrome; IA: Immunoadsorption; IV: Intravenous; IVIg: IV Immunoglobulin; MP: Methylprednisolone; NAC: National Advisory Committee on Blood and Blood Products; NBA: National Blood Authority; PNS: Peripheral Nerve Society; SEATPAC: Southeast Asia Therapeutic Plasma Exchange Consortium; TPE: Therapeutic Plasma Exchange; USA: United States of America; ZikaPLAN: Zika Preparedness Latin American Network

Table 2: Summary of treatment recommendations

Treatment Recommendation	Grade of recommendation
IVIg 0.4 g/kg/day for 5 days: first-line therapy, in patients with relapse[1,4,5]	Strong recommendation
TPE (200–250 ml/kg for 5 sessions)[2,4,6,7,8]	Strong recommendation
High dose IV MP with IVIg[6]	Weak recommendation
Gabapentin or carbamazepine[2]	Weak recommendation
Corticosteroids[3,4,5]	Not recommended
Immunoadsorption[2,3]	Not recommended
Sequential treatment with TPE followed by IVIg or immunoadsorption followed by IVIg[3,4]	Not recommended
Alemtuzumab, eculizumab, brain derived neurotrophic factor, CSF filtration, cyclophosphamide, IFNβ-1a, muronomab-CD3, mycophenolate mofetil or tripterygium polyglycoside[3]	Not recommended

CD: Cluster of differentiation; CSF: Cerebrospinal Fluid; IFNβ: Interferon Beta; IVIg: Intravenous Immunoglobulin; MP: Methylprednisolone; TPE: Therapeutic Plasma Exchange

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Disclosures

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Στόχος της πλασμαφαίρεσης στις αντι-MAG πολυνευροπάθειες είναι η αφαίρεση των αντσωμάτων αλλά η Ανταπόκριση των ασθενών είτε δεν είναι καλή περίπου στο 40% είτε είναι βραχύβια (Gorson, 2001)
Πιο αποτελεσματική στις IgA και IgG γαμμοπάθειες (Cortese, 2011).

The rationale for using TPE is to remove anti-MAG or other antibodies; however, not all patients respond and the response may be short lived. TPE may be more effective for IgA and IgG MGUS-associated polyneuropathy, than for IgM-MGUS (Cortese, 2011). TPE may result in a transient response in anti-MAG neuropathy. In one report of 19 patients with anti-MAG neuropathy who received TPE, 40% had a transient effect, but most of them had a relapse upon stopping TPE (Gorson, 2001). For CANOMAD/CANDA, retrospective studies suggest benefit in 40 to 50% treated with TPE/DFPP; however, the largest study of 45 patients suggests IVIG and rituximab are the most effective therapies (Le Cann, 2020). Currently, other treatments are considered first-line for anti-MAG neuropathy.

ADEM

- If high-dose corticosteroids fail, the next step will be plasma exchange (PE) and there is Class Ib evidence for PE. [40-42] A course of 4–6 PEs have been shown to be associated with moderate to marked and sustained improvement. One could remove a large volume of plasma per exchange if there are no problems of autonomic dysfunction. Predictors associated with improvement include male sex, preserved reflexes, and early initiation of treatment.

ΣΚΛΗΡΥΝΣΗ ΚΑΤΑ ΠΛΑΚΑΣ

- Patients with steroid-refractory relapses can benefit from PLEX, with reported response rates of 40 to 90% (Stork et al. 2018).
- The American Academy of Neurology (AAN) (Cortese et al. 2011) guidelines state that PLEX should be considered for the adjunctive treatment of exacerbations in relapsing forms of MS (Level B).
- PLEX may be considered in the treatment of fulminant CNS demyelinating diseases that fail to respond to high-dose corticosteroid treatment (Level C; the available evidence did not allow to make a recommendation for MS separately).
- PLEX should not be offered for PPMS or SPMS (Level A)
- Σε περιπτώσεις ανθεκτικών στην θεραπεία ώσεων

Once infection is ruled out based on basic CSF results (eg, number of cells) and if biopsy for primary CNS lymphoma or neurosarcoidosis is not a consideration, start acute immunotherapy with high dose corticosteroids (or IVIG or PLEX if steroids are not preferred or contraindicated).

If there is no clinical, radiological or electrophysiological improvement by the end of the initial treatment cycle, add IVIG or PLEX. Consider IVIG first in agitated patients and in those with bleeding disorders. Consider PLEX first in patients with severe hyponatraemia, high thromboembolic (or cancer) risk, and if there is associated brain or spinal demyelination.

Consider starting with a combination therapy of steroids/IVIG or steroids/PLEX from the beginning (as opposed to sequentially) in patients with severe initial presentation (eg, severe NMDAR- antibody presentation, new onset refractory status epilepticus, severe dysautonomia, etc).

Abboud H, Probasco JC, Irani S, et al. J Neurol Neurosurg Psychiatry 2021;92:757–768.

