Treating rheumatoid arthritis to target: an Italian rheumatologists' survey on the acceptance of the treat-to-target recommendations

R. Caporali[1], F. Conti[2], M. Covelli[3], M. Govoni[4], F. Salaffi[5], G. Ventriglia[6], C. Montecucco[1]

[1]Division of Rheumatology, University of Pavia, IRCCS S. Matteo Foundation, Pavia, Italy; [2]Dipartimento di Medicina Interna e Specialità Mediche, Reumatologia, Sapienza Università di Roma, Roma, Italy; [3]Reumatologia Universitaria, A.O.U. Policlinico Bari, Italy; [4]Dipartimento di Scienze Mediche, Reumatologia, Università di Ferrara, Ferrara, Italy; [5]Dipartimento di Scienze Cliniche e Molecolari, Clinica Reumatologica, Università Politecnica delle Marche, Ancona, Italy; [6]Member of SIMG (Società Italiana di Medicina Generale), Pinerolo, Italy.

Abstract

Objective

An educational programme was conducted in Italy in order to favour the diffusion of the rheumatoid arthritis (RA) treat-to-target (T2T) recommendations among Italian rheumatologists. Our objective was to measure the level of acceptance and applicability of the 10 recommendations to treat RA to a target of remission/low disease activity in the Italian rheumatology community, before and after the educational programme.

Methods

One hundred rheumatologists working throughout Italy were invited to participate in this two-stage web-based survey (S1-2). Three questions concerning agreement with, applicability of and possible barriers to the applicability of each of the ten T2T recommendations were administered before (S1) and after (S2) an educational event on the T2T strategy in RA. The agreement with each of the 10 recommendations was measured by a 10-point Likert scale. The applicability of each recommendation was assessed by a 5-point Likert scale (never, almost never, sometimes, almost always, always). Finally, three possible barriers to each recommendation applicability were identified.

Results

Seventy-one rheumatologists participated in S1 and 61 in S2. Level of agreement was high (mean score: 8.9 in S1, 9.1 in S2), with each recommendation receiving a score ≥7.9. The highest agreement score was achieved by recommendation 7 in both surveys. Recommendation 8 received the lowest overall agreement in both surveys. Concerning applicability, the majority of responses was "almost always". Following the educational programme, the mean degree of agreement with the recommendations increased significantly for recommendations 3, 4, 6, and 10.

Conclusion

The level of knowledge of and agreement with the T2T recommendations for RA among Italian rheumatologists is high and increased significantly for some recommendations following a specific educational event, indicating that a deeper knowledge of the T2T strategy may increase agreement and acceptance.

Key words

rheumatoid arthritis, survey, recommendations

Roberto Caporali, MD
Fabrizio Conti, MD
Michele Covelli, MD
Marcello Govoni, MD
Fausto Salaffi, MD
Giuseppe Ventriglia, MD
Carlomaurizio Montecucco, MD

Please address correspondence to:
Roberto Caporali, MD,
Division of Rheumatology,
IRCCS S. Matteo,
Piazzale Golgi 2,
27100 Pavia, Italy.
E-mail: caporali@smatteo.pv.it

Received on September 26, 2013; accepted in revised form on November 22, 2013.

Competing interests: none declared.

Introduction

As for many other chronic conditions, such as hypertension (1), diabetes (2, 3) and hypercholesterolaemia (4), standards to treat to therapeutic target were defined also for rheumatoid arthritis (RA) in 2010 (5) (Table I). An international task force involving rheumatologists and RA patients all over the world has worked to first define the therapeutic targets for RA and then elaborate 10 recommendations, based on a literature review and expert opinion, aimed at providing rheumatologists and patients with appropriate pathways to reach the set therapeutic targets. The eventual objectives were to provide RA patients with the best standards of care, obtain a tight control of the disease and thus better clinical outcomes.

