

EPIDEMIOLOGICAL ANALYSIS AND GEOGRAPHICAL DISTRIBUTION OF PATIENTS SUFFERING FROM RHEUMATOID ARTHRITIS, ELIGIBLE FOR FIRST-LINE THERAPY/MONOTHERAPY TREATMENT WITH SUBCUTANEOUS FORMULATION OF TOCILIZUMAB IN THE REPUBLIC OF MACEDONIA

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ABSTRACT

Rheumatoid arthritis is an inflammatory arthritis characterized by synovial tissue inflammation that leads to structural damage and disability. There are several treatment options available, which include glucocorticoids, DMARDs and biologics given alone as monotherapy or in a variety of combinations. Recent evidence has shown that early treatment is important in reducing the rate of progression of erosions and decreasing disability. The lack of adequate statistical data on number of patients that are eligible for first-line therapy/monotherapy of rheumatoid arthritis in Macedonia, triggered this epidemiological analyse describing eligible patients for first-line treatment/monotherapy distributed by gender, age and geographical allocation. The study was conducted by fulfilling a tailored questionnaire every two months in a period of six months (September 2017-February 2018) by including summarized data not related to personal data of patients nor specific drug information. The results have shown that a total of 115 patients in Macedonia are eligible for first-line therapy, whereby 54 (46%) patients were eligible for monotherapy of rheumatoid arthritis. Precise determination of these data provides patients' determination by geographical allocation and proper selection of the best treatment option and optimized therapy for each patient, furthermore when subcutaneous formulation of tocilizumab is available as an effective clinically proven treatment option for RA.

Keywords: Rheumatoid arthritis, tocilizumab, first-line treatment/monotherapy, subcutaneous

INTRODUCTION

Rheumatoid arthritis (RA) is a common autoimmune systemic inflammatory disease with an unknown aetiology that exerts its greatest impact on those joints of the body that are lined with synovium, a specialised tissue responsible for maintaining the nutrition and lubrication of the joint. It typically affects the small joints of the hands and the feet, and usually both sides equally in a symmetrical distribution, though any

synovial joint can be affected. RA results in joint pain, stiffness, swelling, and destruction [1]. Regarding diagnosis, American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) have developed a new set of criteria to classify RA based on new laboratory parameters such as anti-citrullinated peptide antibodies (anti-ACPA), C- Reactive protein (CRP), and Rheumatoid factor (RF). The new

set of criteria aims to identify early RA patients in order to institute early drug therapy, thereby reducing the functional disability and articular lesions [2]. RA affects approximately 1% of the worldwide population [3], being more common in women than in men, and at ages between 40 and 60 years [4].

RA is one of the most common chronic inflammatory diseases, and in contemporary eras has become a prototype disease entity for defining the molecular and pathological basis of chronic inflammatory syndromes [5]. It causes functional disability and premature death. Approximately 70% of patients have irreversible joint destruction and 80% of active young adults in the labour market are affected by stiffness and devastating pain. This situation generates a big loss of daily activities and vocational productivity resulting in significant reduction in quality of life. Additionally rheumatic diseases are considered public health problems affecting millions of people worldwide resulting in high and rising health-care costs [6]. There are several treatment options available, which include glucocorticoids, DMARDs and biologics given alone as monotherapy or in a variety of combinations. Recent evidence has shown that early treatment is important in reducing the rate of progression of erosions and decreasing disability [7-9]. There is no uniform agreement among rheumatologists on the best first-line DMARD in early RA, and there is considerable inter-individual variation in drug prescription [10].

