ANNUAL NARRATIVE REPORT

Association of citizens for rare diseases LIFE WITH CHALLENGES

JANUARY – DECEMBER, 2019, REPUBLIC OF NORTH MACEDONIA

Contents

LEARNING ABOUT RARE DISEASES 2019

During the month of February 2019, before Rare Disease Day, our volunteer Gordana Loleska, in cooperation with LIFE WITH CHALLENGES and Super Radio Ohrid managed to organize a national campaign for raising awareness on rare diseases.

In February, the month that patients with rare diseases call it rare month, we tired to educate the public about 28 different rare diseases. The statistical data about rare diseases in North Macedonia is not yet official as the registry is a work in progress. We estimate that there are over 2000 patients that face life with a rare disease in North Macedonia with over 100 different diagnoses.

This is why we shared the challenges and problems around diagnosis, treatment, disease management, access to orhpan drugs …

Information on 27 different rare diseases was shared on national, regional and local televisions, radio, web portals and newspapers. We also had a very strong social media campaign using Facebook and Instagram as to reach as many people as possible.

As result we had meeting with the Ministry of Health and Ministry of labor and social policy, we got 10 new members, and we also had more than 5 interviews on TV shows.

Raising awareness is still one of our crucial activities as without that rare diseases are easily forgotten and left on the margins of society. With activities happening almost each month of the year we keep the media attention, the public attention and most importantly the attention of the institutions that need to take steps toward resolving problems and challenges of people and families with rare diseases.

LIFE WITH CHALLENGES
RARE DISEASE DAY 2019

For 2019 the association for rare diseases LIFE WITH CHALLENGES had different events in different cities.

In Bitola we organized an event on 21st of February, together with HEPAR Center Bitola, with the support of Center for Culture Bitola, Municipality of Bitola, and two high schools – Josip Broz Tito and Jane Sandanski.

We had a showing of the film “The Faces of Lafora”, where also the director Denis Bojik, was present for a discussion about the difficult life of families with rare diseases, for which there is no treatment available in the world.

In Ohird, on 22nd of February, we also had a showing of the film “The Faces of Lafora” and after that we had a party where people were coloring their faces in support of rare diseases. The event was organized by Gordana Loleska and supported by the citizens of Ohrid.

In Skopje on 28th of February we supported the Macedonian association of medical students in organizing lectures for the students about rare diseases. 300 students were in the audience. We are happy that so many are interested in rare diseases.

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14:00-14:10 *Проф. Д-р Елена Шукарова-Ангеловска - Вовед за ретките болести*

14:10-14:30 *Студент Симона Наумоска – „Цистична фиброза", ментор проф. Д-р Стојка Нацева-Фуштиќ*
Студент Евгенија Николова - „Приказ на случај за Цистична фиброза", ментор проф. Д-р Стојка Нацева-Фуштиќ

14:30-14:45 *Проф. Д-р Анита Арсовска – „Факоматози: Приказ на случај со синдромот на Sturge-Weber"*

14:45-15:05 *Студент Благица Смилкова – „Синдром на Prader-Willi ", ментор проф. Д-р Елена Шукарова-Ангеловска*
Студент Мартина Савевска - „Приказ на случај со синдром на Prader-Willi",
ментор проф. Д-р Елена Шукарова-Ангеловска

15:05-15:20 *Проф. Д-р Љубинка Дамјановска – „Макрофаген активационен синдром кај системски облик на јувенилен артритис"*

15:20-15:40 *Студент Тамара Атанасова – „Стекната хемофилија", ментор Асс. Д-р Лазар Чадиевски*
Студент Софија Колева - „Приказ на случај со стекната хемофилија", ментор Асс. Д-р Лазар Чадиевски

LIFE WITH CHALLENGES also supported the event organized by the National Alliance for Rare Diseases of Macedonia on 28th of February, with a goal to fight together for national strategy for rare diseases in North Macedonia.

SKOPJE MARATHON - RAISING AWARENESS ON RARE DISEASES

MAY, 2019 RUNNING FOR BETTER LIFE

In 2019 we continued with our tradition to participate in the Skopje Marathon and raise awareness on rare diseases. This was done with support from the group Skopje Night Running. For the first time we started in 2013 and here we are 6 years later still running for better life.

On 4th of May, 2019, around 50 participants ran on 5, 21 and 42 kilometers for the patients that have no available therapy. We hope for a better future for families that face life with rare diseases.

Statement from Vesna Aleksovska, president of LIFE WITH CHALLENGES

„This year we run for the patients that have no existent therapy. From 8000 rare diseases, only 5% have available therapy that improves their life. Others face diagnosis that need additional social and health services and inclusion in society. This year we run for better rehabilitation (physical and mental), for available psychological support, for emotional support, physiotherapy at home, day centers in more cities, we want patients to be included in clinical studies, to have a possibility for compassionate use of drugs. In our association there are around 100 different diagnosis. For a lot of them there is no therapy in the world. One of those is Ichthyosis, others are Epidermolysis Bulossa, Friedrich Ataxia, Allagile syndrome, Muscular dystrophy, Churg Strauss, Gillian Bare syndrome, Alport Syndrome, ALS Lu Gerick syndrome, Huntington disease, Neurofibromatosis, Rendu-Osler Weber syndrome, Barter syndrome, Lowe syndrome, Williams's syndrome, Aspergillosis, West syndrome and many others …

We will continue to communicate and cooperate with institutions to provide appropriate social and health care services for rare disease patients. These families deserve multidisciplinary approach to disease management and holistic care. In the past 10 years we should that things can change for the better and we will do even more further, together all of us patients and families."

***Statement, Josif Mishevski, patient with** Ichthyosis*

„I am just one of the patients with rare diseases where there is no treatment that can significantly improve my condition. Our society needs to make steps towards inclusion of these people. The month of May is a month for raising awareness on my diseases and last year we made a short video showing the challenges and problems that patients face. "

Statement, Iskra Toseva, Skopje Night Running

„We started supporting patients with rare diseases years ago and we will continue this tradition. With our initiative we hope that others will join the cause and support families that face life with rare diseases. Every person deserves a chance for better life."

OHRID RUNNING - RAISING AWARENESS ON RARE DISEASES

Marko Pejchinovski made a call to the public to join the team building group rare diseases, at the Ohrid running Marathon. Marko is a young hero from Ohrid who swam across the Ohrid Lake for 9 hours. He is only 13 years old. His health problem was the reason that he started to swim trying to achieve a dream. His energy is towards raising awareness for rare diseases. As children with rare diseases face many different problems and challenges.

This is why you need to show how rare you are. Run for better social and health care for rare diseases, run for support, for early diagnosis, access to information, day centers, and better conditions for involvement in clinical studies. At this marathon we were together with the doctors and nurses also raising awareness on bone marrow transplant and bone marrow donors.

Run for better life! We are thankful to Gordana Loleska from Ohrid who coordinated this event in Ohrid and to her son with Alport syndrome who ran 5 km with success.

CALL FOR ACTION – DONATE 0,033 EUR PER 1 METER CLIMBED FOR RARE DISEASES

In 2019 we managed to make a call for action and it will continue in 2020. It is our pleasure to inform you that you have a possibility to get involved in the action for the support of families that face rare diseases.

The association of citizens for rare diseases LIFE WITH CHALLENGES for several years has a helpline for support and help of families and patients that face life with rare diseases.

The association is opened for cooperation with medical professionals, scientists, volunteers and supporters that are willing to advocate and support a better quality of life of patients and families with rare diseases.

This year through the helpline in the period of January to end of April 2019, we managed to accomplish the following:

- over 200 telephone calls and over 40 face to face meetings with patients and families
- 2 newly founded associations that we supported to start advocating
- we connected over 10 families from North Macedonia with families in the region that have the same rare disease
- 20 people are already using our psychological services
- we started with the translation of information for 1000 rare diseases
- continuously we are sharing new information on our web site and social media, that are of interest for rare diseases.

With the goal to continue with our successful work, we are gathering financial resources for the next year so that we continue to support families and patients with rare diseases from North Macedonia.

In June, July and August we have an action for climbing mountain tops, where the group of mountaineers (Milenka Sarovik, Hristofor Sarakinov, and Vasko Rusevski) will climb 11980 meters.

This will happen on Elbrus (highest mountain top in Europe), Triglav (highest mountain top in Slovenia), Punta Penia (Italy), Grossglockner (highest top in Austria) and Cugshpice (highest mountain top in Germany).

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It will be of great help if you can support this action and donate 0,003 EUR per meter climbed. Support our helpline, support families and patients with rare diseases from North Macedonia.

A donation will be realized in a number of meters that you choose. All donors will be published on our web page, in press releases for media and company logos will be put on a flag that will be carried on the climbs.

Thank you for supporting us ☺

If you are interested to donate on this link you will find the call and our bank account details.

http://challenges.mk/en/%d0%bf%d0%be%d0%b2%d0%b8%d0%ba-%d0%b7%d0%b0-%d0%b0%d0%ba%d1%86%d0%b8%d1%98%d0%b0/

REGIONAL CONFERENCE ON RARE DISEASES

7-9 JUNE, HOTEL DRIM, STRUGA, REPUBLIC OF NORTH MACEDONIA

It was a pleasure being a host to a great event which included 3 conferences directed towards exchange of experiences and knowledge for improvement of life of families that live with rare diseases.

As an association of citizens for rare diseases LIFE WITH CHALLENGES, this year marked the 10th year of existence, 10th year of activities focused on advocating for the rights of patients with rare diseases.

This conference was made possible with the cooperation of the associations and alliances from the region (Croatia, Serbia, Albania, Bulgaria, Bosnia and Herzegovina, Montenegro, Greece, World Duchenne Organization, International Gaucher Alliance, EURORDIS, Borka, IAPO, Rett syndrome Europe), the Genetic engineering department at the Macedonian academy for science and arts, the Doctor association for rare diseases, institutions from Republic of North Macedonia, volunteers from our association and many more.

The opening of the conference started on 8th of June at 9.00h. We had the honor to open the conference with a speech from the First Lady of Republic of North Macedonia, Elizabeta Gjorgievska, which was followed by the speech of the Minister of Health, Venko Filipce. After that we had a statement from Jagoda Shapaska, vice president of the commission of health at the parliament of Republic of North Macedonia and from Aleksandar Dimovski, director of the research center for genetic engineering and biotechnology.

