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Last Name: de Nettancourt
Email: annabel.denettancourt@aphp.fr
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Bendamustine-rituximab for anti-myelin-associated-glycoprotein neuropathy: a retrospective study of 33 patients.

Annabel de Nettancourt, Rabab Debs, Karine Viala, Cécilia Even, Thierry Maisonobe, Thimothée Lenglet, Sylvain Choquet, Inès Boussen, Véronique Morel, Nicolas Gauthier, Adrien Grenier, Pascale Ghillani-Dalbin, Lamia Hassani, Véronique Leblond, Marine Baron, Damien Roos-Weil

Anti-myelin-associated glycoprotein (MAG) neuropathy is a rare and disabling condition characterised by progressive demyelinating ataxic sensory-motor polyneuropathy. The most commonly used first-line therapy in symptomatic patients is rituximab monotherapy, which leads to neurological improvement in approximately 30-50% of cases with a median delay of 9-12 months. While chemoimmunotherapy (CIT) has been demonstrated to yield deeper and longer responses than rituximab in WM, CIT regimens have not been extensively studied in anti-MAG neuropathy.

The present study aimed to investigate the neurological and hematological responses in patients with anti-MAG neuropathy treated with bendamustine-rituximab (BR) in Pitié-Salpêtrière hospital, Paris. Thirty-three patients were retrospectively identified through medical and biological records. Clinical, biological, and EMG features at the initiation of treatment and at subsequent time points (M3, M6, M12 and M24) were collected. The degree of neurological disability and the response to treatment were evaluated using the Clinical Global Impression (CGI) scale, the modified Rankin scale (mRS), and the Overall Neuropathy Limitations Scale (ONLS).

At BR initiation, the median age of the cohort was 60 years (IQR25-75, 54-67). The median time between onset of symptoms and treatment initiation was 13 months (IQR25-75, 5-16). The median IgM peak and anti-MAG titer were 4.9 g/L (IQR25-75, 1.0-7.3) and 28045 U/mL (IQR25-75, 19245-38281) respectively. The most frequent type of neurological presentation was progressive worsening (61%). The most common symptoms were paresthesia (78%), sensory deficit (76%) and ataxia (70%). Forty-two percent had distal lower limb motor deficiency. The most frequent EMG pattern was sensory-motor length-dependent demyelinating neuropathy.

The median ONLS and mRS were 3.5/12 (IQR25-75, 2-5) and 2.6/5 (IQR25-75, 2-4) at BR initiation. BR was administrated as first-line, after rituximab monotherapy or after CIT in 19, 7 and 7 cases, respectively. All patients received BR 50-90 mg/m2 D1-2, 4-6 28-day cycles. No toxic deaths were reported, one patient discontinued BR after 4 cycles and three experienced dose reductions due to adverse events (AEs). AEs included 24% grade 3+ neutropenia and 15% all grade skin reactions.

Median follow-up was 34 months (IQR25-75, 21-43). Twelve months after starting BR, median ONLS and mRS were 2.3 (IQR25-75, 1-3) and 1.7 (IQR25-75, 1-3), respectively. 76% had a neurological response as assessed by CGI, while 90% and 43% improved their ONLS and mRS at M12 with median changes of 1.1 and 0.6 points (range, -1 to 4 and -1 to 2), respectively. Electrical improvement was seen in 12/25 patients (48%) at M12. The median time to first clinical response according to CGI and ONLS was between 3 and 4 months. Clinical motor improvement was observed in 6 out of 11 evaluable patients. Biological CR was obtained in 7/22 evaluable patients (31%) with a median IgM decrease of 58%. Six patients (18%) required a new line of treatment after BR.

BR is a promising approach for first-line or relapsed refractory anti-MAG neuropathy, resulting in rapid efficacy and high response rates that compare favorably with rituximab monotherapy. A matched analysis with patients receiving rituximab monotherapy will be presented at the IWWM meeting.

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Paris, the 15th July 2024,

I hereby certify, Pr Damien Roos-Weil, that Ms Annabel de Nettancourt is a delegate in training in our hematology unit, that she is submitting the work carried out in our unit entitled "Bendamustine-rituximab for anti-myelin-associated-glycoprotein neuropathy: a retrospective study of 33 patients" and that she will applied for a YIA grant.

Best regards

Pr Damien ROOS-WEIL
Hématologie Clinique
PU-PH
GH Pité-Salpêtrière-CFx
47-83 Boulevard de l'Hôpital – 75651 Paris Cedex 13