The duration of GC therapy in PMR patients should be individualised and be the shortest to achieve adequate efficacy (5, D).
LoE: 2-5; SoR: B-D; LoA: 9.0 (9.0, 10).

Summary of guidelines. The search identified 2 CPGs that addressed the scheduling and route of administration of the first-line therapy (AGREE rating: R = 2).
Recommendation/supporting evidence. ACR/EULAR 2015 (13), S3 2018 (14).
Evidence to recommendation. The panel endorsed the recommendations included with regards to the initial dose of GCs, but it did not recommend doses > 25 mg prednisone equivalent per day. From the results of a clinical trial (25), intramuscular (i.m.) methylprednisolone (starting dose of 120 mg methylprednisolone i.m. injection every 3 weeks) can be considered as an alternative to oral GCs, but its use is not common in the Italian setting. The position of the panel was not unanimous with regards to the administration of multiple daily doses of oral GCs in special situations, such as prominent night pain, while tapering GCs below the low-dose range (prednisone or equivalent <5 mg daily). Such regimen may be considered at the discretion of the treating physician, but it is not the usual clinical practice in the Italian setting.

RECOMMENDATION 7:
Second-line treatment

The early introduction of methotrexate (MTX) in addition to GCs should be considered particularly in patients at high risk of relapse and/or prolonged therapy as well as in cases with risk factors, comorbidities and/or concomitant medications, where GC-related adverse events are more likely to occur. During the follow-up, MTX may also be considered in patients with relapse or experiencing GC-related adverse events. MTX has been used at oral doses of 7.5–10 mg/week in clinical trials (1, A).
The use of TNFα blocking agents for the treatment of PMR is not recommended (1, A).

No specific recommendation can be made for other biologic agents, including interleukin-6 inhibitors.
LoE: 1; SoR A; LoA: 10 (9.75, 10).

Summary of guidelines. The search identified 2 CPGs that addressed the choice of second-line therapy in PMR (AGREE rating: R = 2).
Recommendation/supporting evidence. ACR/EULAR 2015 (13), S3 2018 (14).
Evidence to recommendation. The panel endorsed the recommendations from the CPGs included and agreed that no specific recommendation can be made also for other non-biologic DMARDs due to the absence of clinical studies in PMR, with the exception of hydroxychloroquine, which was ineffective in preventing disease flares in a retrospective clinical study (24).

RECOMMENDATION 8:
Non-pharmacological interventions

An individualised exercise programme should be considered for PMR patients aimed at maintaining muscular mass and function, and reducing risk of falls especially in older persons on long-term GCs as well as in frail patients.
LoE: 5; SoR: D; LoA: 9.5 (8.5, 10).

Summary of guidelines. The search identified 2 CPGs that addressed the non-pharmacological interventions in PMR (AGREE rating: R = 2).
Recommendation/supporting evidence. ACR/EULAR 2015 (13), S3 2018 (14).
Evidence to recommendation. The panel endorsed the recommendations from the CPGs included.

Recommendations for the follow-up of PMR

RECOMMENDATION 9:
Target of treatment and follow-up

Treatment of PMR patients should aim at providing the best care and must be based on a decision shared by the patient and the treating physician (5, D).
Patients should have an individualised PMR management plan. Patient per-

spective and preferences should be considered in the individualised choice of the initial GC dose and the subsequent tapering of GCs in PMR (5, D).
Patients should have access to education focusing on the impact of PMR and treatment (including comorbidities and disease predictors) and advice on individually-tailored exercise programmes (5, D).
Every patient treated for PMR in primary or secondary care should be monitored with the following assessments: risk factors and evidence for steroid-related side effects, comorbidities, other relevant medications, evidence and risk factors for relapse/prolonged therapy. Follow-up visits are recommended every 4–8 weeks in the first year, every 8–12 weeks in the second year, and as indicated in case of relapse or as prednisone is tapered and discontinued (5, D).
It is important for patients to have rapid and direct access to advice from doctors, nurses or trained healthcare staff to report any changes in their condition, such as flares and adverse events (5, D).
LoE: 5; SoR: D; LoA: 9.5 (8.75, 10).

