The role of high-dose intravenous immunoglobulin in rheumatology

Prashantha M. Vaitla and Elizabeth M. McDermott

Abstract

For many years, non-steroidal anti-inflammatory agents, steroids and immunosuppressive drugs have been the mainstay of treatment for rheumatological disorders. Over the last few years, the emergence of biologic treatments has dramatically changed the management of numerous rheumatological diseases. However, immunoglobulin treatment has been used for decades and its use has still not been superseded in certain rheumatological diseases. In fact, despite the introduction of newer immunomodulatory drugs, there has been an ever-increasing number of clinical indications for which intravenous immunoglobulin (IVIG) has been tried. Immunoglobulins are plasma proteins secreted by plasma cells, forming a major component of the adaptive immune system. IVIG is a blood product prepared from plasma, each batch prepared from a pool of 10,000–20,000 donations. Multiple purification steps during the manufacturing process aim to eliminate all known transmissible pathogens, but cannot completely exclude the risk from unknown pathogens. It should be noted that there has been the transmission of hepatitis C in one batch of immunoglobulin, reported in 1994, resulting in more than 200 patients in the USA and Europe being affected. Nevertheless, IVIG remains relatively safe compared with other immunosuppressive drugs. Headaches and fatigue are common side effects but fortunately the more severe problems such as aseptic meningitis, venous thromboembolism and acute renal failure remain rare. High-dose immunoglobulin when administered i.v. has immunomodulatory properties. The precise mechanism of action of IVIG is complex and not yet fully understood.

Key words: Immunoglobulin, IVIG, Therapy, Kawasaki disease, Dermatomyositis, Vasculitis, Systemic lupus erythematosus, Juvenile idiopathic arthritis, Anti-phospholipid syndrome, Polymyositis.

Introduction

For many years, non-steroidal anti-inflammatory agents, steroids and immunosuppressive drugs have been the mainstay of treatment for rheumatological disorders. Over the last few years, the emergence of biologic treatments has dramatically changed the management of numerous rheumatological diseases. However, immunoglobulin treatment has been used for decades and its use has still not been superseded in certain rheumatological diseases. In fact, despite the introduction of newer immunomodulatory drugs, there has been an ever-increasing number of clinical indications for which intravenous immunoglobulin (IVIG) has been tried.

Immunoglobulins are plasma proteins secreted by plasma cells, forming a major component of the adaptive immune system. IVIG is a blood product prepared from plasma, each batch prepared from a pool of 10,000–20,000 donations. Multiple purification steps during the manufacturing process aim to eliminate all known transmissible pathogens, but cannot completely exclude the risk from unknown pathogens. It should be noted that there has been the transmission of hepatitis C in one batch of immunoglobulin, reported in 1994, resulting in more than 200 patients in the USA and Europe being affected [1, 2]. Nevertheless, IVIG remains relatively safe compared with other immunosuppressive drugs. Headaches and fatigue are common side effects but fortunately the more severe problems such as aseptic meningitis, venous thromboembolism and acute renal failure remain rare.

High-dose immunoglobulin when administered i.v. has immunomodulatory properties. The precise mechanism of
action of IVIG is complex and not yet fully understood. Interaction between the Fc fragment of IgG and the Fcγ receptor on target cells appears to be essential for many anti-inflammatory effects. Recent work has highlighted further the numerous actions involving both the innate and adaptive immune system [3].

IVIG has been used in various inflammatory disorders, and although benefit has been shown in some conditions such as Kawasaki disease (KD), in most cases evidence has been anecdotal in the form of case reports with few randomized controlled trials (RCTs). Many of these reports discuss small numbers of patients treated with IVIG when standard therapy has failed. Pyne et al. [4] reviewed the literature for the use of IVIG in autoimmune rheumatic diseases in 2002. Although there have been many reports since, evidence from large RCTs has been limited. Use in inflammatory diseases has increased and a recent literature search revealed more than 150 off-label usages of IVIG, which included 6781 patients in clinical trials and 362 patients in case reports [5]. In this review, we discuss the problems of IVIG shortages experienced in recent years and the method of prescribing IVIG in the UK, following the recent introduction of the UK demand management plan. We then discuss the evidence of benefit of IVIG in different rheumatological diseases.

Supply shortages and the UK’s Department of Health demand management programme for IVIG—how does this affect the UK rheumatologist?

