MIJELOM CRO 2011 - 2021

What are the barriers to the availability of clinical studies in Croatia?

Defining Key Barriers and Creating Possibilities for Access to Clinical Trials

Mira Armour

14th Croatian Cochrane Symposium - Split 1. September 2022

MijelomCRO
Udruga za podršku oboljelima od multiplog mijeloma (plazmocitoma)

Why do we want them?
How do we get them?
How do we find out about them?

Myeloma in the Croatia: key facts

Approximately **330 people diagnosed with myeloma** a year

Around **1,330 people living with myeloma** in Croatia

Myeloma accounts for **15% of blood cancers** and **1% of cancers** generally

Myeloma mostly affects people **over the age of 65**, but it has been diagnosed in people much younger

https://mijelom.hr/Publikacije
RAKK-Putokaz-za-ranu-dijagnozu-multiplog-mijeloma.pdf

Ana Rukavina (1977 – 2006)

…everything is to do with ACCESS!

…ono što je bitno je DOSTUPNOST lijekovima

“Apsolutno vjerujem svojim liječnicima, ali znam gdje živim, stoga Vas najljubaznije molim da mi pomognete.” 2006.

“I trust my doctors implicitly, however I know where I live, so I ask you most politely to help me.”

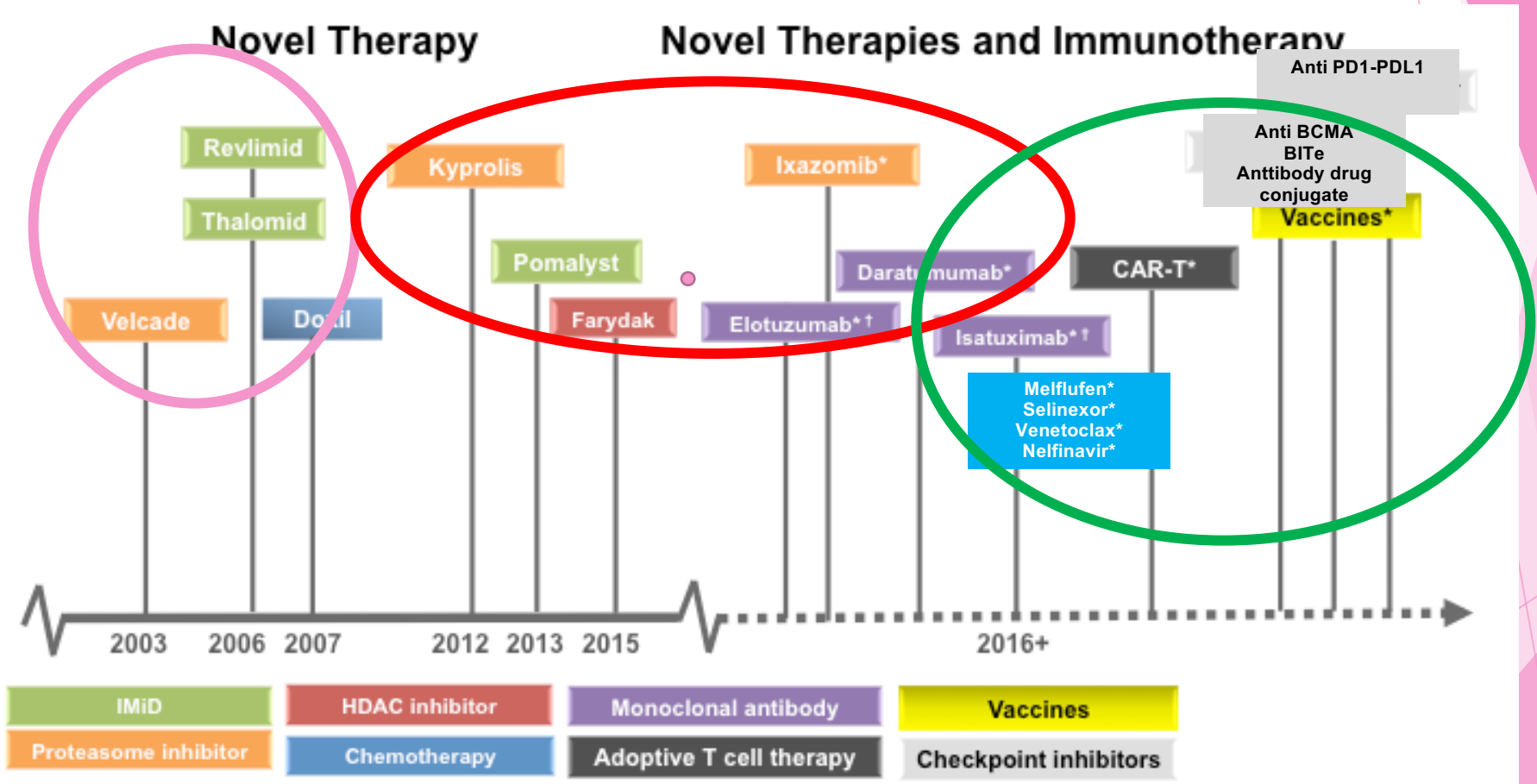
…has access improved?