The main clinical targets were defined as remission and sustained remission. Reaching a low level of disease activity, while representing a major alternative goal, was considered as the main objective only for patients with long-standing disease, who may have become refractory to therapy (5). The level of agreement among the rheumatologists participating in the task force on most of the treat-to-target (T2T) recommendations was very high, suggesting that recognition and consensus were wide and international, at least in the selected group of experts. On the other hand, as stated by the authors themselves, the recommendations were formulated with the optimal outcome of RA in mind, not taking into account potential financial or logistical constraints or access to particular therapies. Now, treating RA to therapeutic target is entering into clinical practice, and little is still known on the level of acceptance and implementation of the recommendations by rheumatologists in their daily practice (6). Haraoui *et al*. published the results of a multinational assessment reporting a great support of the T2T recommendations among the international rheumatology community and the willingness to further improve clinical practice according to the recommendations. However, the rate of response to that questionnaire by Italian rheumatologists was very low (3% of contacts), possibly due to inappropriate means of distribution (7).

With the aim of favouring the diffusion and the acceptance of the T2T recommendations among Italian rheumatologists, one hundred of them were invited to a national educational programme, chaired by the Italian representatives of the T2T task force, during which each recommendation was presented in details and proposed for discussion. Furthermore, in order to assess the level of agreement with and applicability of the T2T recommendations, all the rheumatologists participating in the educational programme were invited to also participate in a web-based survey. The survey was submitted twice, before and after the educational event, with the secondary objective to evaluate if education had improved the level of acceptance of the recommendations. The present paper summarises the results from the double survey among Italian rheumatologists. In details, the objectives of the survey were:

i) to evaluate the level of agreement with T2T recommendations on a global scale;
ii) to determine how much these recommendations were considered applicable in the daily clinical practice;
iii) to find out the main barriers rheumatologists recognised in the implementation of the recommendations.

Methods

One hundred rheumatologists from different parts of Italy were randomly selected and invited by a steering committee of Italian rheumatologists to participate in an educational programme on the T2T recommendations in RA and in the two-stage survey. The first step was the first preliminary survey (S1). Rheumatologists were contacted by e-mail and asked to anonymously answer to a web-based questionnaire. The first part of the questionnaire concerned demographic information. Then a 10-point Likert scale (1 = fully disagree, 10 = fully agree) was proposed to measure the level of agreement with each of the 10 T2T recommendations. Furthermore, the extent to which each recommendation was considered applicable in current daily practice was assessed by a 5-point Likert scale (never, almost never, sometimes, almost always, always). Finally, for each recommenda-

Table I. Recommendations for treating RA to therapeutic target (5).

Overarching principles	
A	The treatment of rheumatoid arthritis must be based on a shared decision between patient and rheumatologist.
B	The primary goal of treating the patient with rheumatoid arthritis is to maximise long-term health-related quality of life through control of symptoms, prevention of structural damage, normalisation of function and social participation.
C	Abrogation of inflammation is the most important way to achieve these goals.
D	Treatment to target by measuring disease activity and adjusting therapy accordingly optimises outcomes in rheumatoid arthritis
Ten recommendations on treating rheumatoid arthritis to target based on both evidence and expert opinion	
1	The primary target for treatment of rheumatoid arthritis should be a state of clinical remission.
2	Clinical remission is defined as the absence of signs and symptoms of significant inflammatory disease activity.
3	While remission should be a clear target, based on available evidence low disease activity may be an acceptable alternative therapeutic goal, particularly in established long-standing disease.
4	Until the desired treatment target is reached, drug therapy should be adjusted at least every 3 months.
5	Measures of disease activity must be obtained and documented regularly, as frequently as monthly for patients with high/moderate disease activity or less frequently (such as every 3–6 months) for patients in sustained low disease activity or remission.
6	The use of validated composite measures of disease activity, which include joint assessments, is needed in routine clinical practice to guide treatment decisions.
7	Structural changes and functional impairment should be considered when making clinical decisions, in addition to assessing composite measures of disease activity.
8	The desired treatment target should be maintained throughout the remaining course of the disease.
9	The choice of the (composite) measure of disease activity and the level of the target value may be influenced by consideration of co-morbidities, patient factors and drug-related risks.
10	The patient has to be appropriately informed about the treatment target and the strategy planned to reach this target under the supervision of the rheumatologist

