EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR INTERNAL MARKET, INDUSTRY, ENTREPRENEURSHIP AND SMES

# Multi-stakeholder Workshop on Biosimilar Medicinal Products

*A follow-up event to the Process on Corporate Responsibility in the Field of Pharmaceuticals*

**Brussels, 30 October 2019**

## Summary

*Information on the workshop (agenda, presentations, etc.) are available at: https://ec.europa.eu/growth/content/fifth-stakeholder-conference-biosimilar-medicines_en*

**Disclaimer:** the views expressed in the meeting and debates are personal views of the individual speakers. The European Commission thanks all speakers and audience for their active participation.

## FRAMEWORK AND OBJECTIVES

The European Commission – DG GROW (Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs) organised a multi-stakeholder event on biosimilar medicinal products in Brussels on 30 October 2019. It was the fifth event of a series of annual workshops on biosimilars, which had started with the first one organised in 2015.

The focus of this year's workshop was on the sustainability of the biosimilar medicines sector. Participants included representatives from patients', physicians', nurses' and pharmacists' organisations, academy, pharmaceutical industry, Member States permanent representations at the EU, Member States competent authorities and payers.

Biological medicines, including biosimilars, have a significant impact on society: they help save lives and significantly improve the health of patients with serious diseases like diabetes, autoimmune disease and cancers.

Biosimilars are medicines that have been evaluated by the European Medicines Agency (EMA) as equivalent in efficacy, safety and quality to the originator biological medicines[1]. They can enter the market with competitive prices after patent expiry of the original biological medicine. The use of biosimilars can increase access to biological medicines to more patients and can create savings across healthcare systems, freeing up resources also for new innovative medicines.

Biosimilar market penetration rapidly increased in the last five years following patent expiry of many biological medicines. However, there are still huge differences between Member States, ranging from market penetration of biosimilars up to 90% in Danish hospitals to percentage lower than 10% in many other Member States, particularly in some Eastern European countries.

The European Commission sets the regulatory framework for market approval of medicines, including biosimilars, whose marketing it authorises, and encourages dialogue among stakeholders to promote patients access to medicines and long-term sustainability of healthcare systems[2]. EU Member States are responsible for decisions regarding the organisation of healthcare systems and delivery of healthcare, including the pricing and reimbursement of medicines.

Starting from updated data on the market penetration of biosimilars in Europe, the event offered an opportunity to participants to exchange views on why timely access to biological medicines is not yet equally available to patients across the European Union and share experiences on how and when best practices can be applied to different systems. The main objectives of the event were to:

(1) Focus on initiatives that aim to disseminate science-based information and fight against biased information on biosimilars.
(2) Announce the availability of the guide on biosimilar medicines for healthcare professionals, now completed for all 23 EU languages – a project based on the cooperation between European Commission with the European Medicines Agency.
(3) Present the results of the 2019 IQVIA report on the impact of biosimilar competition in Europe.
(4) Show examples of current practices and pilot projects on education, dissemination and procurement of biosimilar medicines in various Member States.

[1] https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview

[2] https://ec.europa.eu/growth/sectors/healthcare/competitiveness/corporate-responsibility_en

## INTRODUCTORY PRESENTATION: POTENTIAL TOOLS TO OPTIMIZE THE BENEFITS OF BIOSIMILARS FROM THE SOCIETAL PERSPECTIVE

***Zoltán Kaló, Prof. of Health Economics, Centre for Health Technology Assessment, Semmelweis University, Budapest, Hungary***

Prof. Kaló underlined the differences in access to biologic treatment between lower income and higher income European countries. He showed data on 5-year net survival after breast cancer, indicating greater unmet need for biological medicines in Eastern Europe compared to Western Europe.

He pointed out as reasons to the scarce uptake of biosimilars in certain Member States:

- ✓ Lower acceptance by policy makers and regulators (in some countries) of international scientific data on efficacy and safety to biosimilars. Fear of immunogenicity is based on hypothetical and unproven risks. Empirical evidence shows that switching to biosimilars is not accompanied by increased risk of immunogenicity, significant adverse effect or loss of efficacy.
- ✓ Attempts of originators for product differentiation, such as marketing of different formulations that may not have significant benefits compared to the original product. For instance, based on a review of 42 publications, the added value of subcutaneous formulation of a medicine could not be validated in Eastern Countries: self/home administration of the subcutaneous product was not feasible - particularly in cases of concomitant intravenous chemotherapies - and time saving with subcutaneous product was insignificant, due to fairly long waiting time of patients for treatment administration.

Prof. Kaló argued that, in order to achieve significant improvements in patient access to biological treatment in Eastern countries, a top-down approach establishing targets and quota for procurement of biosimilars should be applied. Such an approach has already proven as successful in Scandinavian countries.