Over recent years, there has been an increasing shortage in the supply of immunoglobulin. This has been due to several reasons, but importantly the increased use of immunoglobulin for the treatment of assorted new clinical indications, often used without evidence of benefit in the literature. Other factors have affected supply and production costs, particularly in the UK. The problem of variant Creutzfeldt–Jakob disease required plasma to be bought from the USA rather than being sourced from the UK, and the closure of the Scottish National Blood Transfusion Service further limited UK supply. With the development of recombinant coagulation factors, the demand for plasma-derived factors has decreased further adding to increased production costs generally. These supply shortages have adversely affected the treatment of conditions and diseases where immunoglobulin is the treatment of choice, backed up by evidence of benefit. Supply has even limited treatment in primary immune deficiency patients where IVIG is known to be life saving.

In 2006, the Department of Health in the UK started a process to review the use of immunoglobulin. They set up a demand management programme to ensure that supply met demand by promoting the use of IVIG, based on evidence of benefit and addressing procurement and funding issues [6]; www.ivig.nhs.uk). An expert working group was set up, and clinical guidelines were published indicating the level of evidence of benefit in various clinical indications for both short- and long-term use. These indications were divided into red, where there was good evidence of benefit as the treatment of choice (high priority), blue where there was some evidence but alternatives were available (medium priority), grey where there was little evidence of benefit (low priority) and black where use was not recommended. The grey indications were often rare clinical conditions or diseases where evidence of benefit from clinical studies was understandably limited. Each hospital was required to set up a local panel of experts to aid in the decision to treat blue and grey cases so that each request could be reviewed on a case-by-case basis. Each request had to be documented on a national database, which assisted in the funding process. This plan was fully implemented in April 2009.

Certainly, this programme has already reduced the demand for immunoglobulin and is ensuring good supply for those indications deemed as high priority. However, it has complicated the process for prescribing immunoglobulin for a patient with a ‘blue’ or ‘grey’ clinical indication. For these cases, the physician needs to first obtain approval from the local hospital immunoglobulin panel. In grey cases, the panel also needs to seek agreement for funding from the primary care trust (PCT). Without agreement from these bodies, immunoglobulin should not be given. For cases not listed in the clinical guidelines, the process is the same as for grey indications.

UK rheumatologists are therefore able to prescribe short-term immunoglobulin therapy for KD, DM and juvenile DM (JDM) without prior approval from the local immunoglobulin panel. These indications are high priority and hence supply should be guaranteed even in periods of immunoglobulin shortage. Long-term immunoglobulin treatments of DM and JDM are deemed blue indications, so require approval from the local immunoglobulin panel. However, approval has to be sought both from the local immunoglobulin panel and funding approved by from the PCT before immunoglobulin treatment can be given for grey indications; juvenile and adult SLE, systemic vasculitis and ANCA disorders, systemic juvenile idiopathic arthritis, catastrophic anti-phospholipid syndrome (APS) and PM. In times of immunoglobulin supply shortage, therapy for these grey indications will be restricted. Rheumatologists will now not be able to prescribe immunoglobulin therapy for IBM or RA as these are listed as black indications.

This raises the question of clinical trials looking at the benefit of immunoglobulin therapy in rare conditions. Clearly good quality research is still needed. In rare conditions, it may be appropriate to use n – 1 patient studies. These studies would of course require support by local commissioners, and the national immunoglobulin database (www.ivig.nhs.uk) would be used to record the efficacy.

Evidence for immunoglobulin use in rheumatology

KD

KD is a systemic vasculitis presenting in young children, common in Japanese and Korean children. It was first
described in 1967 by Kawasaki [7] as ‘acute febrile mucocutaneous syndrome’. It has been well known for some time that prompt use of IVIG in children with KD prevents the development of coronary artery aneurysms (CAAs).

There is plenty of evidence to support the use of IVIG in KD. Oates-Whitehead et al. [8] published a Cochrane review in 2003. Evidence suggested a significant reduction in new CAA on treatment with IVIG when compared with placebo at 30 days. There was no significant difference in efficacy between different IVIG preparations, and the number of adverse events did not show any difference between different groups. A meta-analysis of different IVIG regimens compared with a single dose of 2 g/kg showed a significant reduction in CAA at 30 days in favour of a single high dose. There was also a significant difference in fever with high dose.