tion three possible barriers to its applicability in the current clinical practice were hypothesised by the steering committee and proposed in the questionnaire, and the respondents were asked to choose the one that best fitted with their personal experience. After the first survey, the same rheumatologists were invited to attend a one-day educational event aimed at increasing the knowledge and favouring the diffusion of the T2T recommendations, where objectives and recommendations for treating RA to therapeutic target were presented and deeply discussed. Finally, the rheumatologists who had answered the S1 questionnaire and attended the educational session were asked to complete once again the same questionnaire for the second survey (S2). Data are presented using standard summary statistics including paired *t*-test.

Results

Demographic data

Of the 100 invited rheumatologists, 71 participated in S1: 32 (45%) were males, 33 (46%) were aged <40 years, 19 (27%) between 40 and 50 years, and 19 (27%) >50 years. Twenty-four (34%) were based in Northern Italy, 18 (25%) in Central Italy, and 21 (41%) in Southern Italy, including the main islands. Eighty-five rheumatologists attended the educational event on T2T recommendations and 61 participated in S2; all the 61 completers of S2 participated in both S1 and the educational event

Level of agreement with the recommendations

Agreement with the recommendations was high in S1 (overall mean score 8.9) and slightly increased in S2 (overall mean score 9.1), with each recommendation obtaining a score ≥7.9 (Fig. 1). The highest agreement scores were received by recommendation 7, both in S1 and in S2, followed by recommendation 10. Recommendation 8 obtained the lowest overall agreement scores in both S1 and S2. Following the educational programme on T2T recommendations, the agreement score significantly increased for recommendations 3 (p=0.004), 4 (p=0.003), 6 (p=0.02), and 10 (p=0.009).

Applicability of the T2T recommendations to daily clinical practice

Altogether, "almost always" and "always" accounted for the great majority of the answers on the applicability of each T2T recommendation, ranging from 63.4% for recommendation 8 in S1 to 93.4% for recommendation 10 in S2 (Fig. 2). The highest percentage of "never" and "almost never" were received by recommendation 5 (9.8% in S1 and 7.0% in S2). No statistically significant change was observed in the clinicians' judgment of applicability for any of the 10 recommendations after the educational event. Only recommendation 4 showed a trend towards a significant increase in applicability, which however did not reach statistical significance.

Barriers to the application of the T2T recommendations

Among the barriers most frequently identified (Table II) there was lack of time during the outpatient visit (recommendations 4, 5, and 6). Difficulties in convincing patients to continue treatment when they feel good enough were judged the main barriers to the application of recommendations 8 and 9. Similarly, in the application of recommendation 10, difficulties are encountered in convincing patients with early phase RA to accept an intensive treatment or patients with mild symptoms on the need of adjusting medications. Other barriers were identified in attaining the fixed clinical targets: "only a minority of RA patients actually achieve clinical remission" was primarily objected to recommendation 1, and even low disease activity was judged difficult to obtain in long-standing disease patients (recommendation 3). Barriers to the application of recommendation 7 were not only lack of time but also lack of adequate tools to objectively assess functional impairment.