Proposed policies to maximise societal benefits include:

- ✓ Expedited price and reimbursement processes for biosimilars to reduce obstacles to their timely entry on the market.
- ✓ Administrative tools and policy measures to incentivize use of more affordable biosimilars.
- ✓ Mandatory switch of patients, after patent expiry, from the original biological medicine to the more affordable biosimilar alternative, under medical supervision.
- ✓ Biosimilar set as first line biological therapy for all naïve and maintenance patients.
- ✓ No separate reimbursement categories foreseen for biosimilars and original biologicals or its modified formulations (e.g. subcutaneous vs intravenous), unless the modified formulation has proven benefits to patients or healthcare systems.
- ✓ Establishment of information exchange platforms between Member States.
- ✓ Physicians not only informed about scientific evidence on biosimilars, but also guided on how to educate appropriately their patients on these medicines.
- ✓ Clinical guidelines amendments recommending earlier/extended use of biosimilars, if justified by health benefits such as giving access of biologicals to more patients.

## SESSION 1: WHAT ARE THE FORCES DRIVING THE BIOSIMILAR MARKET?

# IQVIA Report 2019: A Snapshot of the biosimilar market dynamics

***Per Troein, IQVIA***

The IQVIA Report 2019 - The Impact of Biosimilar Competition in Europe - was drafted using data of 2018, with contributions to the content from the pharmaceutical industry (EFPIA, Europabio and Medicines for Europe).

The report includes some key data:

- ✓ Biosimilar competition is able to reduce the overall medicine expenditure significantly. Total savings vary from country to country: up to 8% and on average 4-6% of total medicine expenditure.
- ✓ An increasing number of biosimilar medicines was launched in Europe in the past 10-years: 10 biosimilars were available in 2009 and 55 are available in 2019.
- ✓ Discounts up to 80% were reported in Nordic Countries for biosimilars of major biological medicines such as Humira.
- ✓ Originator manufacturers have changed competition strategy and, in some cases, they have rebated prices of original medicines up to 89% (e.g. in the Netherlands).
- ✓ Access is not yet increasing for all molecules and in all countries after biosimilar introduction, particularly for cancer treatment in Eastern Europe.
- ✓ In 2019, 95 approved biosimilars are in use across the globe. Estimates show that only about one third has earned back the estimated development costs (100 million $) and only 13 products reach the 300 million euro investment mark. More is needed to create a sustainable market for biosimilar manufacturers.

# Market dynamics from a DG COMP perspective

***Harald Mische, Directorate-General for Competition (DG COMP), European Commission***

Mr Mische outlined the main differences between generics and biosimilars in terms of competition. Investments to bring a biosimilar to the market are higher, authorization requirements are more complex and more sales may be needed to earn a sufficient return; health systems generally do not rely on automatic pharmacy substitution for biosimilars, but on doctors and patients who, however, may be reluctant to switch from originals to biosimilars. Consequently, market entry barriers can be higher compared to generics and thus, after loss of exclusivity, originators may maintain a strong market position for a longer period.

Mr Mische summarized the results of the '2009 Sector Inquiry'. This DG Competition inquiry observed that industry used a toolbox for delaying generics entry on the market. The risk is that similar practices may be used also for biosimilars. The toolbox included:

- ✓ Product hopping, i.e. launch of 2nd generation products around the time of loss of exclusivity of the 1st generation product to switch patients to the 2nd generation product before effective generic competition kicks in.
- ✓ Creating clusters of secondary patents to create legal uncertainty and to raise barriers to generic entry.
- ✓ Lengthy patent-related litigations.
- ✓ Settlement agreements.
- ✓ Interventions before Marketing Authorisation and Pricing and Reimbursement Authorities.

Following the 2009 Sector Inquiry, the Commission focussed its enforcement initially on prohibiting 'Pay for delay agreements', i.e. agreements whereby the originator pays the generic competitor for its commitment to stay out of the market. Such agreements may be concluded within the context of a patent dispute. In 'Pay for delay agreements' the originator and generic companies gain, while patients and health care systems lose.

In December 2019, Advocate General Kokott will issue her opinion in the Paroxetine preliminary ruling case referred by the UK on whether under EU law 'pay for delay' agreements restrict competition by object.

The Commission and national competition authorities have further adopted infringement decisions relating to other exclusionary abuses. These concern: providing misleading information to obtain supplementary protection certificates; misuse of government procedures; an exclusionary patent acquisition; disparagement practices to hinder generics; and exclusionary discounts.