…imamo li bolju dostupnost?

“… because of the situation in our country, I live in permanent fear, that there will come a day when they will find a drug that would make it possible to live longer with my twelve year old daughter, my husband and my family, and I will not be able to get it or to pay for it"

Snježana, alo-transplanted in May 2017.

Myeloma Drug Development
What are the newer agents?



IMiD, immunomodulatory drug; HDAC, histone deacetylase; KSP, kinesin spindle protein, SINE, selective inhibitor of nuclear export
*Not yet FDA-approved for MM; only available in clinical trials
†Treatments studied in MMRC trials

Prof Jean Luc Harousseau, Mijelom CRO Susret s pacijentima Zagreb 2018

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Lack and delay in access to drugs in Croatia:

- Bortezomib - in first line March 2018. (3.rd line in 2006, 2. line in 2014.)
- Lenalidomide – in 2. and 3. line (after bortezomib) 2018 (was 3. line since 2014.)
- Thalidomide – not registered in Croatia
- Pomalidomide - in 3+ (only IF Rev and Bort given previously (in EU 2013)
- 3 new drugs in Sep 2019
- No new drugs since
- Some early access schemes – slow and heavy paperwork
- Clinical trials - very few with limiting criteria
- Applications for latest drugs in the pipeline are taking time

Why do we need clinical trials?

- **The nature of the beast - there is still no cure for multiple myeloma**
- **Clinical Trials give access to drugs which are not otherwise available**
- Additional (often better) care then is standard in clinical practice
- A sense of hope and also of doing something for future patients
- Manage rare diseases (Extramedullary MM, Primary plasma cell leukemia, etc)
- Income for further development of clinical programs and improvement of health care services (infrastructure, personnel, laboratory services etc)

Methodology - finding out what is available

First stage:

CROATIA:

- Writing to Croatian Ministry of Health and HALMED – Oct 2021.
- Creating content for our web page with information on how to find out about clinical trials in Croatia – Dec 2021.
- Speaking at the Spring Meeting of Croatian MM Working Group in Beli Manastir. Leading discussion on barriers to clinical trials in Croatia. - 26.03.2022.

COUNTRIES IN THE REGION:

- Interviews with different stakeholders in Croatia, Serbia, Bosnia and Hercegovina, Kosovo, North Macedonia and Rumania. Feb to April 2022

Second Stage:

Convening a virtual meeting with hematologists and regional stakeholders 28th April 2022

Third Stage:

In Progress: Analysing, collating and writing a joint paper; Defining Key Barriers and Creating Possibilities for Access to Clinical Trials

MijelomCRO
Udruga za podršku oboljelima od multiplog mijeloma (plazmocitoma)