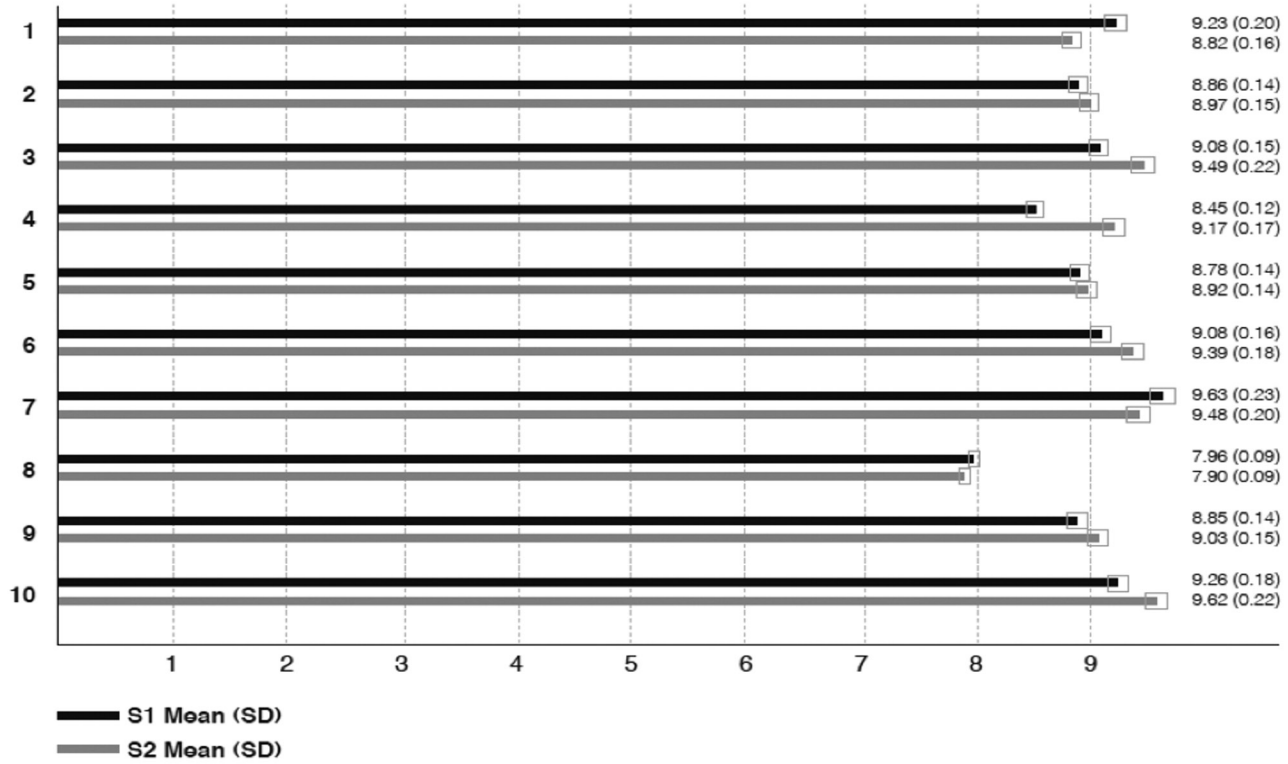

Fig. 1. Average agreement scores for the 10 T2T recommendations in the two surveys, S1, before the educational event on treating rheumatoid arthritis to therapeutic target, and S2, after the educational event. S1, n=71; S2, n=61.