Exclusionary rebate schemes have not played any important role concerning generics. However, market dynamics of biosimilar competition are different. Recent developments such as the UK's Remicade decision or the Dutch inquiry into biosimilar competition regarding TNF-Alpha-Inhibitors suggest certain concerns that biosimilars may be vulnerable to exclusionary rebate schemes. Competition authorities have issued warnings that they will intervene if rebate schemes hinder or foreclose biosimilar competition.

## Discussion Session 1

***Moderator*: Zoltán Kaló, Prof. of Health Economics, Centre for Health Technology Assessment, Semmelweis University, Budapest, Hungary**

***Panel*: Per Troein (IQVIA), Rainer Becker (EC, DG COMP), Isabell Remus (Medicines for Europe), Kristine Peers (General Counsel EFPIA)**

During the discussion, session 1 speakers and panellists raised the following points:

- ✓ In lower income countries (e.g. in Eastern Europe), resistance to use biosimilars leads to insufficient price competition and ability to increase treatment that often reduces survival following serious illnesses such as cancers: with limited resources, only few patients are treated appropriately.
- ✓ All Member States should timely update clinical guidelines to reflect the most cost-efficient treatment, according to latest publicly available international science.
- ✓ Training to understand and use biological medicines is needed for physicians in all Member States. These modern treatments are often unknown to doctors, who use older and cheaper chemical therapies with higher adverse side effects.
- ✓ Multi-winner tenders are crucial to avoid medicines shortages and in general for long-term sustainability of health systems.
- ✓ After patent expiry of original products, tenders to biosimilars should be opened soon, not months/years later. Prices should also be negotiated within reasonable timelines.
- ✓ Race to the lowest price is a danger for long-term sustainability. Tenders should not be based solely on price, but also on factors like supply reliability and added service.
- ✓ Access to biological medicines to the widest number of patients is the goal. This can be achieved by fostering biosimilars uptake, but also by encouraging lower prices for biological medicines through fair competition mechanisms.

- ✓ Developing a biosimilar takes 8 years: investments need assurance that fair competition mechanisms are set in all Member States to allow reasonable expectations to recuperate costs.
- ✓ Patents of many orphan medicines will expire soon: conditions are needed for biosimilars, given the small sale volume of these products.

## SESSION 2 HOW TO ENSURE A SUSTAINABLE BIOSIMILAR MARKET?

## Member States experiences with biosimilars

***Mathias Flume, Head of Business Unit Prescription Management, Kassenärztliche Vereinigung Westfalen Lippe, KVWL, Germany***

Mr Flume indicated that Germany is a free pricing market: "open-house" contracts allow manufacturers fulfilling certain contractual conditions to supply the market. Biosimilars have full market access and reimbursement from day one after patent expiry. In hospitals, individual procurement tenders are price-dependent and obtain high rate of use of biosimilars even in the oncological sector. New rules under discussion in Germany (enter into force expected in 3 years) allow biosimilars substitution also at public pharmacy level.

In Germany, cost reduction obtained by biosimilars compared to originators can be up to 35% and in some cases even 50%. However, initial prices are still overall significantly higher than in other Member States. Therefore, even with the price reduction obtained with biosimilars, prices are often higher in Germany than in other Member States.
Regional differences exist, with room for improvement in some regions.

The experience in Westphalia shows that, when physicians are well informed, they not only prescribe more biosimilar medicines to achieve agreed quotas, they sometimes fully switch their patients. Since 2017, in Westphalia, a position paper for physicians clearly states that biosimilars are equivalent to their biological reference product. A lot of mirror-information is provided also individually to physicians with percentages of biosimilars use, comparisons of prices and number of switched patients. In each therapeutic situation, physicians can make an informed choice together with their patients. A patient information centre has also been established.

In Westphalia, physicians actively prescribe more than one biosimilar medicine: switch from biosimilar to biosimilar happens without any adverse effect.

***Tomáš Tesař, Union Health Insurance Fund, Ministry of Health, Slovakia***

Mr Tesař illustrated a study estimating that Slovakia could save 40 million € per year if biosimilars were fully available on their market (assuming a 25-35% decrease in price, based on a 2016 study by Simon et al).

In August 2019, out of the 54 biosimilars authorized by the European Medicines Agency, 24 were available in Slovakia, 27 in Hungary, 28 in Poland and 29 in Czech Republic. Since Slovakia invested more resources than the other 3 Eastern countries, it is clear that factors other than resources availability influenced the uptake of biosimilars.

Mr Tesař indicated as main factors leading to the low access to biosimilars in Slovakia a small market size and legislative barriers such as poorly designed tender processes.