Clinical Trials in Croatia

- **Prior to pandemic there were 50 to 60 new clinical trials for medicine and medical devices per annum. Only two in MM (2015).**

- ClinicalTrials.gov Identifier: NCT02195479 - 2014
Phase 3, Randomized, Controlled, Open-label Study of VELCADE (Bortezomib) Melphalan-Prednisone (VMP) Compared to Daratumumab in Combination with VMP (D-VMP), in Subjects with Previously Untreated Multiple Myeloma who are Ineligible for High-dose Therapy.
- ClinicalTrials.gov Identifier: NCT02312258 - 2014
A Study of Oral Ixazomib Maintenance Therapy in Participants With Newly Diagnosed Multiple Myeloma (NDMM) Not Treated With Stem Cell Transplantation (SCT)

- In 2020. all clinical trials were stopped for several months – the healthcare system was restructuring to cope with pandemic.

- Exception were CTs related to COVID-19 and recruiting participants into ongoing clinical trials

"There are over 3000 clinical trials in MM, and there are not enough patients"

Philippe Moreau MD and Thierry Facon MD, France @COMy2022

Why no MM CTs in Croatia?

REASONS GIVEN BY HEMATOLOGISTS:

- *Patients are unwilling to take part*
- *small market*
- *there is no central registry, only institutional registries*
- *legal restrictions for paying HCP for their work*
- *COVID has made it even more difficult*

Upitnik sa susreta s pacijentima i liječnicima 2016

MijelomCRO

		% ispitanika	
Je li vam ikad liječnik koji vas je liječio (u bilo kojoj fazi bolesti) ponudio sudjelovanje u ispitivanju novog lijeka ili kliničkoj studiji, a vezani uz liječenje multiplog mijeloma?	ne	26	93%
	da	1	4%
	ne znam	1	4%
Broj ispitanika		28	100%

		% ispitanika	
Jeste li voljni sudjelovati u kliničkom ispitivanju lijeka za liječenje multiplog mijeloma?	ne	2	8%
	da	18	69 %
	ne znam	6	23 %
Broj ispitanika		26	100%

?

Clinical studies in Serbia

- In the last 5 years, a total of 2 phase III clinical studies have been conducted for RRMM. Completed.
- The course of the study was sequential, not at the same time.
- The number of patients included per study was 7-10.
- Both studies have been completed.
- There are currently no active clinical trials.

- Good clinical practice (GCP) must be followed when designing, conducting, recording and reporting clinical trials. Following GCP recommendations of a specific CRO Agency, which is hired by a competent professional association / agency / sponsor of the clinical trial.

- All clinical trials must be approved by the Ethics Committee of the Medicines Agency of the Ministry of Health of the Republic of Serbia, and then meet the legal regulations of the Medicines Agency of the Ministry of Health, as well as the competent Center involved in clinical trials.

"Our professional Association (doctors) cooperates and exchanges experience and knowledge with Associations from the region through regional and European meetings. The activities of the Association of Myeloma Patients of Serbia are carried out in the same way."

Apart from time-consuming administrative procedures, there are no obstacles to increasing the number of active clinical trials.

MIJELOM U BIH - BOSNIA AND HERCEGOVINA

- “ U BiH postoji Registar prijavljenih malignih bolesti gdje se iz svih centara (Sarajevo, Tuzla, Mostar i Zenica) prijavljuju SVI evidentirani maligniteti. Taj registar pripada Zavodu za javno zdravstvo FBiH - dakle i u ovom slučaju govorimo samo o Federaciji, a Republika Srpska se ne spominje. CANCER REGISTER OF HEALTH INSUIRANCE FUND OF BIH