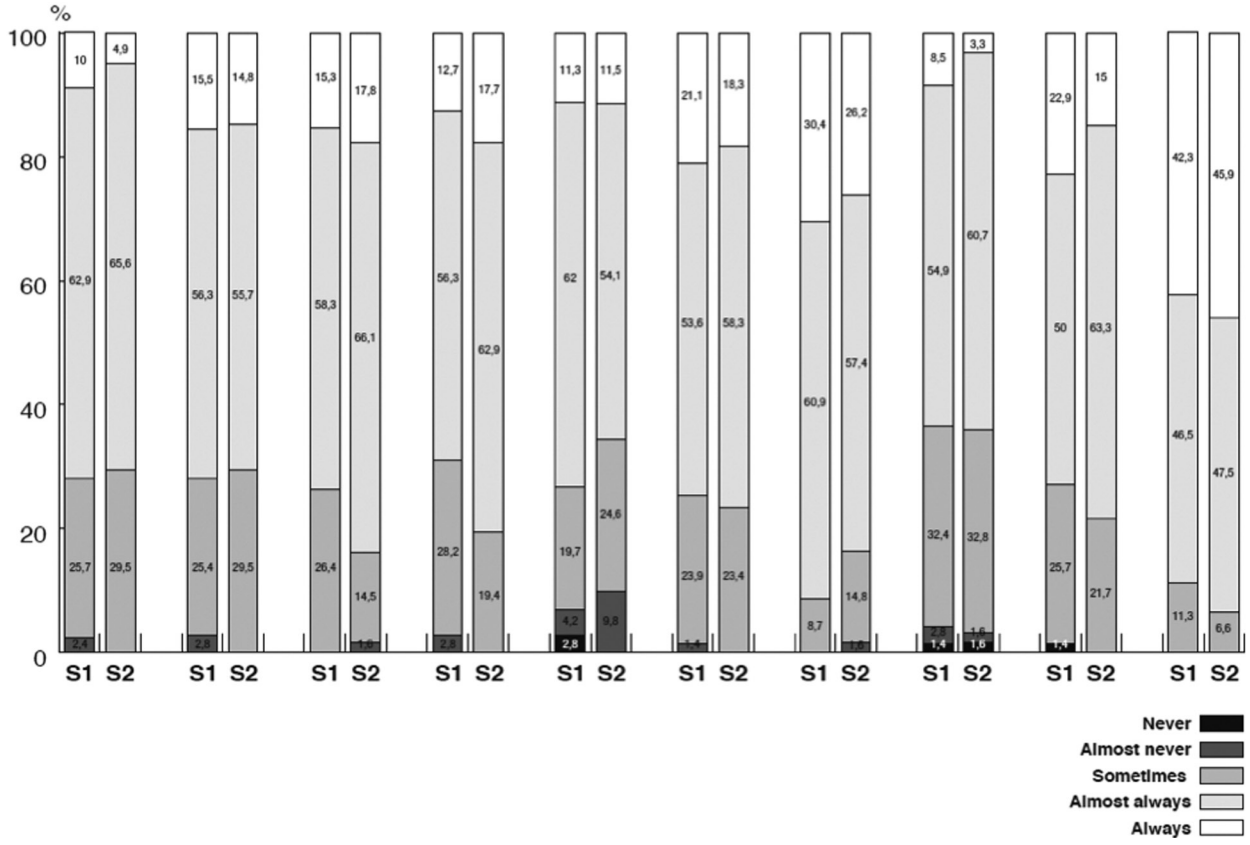

Fig. 2. Applicability of each of the 10 T2T recommendations in daily clinical practice, as judged before (S1) and after (S2) the educational event. S1, n=71; S2, n=61.

Discussion

The results of this Italian assessment questionnaire indicate a high level of knowledge on the recommendations to treat RA to therapeutic target by Italian rheumatologists, even before attending an educational session specifically dedicated at clarifying and discussing this subject. These results also reveal that the mean level of agreement on the recommendations was globally high, even before the educational programme, and increased, though slightly, after it. Similarly to Haraoui's results (7), recommendation 10 received one of the highest agreement scores, underlining once again the importance of patients' involvement in the therapeutic strategy in order to achieve the defined target. This is clearly stated also in the overarching principles to T2T recommendations, stating that "the treatment of RA must be based on a shared decision between patient and rheumatologists" (5).

The other recommendations obtaining the highest agreement in our survey was recommendation 7: Italian rheumatologists seem to take into great account structural damage and functional disability, beyond composite indexes, when making clinical decisions. As a matter of fact this seems in line with the need to obtain a comprehensive disease control when treating RA, in order to achieve clinical remission, halting of damage progression and absence of disability (8).