The example of a tender in 2018 in Slovakia was given, where the winner of the tender offered a discount of 57% versus the original biological price. Since no volume-based

agreement was made, other competitors offered the same discount, resulting in the winner of the tender unable to gain market share. In the tender process for the same molecule in 2019, learning from experience in 2018, the winner offered only a 25% discount, rendering the tender process ineffective. Mr Tesař commented that multi-winner contracts, if not accompanied by quotas for tender winners, do not necessarily decrease prices of biological medicines, nor do they ensure wider access to patients to those medicines.

He presented policies currently under discussion in Slovakia to stimulate biosimilar competition. Future contracts between healthcare providers and insurance funds might include switching targets for physician based on the total number of patients receiving biologic treatment on a given indication. Other measures under consideration are financial incentives for healthcare providers achieving the set targets and a guideline by the Public General Health Insurance Company addressed to healthcare providers.

Finally, he showed results of a study indicating that in Hungary, the switch for many indications after patent expiry of an originator medicine was rather to other patent protected biologicals than to biosimilar alternatives. This confirmed how the access to the market for biosimilars in Eastern Europe is still difficult.

***Floriane Pelon (Social Security Directorate, Ministry of Solidarity and Health, France***

Ms Pelon illustrated how France is trying to promote the use of biosimilars. She indicated that, although the objective for 2022 is to get a market share for biosimilars of 80%, the actual penetration of biosimilars in France one year after patent expiry is today rarely above 10%. Despite the strong efforts to share available information to prescribers and create targets for physicians' prescriptions, results were limited. Therefore, the French government decided to finance a pilot project dedicated to biosimilar medicines in hospitals with the following actions:

1) Appropriate information to health professionals when a biosimilar enters the market.
2) Higher incentives (30% vs current 20%) on savings produced for prescribed biosimilars payed directly to the care units concerned, rather than to the hospital.
3) Raise awareness of hospital prescribers of the financial impact of their prescriptions for outpatients, with the goal of promoting use of biosimilars outside the hospitals too.

The pilot project started in October 2018, will last for 3 years on three molecules across 62 hospitals (clinics & public hospitals). The first results show that the initiation rate has raised to 50% and the switching from originals to biosimilars has doubled.

## Sustainable procurement of medicines: a perspective from DG GROW

***An Baeyens, Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs (DG GROW), European Commission***

MS Baeyens started her presentation by noting that EU countries spend circa 10% of their GDP in health budget. A considerable part of that budget is distributed to medicines through public procurement contracts, by various contracting authorities – national, regional, public and non-public insurance companies.

She presented data on tenders for pharmaceuticals registered in 2010-2017 in the supplement of the European Official Journal 'Tenders Electronic Daily' database (TED). All EU wide tenders over 125000 euros (if local) and 230000 euros (if central) should be

published on TED. A search in the database concerning 298 molecules in the hospital market of 21 Member States (small Member States missing) were included in the analysis. Results revealed that the top 50 gross sales molecules account for 88% of all sales, and the top 25 for 71%. The total amount of the top 25 molecules published in TED in 2010-2017 was 2.6 billion euros with about 20.000 awards.

The number of Contract Awarding Notices varies greatly across Member States, with the highest numbers for Poland, Spain and Portugal. For several countries, there is no publication at all. One third of the 25 molecules is procured under non-competitive procedures and, in many cases, there is only one offer (no competition) or, when there are more offers, they are never published before 3 years after patent expiry.

It was reminded that EU public procurement directives apply to tendering of biosimilars and that rules have to be applied in a smart way, i.e. not only using lowest price as determining factor, but rather ratio between best price and quality, delivery, availability, training of physicians/patients/payers and innovation. Procurements should also consider that ingredients are increasingly produced by subcontractors in India/ China and thus use procurement as a leverage to improve social inclusion and environmental aspects.

In order to tap the full potential of tender tools made available by the 2014 Directives, it is important for public buyers to bundle knowledge, skills and expertise. In order to bring the professionalization of public buyers to a higher level, the Commission has taken several initiatives:

1) Innovation Guidance: with examples also for the health sector.
2) Big buyer project: running until May 2020, with the aim to push public buyers to work together on public projects sharing knowledge to write smart procurements.
3) Innovation procurement brokers: running until Aug 2020, to bring public buyers closer in contact with companies for innovative solutions, creating a business model and a working methodology.
4) European Qualification Framework: detailing different competences that public buyers should have.

