

Pagnoux C, Mahr A, Hamidou MA, Boffa JJ, Ruivard M, Ducroix JP, Kyndt X, Lifermann F, Papo T, Lambert M, Le Noach J, Khellaf M, Merrien D, Puéchal X, Vinzio S, Cohen P, Mouthon L, Cordier JF, Guillevin L; French Vasculitis Study Group.

*Collaborators (171)*

*Rispa P, Baidi N, Chrétien O, Cevallos R, Smail A, Darmaillacq JG, Dubas F, Maghakiam MN, Moreau C, Dubos-Arvis C, Frogner R, Gobert P, Pollini J, Pingat D, Janin-Manificat L, Lafon B, Kettaneh A, Moiton M, Ragnaud JM, Viillard JF, Boudray C, Raphanel B, Renand JP, Roux M, Bonnaire G, Guiso A, André JM, Hanrotel C, Perrichot R, Louvet J, Artigues N, Hurault de Ligny B, Le Hello C, Letellier P, Lobbedez T, Ollivier Y, Pujo M, Ryckelynck JP, Montseny JJ, Pertuiset E, Collet P, Ayach B, Dion JJ, Mouawad H, Damade R, Dupouët L, Asgaraly K, Depernet B, Colin T, Ioos V, Rieu V, Belmatoug N, Foulon L, Jebrak G, Du Coedic L, Merrien D, Bachmeyer C, Dumoulin A, Godeau B, Michel M, Pastural M, Schaeffer A, Geffroy M, Bielefeld P, Fichet D, Saraux JL, Imbert P, Ehrlicher P, Azria A, Mariette X, Tiab M, Delansorne D, Boullanger N, Closs-Prophette F, Goldstein A, Bouscaud L, Meunier V, Hachulla E, Hatron PY, Launay D, Hottelart C, Liozon E, Longuet O, Loustaud-Ratti V, Soria P, Vidal E, Geffray L, Henri P, Landru I, Guillemot JM, Cottin V, Gentil B, Demolombe-Rague S, Girard-Madoux MH, Ninet J, Pinède L, Meynieux JP, Serratrice J, Xeridat B, Bagnères D, Roudier J, Denis B, Boillet N, Geraads A, Teyssandier R, Degraeve F, Le Quellec A, Rivière S, Rogé C, Fauchay JP, Wahl D, Agard C, Meker D, Bensakel S, Vecina F, Aubier M, Foulon G, Jebrak G, Lelièvre P, Lidove O, Mignon F, Meyer O, Piperaud M, Queffeuilou G, Vrtovsnik F, Aouba A, Arène JP, Bérezné A, Bienvenu B, Le Guern V, Benveniste O, Dimitri D, Lê Thi Huong D, Généreau T, Bergeron A, Bourgarit A, Farge D, Martinez F, Sérénis D, Aslangul E, Le Jeunne C, Arnal C, Cadranet J, Daugas E, Pelle G, Rossert J, Wislez M, Gayraud M, Bruet A, Hillion Y, Paccalin M, Roblot P, Léone J, Pennaforte JL, Delaval P, Barbier S, Legallicier B, Dominique S, Charasse C, Coëtmeur D, Duhamel E, Goulias JP, Bournérias F, Gautherie P, Schlienger JL, Vidal A, Diot E, Diot P, Vanhille P, Bindi P, Cervantes G.*

*Université Paris Descartes, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, Paris, France. pagnoux@cch.aphp.fr*

**BACKGROUND:** Current standard therapy for Wegener's granulomatosis and microscopic polyangiitis combines corticosteroids and cyclophosphamide to induce remission, followed by a less toxic immunosuppressant such as azathioprine or methotrexate for maintenance therapy. However, azathioprine and methotrexate have not been compared with regard to safety and efficacy.

**METHODS:** In this prospective, open-label, multicenter trial, we randomly assigned patients with Wegener's granulomatosis or microscopic polyangiitis who entered remission with intravenous cyclophosphamide and corticosteroids to receive oral azathioprine (at a dose of 2.0 mg per kilogram of body weight per day) or methotrexate (at a dose of 0.3 mg per kilogram per week, progressively increased to 25 mg per week) for 12 months. The primary end point was an adverse event requiring discontinuation of the study drug or causing death; the sample size was calculated on the basis of the primary hypothesis that methotrexate would be less toxic than azathioprine. The secondary end points were severe adverse events and relapse.

**RESULTS:** Among 159 eligible patients, 126 (79%) had a remission, were randomly assigned to receive a study drug in two groups of 63 patients each, and were followed for a mean (+/-SD) period of 29+/-13 months. Adverse events occurred in 29 azathioprine recipients and 35 methotrexate recipients (P=0.29); grade 3 or 4 events occurred in 5 patients in the azathioprine group and 11 patients in the methotrexate group (P=0.11). The primary end point was reached in 7 patients who received azathioprine as compared with 12 patients who received methotrexate (P=0.21), with a corresponding hazard ratio for methotrexate of 1.65 (95% confidence interval, 0.65 to 4.18; P=0.29). There was one death in the methotrexate group. Twenty-three patients who received azathioprine and 21 patients who received methotrexate had a relapse (P=0.71); 73% of these patients had a relapse after discontinuation of the study drug.

**CONCLUSIONS:** These results do not support the primary hypothesis that methotrexate is safer than azathioprine. The two agents appear to be similar alternatives for maintenance therapy in patients with Wegener's granulomatosis and microscopic polyangiitis after initial remission. (ClinicalTrials.gov number, NCT00349674.) 2008 Massachusetts Medical Society