The current therapies used to treat RA include nonsteroidal anti-inflammatory drugs (NSAIDs), used for the management of pain and inflammation; disease-modifying anti-rheumatic drugs (DMARDs), used as first-line therapy for all newly diagnosed cases of RA; and biological-response modifiers, targeted agents that selectively inhibit specific molecules of the immune system. Glucocorticoids and other anti-rheumatic drugs are also used to treat RA. DMARDs include methotrexate, hydroxychloroquine, sulfasalazine, and leflunomide. NSAIDs and glucocorticoids are effective in controlling the pain, inflammation, and stiffness related to RA. Unlike NSAIDs, they slow down clinical and radiographic progression of RA. The biological-response modifiers include: tocilizumab, a humanized monoclonal antibody against the interleukin-6 receptor (IL-6R); infliximab, etanercept, and adalimumab (inhibitors of tumor necrosis factor [TNF]- α); anakinra, a recombinant

inhibitor of interleukin-1; abatacept, the first costimulation blocker; and rituximab, a chimeric anti-CD20 monoclonal antibody. [11] Given the superior efficacy that tocilizumab has shown versus long time block buster adalimumab with the clinical study ADACTA [14], tocilizumab should be taken into consideration as first choice when treating patient with biologic agents.

Tocilizumab, in combination with methotrexate (MTX), is indicated for:

- the treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with methotrexate (MTX).
- the treatment of moderate to severe active RA in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists. In these patients, tocilizumab can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

Tocilizumab has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function when given in combination with methotrexate [15] According to the data from the University Clinic of Rheumatology, Skopje, 1100 patients suffering from rheumatoid arthritis (RA) are registered at the Clinic. Most of them are treated with DMARDs and corticosteroids. Patients suffering from more severe forms of RA are treated with biologics. In the Republic of Macedonia until recently patients with more severe forms were treated only with second-line biologic treatment. The motive for undertaking the study was precisely the lack of adequate statistical data on number of patients that are eligible for first-line therapy/monotherapy of RA in the country, in accordance with patients' gender, age and geographical allocation. We aim that the study will provide data for the epidemiological characteristics of rheumatoid arthritis in Macedonia, including geographical allocation of patients, which data will be useful in the future planning and organization of the health care, and selection of the most appropriate treatment option for each patient eligible for first-line therapy/monotherapy for treatment of rheumatoid arthritis. This is particularly important given the situation where effective and easy to use subcutaneous formulation of tocilizumab is available for RA patients (patients may be self-administered with pre-filled syringe of tocilizumab after proper training by medical personnel).

MATERIAL AND METHODS

Objectives

The main objective of the study was to provide epidemiological data on patients with rheumatoid arthritis treated at the University Clinic of Rheumatology (UCR), Skopje, Macedonia eligible for first-line therapy/monotherapy with subcutaneous formulation of tocilizumab, covering the period from September 2017 until February 2018. The epidemiological assessment included information on patients with RA in accordance with their geographical allocation in order to provide a precise distribution of patients across the country. Our goal was to help improve the selection of each patient eligible for first-line treatment/monotherapy for RA in light of availability of subcutaneous formulation of tocilizumab for first-line treatment/monotherapy of RA. Precise determination of these data provides a proper selection of the best treatment option and optimized therapy for each patient at the University Clinic of Rheumatology (UCR), Skopje and dispersed healthcare centres across the country.

Design

A standard questionnaire was developed only for this study and discussed with local RA experts to ensure relevance and easy comprehension. The questionnaire contained questions related to number of patients eligible for first-line therapy distributed by gender, geographical allocation and age, and number of patients eligible for monotherapy as well distributed by geographical allocation.

The questionnaires comprised of closed questions (Y/N questions) and questions that could be answered only numerically (Appendix). The collected data were not related to an individual patient, but only to the total number of patient eligible for treatment of the specific disease area in scope. The summarized report did not include any personal data of the patients or data related to any specific drug information. This observational study was conducted over a period of six months (September 2017-February 2018).

Study population

All patients included in the study were diagnosed with rheumatoid arthritis, distributed by

gender and geographical allocation. This assessment of patients eligible for first-line therapy/monotherapy for rheumatoid arthritis included only patients that were present and treated at the University Clinic of Rheumatology in Skopje, Macedonia, in sixth month period from September 2017 until February 2018.