A single dose of 2 g/kg is effective in children who receive treatment within 2 days of onset of illness. A RCT looking at 178 acute KD patients has shown that a combination of corticosteroids and IVIG improved clinical course and coronary artery outcome without causing untoward effects [9]. Another RCT looking at 24 immunoglobulin-resistant acute KD cases after the first dose of IVIG showed no significant difference in the groups who had infliximab or a second dose of IVIG [10]. Studies have also shown that at a cellular level, IVIG infusion restores the T- and B-cell abnormalities, especially CD5+ B-cell abnormalities found in patients with acute KD [11].

There is strong evidence for the prompt use of IVIG, in addition to low-dose aspirin. In patients who do not respond to the first dose, a further dose of IVIG should be tried. High-dose steroids can have an additional benefit and could be considered in resistant cases.

### JDM

There are no RCTs for the use of IVIG in JDM. The available evidence so far is from open studies. A 4-year review detailed the progress of nine patients with JDM, who failed on conventional treatment or had side effects and were treated with IVIG. All patients showed clinical improvement at some point following treatment with IVIG, and the dose of prednisolone was reduced in six cases [12].

Tsai et al. [13] reported that IVIG was useful when used as an add-on therapy in seven children with JDM. Six out of seven children had clinical improvement when given IVIG once a month, but four initial responders had deterioration sometime after discontinuing IVIG.

A retrospective study by Al-Mayouf et al. [14] showed the ability of IVIG to markedly reduce the dose of steroids in 12 out of 18 children with JDM who were steroid resistant or steroid dependent. The corticosteroid dose was reduced by >50% for >3 months without clinical or biochemical flare. In summary, there are no RCTs but the current evidence would support the use of IVIG in JDM cases refractory to conventional treatment.

### SLE

To date there have been no large RCTs looking at the efficacy of IVIG in SLE. Most of the data comes from small clinical trials, case series and case reports. A study of 20 patients treated with high-dose monthly IVIG showed a beneficial clinical response in 85% of patients. Arthritis, fever, thrombocytopenia and neuropsychiatric lupus responded well compared with other symptoms. Mean SLAM score evaluated before and after treatment in nine of these patients showed a significant reduction (P < 0.0001) [21].

A retrospective analysis of 62 SLE cases that received low-dose IVIG (0.5 g/kg body weight) showed clinical improvement in many disease manifestations with a continuous decrease in SLEDAI, but thrombocytopenia, alopecia and vasculitis did not improve [22]. Various case reports suggest improvement of clinical manifestations of SLE that include myocarditis [23], cardiac tamponade [24], end-stage renal disease [25], chorea [26], polyradiculopathy [27], neuropsychiatric lupus [28], myelofibrosis [29] and pneumonitis [30]. A retrospective analysis of IVIG treatment for thrombocytopenia
(platelet count <50) in SLE revealed a transient response only in 60% of patients [31].

Levy et al. [32] studied seven patients with membranous or membranoproliferative lupus nephritis who were given one to six courses of IVIG and showed that all patients had a reduction in proteinuria with the benefit lasting for at least 6 months. However, a pilot study by Schroeder et al. [33] showed only temporary beneficial effects in mildly to moderately active SLE.

The only small pilot, randomized trial comparing IVIG with a conventional immunosuppressive drug, cyclophosphamide, was in membranoproliferative nephritis [34]. Fourteen patients (Grade III and IV nephritis) were enrolled in the trial and they all received cyclophosphamide and prednisolone for 6 months followed by either cyclophosphamide or monthly IVIG. There was no statistically significant difference in terms of proteinuria and creatinine clearance between the two groups.

In summary, there is some evidence in the form of small clinical trials suggesting the beneficial effect of IVIG in SLE; however, there is also a case report describing the onset of vasculitis [35] following the administration of IVIG. There is no role for IVIG as a first-line treatment in SLE, but it may be an option in cases resistant to conventional treatment.

DM/PM

DM and PM together are described as idiopathic inflammatory myositis and are characterized by skeletal muscle weakness, biochemical or histological evidence of muscle inflammation, skin lesions and systemic organ involvement. The only double-blinded, randomized, placebo-controlled trial investigating the use of IVIG in DM was conducted by Dalakas et al. [36]. They studied 15 patients with DM resistant to other therapies. When randomized to IVIG or placebo and crossed to the alternative therapy after a washout, there was a significant improvement in the symptom score while on IVIG in both groups. Repeated muscle biopsies in patients whose strength improved to normal showed an increase in muscle-fibre diameter, decrease in diameter of capillaries, resolution of complement deposits on capillaries and a reduction in intercellular adhesion molecule 1 and MHC class I antigens.