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The participants were able to learn about the challenges and problems in North Macedonia and how we managed to find solutions, about news in the registry for rare diseases, the increased finance in the program for rare diseases, the news in diagnostic and treatment possibilities. Conclusion was that when doctors, patients, associations, pharma companies and institutions work together, then it is easier to find suitable solutions and overcome obstacles. As together we are definitely stronger.

Participants and lecturers at the conferences were doctors, nurses, researchers, patient advocates, patients, parents … 300 people, coming from many different countries as North Macedonia, Albania, Kosovo, Bulgaria, Greece, Czech Republic, Croatia, Serbia, Slovenia, Bosnia and Herzegovina, Montenegro, Germany, United Kingdom, Australia … The programs for the conferences in full can be found on the following links on our web site:

- Scientific conference – 7th South East European Meeting on Rare Diseases: http://challenges.mk/en/7th-rare-diseases-in-south-east-europe-meeting-7-9-june-2019/
- Regional conference of patient advocates coming from national alliances for rare diseases: http://challenges.mk/en/4767-2/
- Regional conference for families and medical professionals for Gaucher disease: http://challenges.mk/en/4769-2/

At the same time on 8th of June, we organized symposium for physiotherapists in cooperation with the Macedonian society for physiotherapists and with the World Duchenne organization. The lecturer was Prof. D-r Marion Main, coming from UK. She held theoretical and practical part for around 20 physiotherapists present from North Macedonia. The lecture was also opened to patients with Duchenne Muscular Dystrophy and Spinal Muscular Atrophy.

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Conclusions from the event:

- The countries in this region have similar problems and challenges and they strive towards similar solutions
- National plans for rare diseases work in some of the countries where there is good structure in terms of shared responsibility, clear obligations for the different institutions, strong commitment from the patient organizations and the medical professionals.
- Holistic care is something that patient organizations strive to, but there is still lack of understanding and commitment from the institutions.
- Early diagnosis and treatment are crucial for improvement of lives of families with rare diseases and lack of knowledge and expertise are only some of the obstacles to reach a higher level of diagnostics. In some countries there are problems with getting genetic analysis and accurate tests for control and management of rare diseases.
- There is a lack of multidisciplinary approach not just in treatment and management but also in diagnosis.
- Registries should be established and used to gather epidemiological data which is important for prevention, screening and control of rare diseases, and not just for keeping up with the number of patients and diseases.
- Medical professionals and patient organizations need to work with institutions and try to establish regional network for rare diseases that will provide a platform for exchange of experience, knowledge and expertise in diagnosis, treatment, prevention, management, screening and control of rare diseases.
- Reimbursement criteria should be more transparent and clear to the public so that patients can understand them and accept them.
- There is lack of cost effectiveness analysis and health technology assessment. As countries in the region are small and with many challenges, the idea of regional health technology assessment sounds like a future plan that needs to be developed by the responsible institutions in the countries.
- As the cost of medicines for rare diseases is a crucial point of discussion, the idea of regional public bidding for medicines is another idea that needs to be considered.
- Social services for rare diseases and special orthopedic devices are a neglected subject that needs to gain focus and commitment.

- Political crisis and corruption is a shared problem between countries that we need to overcome with higher transparency.
- When all stakeholders work together the progress is inevitable.

We hope that this event is just a beginning of such events that gather doctors, researchers, nurses, patients, pharma, associations and institutions together. It is clear that it helps in promoting holistic treatment and care for patients with rare diseases. And if we work on regional level it will be much easier for our countries to find different innovative ways to improve healthcare and social care for rare diseases.

At the end I would like to say thank you to all of our volunteers and donors who made this event possible. To learn more about LIFE WITH CHALLENGES, our activities, volunteers, members and supporters please download our 10 year anniversary brochure at the following link: http://challenges.mk/wp-content/uploads/2016/07/Brochure-10-years-EN.pdf

This event was supported by:

SANOFI GENZYME

Pfizer BIOMARIN MEDIJA PLANET ТРАЈНИ МУКАЕТОВ ALKALOID SKOPJE Health above all

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DETAILED INFORMATION ABOUT THE CONFERENCE

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The 7th South East European meeting on rare diseases / First Congress of the Macedonian Society for rare diseases for medical professionals and researchers was organized in cooperation with the Macedonian society for rare diseases, and the research center for genetic engineering and biotechnology Georgi D. Efremov. The organizing committee consisted of: Zoran Gucev – President, Velibor Tasic – Secretary, Vesna Aleksovska, Aleksandra Jancevska, Gordana Loleska, and Bojan Teov. The scientific committee: Aleksandar Dimovski, Momir Polenakovic, Zoran Gucev, Velibor Tasic, Dijana Plaseska Karanfilska, Katerina Stavric, Irina Panovska Stavridis, Bojko Bjelakovic, Kristina Mironska, Vesna Ambrakova.

As guest speakers we had the opportunity to hear two amazing lectures from Timothy Cox, University of Cambridge, UK, about ***Sphingolipids: a conspectus in health and disease*****, and from** Christina Lampe, University of Giessen, Germany about ***Skeletal dysplasia in MPSs diseases*****.**

Then there was a session on ***Familial Amyloid Polyneuropathy***, a lecture that combined the experience of the doctors from North Macedonia and Bulgaria.

For the first time after 7 years of the doctor congress on rare diseases in North Macedonia we had a ***hematology session*** on rare diseases with the cooperation of the director of the University hematology clinic, Irina Panovska Stavridis. The topics were: Overview of the hematological rare disease and experience with orphan drug polatuzumab – vedotin, Aplastic anemia- Experience in the Republic of North Macedonia, Diagnosis of mieloproliferative Neoplasms in the Republic of North Macedonia, Langerhans cell histiocytosis in adults, overview and case report, Flow cytometry imunophenotyping in diagnosis and contemporary treatment of paroxysmal nocturnal hemoglobinuria (PNH), New treatment modalities in thrombotic thrombocytopenic purpura (TTP), and Emicizumab a new treatment option for people with hemophilia A.

The meeting continued with lectures from the ***regional lecturers on different cases of rare diseases***: Homozygous Familial Hypercholesterolemia in Childhood – The first case report in Southeast Europe – Bojko Bjelakovic, Serbia, PHENYLKETONURIA: why newborn screening and early dietary treatment are of crucial importance?, Astrinia Skarpalezou, Greece, Epidermolysis bullosa – an overview of medical problems and complications – Slobodna Murat-Sušić, Croatia, Diagnostic challenges and modern pharmacological treatment of Idiopathic Pulmonary Fibrosis – Jasna Tekavec Trkanjec, Croatia.

The lectures were all followed by a lot of questions and discussion as in the audience we had also medical students and young doctors who are entering the field of rare diseases and are eager to learn.

Lectures continued on: Growth Hormone Deficiency; Diagnostic Pitfalls and Treatment Outcomes – Liljana Saranac, Serbia, Global issues Sustainable development goals – Liesbeth Siderius, Netherlands, Genomic testing in the age of rare diseases: Opportunities and challenges – Todor Arsov, Australia, Latest research of treatment and care of patients with Spinal Muscular Atrophy – Marco Castillo, Switzerland, Challenges in diagnosis and treatment of patients with GHD in Kosovo – Vjosa Mulliqi Kotori, Kosovo, Rare forms of short stature, Zoran Gucev, North Macedonia, Clinical significance of life-threatening and chronic hyperammonemias – Danko Miloshevic, Croatia, Nephropathic cystinosis – outcome and treatment – Velibor Tasic, North Macedonia, Hunter syndrome (HS; Mucopolysaccharidosis type II) – Zoran Gucev, North Macedonia.



At the end of the scientific conference there were presentations of more than 20 posters all on different cases of rare diseases. It seems that the field of rare diseases is becoming more attractive and interesting for medical professionals, researchers and medical students which is very important for the future of families that face rare diseases.

The main conclusion of this meeting was that it is always good for patients and medical professionals to cooperate as it was the first time of having such regional conference together. And of course when there is cooperation between all of us on regional level it will be much easier to consult on diagnostics, treatment, management, control, prevention and much more for better quality of life of patients with rare diseases.

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First symposium for physiotherapists on spinal muscular atrophy and muscular dystrophy

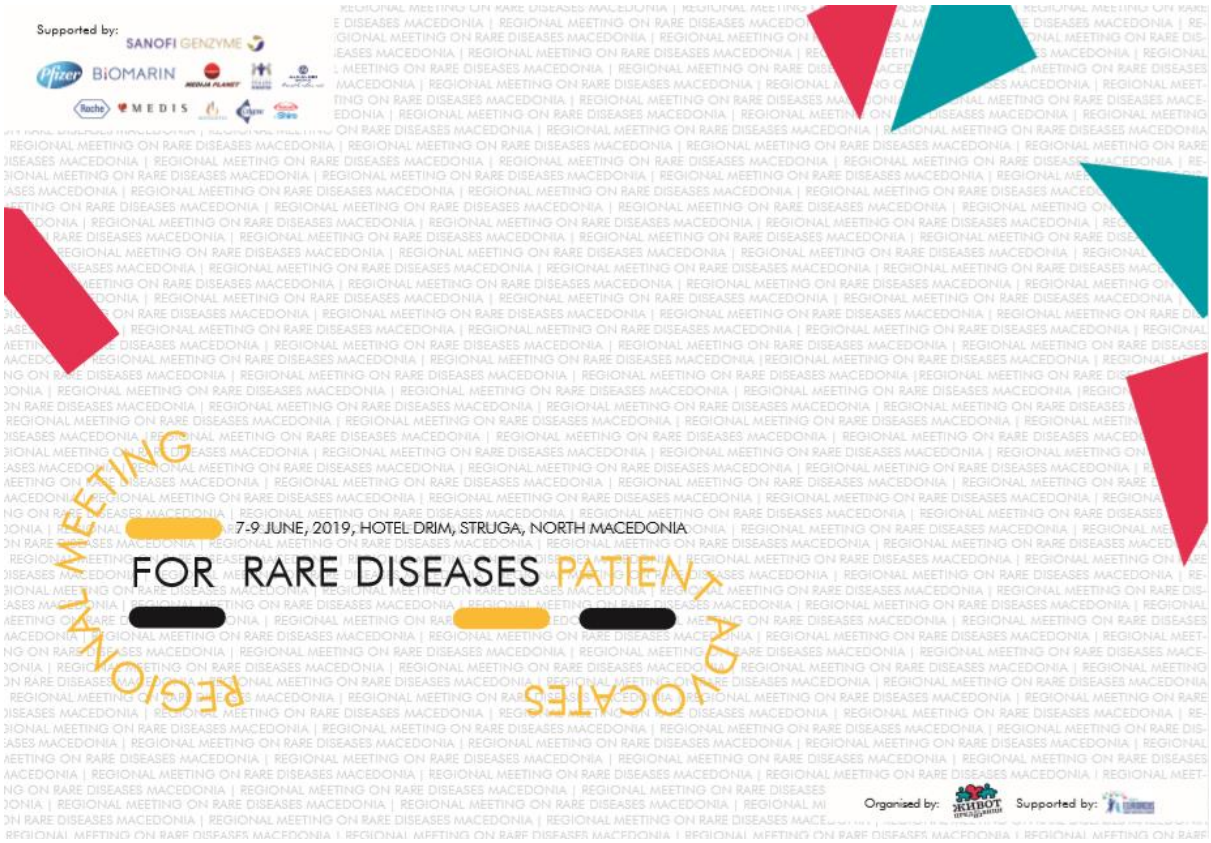
On 8th of June, we organized symposium for physiotherapists in cooperation with the Macedonian society for physiotherapists and with the World Duchenne organization. The lecturer was Prof. D-r Marion Main, coming from UK.