Summary of guidelines. The search identified 2 CPGs that addressed the target of treatment and follow-up in PMR (AGREE rating: R = 2).
Recommendation/supporting evidence. ACR/EULAR 2015 (13), S3 2018 (14).
Evidence to recommendation. The panel endorsed the recommendations from the CPGs included.

DISCUSSION AND CONCLUSIONS

This is the first guidance on management of patients with diagnosis of PMR for clinical practice in Italy, so far. These recommendations were developed from current international consensus and adapted for the context of the NHS.
Glucocorticoids are acknowledged as the mainstay of the first-line PMR treatment. In clinical practice, the initial dose was observed to be between 12.5 and 25 mg prednisone equivalent daily (26), although the scheduling, as well as the duration of therapy, were scarcely investigated (27) and the evidence backing this recommendation is currently limited. Patient reported outcomes, such as visual analogue scale for recording pain measures and fatigue, modified Health Assessment Questionnaire and Medical Outcomes Study Short Form-36 in addition to inflammatory markers, proved to perform well (28) and may help clinicians in tailoring the treatment schedule. The rapid control of symptoms and the regular recovery achieved thanks to the treatment allow the patients to be managed usually in primary care, unless the presence of atypical presentation, unresponsiveness to therapy, relapses and/or prolonged (>24 months) treatment, which is frequently observed (29, 30), may require a specialist referral. In this subset of patients, after a careful re-assessment of the diagnosis to exclude mimicking conditions, like paraneoplastic syndromes, the (early) introduction of MTX is strongly suggested to achieve disease remission as was consistently observed in an Italian cohort of PMR (31). The role of the biological therapy in PMR is still unclear. The use of TNF inhibitors is not recommended on the basis of RCTs with no evidence of large effect due to the administration of infliximab (32) and etanercept (33). The first results from clinical trials on tocilizumab seemed to be promising (34, 35), yet still insufficient to provide an evidence basis for clinical guidance. The role of non-pharmacologic treatments were considered as part of a comprehensive approach to PMR, but this recommendation was supported only by expert opinion, since clinical studies are not yet available.
Comorbidities are frequently observed in patients with PMR and may influence the choice of treatment as well as the disease course (36). The development of cataracts may be observed due protracted therapy, but the rates of other morbidities linked to GCs, such as diabetes mellitus, hypertension (requiring medical therapy), and symptomatic vertebral fractures, are not more common in PMR compared to controls of similar age and sex (37). The need

for a thorough clinical assessment is recommended, because of the widespread clinical experience with a number of conditions which may mimic PMR symptoms, including rheumatoid arthritis, infective, and neoplastic diseases. However, the actual need for additional investigations should be always determined by the treating physician in order to avoid extensive screenings with negligible benefit for the patient compared to the use of the required resources. Particularly, FDG-PET/CT imaging should be used only in the specialist setting, since the indications are mainly limited to confirm the suspicion of concurrent large vessel vasculitis (8, 38). However, the role of imaging is still unclear with regards to its probability of detecting large vessel vasculitis in patients with PMR without apparent clinical signs and its potential role in monitoring the efficacy of the treatment.

Finally, the follow-up of PMR patients is heavily influenced by the definitions of disease remission and relapse due to lack of agreement. The treat-to-target strategy may be a valid concept for PMR (39), although further studies are needed before specific outcome measurement sets could be recommended (40) in accordance with patients' priorities (41).

The key strength of these guidelines is the integration of the most recent high-quality international recommendations, while the process of adaptation to the NHS context is ensured by following an acknowledged method. However, there are some limitations. Firstly, the last update of literature search is dependent upon the end-of-search date of the most recent CPGs (July 2016) (14) and subsequent evidence was not considered. Secondly, the majority of recommendations are based on low quality of evidence or expert opinion, particularly with regards to the clinical and laboratory assessment, the GC schedule, non-pharmacological interventions, and disease follow-up. This weakness is due to the absence of (high-quality) studies on PMR and should prompt more research for future recommendations.

In conclusion, these recommendations provide updated guidance including the current international consensus for the management of PMR for the Italian healthcare context. These are also endorsed by SIR as "guides" only and they do not substitute the individual clinicians' judgment, since they may not apply to all patients and all clinical situations.

Plans for updates

SIR is committed to review and update these recommendations in the future in order to keep them up-to-date and reflect the development of future treatments or advances in the management of PMR.

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