Clinical experience of Cherin et al. [37] in 30 patients with PM or DM suggested a significant improvement in global scores and clinical improvement evaluated by muscle test scores. The same group [38] reported long-term efficacy of IVIG in chronic refractory PM. Thirty-five patients were included in the study and received 1 g/kg/day of IVIG for two consecutive days per month for 4–6 months. Significant clinical and biochemical improvement was shown in 70% and this response remained stable in 50% of responders for over 3 years.

Danielli et al. [39] studied the efficacy of IVIG as an adjuvant therapy for DM or PM patients. Twenty patients were initially treated with prednisolone and CSA. Thirteen out of 20 patients were refractory to this initial treatment and received a trial of IVIG with or without plasmapheresis. These patients had a significantly higher incidence of clinical remission at the end of the 4-year follow-up period ($P < 0.001$). No additional benefit was described from the plasmapheresis.

The only study to determine the efficacy of IVIG as first-line therapy in PM and DM involved 11 patients [40]. This was an open-label study and significant clinical improvement was noted in only three patients with no response in eight. There was no significant improvement in mean muscle power post-treatment.

Therefore, with the available evidence, it is reasonable to use IVIG in the treatment of refractory cases of DM and possibly PM as an additional treatment. There is no evidence to suggest that IVIG should be used as first-line treatment and rather should be reserved for resistant cases.

SSc

To date, there is limited evidence for the use of IVIG in SSc. Current evidence comes from small case studies and case reports. Nacci et al. [41] conducted a pilot study in seven patients with SSc, five with limited and two with diffuse SSc. These patients had severe and refractory joint involvement in spite of treatment with MTX and cyclophosphamide pulse therapy. They were treated with six consecutive courses of IVIG (2 g/kg body weight during 4 days a month). Assessment at 6 months post-treatment showed significant reduction in joint pain and tenderness ($P < 0.03$), improvement in hand function ($P < 0.02$), improvement in quality of life ($P < 0.03$) and significant reduction in skin score ($P < 0.003$). All but one patient showed improvement suggesting a beneficial effect in SSc patients refractory to conventional anti-rheumatic agents.

Amital et al. [42] studied eight patients with fibrotic diseases (three had scleroderma) and reported that fibrotic excess was reduced in all these patients on treatment with IVIG. They suggested IVIG might enhance resorption of fibrosis and promote healing. Another study of 15 SSc patients showed significant improvement in the mean skin score ($P < 0.001$) with IVIG, but further analysis revealed that the improvement was more pronounced in patients with longer duration of disease. Therefore, some of this improvement could be attributed to the natural course of disease [43]. Despite these studies, the lack of evidence from larger studies and RCTs limits the certainty of benefit in SSC.

ANCA-associated systemic vasculitis

ANCA-associated systemic vasculitis (AASV) is a group of systemic small-vessel vasculitic disorders associated with a positive ANCA. It comprises WG, microscopic polyangiitis (MPA) and Churg–Strauss syndrome (CSS). ANCA is a pathogenic antibody associated with neutrophil degranulation and release of lytic granules. The ability of IVIG to regulate autoantibody production by B cells through idioype–anti-idiootypic reactions made this an attractive treatment option for systemic vasculitis in the 1990s. In vitro studies showed that $F(ab')2$ fragments of IVIG could block...
ANCA binding to antigen in a dose-dependent fashion [44].

To date, there has been only one randomized, double-blinded, placebo-controlled trial, investigating the efficacy of a single course of IVIG (total dose of 2 g/kg) in previously treated patients with persistent disease [45]. Thirty-four patients were randomized to receive IVIG or placebo (17 in each group). Patients with WG or MPA who had ongoing disease activity despite at least 2 months treatment with prednisolone and one other immunosuppressant were included. Results showed some improvement in disease activity (as assessed by the Birmingham Vasculitis Activity Score) in the IVIG group (P < 0.01) and a fall in CRP, but this effect was not maintained beyond 3 months. However, there was no difference in mortality, time to relapse and need for rescue therapy between the two groups.

