Attitude, Skills, and Knowledge in Oncology Biosimilars

ASK 'Adapting to a changing landscape: switching to oncology biosimilars' transcript

Slide 1

Emma Foreman: Hi everybody and welcome to our first webinar "Adapting to a changing landscape and switching to oncology biosimilars"

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Emma Foreman: A few words about the educational funding of tonight's webinar. This webinar been supported by grant funding from Pfizer. PCM scientific is the medical education company acting as scientific secretariat an organiser for this programme, the activities run independently of the financial support and all content is created by the faculty, so no funder has had input into the content of this activity.

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Emma Foreman: We want this to be an interactive webinar, so please feel free to participate throughout the session. Please post your questions to the panellists using the Q&A box and please note that the chat function is disabled. Use the Q&A box and myself and the speakers will get to incorporate your questions and comments throughout the webinar to facilitate discussion, and we'd like it to be as interactive as possible.

There will be some interactive questions which will display on the screen and when you see the polling box pop up, just choose your answer by selecting the options when they appear on the screen. If you're watching this on archive footage, you won't be able to take part in the polls.

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Emma Foreman: So, without further ado. Let me introduce the faculty. I'll be chairing the webinar: my name is Emma Foreman and I'm a consultant pharmacist at the Royal Marsden Hospital in London in the UK.

From France we have Philippe Arnaud, who is a senior consultant hospital pharmacist with many, many years' experience and who has also been a university professor. He has done lots of research and has many publications. Phillipe has also taken part in several national agencies and ministerial committees.

From Canada we have Glenn Myers. Glenn is a clinical pharmacist at the Doctor Sheldon H Rubin Oncology Clinic, and is an active member of the Canadian Association of Pharmacy in Oncology, and I've had the pleasure of collaborating with him on several projects recently.

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Emma Foreman: These are the disclosures from the faculty members. Philippe has no disclosures. Glenn and I have a list of honoraria and some working relationships which we declare here.

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Emma Foreman: Here are our learning objectives. At the end of this webinar, you should be able to:

- Recall effective strategies for ensuring patient safety and efficacy when switching between different brands of biologic pharmaceuticals, including pharmacovigilance requirements.
- Describe key considerations across a multidisciplinary team when switching from an originator biologic to a biosimilar
- Discuss the potential savings and access to innovation opportunities created by switching from an originator biologic to a biosimilar.

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Emma Foreman: I'm going to hand you over to Philippe now who's going to kick us off with an introduction to oncology biosimilars.

Philippe Arnaud: Thank you very much Emma for that nice introduction.

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Philippe Arnaud: Not many of our participants are experts in the field of biosimilars. Fewer than 20% use biosimilars routinely in their practice, and 33% never use biosimilars.

Biologics are varied in the field of oncology. Many new drugs prescribed by physicians and used in our practice are biologic drugs.

This class includes monoclonal antibodies, but also some conventional molecules, e.g., low molecular weight heparin. The molecular weights of biosimilar drugs are very different.

Let us come start at the beginning of the story of biosimilars. Guidelines defining biosimilars were introduced - 10 to 15 years ago, beginning in Europe. The European guidelines on biosimilars were followed by other agencies, e.g., the FDA, Japan and other countries.

Before biosimilar guidelines, each company could develop their own definition. For example, with insulin one company developed a complete market document for commercialisation and another company developed another common technical document for insulin and at that time nobody said there are differences between, for example, enoxaparin or insulin.

When monoclonal antibodies became available, there was lobbying from pharmaceutical companies, health authorities, patients and physicians, who wanted to clarify that biosimilars are similar, but not the same, and this could create issues for some patients.

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Philippe Arnaud: Effectively, biologic drugs undergo patent expiration. When a patent expires, other companies can develop other drugs. In the field of biological products, the development of that product is called a biosimilar.

The first point is all the drugs have the authorisation from a Health authority, e.g., the EMA in Europe or the FDA in the USA, which means that all the drugs are of the same quality, the same safety, and the same efficacy. That is a very important point, and it is very interesting to say all the products are drugs with an official market authorisation.

As the products are from biological systems it is very difficult to have strictly the same composition. In fact, because of the products are from cells, animals, plants for example, manufacturing by

natural systems induces small differences in terms of the structure of the product. For that reason, it is not strictly the same structure as the innovator. They are presented as biosimilars, and the term “similar” is very important. It means that it is not strictly the same, but similar and, in fact, that products have the same efficacy, the same quality, and the same safety as the originator.