Statistical analysis

All data were obtained from fulfilled questionnaires collected every two months, afterward a summarized report was prepared, in a period of six months (September 2017 - February 2018). Collected data were analysed as available without source data verification. The database was locked at the end of February 2018, with a total of 3 summarized valid questionnaires covering the following periods: September-October 2017, November-December 2017 and January-February 2018. Analysed data were presented as an absolute number and percentage (%) of patients eligible for first-line therapy/monotherapy for RA presented at UCR, Skopje. Descriptive statistics was used to report the results in terms of percentage of eligible patients distributed by gender, age and geographical allocation.

RESULTS

The study included 115 patients in total, diagnosed with rheumatoid arthritis and eligible for first-line therapy, whereby 29 (25.22%) were males and 86 (74.78%) females, as shown in Table 1.

Table 1. Distribution of patients eligible for first-line therapy by gender

Number of patients eligible for first- line therapy	Male	Female	Total	Period
DISTRIBUTION BY GENDER	10	26	36	Jan-Feb 2018
	7	32	39	Nov-Dec 2017
	12	28	40	Sep-Oct 2017
	29	86	115	Total
%	25.22	74.78		100

In order to gain a detailed insight and determine the current number of patients eligible for first-line treatment/ monotherapy, the patients

were additionally distributed by geographical allocation and age, as shown in Table 2, 3 and 4. According to the results showed in Table 2, the highest number of patients, 34 pts (29.57%) that were eligible for first-line therapy were between the age of 51-60 years, while the lowest number of patients, 12 pts. (10.43%) eligible for first-line therapy were older than 60 years.

These data are followed by 13 patients (11.30%) eligible for first-line therapy aged less than 30 years, 22 patients (20.00%) aged between 30-40 years and 33 patients (28.70%) aged between 41-50 years. The number of patients eligible for first-line therapy younger than 60 years was 103 patients or 89.57% of total number of RA patients.

Table 2. *Distribution of patients eligible for first-line therapy by age*

Number of patients eligible for first-line therapy	<30 y.	30-40 y.	41-50 y.	51-60 y.	>60 y.	Period
DISTRIBUTION BY AGE	1	9	12	11	5	Jan-Feb 2018
	6	11	10	7	5	Nov-Dec 2017
	6	3	11	16	2	Sep-Oct 2017
	13	23	33	34	12	Total
%	11.30	20.00	28.70	29.57	10.43	100

The study has shown that the highest rate of patients eligible for first-line therapy is observed among patients aged between 30 to 60

years, 90 pts. in total (78.27%) out of 115 patients included in the study (Figure 1).

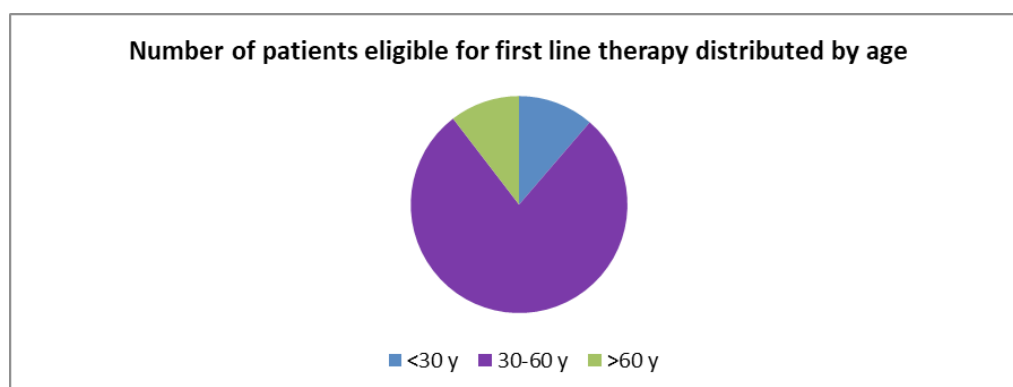


Figure 1. *The highest rate of patients eligible for first-line therapy*

On the other hand, statistical data show that according to the last publication of available labour force in Macedonia distributed by economic activity, gender and age in 2017 the highest rate of labour force consists of inhabitants aged 25 to 54 years. Out of 954212 force labour in total, 616154 are aged 25 to 54 years which represents 64.57% of the work capable population whereby 433308 are females and 295494 males [16]. Table 3 shows the number of patients eligible for first-line therapy distributed by geographical allocation whereby the highest number of patients eligible for first-line therapy are allocated in Skopje, 52 pts (45.22%), while the lowest number of patients

eligible for first-line therapy are 2 (1.74%) located in Gevgelija followed by 1 (0.87%) in Bitola.