There have been a number of open-label studies investigating the use of IVIG. The most recent study by Martinez et al. [46] was a multi-centre, prospective, open-label study of 22 patients. They evaluated the safety and efficacy of IVIG administered for 6 months to treat relapses of WG (19) or MPA (3) occurring either under treatment or during the year following discontinuation of corticosteroids and/or immunosuppressants. Patients were treated with IVIG 0.5 g/kg/day for 4 days every month for 6 months. All patients responded initially, but at 9 months only 13 patients showed complete remission and 1 had partial remission. This response persisted in 8 of the 14 patients in remission at 24 months. Seven patients experienced minor side effects. This study could be criticized because patients were also on immunosuppressant agents and additional steroids were allowed to treat relapses, making it difficult to identify how much of the benefit was attributable to the IVIG alone [47].

Jayne et al. [48] used IVIG as the sole therapy in six newly diagnosed cases of AAVS and showed that four patients had full remission after 1 year, out of which two relapsed at between 16 and 48 months of follow-up. The same group [49] also showed in an open-label trial that IVIG induced remission in 15 out of 16 patients with systemic vasculitis although the response was sustained in only 8 patients.

In 1995, Richter et al. [50] studied IVIG (single/multiple courses of 30 g/day for 5 days) in poor responders to conventional treatment. Although six patients (40%) had clinical benefit, improvement was confined to single organ manifestations (skin, ENT findings). No improvement was seen with conjunctivitis, scleritis, pericarditis or nephritis. They also found that repeated courses of IVIG were no more effective than a single course.

In 1999, Levy et al. [51] investigated the benefit of IVIG in 10 patients resistant to conventional therapy. These patients received IVIG 2 g/kg monthly (5 day schedule). This was an uncontrolled study and each patient received between one and six courses of IVIG. They reported a clinical response in 6 of these 10 patients (60%).

Most of the above-mentioned studies involved patients with WG and MPA. The efficacy of IVIG has been studied separately in CSS patients. In 1991, Hamilos and Christensen [52] first reported the successful treatment with IVIG therapy in a 33-year-old lady with CSS, who was resistant to conventional steroid treatment. She showed a marked improvement in her vasculitic symptoms with normalization of eosinophil count. In 2004, Tsurikisawa et al. [53] showed a significant improvement in neurological and cardiac manifestations in 15 patients with CSS, who were not responsive to corticosteroids with or without cyclophosphamide. There was also a significant improvement in muscle performance (assessed by manual muscle test). Danieli et al. [54] studied long-term effectiveness of IVIG with plasmapheresis as an adjunctive treatment along with prednisolone and cyclophosphamide in CSS. This open-label study showed rapid and sustained recovery, which persisted at long-term follow-up (a mean of 3 years) in the study group when compared with the control group who had prednisolone and ciclophosphamide only. Although the results are in favour of IVIG, given that the study and control groups were not randomized and the numbers were small, interpretation should be cautious.

In summary, there is some evidence to suggest that IVIG is beneficial initially, but the response is not sustained in most cases. It is possible that some organ manifestations respond better than others. The current evidence suggests that IVIG could be considered when other conventional treatment options have failed.

Other vasculitis

Most of the clinical trials in the literature have concentrated on AAV. There have been some isolated case reports of the use of IVIG in HSP. Beneficial effects were reported mainly in the context of severe gastrointestinal manifestations of HSP [55, 56]. In contrast, paradoxical and persistent renal impairment was also reported in a HSP patient with IVIG treatment [57].

APS

IVIG has been used in pregnant women with APS either primary or secondary to SLE. In 1988, Carreras et al. [58] first used IVIG in a pregnant woman with APS who had early miscarriages and reported a successful live birth following monthly treatment with IVIG. In 2000, Branch et al. [59] conducted a multi-centre, randomized, double-blinded, placebo-controlled trial enrolling 16 pregnant women with APS. The study group received IVIG in addition to standard treatment (low-dose heparin and aspirin), whereas the control group received placebo and standard treatment. Both groups had excellent obstetric outcomes and IVIG did not show any statistically significant benefit beyond the standard treatment. A prospective observational study by Jeremic et al. [60] compared low molecular weight heparin (LMWH) and aspirin together vs additional IVIG in 40 patients, but failed to show any statistical difference in pregnancy outcomes between the two groups.
Moreover, there have been two RCTs reported suggesting standard therapy with LMWH and aspirin is superior to IVIG. The first study was in 2003 by Triolo et al. [61] that included 40 patients and showed the standard therapy group had an 84% live birth rate compared with 57% in the IVIG group. More recently, Dendrinos et al. [62] published the results of a prospective, multi-centre, RCT (conducted between 2002 and 2006) comparing LMWH plus low-dose aspirin vs IVIG for recurrent abortion associated with APS. Eighty-five patients aged 18–39 with recurrent spontaneous abortions (RSAs) before 10 weeks of gestation were enrolled in the study. Women treated with LMWH plus low-dose aspirin had a higher rate of live births (72.5%) than those treated with IVIG (39.5%) \( P = 0.003 \).