On the other hand, the recommendation receiving the lowest agreement and the most objections was recommendation 8. Italian rheumatologists seem to have reserves on the possibility to maintain the therapeutic target set initially for the whole course of the disease. Their main objection is that it is quite difficult to motivate patients to continue therapy when they feel better enough. This, together with the barriers identified to the application of recommendations 9 and 10, stresses once again the difficulties in treating RA patients to therapeutic target in the absence of thorough information and deep involvement of patients themselves in the decisions about the treatment strategy, consistently with the first overarching principle of the T2T recommendations (5). This finding probably reflects, almost in part, a well-known discordance between the physician and patient assessment of global disease activity. Actually, to this purpose, a patient version of the T2T international recommendations has been published (9); actually, an Italian translation may be useful for our patients in order to help a correct patient-rheumatologist interaction and to overcome the barriers and to improve application of recommendations 8, 9, 10.

Adherence to a T2T strategy is another issue that needs consideration (10). Vermeer *et al*. observed in a random sample of the Dutch Rheumatoid Arthritis Monitoring (DREAM) cohort a level of adherence of 69.3%, which they believed quite good (11).

In our study, adherence also seems to be quite good, even if some practical aspects of daily clinical practice, such as lack of time and lack of support, were shown to influence the clinicians' attitude towards some recommendations, especially those concerning the frequency of monitoring and the use of validated composite measures of disease activity. However, it is to be kept in mind that measuring disease activity should be considered as essential in evaluating patients with RA, and that tight control should be applied not only in clinical trials but also in clinical practice (12). The routine use of clinimetric assessment is also essential in evaluating patients treated with biological drugs (13).

Remission as the ultimate treatment goal emerged as another controversial aspect. It seems that rheumatologists, while conceptually agreeing with the T2T principle that clinical remission should be the therapeutic target, find it often difficult to obtain in clinical practice (14) and consider the achievement of low disease activity a good enough goal, especially in patients with long disease duration. It is conceivable that a more strict definition of clinical remission, as recently licensed by the EULAR/ACR working group (15), should be helpful, as well as a better understanding that T2T strategy allow a higher rate of remission, particularly in early disease.

Concerning the effectiveness of the educational programme in favouring the acceptance of the T2T recommendations, globally a slight increase in the agreement scores was obtained, but this should be evaluated in view of the very high level of agreement already obtained in the pre-educational survey. On the other hand, the agreement significantly increased for 4 selected recommendations, clearly suggesting that the opportunity to more deeply know and discuss the recommendations increased their acceptance, especially concerning clinical remission as the ultimate target, and tight control as a necessary

Table II. Main barrier to the application of each T2T recommendation identified by respondent rheumatologists.

Recommendation	Main barrier	S1 (%)	S2 (%)
1	Clinical remission is achieved by a minority of patients	38.6	30.7
2	Absence of signs and symptoms of inflammation does not necessarily mean clinical remission	88.7	82
3	Difficult to reach both clinical remission and low disease activity in established long-standing disease	65.7	57.8
4	Difficult to warrant to patients such a frequent monitoring	51.4	68.8
5	Lack of time during outpatient visit	42.3	54.3
6	Lack of time during outpatient visit	50.6	65.2
7	Lack of time and inadequate tools to assess functional impairment	48.6	53
8	Difficult to motivate patients to continue therapy when they feel good enough	43.7	37.8
9	Difficult to motivate patients to continue therapy when they feel good enough	62.7	58.2
10	Difficult to convince early arthritis and mild symptom patients undergoing intensive therapy to reach the clinical target	55.1	50

requirement to obtain it, even if difficult to routinely perform in clinical practice. One limitation of this assessment is the low number of participating rheumatologists that might not be representative of the global Italian rheumatology community. Furthermore, the fact that this type of assessment does not allow determining to what extent the recommendations are actually applied can be considered another study limitation. To this end, a much more complex methodology, implying direct audits to the involved clinics, would be required, which was beyond our scope and possibilities in this phase.