She held theoretical and practical part for around 20 physiotherapists present from North Macedonia. The lecture was also opened to patients with Duchenne Muscular Dystrophy and Spinal Muscular Atrophy. Prof. Marion Main in her presentation had a focus on the right use of appropriate tests to make a physiotherapeutic estimation. These tests are used in the UK in the centers of rehabilitation.

During the symposium, she showed short physiotherapeutic estimation and plan for rehabilitation for every child that was present in the conference room (with DMD and SMA). She also gave them recommendations for further treatment.

It was very exciting since physiotherapists in North Macedonia had never attended lecture on Muscular dystrophy and Spinal Muscular Atrophy and it was a learning moment for the professionals but also for the parents. We hope that we can continue to cooperate in education of physiotherapists in North Macedonia, since both sides understand the value of specific exercises for specific rare diseases. We hope that we can continue to cooperate in education of physiotherapists in North Macedonia since both sides understand the value of specific exercises for specific rare diseases.

Physiotherapists from North Macedonia were able to directly learn the ways of how physiotherapy is implemented in the treatment of patients with SMA and DMD. This symposium was a great opportunity to directly communicate with patients and discuss their needs and challenges.



The regional meeting for rare diseases patient advocates **was organized with the help of the National Alliances from the countries in the region and in cooperation with EURORDIS – European Organization for Rare Diseases.** Its goal was to discuss about our mutual challenges and problems and propose suitable solutions and activities for our future advocacy efforts. It seems that many countries from the region have similar problems and it is almost always connected with finance, corruption, politics, political crisis, education, knowledge, expertise in doctors and much more …

Davor Duboka from Serbia talked about different recommendations and led the discussion with the patient advocates present.

- It seems that the first challenge are the national plans/strategies for rare diseases. Although recommended, and adopted in many countries in Europe and in the region, still there is a lot to do here. Some plans expire and no new plans are developed. There is no financing for the strategies. There are no responsible people on positions needed to realize action points in plans.
- Reimbursement is different in all countries, and criteria is not always transparent on how, when and who gets medicines.
- There is a lack of cost effectiveness analysis, lack of health technology assessment
- Another significant problem is that usually governments focus on medicines for rare diseases and how expensive they are, but it is rare that someone actually understands the real burden of the disease.
- The focus needs to be on diagnosis, prevention, treatment, management and control, and even research although it seems something far away for the countries in the region. But the involvement in clinical research is of crucial importance for families with rare disease.
- There is a lack of multidisciplinary work among medical professionals in the region and this is what patients need. Not just for treatment and management of the disease but also for diagnosis as to get guidance in the search for diagnosis.
- Registries should be established and used to gather epidemiological data which is important for prevention, screening and control of rare diseases.

There was a very interesting discussion on the topic of **public health finance** in the area of **medicines reimbursement**, the different programs and ways of reimbursement, the approval of drugs, the registration of orphan drugs in the countries and of course the access to treatment. At the end transparency and criteria are of paramount importance for trusting the system that will finally work for the benefit of the patients.

We had a guest speaker from the Health insurance fund from North Macedonia, Vladimir Dimkovski, as we already cooperated with him on his previous work as researcher in Studiorum, working together on a research about rare disease challenges and recommendations on how to overcome obstacles and improve quality of life of patients with rare diseases.

It is very difficult to coordinate efforts in access to treatment between EU and not EU member countries. There is a rise in research, development and approval of orphan drugs, but there is also the rise of prices that at the end even EU countries have difficulties in reimbursement. There is a need of ***a transparent European Cooperation Framework for the Determination of Fair Prices and of Sustainable Healthcare Budget Impacts***. The collaborative approach is a way forward in dealing with high prices and access to treatment.
There are many suggestions on how to go forward as:

- Apply consistent approach on **value principles**, **value determinants** for assessment and **European HTA clinical assessment**
- **Flexible agreements** based on outcomes or other financial aspects
- Discounts on **uncertainties**, and allowing price to fluctuate over time based on additional generated evidence
- Registries and post-marketing authorisations activities coordinated cross-border
- **Joint purchasing**
- Focus on **smaller population** first then progressively expands negotiations to more prevalent diseases
- Differential pricing + control over parallel trade

Social services were also a topic of discussion among the patient advocates as they are often forgotten and neglected as such. But the holistic care approach is something that patients and families need to have a better quality of life as from 8000 rare diseases, only for 5% there is some kind of treatment, the others have nothing left and often are included in groups such as people with dysfunctionality or people with special needs. People with rare diseases are different and they need to be in the system as such.

In this session we had the opportunity to hear different stories and examples such as:

- The **helpline services** in Croatia, Serbia and North Macedonia. While in Croatia and Serbia they have employed psychologist to answer the helpline and schedule separate meetings in North Macedonia, the free psychological support is guided by the association but it is available for all rare disease patients, and for their family members as the burden of the disease is on the whole family not just the patient. The helplines also provide information

on rare diseases, doctors with expertise, centers of expertise, they help in writing requests to institutions, and they guide patients through the health and social system in the country. As we are all connected on regional level we also connect families on regional level for exchange of experience and best practice on different rare diseases.

- Vlasta Zmazek from Croatia also presented the work that **Debra** Croatia is doing for the families living with Epidermolisis Bulosa as an example on how much more can an association do for the patients when the system is not providing enough.
- We also had the presentation of Danijela Szili, from **RETT syndrome Europe**, providing information on how peer to peer support and how association support and help is crucial to families when there are no medicines in the world that can help and there is not enough expertise in medical professionals as the numbers of patients are very low in different countries.

At the session on HTA, Clinical trials, and organ transplant the leader of the discussion was Anja Bosilkova Antovska from the National Alliance of North Macedonia. The first speaker was Prim Dr **Neda Milevska Kostova**, President of the NGO Studiorum (North Macedonia) and Board Member of the International Alliance of Patient Organizations - IAPO (UK), who discussed the involvement of patients in health research and the role of IAPO as a bridge between patients and research. Giving a brief overview of the work IAPO does, Milevska Kostova stressed the main aim of IAPO - giving a voice to patients and patient's organization to effectively advocate on relevant aspects of healthcare policy, along with the research done on health policies, quality of life and quality of care. She discussed the patient's path and experience with (rare) diseases and the importance of the patients involvement in reviewing clinical guidelines and health policies by sharing their own experiences, values, preferences and needs, and opportunities for participation in clinical trials.

While Milevska Kostova touched upon patient involvement activities for individual HTAs, the next speaker - **Biba Dodeva,** President of the Association against cancer BORKA (North Macedonia) spoke about Health Technology Assessment (HTA) in more detail and discussed how HTA is used in our countries. Dodeva presented the process of HTA as a systematic evaluation of the effects and consequences of a certain health technology (e.g. drug development, medical devices, diagnostics or other medical procedure etc.) with the aim to inform decision-making about that health technology. Dodeva discussed the importance of patients and organizations using HTA as a tool to advocate about the effectiveness, safety,

cost-effectiveness of the different technologies, as well as the social, economic and ethical aspects of using those, in order to achieve the best value.

Finally, **Pavlinka Nesovska Baliska**, President of NEFRON (North Macedonia) presented about organ transplantation and discussed about the importance of organ donation. After explaining the process of organ transplantation and donation, as well as giving answers to the most frequently asked questions on this topic, Nesovska Baliska discussed the availability of this procedure to patients with rare diseases and the challenges related to this. She also presented the current legislation on organ transplantation and donation in Macedonia, and the history of these procedures in the country. The presentations were followed by a discussion on reimbursement decisions by national health and insurance institutions in the countries of the region when it comes to treatment of rare diseases, and a follow-up discussion regarding organ donation and transplant procedures.

This meeting was also a possibility for patients to meet and talk with each other and with doctors. MPS 4 families from North Macedonia and Montenegro met with Christina Lampe and the doctor that is leading their case in North Macedonia – Zoran Guchev, to exchange experience and talk about the future.

RETT syndrome families from North Macedonia had a meeting with Danijela Szili from RETT syndrome Europe to discuss about the hope and possibilities that future in research brings.

Epidermolysis Bulossa families from North Macedonia had a meeting with Vlasta Zmazek from DEBRA Croatia as to see how patients in North Macedonia can get more support and be more involved regionally.

There were additionally lectures at the scientific meeting that were of interest to patients from North Macedonia such as Phenylketonuria, Epidermolysis Bulossa, Idiopathic Pulmonary Fibrosis, MPS 4 – Morquio Syndrome, Spinal Muscular Atrophy. In this case patients were able to meet expert doctors and discuss their condition and possible improvement in treatment and management of the rare disease.