- Registar kao ni baza podataka vezanih samo za MM ne postoji. NO MM REGISTER

- "Myeloma Balkan Study Group" je podijelila sa hematolozima dio potrebne dokumentacije za prijavu u njihov registar. Problem nastaje u administraciji, konkretno Klinickog Centra u Sarajevu, gdje po riječima hematologa ne doživljaju podršku od trenutne uprave KCUS. Također, kočnica se nalazi i u zakonskoj problematici jer nije regulisan način razmjene podataka pacijenata, odnosno nije regulisano koliko i kako se podaci pacijenata smiju ustupiti dalje. Znači potrebno je da se dobije EU saglasnost za razmjenu podataka za koju doktorica Ibričević sumnja da će je dobiti radi gore navedenih problema. GDPR DATA PROTECTION between EU and non EU countries

- Kada govorimo o kliničkim studijama, niti jedan pacijent u BiH nije učestvovao u jednoj takvoj studiji. Problem je taj što oni koji organizuju kliničke studije Bosnu i Hercegovinu smatraju neatraktivnom radi malog broja pacijenata, te financijski neisplativom i jednostavno za svaku prijavu do sada su se zahvalili i rekli da sav taj proces regrutacije pacijenata i upisa u kliničku studiju se njima ne isplati (financijski, administrativno i mali uzorak). ”

- NO PATIENTS TOOK PART IN CTs

”Too expensive for Pharma to run them in our country (low patient numbers)”

Kako dobiti pristup klinickim istrazivanjima?

S kime surađivati?

The Balkan Myeloma Study Group is currently trying to establish a registry of all myeloma patients in the region to increase interest from pharmaceutical companies and policymakers. It is estimated there are around 1500 newly diagnosed patients; with Turkey the number amounts to 3500 annually. Industry representatives highlighted that companies want to undertake studies and get drugs to patients as soon as possible, but they are incentivised to start in larger markets. Including regulatory bodies as a part of the BMSG future meetings should be beneficial so they can learn the challenges and perspectives of each country.

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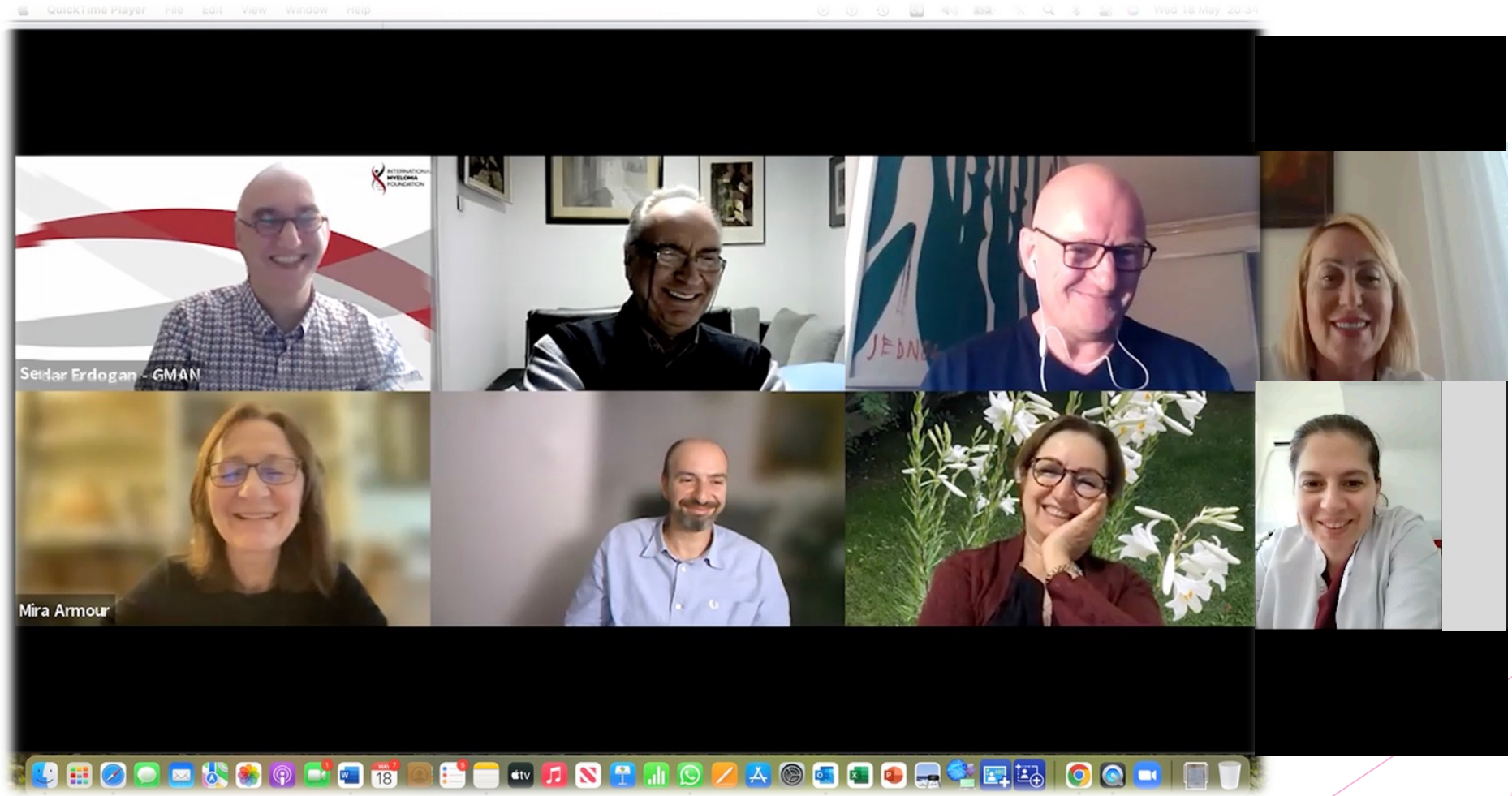
Myeloma Community SEE Meeting 28th April 2022 online event