## Discussion Session 2

***Moderator*: Per Troein, IQVIA**

***Panel*: Mathias Flume (DE), Tomáš Tesař (SK), Floriane Pelon (FR), Evert Jan van Lente (Medicine Evaluation Committee MEDEV), Dorthe Bartels (AMGROS - Regions' Procurement Pharmaceutical Organisation, Denmark), Kelly Burke (Medicines for Europe), Mareike Ostertag (Director Regulatory and Science Policy, Novartis), An Baeyens (DG GROW)**

During the discussion, session 2 speakers and panellists highlighted the following points:

- ✓ Evidence-based guidelines can change clinical practice: molecules (including biosimilars) winning the tenders should be recommended in the guidelines. Guidelines should be updated immediately after tender is concluded, as it happens already in Denmark. In Germany, general recommendations require always using the cheapest alternative, unless there are medical reasons against this.
- ✓ Patients should be involved or at least informed on public procurement and invited in conferences regarding pharmaceutical procurement.
- ✓ There is no "one-fits-all" tool to drive biosimilar competition in the various Member States because of the differences in health systems and overall economy.

- ✓ Sustainability of biosimilars should be ensured for patients, healthcare professionals and industry. Race to the lowest price is a danger for sustainability of industry and long-term supply security. Indication-based (rather than molecule-based) tenders will not help sustainability.
- ✓ Policies allowing multi-winner tenders (even more than 2) are key.
- ✓ An obstacle to biosimilar uptake is that procurement contracts are often agreed just before patent expiry and, when already existing, they are extended not allowing for competition. If competition is considered hampered, complaints can be filed by economic operators, who are those that can legally challenge the practice.
- ✓ Training is a valuable asset, but education needs to be neutral, thus criteria in tenders should not include education. Environmental aspects are inappropriate criteria in tendering: they may rather be dealt by the European Medicine Agency at authorization level.

## SESSION 3: HOW TO IMPROVE EARLY ACCESS TO BIOSIMILARS? LEARNING FROM EXAMPLES

### Pharmacists

***Arnold G. Vulto, Honorary Professor at the Section of Clinical Pharmacology & Pharmacotherapy, Dept. of Pharmaceutical and Pharmacological Sciences, KU Leuven, Belgium and Honorary Professor at the Hospital Pharmacy of the Erasmus University Medical Center in Rotterdam, The Netherlands***

Prof. Vulto mentioned his motto: optimal treatment for all patients at an affordable cost. Science is the best possible description of the world and problems occur because of lack of knowledge or emotion.

He pointed out that biosimilar uptake can be achieved if: a) physicians have sufficient trust in the sameness of biosimilars; b) pharmacists are allowed dispensing biosimilars; c) both have sufficient incentive to do so; d) patients have confidence in the prescribed medicine (avoiding nocebo response).

He cited two key scientific studies that showed the equivalence of biosimilars to originators, concluding that four factors were shown key in acceptance of biosimilars:

1) Educate and involve all healthcare stakeholders in the science-based choice.
2) Have a coherent message coming from all healthcare stakeholders.
3) Share the decision making with patients, ensuring they are informed and consulted, avoiding they get information from unreliable sources.
4) Foresee gain sharing, with compensation to healthcare professionals to account for the additional investment (time, effort) in the biosimilar medicines clinical introduction process (e.g. explanations to patients).

He indicated that the role of pharmacists in hospitals is key to achieve the four factors above, since pharmacists:

a) Provide education in the hospital setting.
b) Support and participate in the decision-making within the drug therapeutic committee.
c) Communicate with the overall hospital staff and patients.
d) Actively design the medicines procurement and logistics (selection of the best value biologic vs lowest price – supply chain and pharmacovigilance reporting).

Reference was made to the EAHP (European Association of Hospital Pharmacists) position on biosimilar medicines (June 2018).

Promoting biosimilars should also require less development costs & large sales volumes. The development of biosimilar medicines currently costs between 100-200 million €. Prof. Vulto indicated that this is too expensive and likely not needed. The requirements for marketing authorization of biosimilars might have to be revisited.

He cited a 2019 EMA-study with 25 molecules showing that clinical trials hardly played a decisive role in decision-making on equivalence and approval of biosimilars. Prof. Vulto commented that, although there are over 55 biosimilar medicines approved in the EU and over 1 billion patients' days' experience showing safety, quality and efficacy of biosimilars, we still need to combat emotions in this field.

## European Medicines Agency EMA

***Rosa Gonzalez-Quevedo, Public Engagement Department/Stakeholders and Communication Division, European Medicines Agency EMA***

Ms Gonzalez-Quevedo reminded that, before any biosimilar is approved in the EU, a rigorous scientific evaluation occurs, followed by post-marketing safety monitoring and evaluation via pharmacovigilance.

From the 95 applications received so far by EMA, 54 have received marketing authorization. The seven cases of post-marketing withdrawals were exclusively based on commercial reasons and not on safety or efficacy reasons. Currently, 14 biosimilars are under review and half of them are oncological medicines.