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The Gaucher regional meeting **was organized with the help of the Gaucher associations and groups from the region and cooperation with International Gaucher Alliance. Around 120 participants were at the meeting (patients, family members, nurses, doctors).**

This meeting started with sharing information on number of patients and available treatment, care and diagnosis. The following conclusions were presented:

- ***Republic of North Macedonia:*** around 12 patients with type 1 on treatment (there are also some older patients – above 70 years old, without treatment), 8 on Imiglucerase, 4 on Taliglucerase, 1 on Eliglustat (expected 2 to transfer to eliglustat from imiglucerase), patients usually start with 60 units per kg, and after they are stable they go on 30 units per kg. There are no patients with type 3, but there were 3 patients type 2 that we know about in the past.
  There is no home therapy, all patients must travel to University hematology clinic in Skopje but there are efforts to get therapy at least in other hospitals in other cities, if not home. Genetic analysis is available at the genetic center at the Macedonian academy for

science and arts, covered by the Health Insurance Fund. All patients are registered at the rare disease registry at the Ministry of Health under the program for rare diseases. The information about Gaucher disease is shared with printed and downloadable brochure in Macedonian and Albanian language available on our web site and in the clinic. There is a helpline and psychological support for all rare diseases available through the association LIFE WITH CHALLENGES.

- ***Serbia:*** 34 patients with type 1, 1 with type 2 and 5 with type 3 Gaucher. Available treatments are imiglucerase, taliglucerase and eliglustat. There is no home therapy, the doses are low in matter of units per kg, there is no reimbursement yet for oral therapy, part of the patients are receiving treatment as donation. Genetic analysis is possible and covered by the government. The association has an informative brochure in Serbian language available for the patients, they have regular meetings, lectures for doctors, social media activities and much more.
- ***Croatia:*** there are 20 patients with type 1 and 2 with type 3 Gaucher. All of them are on treatment and available treatment is imiglucerase, velaglucerase and eliglustat. There are 5 clinical centers that patients go to for therapy. Genetic analysis and diagnosis is available and covered by the government. Home therapy is available for patients on imiglucerase.
- ***Slovenia***: there are 22 patients with type 1 Gaucher, all on treatment. Available at the moment is imiglucerase and velaglucerase. Diagnosis and genetic analysis is available and covered by the government. Home therapy is available for the patients. There are different patient and doctor brochures for information and education.
- ***Bosnia and Herzegovina:*** there are 3 patients type 1 on imiglucerase and velaglucerase. There is a problem in education and information among doctors and no new patients have been diagnosed in the past 10 years or more. Diagnosis is on a very low level and also reimbursement of treatment is a problem so donation is present.
- ***Albania***: there are around 28 patients. Available treatment at the moment is taliglucerase and velaglucerase. All patients must travel to the clinic in Tirana and they are now trying to get therapy in other hospitals in the country as some of them have to travel 4 to 6 hours to get to the clinic. The association is new and they will soon become members of IGA as they asked for support many times and IGA representatives visited Albania. This is the first time that we have included Albania in the regional meeting for Gaucher and we hope to continue cooperating in improving lives of patients and families.
- ***Bulgaria***: there are 22 patients, and 16 are on treatment. Treatment available in the country is imiglucerase, some are on eliglustat after participating in clinical study. Genetic analysis and diagnosis is available and covered by the government. It was the first time that Bulgaria attend a regional meeting in Gaucher disease, and we were very happy that new people are included at the meeting.

At this meeting we also had the opportunity to hear more about **International Gaucher Alliance and the regional manager project.** Marketa Smockova as regional manager for Eastern Europe and Balkan was present at the meeting and besides having a presentation she also had meetings, discussions and conversations with the representatives to learn about the challenges and see how she can help and support the patient associations through the activities of the IGA.

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As a guest speaker from abroad we had the pleasure to listen to a lecture from **Prof. D-r Timothy Cox,** who presented oral therapy and what are the benefits and the challenges with it. As doctors, patients and families were present, they all had a lot of questions and a great discussion.

Doctors from the region had lectures on the treatment, care and management of Gaucher patients in the region. As such we had the following lectures:

Prof. D-r Nadira Duraković from Croatia spoke about thier experience with Gaucher disease, then Prof. D-r Mojca Žerjav Tanšek from Slovenia talked about biomarkers for Gaucher disease, from North Macedonia Prof. D-r Zlate Stojanoski, presented the current situation in management for Gaucher disease, D-r Ermira Dervishi from Albania presented the expereince in Gaucher disease in Albania and from Serbia Prof. D-r Milan Lakočević talked about clinical trials -what are they and how are they done?

Живот со Предизвици / Jeta me Sfida / Life With Challenges

In the program we also had **workshops to discuss different challenges and opportunities** in Gaucher disease for patients, family members and medical professionals. Topics that were discussed were: available treatments, funding, availability of home therapy, quality of life, difference between children and adult patients, existence of referral centres and guidelines, organisation of regular annual check-ups, knowledge about GD among 'non GD professionals', need for screening and genetic counselling, need for multidisciplinary approach, relationship with pharma companies… One of the conclusions was that since 1st regional Gaucher meeting in Slovenia, there is significant improvement in availability of treatment for GD patients in the region, but there are many more issues to deal with beyond the treatment.

Statements from participants at the meeting:

Kristijan, Bulgaria: *As a first time comer to a regional meeting, it was interesting to see people from all over the Balkan states. Even though there are differences between the languages spoken on the Balkan peninsula, it was nice to be able to speak your own language and be understood at the same time (more or less). This makes you feel accepted and part of the whole room. I admit that this way it is harder for the guest lecturers, as they do not speak the language, but you cannot have your cake and eat it too.*

Slovenia:

I would like to congratulate the organizers who have been very nice to us and have prepared lectures where we learned about Gaucher disease, treatment and new findings, and about the situation in other countries. At the workshop on Sunday we met new patients and listened to their stories, which are not only positive, but also unpleasant and difficult. In the end, however, we concluded that there are many positive things in all this Gaucher story, and that is why we have to look positively on the disease and make the most of our lives. (Gaucher patient from Slovenia)

Super meeting, great experience! In the future, I wish a little more focus on sharing groups, discussions among patients, perhaps having a doctor who is treating Gaucher with us in a patient workshop. (Gaucher patient from Slovenia)

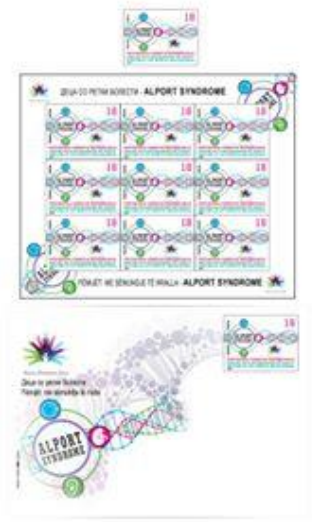
We are very happy and grateful to all organizers that they have brought together many people from several countries, patients and their dearest ones. We got additional information about the husband's disease (Gaucher disease) and were calmed down regarding its impact on our children. All praises to the local organisers and to everyone for a nice and relaxed meeting. (a wife of Gaucher patient from Slovenia)

Biljana, Serbia: *24 of Serbian Gaucher patients and family members attended Regional Gaucher Meeting in North Macedonia 7-9th June. It was a great opportunity to hear very important lectures from leading doctors in the region, and always inspiring prof Tim Cox. We also had time to gather with friends from other countries and share experiences.*

THE FIRST ALPORT SYNDROME POSTAL STAMP

10TH OF JUNE, MACEDONIAN POST OFFICE

On 10th of June, 2020, the Macedonian post office issued a new postal stamp with the name children with rare diseases – Alport syndrome.



With this we are continuing our cooperation with the Macedonian post office on raising awareness on rare diseases not just in our country but worldwide.

This is the first time that this kind of stamp is issued in the whole world. We are proud to have Gordana Loleska as our most active member who advocated for this to happen.

HELPLINE FOR RARE DISEASES

INFORMATION AND PSYCHOLOGICAL SUPPORT

2019, REPUBLIC OF NORTH MACEDONIA

In 2019 through the Help line for rare diseases of LIFE WITH CHALLENGES we are providing psychological and psycho-therapeutic support for families with rare diseases.

The HELP LINE is a project that we started since 2013 as a non-formal info line for families that face life with rare diseases. It is an open communication through telephone, Viber, Facebook, e-mail, face to face meetings, family gatherings … and much more … the help line is for informative support, for direction and support through the health and social system so that patients can get the services they need without spending a lot of time through the institutions.

Usually we have one or 2 calls on a daily basis, not just in work days but also on weekends and holidays. Sometimes we get calls from people who face other kinds of diseases and we try to direct them towards reliable organizations.

With a goal to help more we are in communication with organizations from the region like Croatia, Serbia, Monte Negro, Bulgaria, Bosnia and Herzegovina. We are all enthusiastic and persistent in our work to support patients. We also organize regional conferences, meetings, we share best practices, contacts from medical professionals, we advise and support each other to achieve more for the families who face rare diseases.

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From January, 2019 we signed agreement for cooperation with NEOKORTEX – Center for psychotherapy, psycho-diagnostics, training and education so that we can offer the following services: individual psycho-therapeutic sessions, partner therapy, psychological advice for parents, family therapy, psychological testing and other services needed for the families that face life with rare diseases.

Statement, Vesna Aleksovska, President of LIFE WITH CHALLENGES:
"Supporting the patients in the past ten years, we became aware that psychological support is very important not just for the patients but also for their families. Having a rare disease is not just a burden to the one person that has it, but to the whole family. This is why we decided, part of grant form the Foundation Trajche Mukaetov, that we received at the end of the last year, to be for free psychological and psycho-therapeutic services for the families that face life with rare diseases.

