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MARKOV MODEL PROJECTION OF REMISSION STATUS FOR EARLY VERSUS DELAYED STEP-UP ADALIMUMAB USE IN MODERATE TO SEVERE CROHN'S DISEASE

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Introduction No randomised clinical trials have compared early treatment with anti-TNF agents and conventional delayed step-up treatment for patients with moderate to severe Crohn's disease (CD). The goal of this study was to project remission rates in patients with moderate to severe CD with early versus delayed step-up use of adalimumab (ADA) using a Markov model.

Methods The Markov model considered 4 states: remission, no remission but response, no remission and no response, and discontinuation. Each treatment cycle was 4 weeks. In the early treatment arm, patients with shorter disease duration (onset ≤ 2 years) would start ADA without prior use of immunomodulators (IMMs). In the step-up treatment arm, patients with longer disease duration (onset > 2 years) would be treated with IMMs before switching to ADA owing to lack of response for 2 consecutive months. Transitional probabilities for patients on ADA were estimated using a multinomial logistic model using data from the CHARM trial,¹ specifically the treatment arm of ADA 40 mg every other week. Transitional probabilities for patients on IMM treatment in the step-up treatment arm were derived from literature.² One-year remission rates with early and step-up use of ADA were projected with the estimated transitional probabilities.

Results The multinomial logistic model estimated that patients in the early ADA treatment arm had a higher probability of transitioning from moderate/severe disease to remission during the induction cycle (weeks 0–4) than did patients in the step-up arm (54.8% vs 30.4%, $p=0.0106$). After achieving remission, early use patients had a higher probability of staying in remission than did step-up patients (91.5% vs 78.2%, $p<0.0001$). Using the estimated transitional probabilities, the Markov model projected early use patients to have a remission rate of 46.2% at the end of 1 year, with cumulative time in remission of 0.57 years. For step-up patients, the model projected a remission rate of 37.5% at the end of 1 year, with cumulative time in remission of 0.36 years.

Conclusion Early initiation with ADA was projected in a 1-year Markov model to result in higher remission rates and longer time in remission than delayed step-up therapy.

Competing interests E. Loftus Jr Grant/Research Support from: Abbott, Consultant for: Abbott, J. Chao Shareholder with: Abbott, Employee of: Abbott, M. Yang Shareholder with: Abbott, Employee of: Abbott, P. Pollack Shareholder with: Abbott, Employee of: Abbott, Z. Li Employee of: Analysis Group, under contract with Abbott, R. Thakkar Shareholder with: Abbott, Employee of: Abbott, P. Mulani Shareholder with: Abbott, Employee of: Abbott.

Keywords adalimumab, Crohn's disease, early therapy.

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