Additionally, patients have been distributed by eligibility for monotherapy in accordance with the distribution by geographical allocation and eligibility for first-line therapy as previously described in Table 2, whereby 21 patients with RA (18.26%) out of 52 pts (45.22%) in Skopje, (as the city with the highest rate of pts eligible for first-line therapy) are eligible for monotherapy. The second rate of patients eligible for first-line therapy is Kumanovo (10 patients, 8.7%), followed by Struga and Strumica (5 patients, 4.35%), Kavadarci (4 patients, 3.48%), Tetovo (3, 2.61%), and Prilep (2, 1.74%).

Table 3. *Geographical distribution of patients eligible for first-line therapy*

Number of patients eligible for first-line therapy	Skopje	Kumanovo	Tetovo	Stip	Prilep	Bitola	Struga	Ohrid	Kavadarci	Strumica	Gevgelija	Period
GEOGRAPHICAL DISTRIBUTION	14	3	4	2	2	0	1	0	3	3	2	Jan-Feb2018
	17	7	4	4	0	0	3	0	2	2	0	Nov-Dec 2017
	21	5	3	0	3	1	1	0	5	3	0	Sep-Oct 2017
	52	15	11	6	5	1	5	0	10	8	2	Total 115
%	45.22	13.04	9.57	5.22	4.35	0.87	4.35	0.00	8.70	6.96	1.74	100

Table 4. *Number of patients eligible for first line-therapy – monotherapy*

Number of patients eligible for first-line therapy	Skopje	Kumanovo	Tetovo	Stip	Prilep	Bitola	Struga	Ohrid	Kavadarci	Strumica	Gevgelija	Period
MONO-THERAPY	5	2	0	0	2	0	1	0	3	2	2	Jan-Feb2018
	14	5	3	1	0	0	3	0	1	2	0	Nov-Dec 2017
	2	3	0	0	0	1	1	0	0	1	0	Sep-Oct 2017
	21	10	3	1	2	1	5	0	4	5	2	Total 54
%	18.26	8.70	2.61	0.87	1.74	0.87	4.35	0.00	3.48	4.35	1.74	46.96

Regarding cities with the lowest number of RA patients eligible for first-line therapy Gevgelija, 2 pts (1.74%) and Bitola, 1 pts (0.87%), all three of them are eligible for mono-

therapy 1.74% and 0.87%, respectively. In total 54 (46.96%) patients are eligible for monotherapy out of 115 patients that were eligible for first-line therapy.

Table 5. *Distribution of patients eligible for first-line treatment by region/city*

Region	Total population ^a	No. of patients with RA eligible for first-line treatment	% of patients eligible for first-line treatment in each region (%) ^b	Portion of patients eligible for first-line treatment in Macedonia (%) ^b
Skopje	619279	52	0.0083	0.00251
Kumanovo	108942	15	0.0137	0.00072
Tetovo	91431	11	0.0120	0.00053
Kavadarci	38937	10	0.0256	0.00048
Strumica	56961	8	0.0140	0.00038
Stip	48657	6	0.0123	0.00028
Prilep	75484	5	0.0066	0.00024
Struga	65485	5	0.0076	0.00024
Gevgelija	22764	2	0.0087	0.00009
Republic of Macedonia	2070226	115	0.0055	0.0055
Bitola	92329	1	0.0010	0.00004

a. The data on total population of citizens distributed by cities is extracted from the statistical review of the population on 30.06.2015 and 31.12.2015 by gender and age, distributed by municipalities and statistical regions, NTES 3-2007, Republic of Macedonia, State Statistical Office (<http://www.stat.gov.mk/Publikacii/2.4.16.10.pdf>)

b. The provided data refers to the data collected during the six months investigational period (September-January)