A 2019 article by members of the EMA Biosimilar Working Party resumed the following learnings from the EU regulatory experience:

1) Biosimilars are approved based on a comprehensive assessment & stringent standards.
2) Regulatory framework is robust but able to adapt to science & clinical experience.
3) Adequate balance is achieved between regulatory standards, patient safety and feasibility of biosimilar development.

At the time, biosimilars represented a novel approach to medicines development, but an approach based on well-known scientific principles of comparability assessment. Barriers to uptake are attributed partly to lack of unbiased information.

EMA is putting resources to respond to patients and healthcare professionals need for unbiased information. It has now completed the translation of the guide for healthcare professionals in all the 23 EU languages. It has also updated the guide from 2017 in all languages to account for the newly authorised biosimilar medicines (Biosimilars in the EU, Information guide for healthcare professionals: EN, DE, FR, ES, IT, NL, PL, PT, BG, CZ, EL, DA, ET, FI, HR, HU, LT, LV, MT, RO ,SK, SL, SE).

At international level, EMA actively contributed to the 'International Coalition of Medicines Regulatory Authorities' (ICMRA) and WHO statements on biosimilars published in June 2019 (patients and general public and healthcare professionals)

Within the 2025 EMA strategic reflection to refine goals for regulatory science, dedicated actions are foreseen for biosimilars: communication campaigns to reinforce trust in patients and healthcare professionals, enhanced training to non-EU regulators evaluating biosimilars and resources for upcoming regulatory challenges.

## Patients

***Zorana Maravic, Director of Operations, Digestive Cancers Europe***

Ms Maravic pointed out how - although colorectal cancer is a preventable and in an early phase treatable disease - still half million of patients are diagnosed in EU every year and half of them die. Treatment for metastatic colorectal cancer combines cytotoxic and biological agents. Significant survival progress has been achieved with the multiplication of therapy options over the years, shifting from 6 months survival, when only one chemical medicine was available, to 30 months with today's combined therapies.

However, huge inequalities exist in access to biological treatment, with lower access in Eastern Europe, as shown by the European Society of Medical Oncology (ESMO) survey[3]. Two biosimilars are registered for metastatic colorectal patients but not available yet. Digestive Cancers would like to prepare its patients to the discussions, preventing confusion and misinformation encountered in the past by other medical sectors.

In a series of ESMO workshops, Digestive Cancers inquired what patients think about biosimilars and learnt that patients would like to know how savings are used in practice: to improve facilities, to employ more nurses, to educate clinicians, etc.
Based on these findings, Digestive Cancers published in 2019 a position paper highlighting key principles:

1) Patients' safety is a priority and pharmacovigilance is essential - as for all medicines.
2) Education and involvement of patients is key, but information should be clear and easily accessible: messages should focus on quality, rather than solely on cost differences and should remind that biosimilars are by no means inferior drugs.
3) Patients stable on a medicine should not be forced to switch just with the argument of savings (to prevent the risk of nocebo effect). If appropriately informed, they will trust biosimilars and agree to switch spontaneously.

A multi-tiered educational campaign is now rolling out, focusing on quality and outcomes for patients.

## Physicians

***Prof. Matti Aapro, Executive Board member of the "European School of Oncology" (ESO), board member of "European CanCer Organisation" (ECCO)***

Prof. Aapro illustrated the perspective from an oncology clinician. He stressed that science should be made accessible to everyone because there are still a lot of misconceptions about biosimilars. Manufacturing changes - under regulatory surveillance - of biologic medicines have been numerous over time and regulatory scrutiny has allowed seamless controlled similarity between the different versions.

Why not the same acceptance for biosimilars?

He showed scientific arguments supporting and explaining 5 key facts about biosimilars:

1) Biosimilars are not generics. This is legally true. However, certain aspirin generics were shown in the past to have different absorption compared to the 'original aspirin'. Therefore, the generic had not identical properties as the originator

[3] Cherny C, et al. ESMO European Consortium Study on the availability, out-of-pocket costs and accessibility of antineoplastic medicines in Europe. Annals of Oncology, Volume 27, Issue 8, 1 August 2016, Pages 1423-1443

medicine, but no concerns were raised, differently to the current reluctance to use biosimilars.