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Philippe Arnaud: The big difference between a chemical product, for aspirin, and a biological product, on this slide filgrastim, is the size and the complexity of the molecule because biological products have primary structure, secondary structure, tertiary structure and quaternary structure. It is not a structure that is linear or a simple chemical structure, allowing reproduction of the same structure to create the same product. In the field of biosimilars it is not strictly the same structure due to the complex manufacturing process and due to the use of living cells or other systems.

This means that the documents required to obtain market authorisation of that drug is not the same. In the field of generics, the pharmaceutical company provide only a document about the quality – not about the safety, not about the efficacy, because it is the same drug as the originator. In the field of biosimilars, the pharmaceutical company must produce clinical data that not only document quality, but also to demonstrate the efficacy and the safety of the drug.

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Philippe Arnaud: On the slide is our fundamental question. Our action is the action of all healthcare professionals, physician, pharmacists, nurses and all health colleagues.

First, why are biosimilar developed?

The first reason is to have a low price. I mean a price that is lower than the originator and, on that slide, there is the example of reducing of the price 10 to 50% and now in some cases it is more than 50% discount. Because the price is low, it is possible to improve patient access to an alternative option from the reference drug and, with the marketing of biosimilars, more patients can receive the treatment and that also secures control of supply. In a lot of cases there can be a disruption of supply of drugs. In the field of a chemical drugs, it is easy to produce a drug, by easy I mean in one, two or three months to make the product, the manufacturing and the control of the drug. With biological products the time for production is 3 to 6 or more months, and for that reason it is very important to have secure product supply to avoid a disruption of treatment for the patient, particularly in the field of the cancer.

Biosimilars also improve access to treatment for some very rare indications, maybe in some cases through off-label use for some drugs, because in the treatment of cancer, the research develops more quickly than the market authorisations.

It is very important for a patient to have the drug in the beginning of their disease and not to have the drug months later. Because biosimilars are lower cost than the originator, all the money saved can be used to improve other healthcare services for the patient. We know that a lot of countries don't have the same quantity of money for their own healthcare system.

With biosimilars, in some cases pharmaceutical companies see the biosimilar in use then they innovate. For example, a recent innovation is the development of formulations for subcutaneous

administration and when we compare the pathway of administration between IV or subcutaneous, we see that it is easier for patient to use subcutaneous administration and it is easy for patient to administer subcutaneous formulations at home.

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Emma Foreman: Thank you, Phillippe, and certainly we've seen quite a lot of these benefits as we've introduced biosimilars in the UK.

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Glenn Myers: So this is an important part of the biosimilar switching and implementation, because switching can really mean a different term depending on the country or the continent that you live in. From a biosimilar implementation perspective there's a couple of different safety and risk assessment considerations that we have to take into account, and importantly, one of the first things that we have to think of, which is why we have the regulatory framework for biosimilars, is trying to identify any clinically significant differences between a biosimilar product and its innovator. We all have seen the upside-down pyramid scheme about how to identify any differences with the innovator due to post-translational changes from glycosylation and what have you.

So, once we do determine that there really isn't any clinically significant difference in efficacy, safety, or immunogenicity, then this then provides us the opportunity to provide a framework where we have a solid pharmacovigilance set up with that specific biosimilar product. And this is really on behalf, and it's really the responsibility of the manufacturer to set up a robust pharmacovigilance process so we can identify very rare adverse events and this is really important in real life because in a lot of these studies of biosimilars we're using smaller groups of patients, and we don't have as much of an emphasis on clinical data as we do for the innovator, which is what it's meant to do.

But in the real world, we have to have a way to identify these rare or even delayed adverse events due to a biosimilar just so we can compare them to the innovator biologics, so we're not seeing any major differences in safety. And this is a really important piece of the risk assessment and the final one we have to think of is the supply chain reliability with that specific company, because if a company has a very poor track record for providing drug supply and having drug shortages, it's obviously going to create some doubt in the mind of the clinicians. With these three risk assessment pieces, this gives the clinician the nurse, the pharmacist, and the patient more confidence in adapting the biosimilar into daily practice.