Participants: 25

6 countries

4 presentations

Panel discussion

Agenda

Welcome and Introductions

Mira Armour, CEO Mijelom CRO & Serdar Erdoğan, Director of GMAN

Presentations

Mira Armour

CEO Mijelom CRO
Importance of Clinical Trial for MM Patients in SEE – Setting the Scene

Maša Katić, Ph.D.

Head of Clinical Trials Department, Marti Farm d.o.o., Zagreb, Croatia
Setting up a CT – What is Involved and What are Barriers

Efstathios Kastridis, MD

Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Greece
Overview of Myeloma Balkan Study Group and their Register

Meral Beksaç, MD

Department of Hematology at Ankara University, Director of the Ankara University, Turkey
Running A Clinical Trial – Haematologist Perspective

Balkans: population~160 mil

How many myeloma patients are there in the Balkans?

What are their special needs and characterictics?

What therapies are available ? In which countries?

What can we do to improve access to new therapies and new methods for diagnosis ?

Slide from Efstathios Kastridis, MD

Weaknesses:

- We lack data managers in most countries, no national registries for MM
- Small numbers of patients in each country
- Legal requirements on data protection between EU and non EU countries
- Patients from this region are not involved in design of the CT at the beginning
- Priorities of patient population might be different to patients from other parts of Europe
- We need better diagnostics which would require sufficient resources to run complex clinical trials
- Lack of laboratories for personalized biomarker diagnostics and analysis of immune responses
- Lack of MM relevant Pharma companies' representation in the region
- Different legal framework in each county, hospital

Strong points:

- Work with registries that already exist (setting up national registries which would take time)
- Bigger patient population
- Setting up and running trials in our region will be cheaper than in USA or big 5 countries in Europe
- We need a network of well organized and run centers, one or two in each country
- For countries – An important source of income for further development of clinical programs and improvement of health care services (infrastructure, personnel, laboratory services etc)

What can patient organisations do to help with getting clinical trials?

Panelists answers:

- RWE – no extra benefit for patient, they get what is available, but it includes the whole patient population
- Get evidence, stories, patients experiences
- Have a strong voice in European advocacy setting
- Be heard in Brussels
- Awareness campaigns on regional reality which requires different measures
- Advocate for change in EU guidelines an ensure that small countries are invited to participate in clinical trials

2022.