Table 1. TA in neurological disease (adapted from ASFA Guidelines, 2019) [6]

Disease	TA MODALITY	Indications	Category	Grade	Timeline/procedure frequency
Acute disseminated encephalomyelitis (ADEM)	TPE	Steroid refractory	II	2C	5-7 treatments, every other day, clinical response within days
Acute inflammatory demyelinating polyradiculoneuropathy (GBS)	TPE IA	Primary treatment Primary treatment	I I	1A 1B	Exchange 1–1.5 plasma volumes, 5-6 times over 10–14 days; some patients may need additional treatments
Age related macular degeneration, dry	Rheopheresis	High-risk	II	2B	Clinical benefit of a single course of treatment, reported to last for up to 4 years; repeated treatment over several years not systematically investigated
Amyloidosis, systemic	TPE	Other causes	IV	2C	NA
Chronic focal encephalitis (Rasmussen encephalitis)	TPE		III	2C	NA
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	TPE IA		I I	1B 1B	TPE or IA short-term benefit, rapid deterioration may occur; maintenance treatment may be necessary, with repeated TPE, IA (2-3/week or monthly until improvement); frequency tailored to symptoms and tolerability of the patient
Complex regional pain syndrome	TPE	chronic	III	2C	NA
Lambert-Eaton myasthenic syndrome	TPE		II	2C	Treatment until clear clinical and EMG response, at least 2–3-week course of TPE. Repeated courses in case of neurological relapse. TPE regimens: 5–15 TPE over 5–19 days to 8–10 TPE, at 5–7-day intervals
Multiple sclerosis	TPE IA TPE IA	Acute attack/ relapse Acute attack/ relapse Chronic Chronic	II II III III	1A 1B 2B 2B	Acute MS attack/relapse unresponsive to steroids, 5–7 TPE or IA procedures (response rate: >50%). Frequency: Acute attack/relapse: 5–7 TPE over 10–14 days NA
MG	TPE/IA TPE/IA	Acute short-term treatment Long-term treatment	I II	1B 2B	Acute attack/relapse or unstable disease activity, frequency: 3-6 treatments over 10–14 days; weekly to bi-weekly. Individually adjusted number of treatments for chronic treatment
Neuromyelitis optica spectrum disorders (NMOSD)	TPE IA TPE	Acute attack/ relapse acute attack/relapse Maintenance	II II III	1B 1C 2C	Acute attack/relapse: daily or every other day. 5 procedures on average for acute exacerbation; range: 2–20 procedures. Early initiation of apheresis (≤5 days since clinical onset). Individually adjusted intervals for maintenance treatment

N-methyl-D-aspartate receptor antibody encephalitis	TPE/IA		I	1C	5-12 treatments with TPE or IA over 1–3 weeks; individually adjusted number of and intervals between treatments. If patients do not improve rapidly after TPE or IA, longer periods are required
Paraneoplastic neurological syndromes	TPE/IA		III	2C	NA
Paraproteinemic demyelinating neuropathies; Chronic acquired demyelinating polyneuropathies	TPE TPE TPE TPE	IgG/IgA/IgM Anti-MAG neuropathy Multiple myeloma Multifocal motor neuropathy	I III III IV	1B 1C 2C 1C	Typical course is 5–6 treatments over 10–14 days, regimen guided by clinical response NA NA
Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS); Sydenham's chorea	TPE TPE	PANDAS exacerbation Sydenham's chorea, severe	II III	1B 2B	Daily or every other day. Three to 6 procedures over 1–2 weeks NA
Progressive multifocal leukoencephalopathies (PMLs) associated with natalizumab	TPE		III	1C	NA
Steroid-responsive encephalopathy associated with autoimmune thyroiditis (Hashimoto's encephalopathy)	TPE		II	2C	Daily to every other day 3–9 procedures, mostly commonly 5
Stiff-person syndrome	TPE		III	2C	NA
Sudden sensorineural hearing loss	LA/ rheopheresis/ TPE		III	2A	NA
Voltage-gated potassium channel (VGKC) antibody related diseases	TPE/IA		II	1B	5–10 treatments with TPE or IA over 7–14 days adjusted to the individual curse. Disease activity/symptom severity monitored by anti-VGKC titers. Treatment course: response of clinical symptoms

Disease	Conclusion	Quality
Acute inflammatory demyelinating polyneuropathy/Guillain-Barré syndrome	Established effective	Class I
Chronic inflammatory demyelinating polyneuropathy, short-term treatment	Established effective	Class I
Polyneuropathy with monoclonal gammopathies of undetermined significance		
Immunoglobulin A/immunoglobulin G	Probably effective	Class I
Immunoglobulin M	Probably ineffective	Class I
Myasthenia gravis		
Preoperative preparation	Insufficient evidence	Class III
Crisis	Insufficient evidence	Class III
Fulminant demyelinating CNS disease	Possibly effective	Class II
Chronic or secondary progressive multiple sclerosis	Established ineffective	Class I
Relapses in multiple sclerosis	Probably effective	Class I
Sydenham chorea	Insufficient evidence	Class III
Acute obsessive-compulsive disorder and tics in PANDAS	Insufficient evidence	Class III

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