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Glenn Myers: So further on with the pharmacovigilance discussion, pharmacovigilance, as you can see from the table and the infographic on the left, it really has multiple different considerations, and this can really change depending on the country or even the health registry where the biosimilar is approved. One big thing with a pharmacovigilance plan from a manufacturer is that it has to be very robust, very homogeneous and transparent. There has to be a way to identify specific manufacturing, changes to manufacturing processes and then actually studying the effect of these manufacturing processes on the structure or even the quality or purity of the products. But also as we mentioned in the slide before this, we also have to have a way to trace the biosimilars in real practice and have a way to identify any post-marketing adverse events that may be more frequent,

or more severe than the innovator product. This again could be due to those post-translational changes like glycosylation, or even manufacturing shift, which can happen over time with a with a biologic drug. That's why we must have this really robust structure in place in order for clinicians and patients to have true confidence to adapt biosimilars into practice. I'm speaking from a North American lens here, where you know the last couple of years, we've just been adopting biosimilars, starting in around 2017/2018, but those of you who are here from the EU, or European countries, you guys have had probably over a decade to develop this pharmacovigilance practice and develop various databases and whatnot, which go to help toward the confidence of adopting biosimilars to practice.

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Glenn Myers: When we are collecting data as part of a biosimilar approval, specific drug licences for a biosimilar, depending on the manufacturer, may require that data be collected. The big example here is if a biosimilar were to go through a specific manufacturing change, then that biosimilar manufacturer is required to collect data on that batch to ensure that the changes made from that manufacturing change aren't adversely affecting the efficacy, safety, or immunogenicity of that specific biosimilar. What we might see evolve as we get more experience with therapeutic biosimilars, is there may be an opportunity to provide real-time data collection in real patient populations, as opposed to clinical trial patient populations, where we collect data and actually make them a part of a centralised registry and even try to compare post-marketing adverse events of various biosimilars as they compare to the reference biologic. This will go in to help our confidence into adopting biosimilars into practice, especially those biosimilars we're using in very complex patient populations for chronic disease management, so things like cancer and things like rheumatologic disorders are the ones that come to mind.

What we are hopefully going to be seeing in the future is more robust data collection as part of the drugs' licence in the post-marketing phase.

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Glenn Myers: When we're monitoring for immunogenicity it really has to be appropriate to the setting. In Canada, a lot of the Health Canada monographs that we see for biosimilars do not have any instructions on monitoring for anti-drug antibodies after post-marketing because this would involve testing the patient serum in real-time practice. I certainly can't speak to the European practice and hopefully Philippe or Emma would be able to provide some insight on that.

But essentially, when we're monitoring for anti-drug antibodies, this may be a way to assess for safety and immunogenicity or even effectiveness of a biologic after it's been approved. This could be a more objective way to identify any changes to manufacturing or manufacturing shift that occurs with any biologic that may have an adverse effect on safety or efficacy.

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Glenn Myers: The first way that we'd monitor for anti-drug antibodies, if this were to happen, is more of a reactive therapeutic drug monitoring strategy and this would be more so in the case of in response to where we may see a large percentage of populations losing response to a therapy, maybe increased rates of hypersensitivity reactions or other types of immunogenic reactions or

increased injection site or allergic reactions. This is where having a centralised database within a country or a continental health authority such as the FDA, Health Canada or the EMA, where we can actually have this information available to clinicians in real-time so we can compare rates of loss of response, hypersensitivity or injection site reactions across various jurisdictions, which would be valuable.

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Glenn Myers: The other way that we would also monitor for immunogenicity, again appropriate to the setting, would be more of a routine sampling and this would be something that's done maybe on an annual or semi-annual basis. It can be used in academic research or phase four studies, or academic papers where we can collect serum samples to assess anti-drug antibodies in various different patient populations who are prescribed various other types of medications or have other kinds of complications compared with those that were in their original clinical trials. We may also be able to use these routine serum samples to correlate drug levels or anti-drug antibodies with efficacy of the biosimilar and then, as I mentioned in the prior slide, we could also use these data to create registries or databases to improve the comfort level of adoption of biosimilars into practice.

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Emma Foreman: Thanks Glenn, and just to comment on that slightly – I think in the UK in clinical practice we don't do any sort of serum sampling for immunogenicity testing, although I think in some of the real-world post-marketing studies, that's the sort of thing that would be done.

We do quite a lot and audit things like hypersensitivity rates, adverse event monitoring within various hospitals and institutions so that we can actually set our own minds at rest that we're not affecting patient safety, and that's probably the more common way that we carry out our local pharmacovigilance.