In accordance with the results described in Table 5 the highest rate of patients eligible for first-line treatment who suffer from rheumatoid arthritis, when taking into consideration the total population of each region is found in Kavadarci, 0.0256% while the lowest in Bitola 0.0010%. On the other hand, when comparing the number of patients eligible for first-line treatment compared to the total number of eligible patients in Macedonia, while following

a descending trend the highest rate is found in Skopje 52 pts out of 115 pts, 0.00251% out of 0.0055%, respectively, out of the total population. These values are followed by Kumanovo and Tetovo as described in the last column of Table 5, finishing with Bitola that is under the average with only 1 patient, 0.00004%. It must be underlined that the provided data is based upon the information provided during the investigational period of this observational study.

Table 6. Geographical distribution of patients eligible for first-line therapy (extrapolated data for one year period)

Number of patients eligible for first-line therapy	Skopje	Kumanovo	Tetovo	Stip	Prilep	Bitola	Struga	Ohrid	Kavadarci	Strumica	Gevgelija	Period
Geographical distribution	52	15	11	6	5	1	5	0	10	8	2	6 months investigational period
	104	30	22	12	10	2	10	0	20	16	4	1 year period (extrapolated data) Total: 230 pts

Table 6 describes the extrapolated data of patients eligible for first-line therapy whereby on annual basis it is expected the total number of patients to be 230. Based on the insight gained for the 6 months investigational period (September- January), on annual basis the number of patients eligible for first-line therapy following a descending trend would be: Skopje 104 patients, Kumanovo 30, Tetovo 22, Kavadarci 20, Strumica 16, Stip 12, Prilep 10, Struga 10, Gevgelija 4, and Bitola 2 patients.

DISCUSSION

When taking into consideration the results that have been provided by this observational study it was shown that out of 115 patients eligible for first-line therapy, 29 patients were males and 86 patients were female, 25.22% and 74.78% respectively. The distribution by gender of patients with RA treated at the UCR, once again proves that the incidence of the disease is more often in women than man and this finding is also relevant for population in the Republic of Macedonia [4].

Regarding the distribution by age, RA is the most common in patients aged between 40 and 60 years, taking 58.27% of eligible RA pa-

tients in Macedonia [4]. The total population aged between 31 to 60 years in the Republic of Macedonia accounts 918,031 inhabitants [12] out of 2,070,226 inhabitants, 44.34% in total, accordingly. This statistical result is an indicator that patients eligible for first-line therapy and diagnosed with active rheumatoid arthritis cover the most common age in the Republic of Macedonia, which additionally represents the most productive and work-capable population. Early diagnose of the disease and choosing the suitable first-line treatment for these patients will improve their quality of life, provide a positive clinical outcome and keep patients capable of working correspondingly. As previously described in Figure 1, the highest rate of pts eligible for first-line therapy are aged between 30-60 years, which age at the same time represents the labour force in Macedonia. When comparing the data obtained from the observational study and the statistical data on labour force in Macedonia, it must be noted that RA mostly affects the work capable population which additionally besides the patient himself, also affects the society resulting in decrease of the labour force in Macedonia and enhancement of costs, direct and indirect ones. Considering the symptomatology and manifestation of RA it is expected that prolonged treatment or treatment with low effective therapy will result with enhancement of the number of