In 2019, patients and families with rare diseases can directly contact Ivana Hadzivanova from NEOKORTEKS (psychologists, psychotherapists, educator +38975273768), they can schedule a meeting and get the needed support. We hope that the availability of this service and the guaranteed anonymity will contribute towards greater help and support for the families with rare diseases and for the improvement of their quality of life. Although we are starting with this project in Skopje, we have planned educational workshops for other cities so that further we can start cooperation with other professionals and make a network of support for the families with rare "

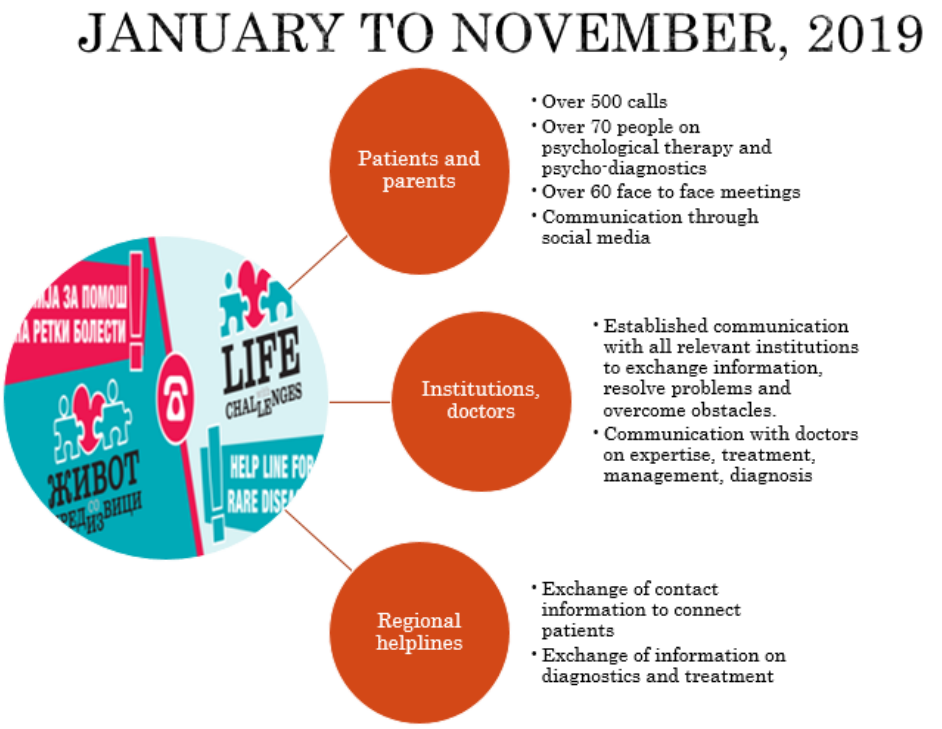
Statement, Ivana Hadzivanova, Psychologist, psychotherapist, NEOKORTEKS

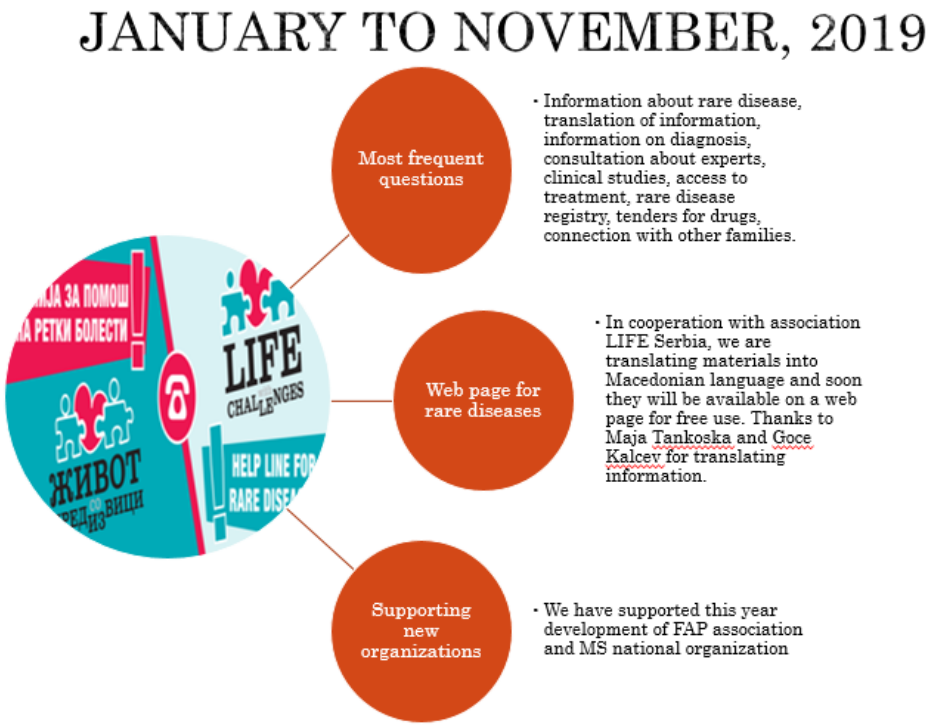
"It is a great honor and happiness for me to start this cooperation with LIFE WITH CHALLENGES as an organization that I respect a lot. I am ready in this year, to give all my professional energy in order to improve the mental health and the psychological condition of the people and the families with rare diseases. I am happy to be a part of the support in overcoming the life challenges when you face a rare disease."

The request for help are usually those bellow:

- Do I have a rare disease or just ordinary one? / Where can I find information?
- Can you translate information for my diseases? / Is there a medicine?
- Is there any other treatment available or not?
- How should I be registered to get a drug?
- Do I have the right to social aid?
- Do you know someone with this diseases? / Can you connect me with others like me?
- Do you know doctors that can explain about my disease?
- Which institution should I contact? / How to write a letter to institution?
- Can you take my documents to the institutions in my name?
- Can you help me gathering documentation?
- Is stem cells treatment useful?
- Who in Health insurance is responsible for rare diseases?
- Who in Ministry of health should I contact?

- Is my special food for my disease refunded? / How can I get refund?
- Is the clinic responsible for provision of my drugs?
- Who decides if I get a drug or not?





INTERNATIONAL, REGIONAL AND NATIONAL CONFERENCES AND MEETINGS

DITA (Drug information, transparency and access) task force at EURORDIS.
Vesna Aleksovska continued to be part of the group in 2019 and now she has been elected again for the next three years to continue to work in DITA.

EURORDIS (European Organization on rare diseases) membership meeting, May, 2019, Bucharest, Romania

International Gaucher Alliance at European Working Group for Gaucher Disease, Clermont de Ferrand, France, July, 2019 – Vesna Aleksovska as chair of IGA gave a presentation about the work of IGA in front of all participants at EWGGD.

Council of National Alliances – EURORDIS, 6th November, 2019

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Rare 2030 meeting, 7th November, 2019, EURORDIS, Bruselss

Council of European Federations, 8th of November, 2019, Brussels, EURORDIS

Regional meeting on Rare diseases, 16-17 November, 2019, Tirana, Albania

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Workshop on National Strategy for rare diseases – October, 2019, North Macedonia

Supporting national patient organizations – events and activities, during 2019

HEPAR center event, July, 2019 and HEMOLOG – hemophilia day April, 2019

NEFRON – organ donor day, October, 2019

Pharma day – safe drugs for all patients , September, 2019

Spinal Muscular Atrophy event, August, 2019 – STOP SMA

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BORKA events

Muscular Dystrophy events, September and October, 2019

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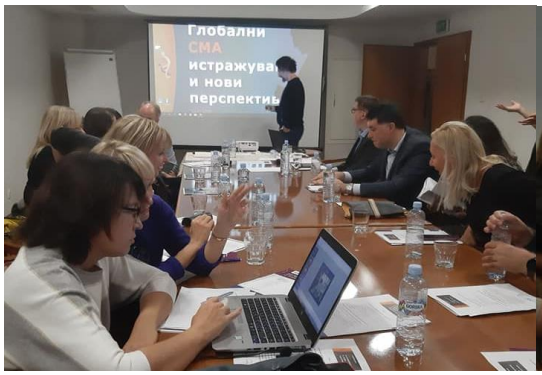
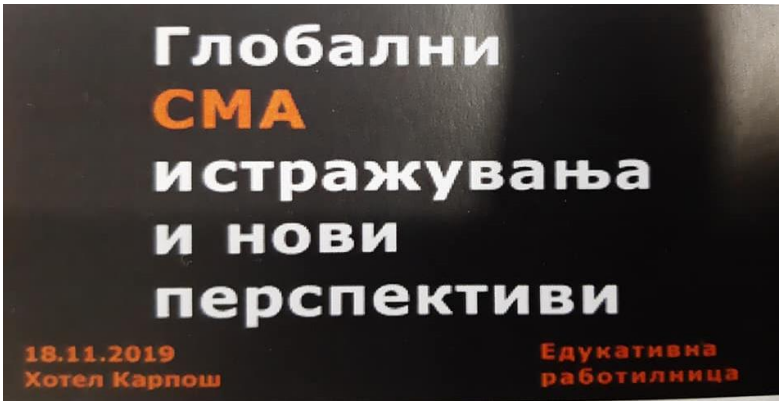
Meeting with the Macedonian Chamber of Doctors to speak about violence and how to resolve the issues and challenges we face between patients and doctors, 24 September, 2019, Skopje, North Macedonia

Special event – **Marko Pejchinovski** takes the challenge to swim 64 kilometers through the Ohrid Lake. Although he did not succeeded in that he managed to raise a lot of awareness as all media attention was on rare diseases. He showed that anyone can support families with rare diseases, anyone can help out … you just need to start doing something for someone else than yourself.

Supporting World Diabetes Day, November, 2019, Skopje, North Macedonia


Supporting educational event from STOP SMA, 18 November, 2019, Skopje, North Macedonia





CLIMBING KORAB – HIGHEST MOUNTAIN TOP IN REPUBLIC OF NORTH MACEDONIA ACTIVITIES FOR RAISING AWARENESS ON RARE DISEASES

8TH OF SEPTEMBER, 2019, REPUBLIC OF NORTH MACEDONIA

We continue with the tradition to raise awareness on rare diseases by climbing the highest mountain top in North Macedonia – Great Korab. On 8th of September, 2019, the Independence Day of North Macedonia with the help of the mountain club Korab we set our rare disease flag on the top of the mountain.