Glenn Myers: Yeah, and that's certainly I think what's being done across the world, and I think as this practice becomes more mainstream, that may develop over time, but certainly that's not standard right now as you had mentioned Emma.

Emma Foreman: Yeah brilliant. I'm going to pass you back to Philippe for building a case for switching.

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Philippe Arnaud: There are different types of switching studies. The first one is very easy – a transition from innovator to the biosimilar – that is very easy. Second is a crossover study, if you start on the innovator, you switch to a biosimilar and if you start on biosimilar you crossover to the originator. The third system is multiple switching. These types of studies exist to cover different clinical scenarios. First, because there may be a change in subscription. Second, the procurement of our hospitals is different and crossover may occur. The third, because of the increasing numbers of patients, in the case of multiple switching, the system of traceability must be perfect.

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Philippe Arnaud: What are different aspects to horizon scanning?

The first is the discussion about our practices at the local, regional, national or international levels. Second is to take regular review of about the status of biosimilars or innovators in terms of safety or efficacy. We must not work alone in our hospital or in our vision, but share our experience in working group and have ongoing taskforces to keep us up to date about biosimilars.

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Philippe Arnaud: The cost is a very important, key consideration. For that reason, hospitals are very limited.

In France cost is not really a critical factor in the system; however, everybody discusses money and cost reduction. In the current usage in a lot of country as the message is “use biosimilars when you can use them”. If you cannot use biosimilars the physician must give a scientific argument to say that for that patient it is impossible to use a biosimilar and as physicians must justify their prescriptions. Biosimilars are becoming more and more used in our healthcare system.

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Philippe Arnaud: The cost is not only the cost of the product because in a lot of cases when there is some change in our practice, it is important to provide training for healthcare providers and for patients. Because in a lot of cases when the prescription is via an electronic system, it is important to introduce the new prescription into the information system.

We should develop the pharmacovigilance, as Glenn said, and also increase our structure of cold storage system for preparing and handling because, for example in France, in some cases each dose, one dose for one patient are prepared at the pharmacy and it is very important not to mix biosimilars with other biosimilars or with the originator.

Monitoring patients is important, as Glenn said, administration and the traceability, and the development of all technology for the traceability, e.g., RFID [Radio Frequency Identification] system. It is very important that up to date medical information is available for physicians and pharmacists and nurses.

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Philippe Arnaud: When biosimilars are evaluated, it is important to consider 3 factors: (1) administration, (2) storage and (3) packaging and labelling.

Because the name is the same, the denomination is the same and, for instance, there is no difference in the international non-proprietary name for the biosimilar, it is very important to have very clear packaging and labelling.

Storage is also very important in terms of light sensitivity and sensitivity to the transport. These products are sensitive to harsh transport conditions,

Administration is an activity for nurses after pharmacists or technicians have prepared a single dose for patient. The time of administration, the routes of administration, the delivery system, all those systems must be clearly defined to avoid mistakes.

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Philippe Arnaud: When and who to switch? In France, for example, switching is only decided by physicians. Pharmacists are not allowed to switch patients, except in a hospital setting because the rules are different – but for outpatients, pharmacists cannot switch medications.

When there is a switching, it is very important to avoid confusion and to maximise the cost reduction. For new patients, you can start with the biosimilar or with the originator. The rule in some countries is now to begin with the biosimilar and to have a large number of patients receiving it to see eventual adverse effects.

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Emma Foreman: OK, I think we're just about to go into the next section. Before we do, can I just ask quickly?

There's a lot of preparation and planning that goes into these switches –how far in advance should people start thinking about planning their switch over before a product comes to market?

Glenn Myers: I would say because of the different levels of planning that have to go into it from an education and just from a technical perspective and a formulary perspective, Emma I would say a minimum of probably 6 months has to be planned in order to switch from an innovator to a biosimilar, especially if it's the first therapeutic biosimilar that a place is switching to, just because there's so much education that needs to happen and as we've seen from prior research, education is really key to stakeholder involvement.

Emma Foreman: And in our UK experience we've found with every subsequent switchover, it gets easier because you're more familiar with the process.

Glenn Myers: Yeah definitely

Emma Foreman: So I'm going to let you continue on now and give us a quick whip through of some of the practical aspects of switching.