RA pts who will not be able to work and will become a burden not only for the family but for the society as well. Over the last two decades, the treatment of patients with rheumatoid arthritis (RA) has changed considerably. Currently, the goal of therapy is not only symptom relief, but in particular prevention of long-term structural damage and functional decline. To this end, an increasing number of effective disease-modifying anti-rheumatic drugs (DMARDs) as well as biologic agents have been developed and have demonstrated clinical value in randomized clinical trials as a first-line therapy/ monotherapy. It has become clear that treatment should start early and must be maintained without interruption to reduce the occurrence of irreversible joint damage.[13] Everyday new therapeutic options are being developed aiming for highly effective medicines with a favourable safety profile. The University Clinic of Rheumatology in Macedonia works on providing new and more effective therapeutic options for RA patients in order to improve the clinical outcomes and the quality of life of these patients. It is a pleasure to share that UCR among other conventional treatment options for RA, also includes Tocilizumab, a contemporary first-line biological treatment option for moderate to severe forms of active rheumatoid arthritis in adults. Tocilizumab, a humanized monoclonal antibody against the interleukin-6 receptor (IL-6R) is characterized with high efficacy and a favourable safety profile established by several clinical studies. For example, the study ADACTA, which is the only head to head study between tocilizumab versus adalimumab (inhibitor of TNF alpha), has shown a superior efficacy and a favourable safety profile of tocilizumab in comparison to adalimumab, as TNF alpha inhibitor. [14] Additionally, the subcutaneous administration of Tocilizumab offers a simple use which can be implemented in the patient's home and spare the patient of making additional expenses. One of the reasons to disperse the administration of Tocilizumab sc is to provide a new possibility for patients to receive the therapy in their homes, their places of living. This is with the purpose to avoid generating expenses and at the same time to provide a possibility for other hospitals to gain experience with the medicine.

It is to be discussed that after initiation and implementation of the previously mentioned idea two cities that have the highest number of patients eligible for first-line therapy, after Skopje, to date haven't have any patient on therapy.

Kumanovo and Tetovo should be reconsidered to start administering therapy to RA patients and adhere to providing a higher treatment comfort.

The UCR always aims to providing the most suitable treatment for each patient with rheumatoid arthritis.

As previously described, this observational study accounts 115 patients that are eligible for first-line treatment, whereby 54 patients are eligible for monotherapy and this data refers to a six month investigational period. Basing upon the principles of linear extrapolation it is expected that on annual basis this number will be 230 patients per year eligible for first-line treatment and 108 patients eligible for monotherapy, respectively.

Rheumatoid arthritis (RA) is a chronic inflammatory disease which, if left untreated, leads to functional disability, pain, reduced health-related quality of life and premature mortality. Between 0.5% and 1% of the population are affected worldwide, and between 25 and 50 new cases evolve in a population of 100,000. If disease course is monitored with adjustment of medication, lifestyle factors, and exercise, as well as physical activity levels, co-morbidities may be prevented in the course of RA. During the last decade, major progress has been made in treating RA through early identification and treatment of the disease. For societies, the economic burden of RA is high in terms of direct and indirect costs, including modern drug treatment. With early treatment of RA patients, with tocilizumab as high effective therapy of choice helps in minimization the impact of the disease, promotion a better health quality and as well in long-term help in saving and rational use of health funds.

CONCLUSION

This study specifically tailored to gain insight in the current situation of patients with RA eligible for first-line therapy/monotherapy with subcutaneous formulation of tocilizumab, showed that the number of eligible patients for first-line therapy was 115 {29 (25.22%) males; 86 (74.78%) females}, whereby 54 (46.96%) patients were eligible for monotherapy, determined in a six months investigational period.

Taking into consideration that the highest number of patients eligible for first-line treat-

ment were between the age of 30 to 60 years (78.27% out of total 115 patients) determined in the six months investigational period, indicated that early diagnose and suitable effective treatment would provide a better life quality of these patients which would result in long-term preservation of their work capacity and also contribute to rational use of health funds.

With the administration of tocilizumab subcutaneously not only health improvement is observed, but it is noted that in long term it will have impact in saving funds. By early diagnose of the patient and on time start with the suitable therapy the patient's quality of life will maintain preserved which will contribute to keep that patient work capable and will not become a burden for the society.