2) Biosimilars are not 'intended copies' or 'non-comparable copy of biologics'. Those 'copies', different from biosimilars, do not always meet international standards of regulatory requirements, nor they are subject to strict pharmacovigilance. However, those 'copies' can be marketed outside the EU and this can create confusion and misconceptions about biosimilars.
3) Extrapolation of indication is common (e.g. it has been used for cytotoxic medicines), but not automatic. A biosimilar is considered equivalent to an original biological medicine only if supported by clinical and non-clinical scientific evidence, including deep knowledge of its biological mechanism of action. If there are any doubts, the European Medicine Agency will ask for further studies.
4) Biosimilars are currently available for use in oncology. Although we often hear the opposite, large experience exists by now. The only immunological reaction observed with an oncological medicine was a long time ago with an originator, not with a biosimilar. We observe that fears about biosimilars are driven by emotion, not by science. Biosimilars uptake in oncology varies across medicines, countries and even across regions, showing a different dissemination of unbiased knowledge.
5) The potential for use of biosimilars in oncology is high. It is only 'silos thinking' that slows down biosimilars acceptance in certain medical sectors. Rheumatologists and gastro-enterologists demonstrated efficacy and safety of biosimilars years ago. We just need more communication between oncologists, rheumatologists, gastro-enterologists, endocrinologists and so on.

Reference was made to the ESMO position paper on biosimilar medicines (December 2016) in reaching out to the oncologist community.

## Nurses

***Ber Oomen, Executive Director European Specialist Nurses Organization (ESNO)***

Mr Oomen explained that ESNO includes institutes and individuals and promotes the harmonization of education of specialized nurses.

ESNO published on their website a position statement on biosimilars and a communication guide on how nurses should communicate to patients when switching to biosimilars "Switch management between similar biological medicines" translated so far in eight languages.

2020 is the international year of the nurses (WHO) and a number of dedicated events will be organised. Over 2020-2022, ESNO will translate their guide into a digital format (digital transition project) to reach out to more nurses and raise awareness at the level of national continuing professional development (CPD) nursing councils.

Awareness in the community setting is still limited: in a recent event in Barcelona, less than 5% of the nurses were aware and informed of the biosimilars guide for nurses.

## Public Competent Authorities

***Nicolai Brun, Director of Division of the new Medical Evaluation & Biostatistics division, Danish Medical Agency DKMA, Denmark***

Mr Brun presented how regulators in Denmark help building trust in biosimilars. Interchangeability, switch, pharmacovigilance are essential components of legal texts. However, interchangeability is a term that might create confusion: once a biosimilar is

approved by EMA, Denmark does not see any issues related to interchangeability and switching is promoted.

Denmark authorities have clearly communicated that, although slightly different from reference medicines, biosimilars are safe and effective and that, ultimately, only safe and effective medicines are used in the EU. The perception from the Danish public opinion is today very positive: biosimilars are seen as an opportunity to provide wide access to biological medicines and to create economic space to implement the use of newer therapies. Transition to biosimilars in Danish hospitals is almost 100%. All treated hospital patients must switch to the winner of the tendering, irrespective whether it is a biosimilar or a reference product. Retention level is also very high in hospitals: patients treated with a biosimilars remain with that treatment for long time.

Key factors to build trust on biosimilars have been:

1) Strict pharmacovigilance: the treatment division must report all adverse events for biosimilars and original medicines.
2) Patients are informed of the percentages of switch in the various hospitals and also of the adverse effects reported, which were in fact very few and minor.

However, the situation is so positive only in hospitals. Biosimilars uptake in Danish primary care is still below 5% and education of general practitioners remains a challenge.

***Akos Karsay, Department of item-based medicine, National Institute of Health Insurance Fund, Budapest, Hungary***

Mr Karsay presented the different mechanisms for financing medicines in Hungary: biobidding, special financing and item based financing (patent protected medicines).

When a medicine loses patent protection, tenders are opened, but solely for treatment of naïve patients. Quotas are legally defined, but not effective.

Access to new biologic medicines is not restricted, since all new substances are available. Competition has allowed reinvestment of the freed-up budget, thus allowing financing more than 30 new medicines.

Resistance to use biosimilar medicines more broadly remains. Often doctors continue to prescribe reference products, even when biosimilars win a tender. Hospitals receive only recommendations to use biosimilars, but no quotas are applied and unbiased scientific information does not reach enough healthcare professionals and patients.

## Discussion Session 3

***Moderator: Arnold G. Vulto***

***Panel: Matti Aapro, Usman Khan (European Patient's Forum EPF), Zorana Maravic, Ber Oomen, Nicolai Brun, Akos Karsay, Rosa Gonzalez-Quevedo.***

During the discussion, session 3 speakers and panellists highlighted the following points:

- ✓ Usman Khan (European Patient Forum EPF) reported a 2016 study, showing that only about 25% of the general population and 50% of diagnosed patients understand what a biological medicine is. However, percentages decrease even further for biosimilars: only about 6% of the general population and 20% of diagnosed patients understands what a biosimilar is. There is a lot of work to do engaging with patients