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Glenn Myers: I think with early engagement it's really important to get everybody on the same page, and this includes the prescribers, the pharmacist, pharmacy management, the nursing staff, pharmacy technicians and patients. When we all have a structured homogeneous process, then things are able to be implemented in a more seamless way. I think from a pharmacy perspective, we always have to identify a lead within pharmacy, as well as nursing, to make sure that things are done consistently and there's a clear message conveyed throughout the process. It's always important to have a multidisciplinary team promote this process, again, physicians need to be involved, and upper pharmacy management, pharmacists, technicians, etc.

As Emma just said, as you get further experience with implementing therapeutic biosimilars, the time for implementation gets quicker and we can use the learnings from prior implementation launches to help speed up the next implementation.

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Glenn Myers: Some processes we have to think of when we are implementing a switch is what are we going to be using for a name on things like labels and electronic databases. Usually this is dictated by the jurisdiction, such as the EMA, Health Canada or the FDA. It's important to be come to a consensus as a team for these needs, because it becomes important for traceability, as Philippe mentioned to us in a previous meeting, this becomes a big issue in France among different hospitals using different biosimilars.

And I think for electronic prescribing indications, various hospitals may use different electronic prescribing or CPOE [Computerised physician order entry] programmes, so it's important to identify and organise this early so that we can develop these changes to the CPOE programme so that the biosimilar is not being mixed up with the innovator biologic. When we're implementing biosimilars at an institutional level, there are always many questions that have to be answered.

Are we going to switch new patients only or is there going to be a plan switch for patients currently on therapy?

And the other questions that come from a pharmacy perspective is, how are we going to stock this?

If we have multiple biosimilars, how are we going to communicate this to our patients and our caregivers and other healthcare providers.

How is the preparation going to change as we implement a biosimilar?

These are all things that we must agree upon as a multidisciplinary team before we even think about implementing it.

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Glenn Myers: Some specific pharmacy considerations that we have to think of that maybe different for biosimilars:

Where the stability might be different. I know this was something from the pegfilgrastim perspective that for instance the stability of pegfilgrastim at room temperature for the biosimilar has improved versus the innovator biologic, and this was something that we had to understand. Understanding the stability in the fridge and room temperature of the biosimilar versus the innovator is important because a lot of our practices are going to be established using the innovator.

Now another thing to think of is the preparation. Is the time to go into solution longer than the innovator?

Does it mix in a different solution, or can we mix it in a more concentrated method? A benefit of a biosimilar is that they can perform these studies when they're gaining market access, because these are things that they've identified as potential barriers in practice with the innovator.

The other thing we have to think of is the shelf-life. So is the dating on it good and is there any risk of drug shortages with a specific company?

Then also having everybody on the same page for labelling as we talked about before as well as the CPOE programmes.

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Glenn Myers: From an administrative perspective, I'm certainly not in that realm in my role, but I think some things we have to consider is how we're going to accurately track and trace biosimilars. The naming is really important here and again this is more so done on a national level most times, but we have to identify that the names have to be consistent among the labels and as well in documentation guidelines and CPOE protocols so that we can link specific post-marketing adverse events to that product.

The other feasibility issue is the time for implementation of the biosimilar, is that going to offset any cost savings that we have? I think from an administrative point of view, if your hospital does a tendering process, this would be a situation where you could actually work the cost of implementation for a specific biosimilar into the tendering process and actually work that into the cost.

Then redirecting the savings is a really important piece, especially for pharmacies. It may be an important consideration to redirect some of the savings into hiring a pharmacist full-time or even part-time to help navigate this biosimilar switch and to help run this programme consistently from a pharmacy perspective.

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Glenn Myers: So the differences in products can certainly affect uptake, and I think educating all the stakeholders on any differences in dosing, preparations, storage, labelling – anything like that – is extremely important across the pharmacy, but also it's important with our nursing colleagues and physician colleagues as well since we want this to be a collaborative and transparent process the whole way through. One biosimilar may be different than another in terms of how it looks or how it's stored in its specific vial. So, we need to educate any differences in these so that mistakes aren't made in the future.

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Training the multidisciplinary team as we mentioned in the prior slide is probably the most important piece of this process, because to make sure that biosimilar implementation and switching is achieved and is successful and we get buy-in from clinicians and patients, we have to make sure that everybody understands the process for biosimilar approval, as well as what is going to be done to identify any risks post-marketing to the patient and any risks in terms of manufacturing and that kind of thing. This only improves the confidence of the prescriber, the whole multidisciplinary team, and the patient.