Our statement to the media was that we are aware of how things are moving forward in improvement of treatment of rare diseases in North Macedonia but there are still many problems that need to be addressed accordingly such as: screening for PKU, a year to year and a half waiting for procurement for medicines for new patients because of public bidding procedures, needed increase of finance for genetic analysis, non-existent multidisciplinary approach to treatment and management of rare diseases.

With this symbolic activity we just raise awareness to remind the public about all the problems and challenges that people with rare diseases face in their everyday life.

INTERNATIONAL GAUCHER DAY
ACTIVITIES FOR RARE DISEASES

1ST OF OCTOBER, 2019, REPUBLIC OF NORTH MACEDONIA

On 1st of October, 2019, in Skopje we marked the International Gaucher Day with a press conference announcing the access to oral therapy for Gaucher patients in our country.

The Minister of Health, Venko Filipche said that he is very happy to continue cooperation with all patient organizations, since working together means addressing key issues for the patients and improving lives. In 2015 patients with Gaucher got imiglucerase as treatment payed from the Program for rare diseases, in 2018 a second infusion therapy taliglucerase was accessable for Gaucher patients and now in 2019 oral therapy – eliglustat is also available in North Macedonia for Gaucher patients.

Vesna Aleksovska, Gaucher patient, said that she is very happy that finally she won't have to go every two weeks in the clinic for infusion and this will mean better quality of life. Also it saves expenses in terms of hospital resources and travel expenses, also you do not need a day off work to go to therapy. She added that the next step would be to get home therapy or to get therapy available in other city than Skopje to improve life of patients with Gaucher disease further in the future.

D-r Dijana Plasheska Karanfilska, from the department of genetic engineering talked about how genetic analysis is done for Gaucher disease in North Macedonia for the patients and for their families. She also stated that from the research done on 700 people, 1 in 100 was a carrier of Gaucher disease. Pesearch also shows that Parkinson is connected to Gaucher so they started testing patients and families for Parkinson. The focus should be on diagnosis, since there are more undiscovered patients in the country, and early diagnosis is the key for better quality of life.

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Prof. D-r Zlate Stojanoski, from the hematology clinic in Skopje, said that it is very good that we have organizations that raise awareness on rare diseases and fight for a better life of the patients and the families. He first encountered Gaucher in 1995 when treatment was not available in North Macedonia. Since than 4 patients got donation from Sanofi Genzyme in 2010 and in 2015 treatment was provided from the government. He said that he is happy to treat and follow the patients and he hopes for better future for all rare diseases.

We also had 2 rare stars nominations from North Macedonia to be included in International Gaucher Day of IGA. Jasmina from Sanofi, for working on the humanitarian aid program and Anne Grethe from Gaucher Denmark for realization of the project Go With Gaucher.

Educational workshop for psychologists and psychotherapists - MENTAL HEALTH –vital in the holistic approach to treatment of people with rare diseases and their families

23RD OF NOVEMBER, 2019, REPUBLIC OF NORTH MACEDONIA

On 23rd of November, LIFE WITH CHALLENGES, together with NEOKORTEKS, organized a workshop for psychologists and psychotherapists. The goal of the workshop was to educate more professional on how to support and help people with rare diseases and their families as in 2019 we had provided psychological support in Skopje. Because of the great results and need we decided to provide this support in other cities in North Macedonia where help is needed such as Bitola, Ohrid, Strumica, Shtip, Tetovo, Negotino, Veles and others.

Ivana Hadzivanova, psychologist and psychotherapist, stated that she feels how with entering in the field of rare diseases was new for her, but she managed to get new experience in heling and supporting people in need. This is why she decided to share her experience so that more professionals in her field will be able to provide much needed help for the people with rare diseases and their families.

Vesna Aleksovska, chair of LIFE WITH CHALLENGES stated that she is very happy that with the help of the foundation Trajce Mukaetov and AlKALOID Skkopje, managed to provide this support through the helpline of rare diseases that exists since 2013. The conclusions are that more than 40 people asked and got psychological support, they were happy that it is not at the clinical center but in a pleasant atmosphere and anonymous. The families were also happy that family counselling is possible as usually only a patient has a right to get psychological support at the clinic.

This education was held in cooperation with the Psychological Chamber of North Macedonia and it was free of charge to all participants.

We hope that in future the government will find funding to support such projects that empower people with rare diseases and their families.

NATIONAL STRATEGY FOR RARE DISEASES OF R. N. MACEDONIA

20TH OF DECEMBER, 2019, REPUBLIC OF NORTH MACEDONIA

On 20th of December the National Alliance for rare diseases of Republic of North Macedonia held a press conference to finally present the agreed national strategy for rare diseases that was made together with the institutions from North Macedonia.

We do hope that it will be accepted from the parliament and implemented in the near future. LIFE WITH CHALLENGES developed the first national strategy in 2014 when we initiated the formation of the National Alliance. From then on, the institutions were following the recommendations but it was not and official document.

In 2017 we had a regional conference to improve the strategy and work together with different rare disease organizations and institution representatives. We included recommendations from regional countries and from EURORDIS.

In 2019 under the Nation Alliance we had several meetings and we finalized the document presented in December.

SPORT ACTIVITIES FOR RAISING AWARENESS FOR RARE DISEASES

2019, REPUBLIC OF NORTH MACEDONIA

Ohrid running supported rare diseases on the ***Marathon in Ljubljana,*** Slovenia on 27th of October, 2019.

Bitola Marathon – Trchaj be, September, 2019

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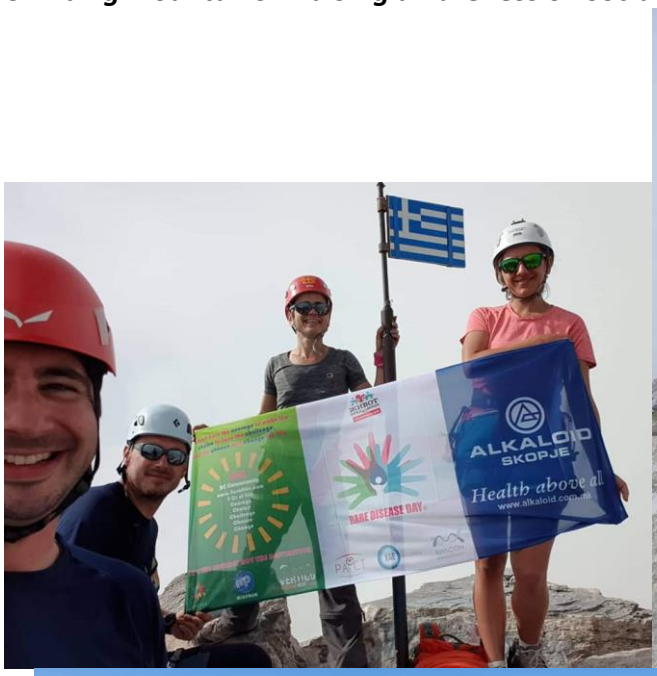
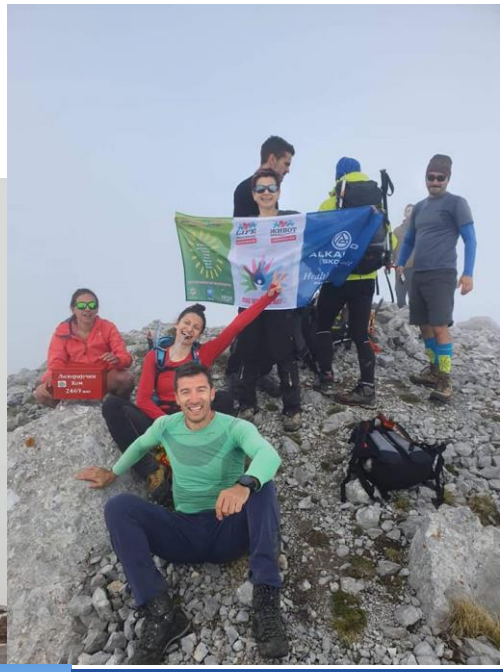
Climbing mountains – raising awareness on social media





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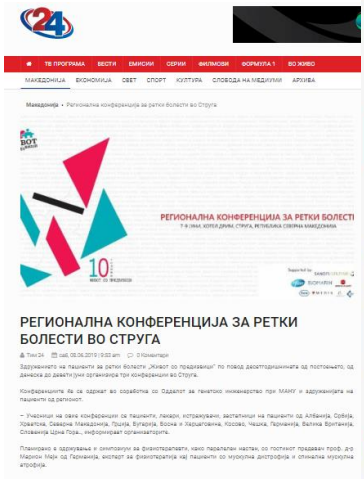
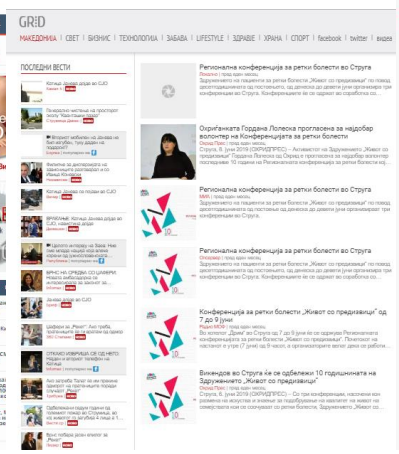
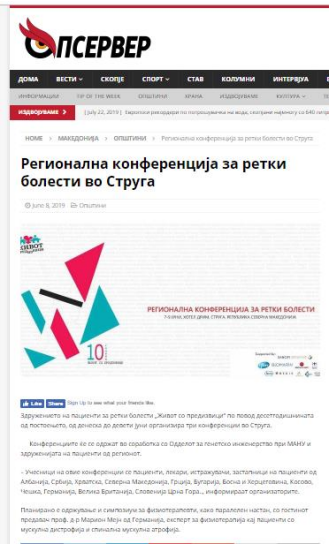
MEDIA COVERAGE ON OUR ACTIVITIES FOR RARE DISEASES

2019, REPUBLIC OF NORTH MACEDONIA

Our activities through the year were widely covered by local, regional and national televisions, radio, newspapers, web portals etc.…