- ✓ In Central Eastern European Countries, the main issue is that instead of 'evidence-based' policies, in many cases, 'eminence-based' policies are in place, relying on academic opinion leaders rather than on evidence from the field. Failure to open the competition has created massive loss of resources in Hungary. A physician-led switching policy is needed to be able to transfer benefits to patients.
- ✓ In the Netherlands, a new initiative will start in 2020 rolling out educational programmes beyond the hospital, involving family practitioners and community pharmacists. Moreover, a document with all patient organisations is under development, so that each patient can retrieve the relevant information for his disease. These initiatives could be replicated in other countries.
- ✓ The International Association of Patient Organisations (IAPO) has developed a valuable biologics/biosimilar toolbox, directed at patients. It is available in a few languages, but can be easily translated and made available in any EU country. Patient organisations better use the best material available instead of trying to invent the wheel again.
- ✓ All patients - including those not yet getting the medicine - should discuss the benefits of switching and be involved in the development of the patient organisation position. In UK, the case of a patient was debated who payed for a biological medicine out of her pocket and survived 12 years instead of the three months expected without that medicine.
- ✓ There is a huge network of underfunded national patients' organisations, yet the knowledge on biosimilars in the patient community is limited. Health literacy remains a problem. Patients self-educate themselves when they need medicines or biosimilars. A solid EU framework for marketing authorization of biosimilars is in place, but there is a need to work much more on education of doctors and patients. Passive distribution of information documents is not enough: there should be active exposure.
- ✓ Suggestions from the various panellists on how to distribute information to patients:
    a) EMA platform for dialogue with patients and healthcare professional (patients and consumers working party and healthcare professionals' working party).
    b) Make understand to patients the science by improving communication between nurses and patients
    c) Digitalisation should support better accessibility and dissemination of guides to doctors, nurses and patients via more widely distributed printed copies
    d) Physicians with experience have to continue raising awareness within the physician community, breaking silos and engaging in physician meetings in oncology and beyond (e.g. with endocrinologists).
    e) Cinema/TV celebrities could serve as an example for the community to show and publicize that biosimilars are safe and effective like originals.
    f) Less than 50% of national medicine agencies have information on biosimilar medicines on their websites. No need to reinvent the wheel; publications are general and can translated from those already accessible in national website (e.g. in Denmark, UK, The Netherlands, Finland). Regulators need to give incentives and be strict, avoiding transmitting sponsored biased information.
    g) Speeding up reimbursement procedure can create great opportunity for savings.

## CONCLUSIONS

All speakers and panellists gave their one-minute take home message:

- Troein: biosimilars are a major economic opportunity for health system to increase access and afford further innovation.
- Mische: regulators and decision makers should be mindful how their choices affect biosimilar competition. Competition tends to lower prices and offer more choice for patients.
- Kaló: in Member States lagging behind, small improvement are not enough and radical top-down approach is needed.
- Tesař: there is no 'one fit-all' solution. A toolbox tailored to each Member State is needed.
- Pelon: trust is key. Implementing incentives directly to the care unit and giving feedback to prescribers has proven useful to educate prescribers and allow patient to understand.
- van Lente: there is still a lot to do. These stakeholders meeting are precious opportunities to learn from each other. We have to monitor what achieved and, if not satisfactory, ask politicians to change rules.
- Bartels: long-term sustainable market is needed: if prices decrease too much, products will not stay on the market.
- Gonzalez-Quevedo: The biosimilar framework and pharmacovigilance system are robust. If there are questions, we have experts to answer. Give us feedback if our information guides need to be improved
- Aapro: not so necessary to talk to those coming to this workshop, but to the others.
- Vulto: after 15 years of experience, we only need to look at science and to bring appropriate information to all patients and doctors at a local level.
- Khan: engage with patients and make sure it is an agreed solution and not an imposed one for each single patient.
- Oomen: with appropriate information, biosimilars have to become common like car security belts.
- Karsay: we need to improve communication with patients and doctors and learn from Denmark positive experience.
- van den Hoven (MfE): if we want to address sustainability in health systems, we need to use biosimilars. We can copy from positive experiences.
- Grimm (Europabio): communication is repetition, repetition and repetition from all players with one coherent voice. Fair competition and innovation have to be supported, adapting solutions to the specificity of the markets. In no way, we should lower the bar of regulatory standards and pharmacovigilance.

Participants thanked the European Commission for the opportunity to express their views and share practices in this multi-stakeholder workshop. Participants also thanked the speakers for their interesting presentations, which stimulated fruitful discussions. In particular, the large spectrum of stakeholders invited and the variety of angles under which the topic was constructively discussed were highly appreciated.

The goal of equal and timely access of best value medicinal treatment to all patients in Europe is not yet achieved, although significant progress has been made.

Several speakers and participants underlined that there is still further progress to make and expressed the wish that a similar multi-stakeholder event is organised next year to continue providing a platform for supporting the use and the sustainability of biosimilars in Europe.