What we found in research is that when we educate the healthcare professionals about biosimilar implementation and the various aspects of biosimilars, then they're able to discuss this with patients in a more seamless way, and therefore we try to limit the nocebo effect, which from the side of clinicians not understanding biosimilars can result in miscommunication to patients which can then result in a nocebo effect, potentially reducing their response to the treatment. So that's why it's so important to have a structured collaborative, but also a transparent process for education.

This can be done via pharma, which we we're probably most familiar with, but I think it's also important to come from academic institutions, academic detailers, various national patient groups,

and national physician and pharmacy groups, so that we can get some balance of non-biased education as well.

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Glenn Myers: Then when we when we do implement a biosimilar, it is important to regularly review the data on new biosimilars that are coming to market, but also review data on post-marketing analysis from that manufacturer based on any manufacturing changes or any safety signals that they see in the post-marketing phase.

This is the other kind of thing to keep in mind here, as Philippe talked about, is actually trying to identify any potential switching studies or studies that are meant to improve the uptake of interchangeability, because this may change how a biosimilar is implemented within a certain health authority.

So, I'll use the example of a multiple switching study: a new one that comes out that gives some great data on it being very safe to switch to a biosimilar from the innovator and back to the innovator on a multiple switch study. This may improve the confidence to actually switch patients on the innovator to the biosimilar and thus have cost savings to the healthcare system where we can improve access to the product.

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Emma Foreman: Brilliant before we go on to the next section, let me just ask if you've got any top tips on using things like electronic prescribing systems or other forms of data collection for keeping tabs on things like traceability or safety concerns?

Glenn Myers: For us, a lot of our systems are electronic and a lot of our checking software in the pharmacy is actually electronic as well, so it's all done via cameras and this is very helpful for tracing, especially for biosimilars, because we can actually see the exact lot expiry and the specific biosimilar whenever we mix it for that certain patient. That really does help with traceability, and I could see how that could be challenging going from province to province in Canada or country to country in the EU or different health jurisdictions, but I think having things electronic is probably the best way to go, and having a kind of a centralised database for adverse event monitoring is really important as well, just so everybody has that same structured view of adverse events.

Emma Foreman: Yeah, that's really useful. We have some sort of adverse event reporting software that we use in the NHS and it can be really useful to just pull off a report of numbers of, say, hypersensitivity reactions reported against time. You can look back and see whether there's been an increase since switched to a biosimilar or not, and that can sometimes help dispel any anecdotal reports of increases in hypersensitivity events and the nocebo effect that you're talking about.

Glenn Myers: I think it just strengthens our cause and the evidence for using biosimilars, and gives us more comfort with that.

Emma Foreman: Let's move on. Access to innovation.

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Philippe Arnaud: Effectively money is a very important consideration with biosimilars, as biosimilars can save a lot of money because drugs in the field of cancer therapy are very expensive. With a very drastic reduction of cost, it is possible to put that money towards innovative medicines, maybe because it is not really easy to have dedicated resources for pharmacists, nurses and also for physicians. In France, there is the possibility for a pharmacy and physician, if they prescribe biosimilars to receive some money, not for us, not for the staff, but for the hospital or the institute.

It is very important to develop new devices. The drug is important, but the good administration without fear or pain for the patient, which is easy to use. It is a very important for the manufacturer to develop new devices. There is a Congress, named the Pharmapack International Congress to develop new devices for that type of product.

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Philippe Arnaud: There are a lot of pharmaceutical companies in the field of biosimilars. The companies are European companies or Asian companies, there are a lot of Asian companies and of course American companies. There is a lot of competition between the different manufacturers and because there is that competition, manufacturers of the originator must be on time and make adaptations, and there is stimulation between the different companies. But in some cases, it is the same company which produces the originator and also produces a biosimilar. In that case, the competition is lower. For that reason, the development of different formulations and also the reduction of excipients, for example, animal excipients, and now in the manufacturing process, there is no bovine serum albumin, and it is to avoid reactions.

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Emma Foreman: Lovely thanks for that, that's a good illustration of how the benefits of biosimilars aren't just down to cost savings, which I think is quite a common misconception. Now I must apologise, we're running a little bit over time, but the next section coming up is very important patient communication, so let's glide straight onto that.

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Glenn Myers: Yeah, so I think and Emma is going to be chatting about some patient communication considerations in the next webinar I believe.