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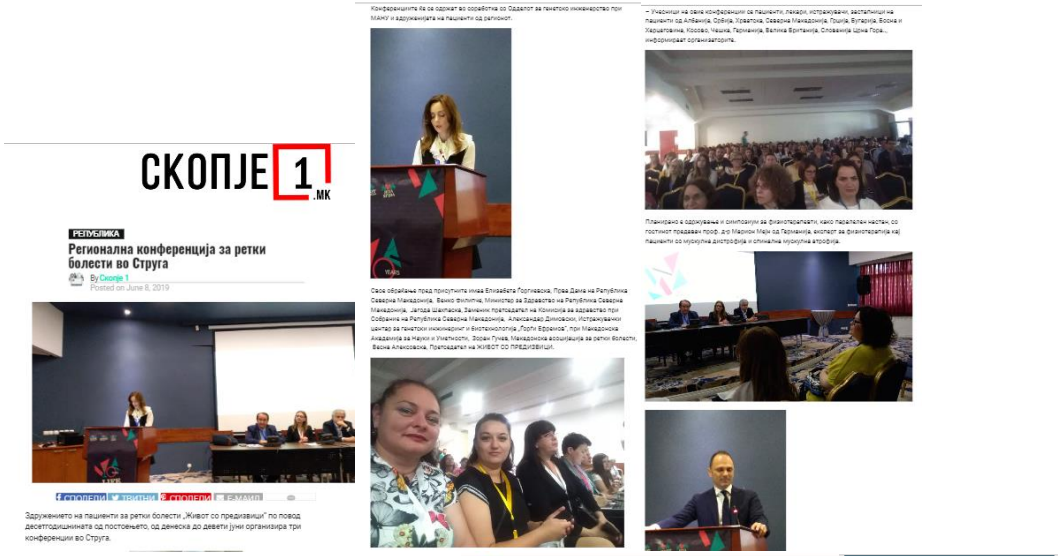

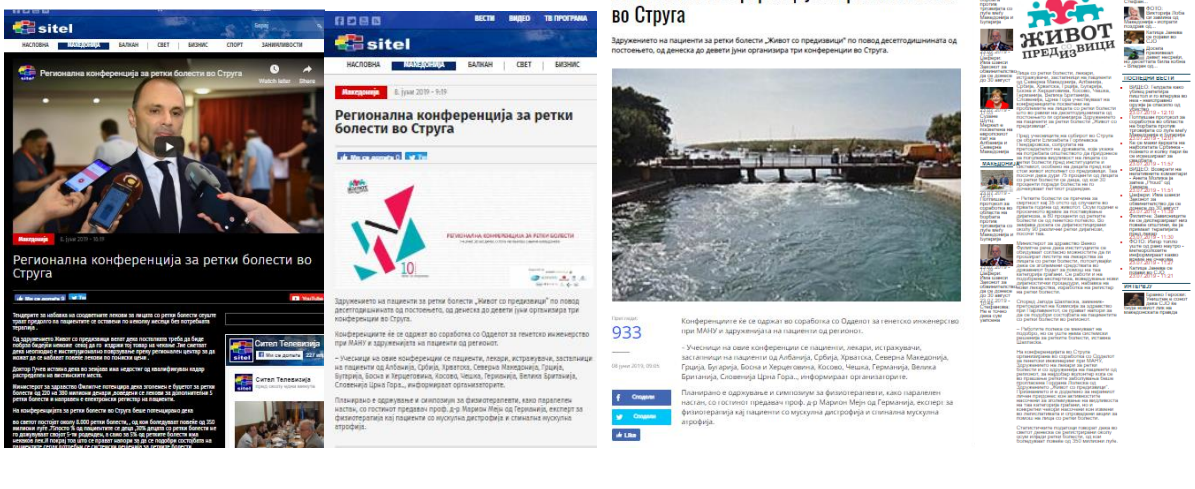

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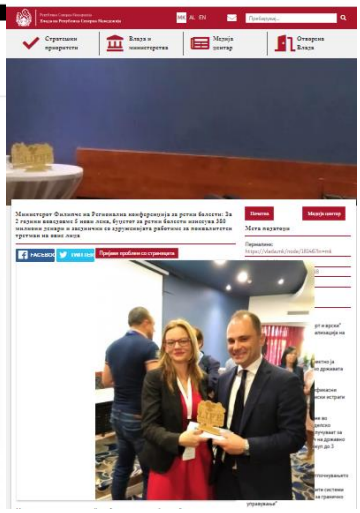

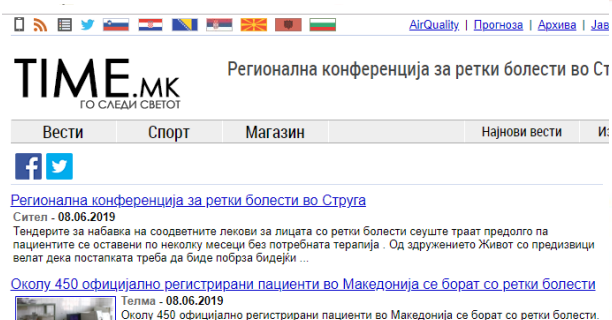

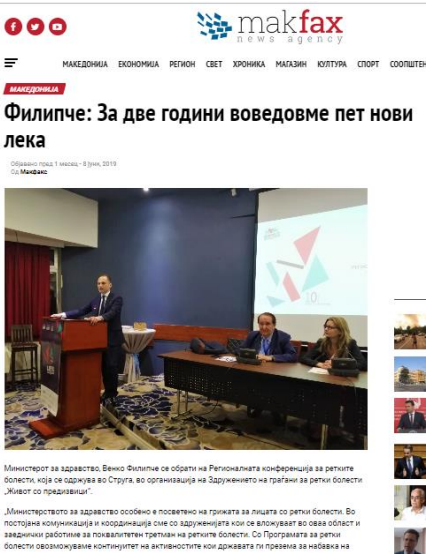

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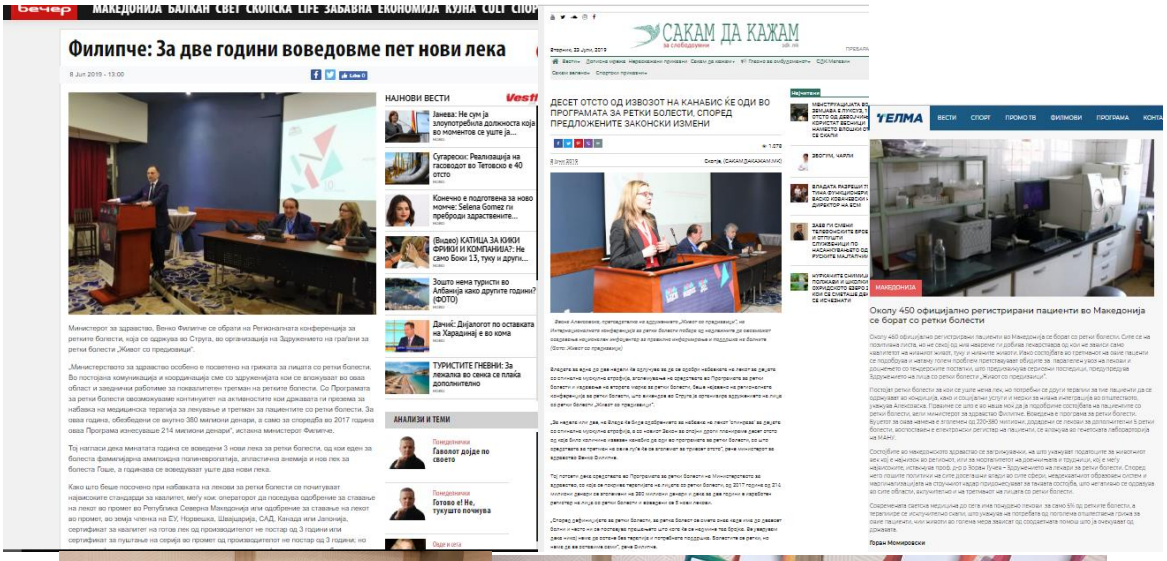

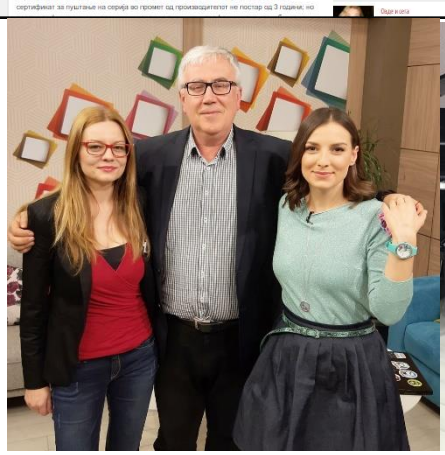

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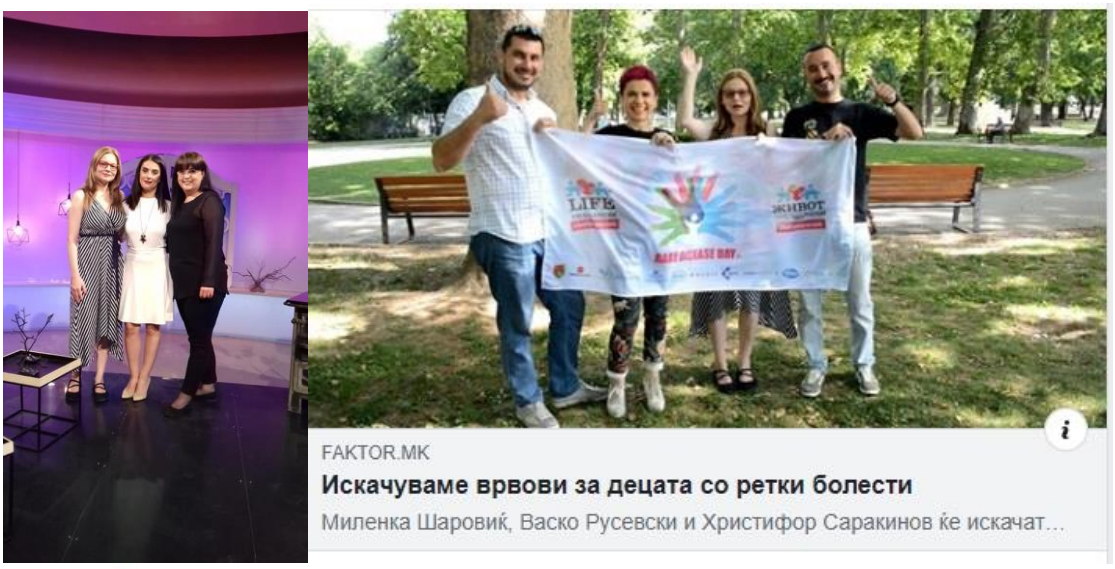

