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ARTICLE SUMMARY: INTERNATIONAL CONSENSUS GUIDANCE FOR MANAGEMENT OF MYASTHENIA GRAVIS (MG)

OVERVIEW
This paper reports the results of an effort by international experts to develop consensus guidance for clinicians worldwide who manage patients with MG.

AUTHORS
Sanders DB, Wolfe GI, Benatar M, Evoli A, Gilhus NE, Illa I, Kuntz N, Massey JM, Melms A, Murai H, Nicolle M, Palace J, Richman DP, Verschuuren J, Narayanaswami P

TERUMO BCT
10811 West Collins Avenue, Lakewood, Colorado 80215-4440 USA

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BACKGROUND

There is no accepted standard of care for patients with MG; and because it is a rare disease, few physicians treat enough patients with MG to be confident in using available therapies. There are only a few randomized controlled trials of treatments for MG and they have limited generalizability due to the heterogeneity of patients with this disease. The Task Force considered a wide range of treatments for MG. This summary focuses primarily on administration of intravenous immunoglobulin (IVIG) and plasma exchange (PLEX).

THE TASK FORCE

In October 2013, the Myasthenia Gravis Foundation of America appointed a Task Force to develop treatment guidance for MG, and a panel of 15 international experts was convened. These included:

Michael Benatar, MD, PhD	Janice M. Massey, MD	Jacqueline Palace, BM, DM
Amelia Evoli, MD	Arthur Melms, MD	David P. Richman, MD
Nils E. Gilhus, MD	Hiroyuki Murai, MD	Donald B. Sanders, MD
Isabel Illa, MD	Michael Nicolle, MD	Jan Verschuuren, MD
Nancy Kuntz, MD	Pushpa Narayanaswami, MBBS, DM	Gil I. Wolfe, MD

TREATMENT GOALS

The Task Force set forth the following as treatment goals:

- Postintervention status (PIS) classification of minimal manifestation status (MMS; patient has no symptoms or functional limitations from MG but has some weakness on examination of some muscles) or better.
- No more than grade 1 common terminology criteria for adverse events (CTCAE) medication side effects (asymptomatic or only mild symptoms; intervention not indicated).

CONSENSUS GUIDANCE FOR SYMPTOMATIC AND IMMUNOSUPPRESSIVE (IS) TREATMENT

- Pyridostigmine (an acetylcholinesterase inhibitor) should be part of the initial treatment in most patients with MG. Pyridostigmine dose should be adjusted as needed based on symptoms. The ability to discontinue pyridostigmine can indicate that the patient has met treatment goals and may guide the tapering of other therapies.
- Corticosteroids should also be used in all patients with MG who have not met treatment goals after an adequate trial of pyridostigmine.
- A nonsteroidal IS agent (azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, or tacrolimus) should be used alone when corticosteroids are contraindicated or refused.
- Patients with refractory MG (PIS is unchanged or worse after corticosteroids and ≥ 2 other IS agents, used in adequate doses for an adequate duration, with persistent symptoms or side effects that limit functioning) should be referred to a physician or a center with expertise in management of MG, and may also consider utilizing:
  - Additional therapies, including chronic IVIG and chronic PLEX.
    - The use of IVIG and PLEX should be done in addition to IS agents
  - Cyclophosphamide
  - Rituximab but note:
    - Evidence of efficacy is building, but a formal consensus regarding its use could not be reached

PLEX AND IVIG

- PLEX and IVIG are appropriately used as short-term treatments in patients with MG in a large number of specific situations:
  - Life-threatening signs, such as respiratory insufficiency or dysphagia
  - In preparation for surgery in patients with significant bulbar dysfunction
  - When a rapid response to treatment is needed
  - When other treatments are insufficiently effective
  - Prior to beginning corticosteroids if deemed necessary to prevent or minimize exacerbations
  - In myasthenic crisis
  - When a prompt, although temporary, response is desired during pregnancy
- PLEX and IVIG may also be considered as maintenance treatments in juvenile MG that is refractory to IS.

CHOOSING BETWEEN PLEX AND IVIG

- The choice between PLEX and IVIG depends on individual patient factors (for example, PLEX cannot be used in patients with sepsis and IVIG cannot be used in patients with renal failure) and on the availability of each:
  - IVIG and PLEX are probably equally effective in the treatment of severe generalized MG.
  - The efficacy of IVIG is less certain in milder MG or in ocular MG.
  - PLEX may be more effective than IVIG in MG associated with antibodies against muscle-specific tyrosine kinase (MuSK). MuSK-MG responds well to PLEX, while IVIG seems to be less effective. Please note that patients with MuSK-MG also respond well to corticosteroids and to many steroid-sparing IS agents but they tend to remain dependent on prednisone despite treatment with steroid-sparing agents.
  - Although clinical trials suggest that IVIG and PLEX are equally effective in the treatment of impending or manifest myasthenic crisis, expert consensus suggests that PLEX is more effective and works more quickly.
- PLEX has a greater risk of hemodynamic and venous access complications and these should be taken into consideration when considering treatment.
- Many of the complications of PLEX may be minimized by using peripheral versus central venous access.

REFERENCES

Sanders DB, Wolfe GI, Benatar M, Evoli A, Gilhus NE, Illa I, et al. International consensus guidance for management of myasthenia gravis. *Neurology.* 2016; 87(4):419-425.

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Terumo BCT, Inc.
10811 West Collins Ave.
Lakewood, Colorado 80215-4440
USA
USA Phone: 1.877.339.4228
Phone: +1.303.231.4357
Fax: +1.303.542.5215

Terumo BCT Europe N.V.
Europe, Middle East and Africa
Ikaroslaan 41
1930 Zaventem
Belgium
Phone: +32.2.715.05.90
Fax: +32.2.721.07.70

Terumo BCT Asia Pte. Ltd.
89 Science Park Drive
#04-25 (Lobby B)
The Rutherford
Singapore 118261
Phone: +65.6715.3778
Fax: +65.6774.1419

Terumo BCT Latin America S.A.
La Pampa 1517–12th Floor
C1428DZE
Buenos Aires
Argentina
Phone: +54.11.5530.5200
Fax: +54.11.5530.5201

Terumo BCT Japan, Inc.
Tokyo Opera City Tower 49F
3-20-2, Nishi-Shinjuku,
Shinjuku-ku, Tokyo 163-1450
Japan
Phone: +81.3.6743.7890
Fax: +81.3.6743.9800