This is really important for me because I work really on the front line with patient education and communication. Hearing the patient voices and communicating switches is probably one of the most important steps in this whole process, because patients, in the end, are the ones that are going to be taking these therapies, and we're going to have to get buy-in from them, and they're going to have to have confidence in accepting biosimilars.

A lot of the things that we have to do with patients come from not only our one-on-one discussions, but also what kind of messages are given from patient advocacy groups on a national or international basis, and even physician advocacy groups, or pharmacy advocacy groups because a lot of these messages have to be in sync in order to improve the patient comfort level with adopting the biosimilar.

Things that we have to explain to the patient include reasons behind switching if we are switching them from the innovator or even starting them as a naïve patient. Explaining that the product is equally safe and effective as the innovator and explaining in a layman's term way of how it goes, how it's approved, and then any practical differences that may come along with this. So in the case of rheumatologic patients who self-inject subcutaneous products, if there's any changes in the injection device itself, then actually going through that with the patient and then what to do in the case of having an adverse event, and always relaying to the patient that the healthcare professionals are there for communication if they do experience an adverse event if weren't anticipating it. It is important too when you are educating the patient to use the international non-proprietary name if you can, and try to be more transparent and honest with the patient. Try to focus on the positive things as I had said and make it very relatable to the patient and provide them with written information that's at their reading level as well. This information would ideally be developed on a national basis with patient advocacy groups or national pharmacy or physician groups, where a robust education tool can be provided.

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Glenn Myers: These are just some tips – I mentioned a couple them already, but again keep the examples simple. Try to give them a mix of written and oral information cause you have to remember that patients will only remember about 10% of what you say in a meeting.

Involve the patient groups and patient advocacy groups when developing materials as I mentioned, usually at a national level if possible.

Have all staff have one voice and make sure everybody is giving the patient the same message.

Build a rapport with the patients, not only when you talk to them about biosimilars, but also when you follow up with them, or if they follow up with you with questions. Always invite feedback on how biosimilar implementation or education can be improved with patients. Again, this isn't just a one-time thing, it's an ongoing thing that may change over time because due to some of the tendering processes, some patients may use eventually maybe two to three biosimilars over their lifetime, so it really is important to invite that feedback that the patient has over time.

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Emma Foreman: Brilliant, thanks Glenn. So instead of closing remarks I want to ask you both slightly controversial question, I think. In the UK we've been using biosimilars for a long time, and we've just recently done a biosimilar-to-biosimilar switch for our biosimilar trastuzumab since a better value product became available. We didn't routinely tell the patients we were switching. We just treated it like one generic being switched to another. And also, the use of biosimilar rituximab has become our standard practice for some years now and we don't tell the patients that it's a biosimilar rituximab that they're going to be started on. And because we just talk about rituximab in its generic form, it's internationally approved name and there's no need to tell them when it is a biosimilar. So now my drug resource manager, he's just looking at an Avastin to biosimilar bevacizumab switch, is saying do we need to tell the patients when switching at all?

So when do you really need to involve patients in this decision and when is it OK not to tell them you're going to switch, If ever?

Glenn Myers: It's very controversial, of course. So I think when you're switching a patient outright from a biosimilar to another biosimilar or an innovator to a biosimilar. I think there's even some chat in North America and Canada about re-consenting a patient at that time, because technically there is a potential for, some safety issues when switching. I think it really depends on the jurisdiction you're in and the comfort level of the multidisciplinary team and the prescribers, pharmacists and nursing staff.

A lot of the data that I've read anyway, there's still a lot of reluctance, especially in North America, for switching patients from an innovator to a biosimilar, because of issues around interchangeability and auto substitution.

I think when you do switch a patient for a non-medical reason to a different biosimilar, I think at that point to make it a more robust process, there has to be a discussion with the patient, even if it's just a very short discussion, emphasising the positive things about switching to a biosimilar and also telling the patient where the savings are going to. I think you're more likely to get a positive response from the patient when you frame it that way, versus if you frame it as and "we're switching you and that's that", because a lot of patients take an active role in their care so they really do want to know what they're getting. I think it's very different for us in the oncology setting because patients just assume that they're getting the right drug because we made that decision for them. In the outpatient setting, where they're giving themselves like a D Mart or something like that, they may question it more because they're seeing a different injectable product, or they're seeing a different vial, so they may come back and say, how come you didn't tell me why I switched. That could turn into more a trust issue later on in that case, but I think it's so important to have that discussion with the patient. But you're right, there's no. clear answer – it's a very grey area.

