Retention and clinical response to abatacept in patients with rheumatoid arthritis: an Italian perspective

Sirs,

Country differences are important considerations when assessing the impact of patient characteristics on clinical response to anti-rheumatic drugs (1). In Italy, the proportion of people aged ≥65 years is one of the highest in Europe (2) and is likely to be accompanied by an increased burden of rheumatoid arthritis (RA) (3). Abatacept is approved as a first-line biologic after disease-modifying anti-rheumatic drug failure in Italy (4). Lower abatacept retention rates have been reported in European countries with easier access to biologics (1). However, Italian patients were among the least likely to discontinue abatacept in the large, 2-year, non-interventional, international ACTION cohort study (NCT02109666) in which prescribing guidelines and reimbursement were uniform across participating countries (5).

To provide a local perspective on the impact of patient characteristics on retention rate and clinical response to abatacept, we analysed the 12-month data in the Italian cohort of ACTION (n=441). Patients ≥18 years old with moderate-to-severe RA were enrolled prospectively at initiation of intravenous abatacept or retrospectively within 3 months of the first abatacept dose according to local requirements (6). Baseline rheumatoid factor (RF)/anti-citrullinated protein antibody (ACPA) serostatus was available for 371/441 patients: 183/371 (49%) were double RF/ACPA-positive; 112/371 (30%) were single RF- or ACPA-positive; and 76/371 (20%) were double RF/ACPA-negative. Baseline body mass index (BMI) was reported in 435/441 patients: 224/435 (51%) were underweight / normal; 130/435 (30%) were overweight; and 81/435 (19%) were obese.

Baseline seropositivity had a significant impact on the crude abatacept retention rate at 12 months (log-rank test: p=0.043; Fig. 1A). Crude abatacept retention rates (95% confidence intervals [CIs]) at 12 months in the Italian cohort were higher in single RF- or ACPA-positive or double RF/ACPA-positive patients (85.1% [76.9, 90.6] and 80.2% [73.6, 85.4], respectively) than in double RF/ACPA-negative patients (70.3% [58.5, 79.4]). Over 12 months, abatacept discontinuation rates due to inefficacy were numerically lower with baseline seropositivity *versus* seronegativity: 25/35, 14/20 and 18/23 patients in the double RF/ACPA-positive, single RF- or ACPA-positive and double RF/ACPA-negative subgroups, respectively. RF/ACPA positivity on abatacept initiation was associated with a trend towards improved good / moderate EULAR response rates (95% CIs) based on Disease Activity Score in 28 joints (erythrocyte sedimentation rate, otherwise C-reactive protein) at 12 months: 83.7% (76.5, 90.8), 73.1% (63.2, 82.9) and 65.9% (52.4, 79.5) in the double RF/ACPA-positive, single RF- or ACPA-positive and double RF/ACPA-negative subgroups, respectively (Fisher's exact test: p=0.056).

Crude abatacept retention rates (95% CIs) at 12 months were similar across BMI subgroups: 75.5% (69.2, 80.7), 82.1% (74.1, 87.8) and 79.4% (68.6, 86.9) in the underweight/normal, overweight and obese subgroups, respectively (log-rank test: p=0.629; Fig. 1B). Over 12 months, abatacept discontinuation rates due to inefficacy were numerically higher in the obese *versus* the underweight / normal and overweight subgroups at 15/17, 37/53 and 18/25 patients, respectively, and were associated with a higher rate of co-morbidity. Discontinuation rates due to intolerance were lower in the obese *versus* the underweight / normal and overweight subgroups: 2/17, 9/53 and 5/25 patients, respectively. There were no significant differences in good / moderate EULAR response rates (95% CIs) at 12 months across baseline BMI subgroups: 76.5% (68.8, 84.1), 75.9% (66.7, 85.1) and 73.3% (60.4, 86.3) in the underweight / normal, overweight and obese subgroups, respectively (Fisher's exact test: p=0.854).

Our findings for the Italian cohort of ACTION demonstrate improved abatacept retention and clinical response with RF/ACPA positivity and are consistent with 2-year results for the overall international population (5), and for a European RA registry analysis (7). Baseline BMI did not impact abatacept retention or clinical response, also consistent with the overall ACTION study and an international registry analysis (5, 8). These findings highlight the relevance of abatacept real-world data in different patient subpopulations to the management of RA in Italy.