Study to Evaluate t(11;14) Status and BCL2 Expression in Adult Participants With Multiple Myeloma (MM) (MEDICI)

Brief Summary:
Multiple myeloma (MM) is a rare cancer caused by abnormal survival of plasma cells (blood cells). Most trial participants with MM relapse (cancer has come back) or become non- responsive to treatment and remission gets shorter after each line of treatment. This is a study to assess t(11;14) and BCL2 expression in adult participants with newly diagnosed and relapsed/refractory (R/R) MM.
Approximately 500 adult participants with newly confirmed or relapsed/refractory (R/R) multiple myeloma (MM) will be enrolled in around 15-20 countries.
Participants will receive standard of care while participating in this study. No drug will be administered as a part of this study.
Participants will attend regular visits during the course of the study at a hospital or clinic and will be asked to provide bone marrow and blood samples.

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Investigator: KBC Zagreb

Novi/relapsni/refraktorni pacijenti

Prisustvo t(11;14) i BCL2

Cilj: 500 pacijenata

Centri u 15-20 zemalja

Standardni protokoli liječenja

Redovni pregledi, uzorak koštane srži io krvi

Patient registries – there is a need for POs to understand what EMA does if we want to be effective in advocating

https://www.ema.europa.eu/en/human-regulatory/post-authorisation/patient-registries

Q1. Regional registries – what is their value ?

Q2. Are they practical to achieve ?

Q3. Maybe only in rare extramedullary and SPCL?

Q4. Maybe for lenalidomide and daratumumab naive patients?

The **initiative for patient registries**, launched in September 2015, explores ways of expanding the use of patient registries by introducing and supporting a systematic and standardised approach to their contribution to the benefit-risk evaluation of medicines within the European Economic Area.

Take away messages:

For MBSG and any other register to become true players in attracting CTs:

Need for a network of centers that can provide:

- ✓ Experience in clinical trials
- ✓ Facilities / infrastructure for clinical trials
- ✓ Access to standard procedures
- ✓ Patient volume to ensure enrollment in reasonable timeframe

Practice in the UK – regional CTs networks

Data Data Data ……

- **Real-World Evidence (RWE) trials**
  - Adequately integrate existing RWE reports in clinical practice, to drive treatment decisions in (the majority of) RRMM patients who are RCT-ineligible,
  - translation of RCT data may not be applicable to these populations

- **Payor data**
  - Increase transparency of insurance companies' data on duration of treatment, time to new therapy, dose reductions, overall survival, comorbidity codes, concomittant therapies, and other available data that could provide more insights in the RRMM population and real-world outcomes

- **Academic trials**
  - Conduct academic trials with less strict criteria to enrol real-life RRMM patients, and to support clinical decision making in underrepresented patient groups

- **Clinical Registries**
  - Create registries that automatically import data from hospital clinical records, since more comprehensive and detailed registries are needed to analyse RRMM population

Transparency and public accessibility of clinical trial information in Croatia: how it affects patient participation in clinical trials

Ivana S̆olić́1, Ana Stipc̆ić́2, Ivanc̆ica Pavlič̆ević́3, Ana Marusi̇̆ć́*4,5

Biochemia Medica 2017;27(2):259-69

Conclusions: Our study demonstrates that there is low transparency of clinical trials in Croatia, and that Croatian patients are not fully aware of clinical trials and the possibilities of participating in them, despite reported availability of Internet resources and good communication with their physicians. There is a need for active policy measures to increase the awareness of and access to clinical trials to patients in Croatia, particularly in their own language.

GOOD NEWS: A list of current CTs in hematology

KroHem – Klinička ispitivanja u tijeku

https://www.krohem.hr/klinicka-ispitivanja/


MijelomCRO
Rak krvnih stanica
Ja nisam 1%, ja sam 100%

Sarajevo

Thank you to
Cochrane Croatia Team for inviting us!

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