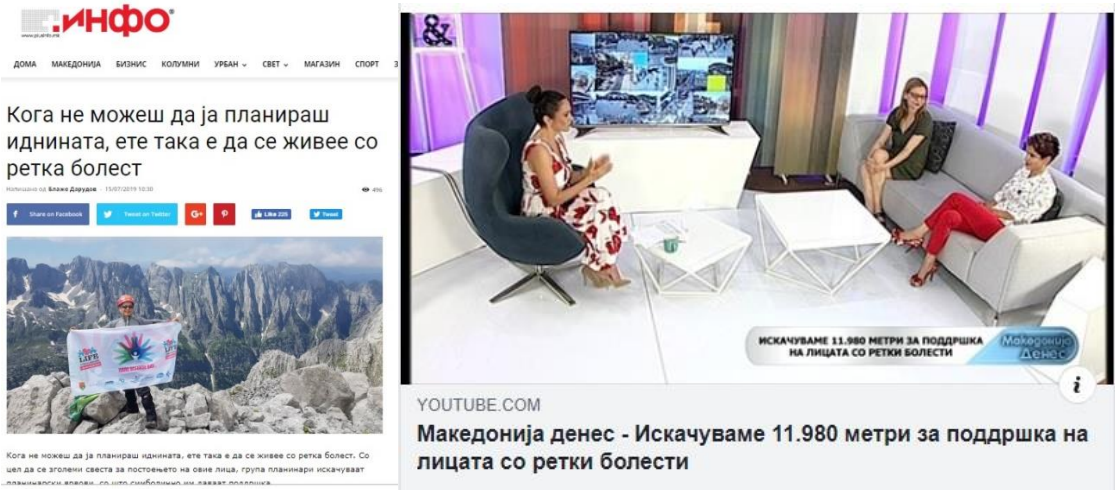

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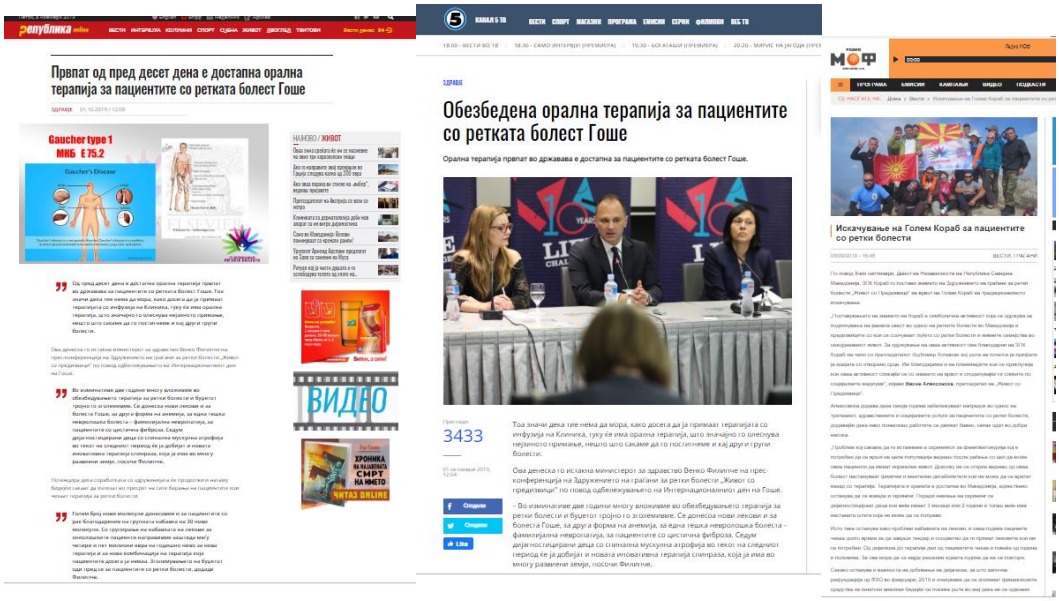

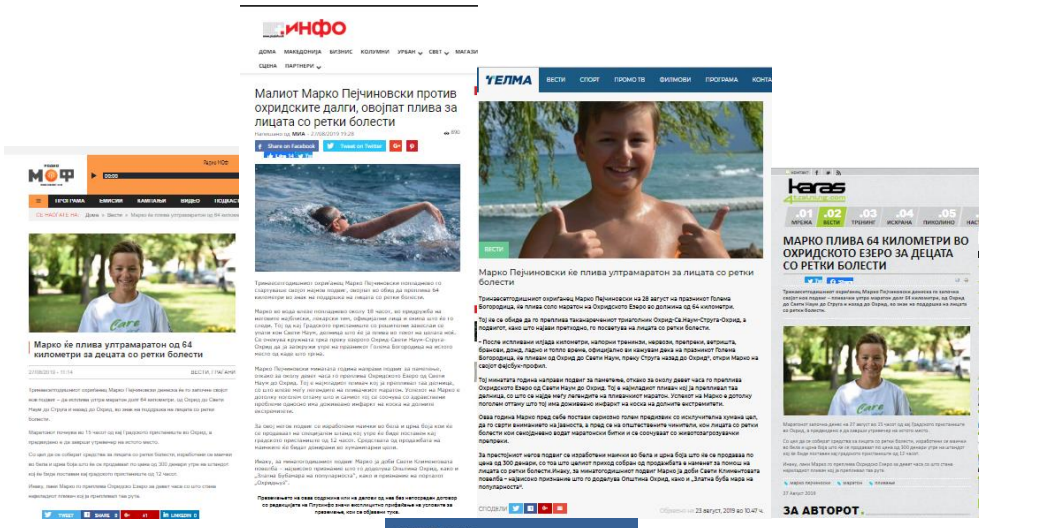

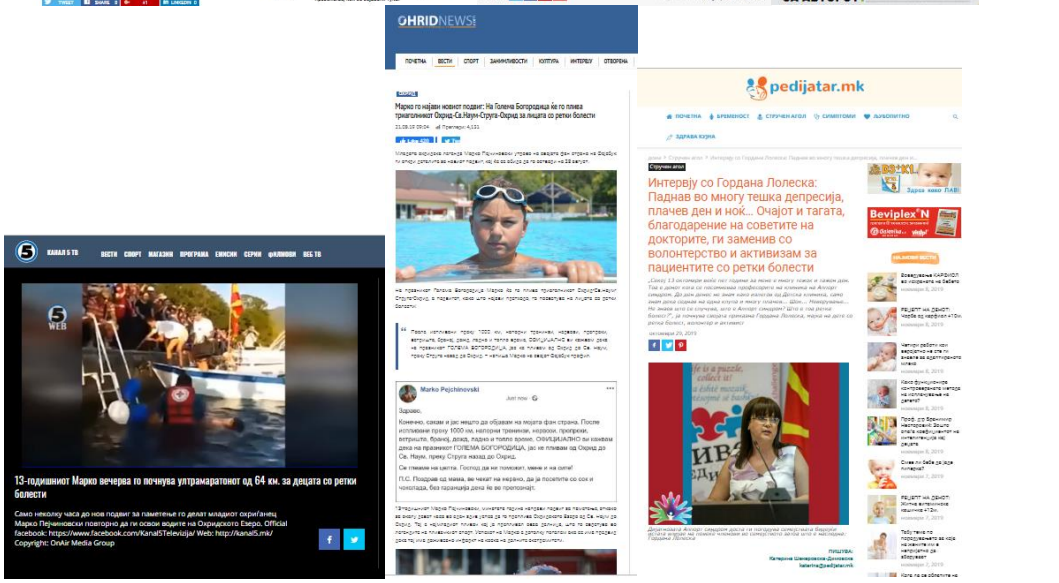

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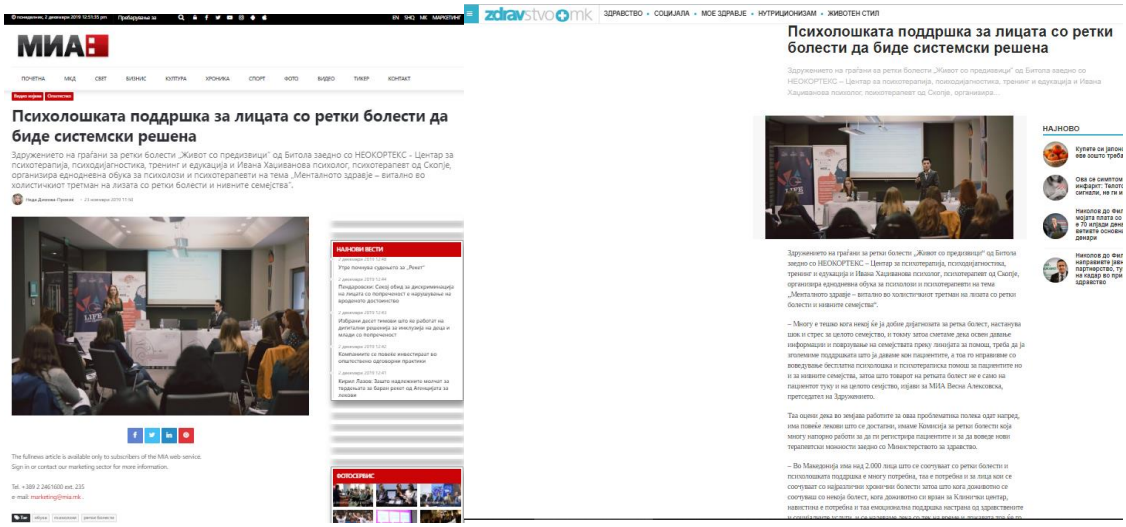

Sincerely,
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