The geographical distribution of patients provides data to more efficiently organize the healthcare of patients suffering from RA by taking RA treatment next to their homes in the native city, avoiding additional costs (travel expenses), minimizing indirect treatment costs and optimizing time spend for treatment, moreover because subcutaneous formulation of tocilizumab may be self-administered by patients after proper training is given by medical personal. According to analysis, 81.74 percent of patients eligible for first-line therapy – monotherapy are out of the capital city of Skopje, where UCR is located; therefore, dispersion of monotherapy, particularly with subcutaneous formulation that patient may be self-administered in distinct cities is rational and effective way of organizing RA treatment across the country.

The University Clinic of Rheumatology in Skopje, Macedonia is able to provide different kind of treatment options for RA including: DMARDs, adalimumab, etanercept and other anti-rheumatic medicines. The UCR has at its disposal subcutaneous formulation of tocilizumab as one of the most effective and easy to use biologic medicines for treatment of RA. By determining the precise number of patients eligible for first-line therapy/monotherapy it

will be much easier to proceed with choosing the most beneficial treatment option for each patient and provide a continuously improving health care system.

Conflict of interest

Authors declare no conflict of interest in performing this study.

Limitation

The study population in this observational study consists of patients suffering from RA referred and presented at the University Clinic of Rheumatology Skopje in the period of six months (September 2017-February 2018), and therefore the presented results and conclusions in this article do not represent the total number of patients suffering from RA in the Republic of Macedonia

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Glossary of abbreviations

RA ----- Rheumatoid arthritis
 UCR ----- University Clinic of Rheumatology
 ACR ----- American college of rheumatology
 EULAR --- European league against rheumatism
 anti-ACPA – Anti-citrullinated peptide antibodies
 CRP -----C-reactive protein
 RF ----- Rheumatoid factor
 DMARDs – Disease modifying anti-rheumatic drugs
 Pts ----- Patient
 Sc ----- subcutaneous

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Резиме**ЕПИДЕМИОЛОШКА АНАЛИЗА И ГЕОГРАФСКА ДИСТРИБУЦИЈА НА ПАЦИЕНТИТЕ СО РЕВМАТОИДЕН АРТРИТИС, КОИ СЕ ПОГОДНИ ЗА ТЕРАПИЈА СО СУПКУТАНАТА ФОРМА НА TOSILIZUMAB КАКО ПРВОЛИНИСКИ ТРЕТМАН/МОНОТЕРАПИЈА ВО Р МАКЕДОНИЈА**

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Ревматоидниот артритис претставува инфламаторен артритис, кој се карактеризира со инфламација на синовијалното ткиво и доведува до структурни оштетувања и инвалидитет. Достапни се неколку видови третмани, кои вклучуваат глукокортикоиди, DMARDs и биолошки лекови како монотерапија или во комбинација со други лекови. Новите докази покажале дека раниот третман е многу значаен за намалување на стапката на прогресија на ерозиите и намалување на инвалидитетот. Недостигот на соодветни статистички податоци за бројот на пациентите што се соодветни да примаат прволиниски третман/монотерапија, резултирале со оваа епидемиолошка анализа, која ги опишува соодветните пациенти што можат да примаат прволиниски третман/монотерапија, дистрибуирани според возраста, полот и географската локација. Студијата е изведена преку пополнување на специфичен прашалник, кој бил дизајниран само за оваа намена на секои два месеци во период од шест месеци (септември 2017 – февруари 2018), преку генерирање сумирани податоци, кои не се поврзани со персоналните податоци на секој поединечен пациент. Резултатите покажале дека од сите 115 пациенти во Македонија што се соодветни за прволиниски третман, 54 (46 %) биле кандидати за монотерапија за третман на ревматоиден артритис. Точното дефинирање на овие податоци овозможува одредување на пациентите според географската позиција и соодветен избор на најефикасната терапија, како и оптимизација на терапијата за секој пациент, особено кога супкутаната форма на tocilizumab е достапна и докажана како ефикасна опција за третман на РА.

Клучни зборови: ревматоиден артритис, tocilizumab, прволиниски третман/монотерапија, супкутана апликација