In conclusion, our assessment questionnaire among Italian rheumatologists reveals good knowledge and high conceptual agreement on the T2T recommendations. Some practical barriers have been identified to their applicability, which however was globally judged fairly high; this confirms that while T2T strategy has been an important breakthrough in RA treatment, strict adherence could be problematic, especially in some contexts and in some patients. The deeper knowledge achieved by the educational programme has significantly increased acceptance of some recommendations and this result leads us to trust that additional initiatives could further improve knowledge and diffusion of the T2T strategy in RA and increase their application in daily clinical practice.

References

1. EGAN BM, LACKLAND DT, CUTLER NE: Awareness, knowledge, and attitudes of older americans about high pressure: implications for health care policy, education, and research. *Arch Intern Med* 2003; 163: 681-7.
2. RACHMANI R, SLAVACHESKI I, BERLA M, FROMMER-SHAPIRA R, RAVID M: Treatment of high-risk patients with diabetes: motivation and teaching intervention: a randomized, prospective 8-year follow-up study. *J Am Soc Nephrol* 2005; 16 (Suppl. 1): S22-6.
3. EEG-OLOFSSON K, CEDERHOM J, NISSON PM,GUDBJÖRNSDÓTTIR S, ELIASSON B; STEERING COMMITTEE OF THE SWEDISH NATIONAL DIABETES REGISTER: Glycemic and risk factor control in type 1 diabetes: results from 13,612 patients in a national database register. *Diabetes Care* 2007; 30: 496-502.
4. PEARSON TA: The epidemiologic basis for population-wide cholesterol reduction in the primary prevention of coronary artery disease. *Am J Cardiol* 2004; 94: 4F-8F.
5. SMOLEN JS, ALETAHA D, BIJLSMA JW *et al*.: Treating rheumatoid arthritis to target: recommendations of an international task force. *Ann Rheum Dis* 2010; 69: 631-7.
6. COHEN MD, KEYSTONE EC: Issues in implementing a treat-to-target approach in RA. *Nature Rev Rheumatol* 2013; 9: 137-8.
7. HARAOUI B, SMOLEN JS, ALETAHA D *et al*.: Treating rheumatoid arthritis to target: multinational recommendations assessment questionnaire. *Ann Rheum Dis* 2011; 70: 1999-2002.
8. GOVONI M, CAPORALI R: Predicting and managing the progression of structural damage in rheumatoid arthritis: where do we stand? *Clin Exp Rheumatol* 2012; 30: 459-63.
9. DE WIT MPT, SMOLEN JS, GOSSEC L, VAN DER HEIJDE DMFM: Treating rheumatoid arthritis to target: the patient version of the international recommendations. *Ann Rheum Dis* 2011; 70: 891-5.
10. SMOLEN JS: Treat-to-target: rationale and strategies. *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S2-6.
11. VERMEER M, KUPER HH, BERNELOT MOENS HJ *et al*.: Adherence to a treat-to-target strategy in early rheumatoid arthritis: results of the DREAM remission induction cohort. *Arthritis Res Ther* 2012; 14: R254.
12. PORTER D: Intensive management of early rheumatoid arthritis: the TICORA and TEAR studies. *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S32-4.
13. CAPORALI R, CONTI F, ALIVERNINI S *et al*.; ITALIAN SOCIETY FOR RHEUMATOLOGY: Recommendations for the use of biologic therapy in rheumatoid arthritis: update from the Italian Society for Rheumatology I. Efficacy. *Clin Exp Rheumatol* 2011; 29 (Suppl. 66): S7-14.
14. BYKERK VP, KEYSTONE EC, KURIYA B, LARCHÉ M, THORNE JC, HARAOUI B: Achieving remission in clinical practice: lessons from clinical trial data. *Clin Exp Rheumatol* 2013; 31: 621-32.
15. JURGENS MS, WELSING PM, JACOBS JW: Overview and analysis of treat-to-target trials in rheumatoid arthritis reporting on remission. *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S56-63.