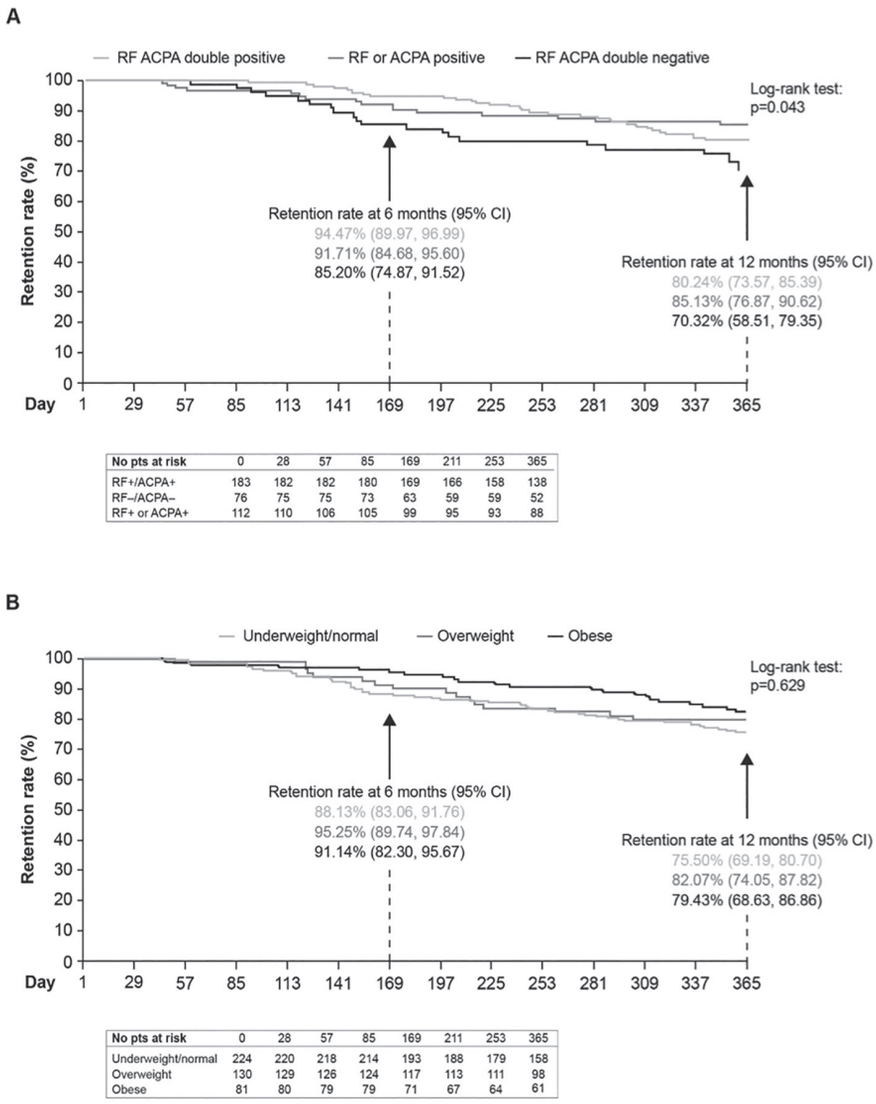

Fig. 1. Crude retention rate of abatacept by a) RF/ACPA serostatus and b) body mass index, in the Italian cohort of ACTION. ACPA: anti-citrullinated protein antibody; CI: confidence interval; pt: patient; RF: rheumatoid factor.

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Competing interests:
R. Alten has received research grants and consulting fees and is on a speaker bureau for Bristol-Myers Squibb. M. Chartier is an employee of Bristol-Myers Squibb. Y. Elbez is an employee of Excelya and has received consulting fees from Bristol-Myers Squibb. M. Le Bars and G. Patanè,are employees and shareholders of Bristol-Myers Squibb. H.-M. Lorenz is a consultant for AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, Sobi, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer and Actelion, and is on speaker bureaus for AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, SOBI, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer and Actelion. H.G. Nüßlein is a consultant and is on speaker bureaus for Bristol-Myers Squibb, AbbVie, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB.
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