A more recent RCT by Perricone et al. [63] compared efficacy of IVIG with prednisolone and NSAIDs in 24 pregnant women suffering with RSAs. There were four patients with SLE, APS and RSA in the IVIG group, but all the remaining patients in both groups were SLE and RSA alone. This study showed a significant clinical benefit as assessed by the Lupus Activity Index-Pregnancy Scale \( P < 0.0001 \) in the IVIG group. In the IVIG group, 100% of patients had successful pregnancies compared with a 25% abortion rate in the steroid group.

IVIG has also been tried in catastrophic APS along with other treatment modalities, but there are no clinical trials reporting the efficacy of IVIG in this condition. One paper [64] reports reduction in mortality by \( \sim20\% \) with the use of full anticoagulation, corticosteroids, plasma exchange and IVIG as first-line therapies, but how much of this reduction could be attributed to IVIG alone is unclear.

As the evidence stands, currently there is no role for IVIG as first-line therapy in treating women with APS and RSA. Conventional treatment with aspirin and LMWH appears superior to IVIG. It could be argued that the study by Branch et al. [59] was small and did not have the power to show the statistical significance of IVIG as an adjuvant therapy.

RA

IVIG has been shown to be ineffective in adult RA by many studies. One randomized, double-blinded, placebo-controlled study of 32 patients with early active RA showed no significant difference in disease activity between high-dose IVIG and placebo [65]. Another randomized, double-blinded, placebo-controlled trial by Kanik et al. [66] investigating the efficacy of low-dose IVIG in 20 patients with treatment refractory RA also failed to show any therapeutic effect. Hence, there is no evidence of a beneficial role for IVIG in adult RA.

Miscellaneous

There are several case reports suggesting a beneficial role of IVIG in the resolution of arthritis [67], refractory vasculitis [68], peripheral neuropathy [69, 70] and dysautonomia [71] associated with SS. However, there are no clinical trials to support this.

A small open-label study evaluated the role of IVIG in treatment of ocular Behçet’s disease [72]. Six eyes of four patients refractory to steroids and CSA were treated with multiple doses of IVIG (0.5/kg of each dose) over a 1-year period. All six eyes showed good response to IVIG. Kaaja and Julkunen [73] used IVIG and corticosteroid to prevent the development of congenital heart block (CHB) in eight high-risk mothers (anti-Ro/SSA-positive and previous pregnancy with CHB), but showed no beneficial role for IVIG in preventing the recurrence of CHB.

There are no case reports or clinical trials for the use of IVIG in AS.

Successful use of IVIG has been reported in Kikuchi’s disease (an idiopathic illness characterized by self-limiting lymphadenitis) [74]. IVIG was used in this case to treat severe head and neck swellings and these swellings improved within 4 days and complete resolution occurred by 8 weeks.

Summary

The role of IVIG in rheumatological disease has been clarified in some conditions over recent years. However, uncertainty still exists in several diseases. Diagnostic difficulties and the absence of clear outcome parameters and measures of disease activity in some conditions are probably responsible for this situation. This illustrates the need for more research of good quality to further identify appropriate and effective use. The recent shortage of IVIG highlights the need for responsible use by all physicians, guided by evidence of clinical benefit. Currently, use in England has to adhere to the newly introduced national demand management plan for IVIG. This is likely to restrict the use in some rare rheumatological conditions but will prioritize use in those where benefit has clearly been established. IVIG therapy may not be new but remains an effective component of the modern rheumatologist’s toolkit.

Rheumatology key messages

- IVIG is beneficial in KD, DM and JDM.
- The UK demand management plan restricts IVIG use where benefit is unproved.
- Further studies in rare conditions are still required to assess IVIG response.

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References


38 Cherin P, Pelletier S, Teixeira A et al. Results and longterm followup of intravenous immunoglobulin infusions in...