Emma Foreman: I think in the UK our level of comfort with using biosimilars has given us this increased confidence, and we do need to probably challenge ourselves more about whether we should be informing patients about these things. So Philippe, how does it happen in France?

Philippe Arnaud: The big problem in the field of biosimilars is framing – we say it is the same product but less expensive. People think that the same product but less expensive is impossible. In their mind, if the price is lower the product is not the same and not a good product.

The communication strategy of health authorities, of pharmaceutical companies, etc., is to say that the main issue is money – this is not a good system for patients. For patients, you must say first that it is the same product, with the same safety, sensitivity and efficacy, and then clarify that the price is lower – do not start with explaining first that the price is lower and then explain that the product is the same afterwards

Emma Foreman: OK, so we've had a comment from one of our attendees. He said that when you switch to a biosimilar, isn't there a risk that patients could be more sensitive to the biosimilar and so you should reconsent then to make sure they're aware of that risk? I accept that, but what I would say is that the level of variation between an originator and a biosimilar really isn't any different to potentially one batch of an originator to the next batch of an originator, or the originator following a manufacturing change – we wouldn't reconsent a patient because we've changed to a different batch of an originator product. I personally don't believe we need to reconsent when we're

switching from originator to a biosimilar, although granted, I think possibly when you're switching someone mid treatment it's important to inform them of a change. What do you think?

Glenn Myers:

I think that's why it's so important to have a unified view from both a national level, but also from a medical agency perspective as well, so the EMA versus the individual countries and Health Canada or the FDA in the individual states. A lot of times with interchangeability and auto substitution, it's left up to the country or the individual province of the state to make that change, whereas I think there needs to be some policy and procedure consensus at a continental level as well. From the EMA perspective, there's no guidance from the EMA or Health Canada about what to do with switching and that kind of thing, so I think that's really important to improve the confidence level of prescribers as well.

Do I agree that patients need to be reconsented? I really like your point Emma I think that's really a valid point, but I think there has to be a more structured way in how we tell patients that they're being switched.

Emma Foreman: Philippe, any last thoughts?

Philippe Arnaud: And yes, I agree with the with you Emma – during the life of a product there is a lot of variation and during 5, 10 or 15 years between the first market authorisation and after the evolution of the manufacturing process and the pharmaceutical company processes. There are in some cases scientific papers about how the difference within the originator product must be more important than the difference between a biosimilar and the originator.

It is important to explain to patients that the same product is not the same product at the time of the market authorisation and 10 years later. This is true for all products, including chemical products – when there are chemical products which are compared 40 years apart, manufacturing processes and techniques are not the same, purity is not the same and there is a lot of variation. It is the same in the field of biologics. With biologics there is one specific problem, namely immunogenicity. Immunogenicity is a very complex issue. Immunogenicity is an individual patient issue – it is not an issue for a lot of patients. One patient can be allergic to one product and not to another product. There was one question in the chat – are some patients sensitive to a biosimilar or to an originator? My opinion is yes, there are some patients who are sensitive to an originator and for them, a biosimilar is a safe and effective choice. Conversely for some patients, they may be sensitive to the biosimilar. When a patient has some trouble with a biosimilar or an originator, my opinion is that before changing the treatment strategy, you should try switching the product and see what happens.

Emma Foreman: Right, so I think we're going to have to stop there as we're really running over time now. It's been really great having this discussion, and I think it's finally stimulated a bit of conversation from the Q&A box.

There was someone asking about defining automatic switch versus clinician-led switch. Glenn has posted an interesting reference there and certainly we define all of those terms in the International Society of Oncology Pharmacy Practitioners position statement. So if you want to read up on the various definitions of how switchovers happen that would be a good place to look.

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Emma Foreman: We have free learning resources available that cover many of the topics that we've covered today. We have a handbook, which is in English currently and is coming soon in French, German, Italian, Japanese and Spanish.

We have an abstract library already on the website and coming soon learning chapters, national guideline summary documents and subtitled webinar archive footage, and that's the website address.

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Emma Foreman: And that's it, thank you for joining this webinar and I hope you enjoy the rest of your day, however long or short it may be, wherever you are. It's been a pleasure speaking to you all and it's been a pleasure to have you with us. Glenn and Philippe, thank you very much for speaking and thank you everyone for coming.

Glenn Myers: Have a great day. Take care.

Philippe Arnaud: Thank you, bye.