



RE: METHOTREXATE IN THE TREATMENT OF ARTHRITIS AND CONNECTIVE TISSUE DISEASE

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We read with interest the article by Wilke et al¹ and would like to comment on *Table 1*, which summarizes the use of low-dose methotrexate for the treatment of rheumatoid arthritis. Under "Unique findings," the authors, referring to the article by Weinblatt et al,² state that HLA-DR2 was found with increased frequency in patients who had a marked response to methotrexate. We have conducted and published two studies demonstrating that HLA-DR2 is not a marker for disease response in patients with rheumatoid arthritis receiving methotrexate. The first study involved a group of 32 patients treated at our institution. Since they were not part of a controlled study, response was evaluated based on available data from the different treating rheumatologists. We found no association between response and DR2 or any other HLA specificity.³ We then conducted a second and more rigorous study that involved 40 of 49 patients from the Cooperative Systematic Studies on the Rheumatic Diseases (Methotrexate-clinical trial).⁴ No association was apparent. Moreover, no significant difference in the frequency distribution of any HLA-DR specificity was found between the eight responders and the 32 non-responders, and no responder was HLA-DR2 positive.⁴ Thus we believe that neither HLA-DR2, nor

any other HLA-DR specificity, can be considered a genetic marker for response to methotrexate.

REFERENCES

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2. Weinblatt ME, Coblyn JS, Fox DA, et al. Efficacy of low-dose methotrexate in rheumatoid arthritis. *N Engl J Med* 1985; **312**:818-823.
3. Alarcón GS, Guyton JM, Acton RT, Barger BO, Koopman WJ. DR2 positivity and response to methotrexate in rheumatoid arthritis (letter). *Arthritis Rheum* 1986; **29**:151.
4. Williams HJ, Willkens RF, Samuelson CO Jr, et al. Comparison of low-dose oral pulse methotrexate and placebo in the treatment of rheumatoid arthritis: a controlled clinical trial. *Arthritis Rheum* 1985; **28**:721-370.

REPLY

We appreciate the letter by Alarcón and associates and agree with their comments. It is clear from their work that no particular DR or other tested HLA locus emerged as a marker for enhanced disease response to methotrexate in their population of patients with rheumatoid arthritis. We included the information about HLA-DR2 in order to thoroughly characterize the differences and special features of the published double-blind controlled efficacy studies of methotrexate in rheumatoid arthritis.

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