WEDNESDAY, 13 JUNE 2018

New drugs – new perspectives: clinical and regulatory issues concerning biosimilars

SP0024 AN UP-DATE ON BIOSIMILARS

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Biosimilars represent a new opportunity for lowering the cost of treatment with biological disease-modifying antirheumatic drugs (bDMARDs). Studies have demonstrated large inequities in the access to bDMARDs across countries and this inequity is related to economic parameters such as gross domestic product. Thus, reduced costs of bDMARDs should potentially lead to better treatment for more patients, especially in countries with low economy.

The regulatory agencies in Europe and in US have set up strict guidelines for approval of biosimilars which include extensive pre-clinical examinations (structure and functional characteristics) but less clinical data than for an originator product. The clinical part of this comparability exercise focuses on efficacy, safety, pharmacokinetics as well as immunogenicity.

Three biosimilars to adalimumab have also been approved but the patent of the reference product has not yet expired (expected to occur October 2018). (expected to occur October 2018). It is a growing acceptance about the use of these biosimilars, also in extrapolated indications when treatment are started or changed for medical reasons. Most rheumatologists will consider the biosimilars on the same level as originator products in these situations.

However, replacing an originator product by a biosimilar is more controversial, but is important because of the large cost-savings. Switching evidence is available from four different types of studies which will be discussed:

- Extension of phase 3 RCTs
- Switching within RCTs
- Real life data (eg from DANBIO)
- Randomising patients on stable long-term treatment

In the NOR-SWITCH trial – totally funded by the Norwegian government – 482 patients on stable treatment with the reference product infliximab across 6 indications (RA, SpA, PsA, UC, CD, PsO) were randomised to continued treatment with the reference product or switch to the biosimilar CT-P13; Jørgensen KK et al. *Lancet* 2017;389:2304–2316). The primary endpoint was occurrence of disease worsening, defined by the disease-specific composite measures or clinically significant worsening leading to a major change in treatment. Overall, disease worsening occurred in 26.2% of patients who continued treatment with the originator infliximab and in 29.6% of patients who switched to CT-P13. The adjusted treatment difference (95% CI) was –4.4% (–12.7–3.9) which was within the prespecified non-inferiority margin of –15%. The occurrence of adverse events, including infusion reactions, was similar across both groups. There were no differences between the two groups in secondary endpoints, including time to study drug discontinuation, remission rates, CRP levels, anti-drug antibody formation and drug trough levels. The extension study (not yet published) showed that switching from originator to biosimilar was not inferior to continued treatment with the biosimilar.

In conclusion, the NOR-SWITCH study demonstrated that switching to CT-P13 was not inferior to continued treatment with originator infliximab, adding to the increasing real-world evidence that switching from originator to biosimilar bDMARD is safe and efficacious.

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SP0025 SHARED DECISION MAKING IN SWITCHING TO BIOSIMILARS

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This presentation will focus on the speaker's experience of switching patients who are on an originator biologic therapy to a biosimilar, using a shared decision making approach. It will initially explore what constitutes shared decision making, why it is important when switching to biosimilars and the benefits of this approach.

The speaker will discuss how this change in therapy was achieved in practice when switching patients to both intravenous and subcutaneous biosimilars. There

will be a focus on the patient consultation itself, recognising patient anxiety and an exploration of why some patients declined to switch.

The speaker will share how loss of efficacy to the biosimilar was managed, and how this influenced the shared decision making approach.

Clinician's concerns will also be considered, specifically the inability to maintain pharmacovigilance (in not having sufficient nursing resources to add patients who had switched to a biosimilar to a national register). This is relevant to shared decision making as providing evidence and reassurance to patients regarding safety of biosimilars relies on this data collection.

The guidance referred to in this presentation is from NHS England, National Institute for Health and Care Excellence and the British Society for Rheumatology, so it has a UK focus. However, the main themes of the talk should be relevant to all audience members as it considers the opposing pressures on Rheumatology nurses to be change agents and make cost savings in implementing this switch to biosimilars. Whilst nurses also need to act as the patient advocate in ensuring shared decision making is a reality: that a face-to-face consultation takes place and that the patient can decline to switch and not feel penalised. The speaker will reflect on how the trust in her relationship with her patients was tested by this experience.

The main recommendation from this presentation is that rheumatology teams need to be proactive in managing this change and securing extra funding for nursing or pharmacy support. This 'invest to save' approach will enable appropriate consultation with patients to allow them to give informed consent to switch their therapy and feel supported whilst this switch takes place. It also enables maximum cost savings by ensuring the switch occurs quickly.

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SP0026 BIOSIMILARS – THE CHANGING VIEWS OF PARE'S MEMBER ORGANISATIONS

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After EULAR PARE's position paper "Biosimilars – what do patients need to consider" published in November 2015 more biosimilars for rheumatic diseases have been approved by EMA (European Medicine Agency), have entered the market in different European countries and more biosimilars will be marketed. New studies and data informing about the use of biosimilars, as well as feedback received from patient organisations and in particular from PARE organisations, have made it necessary to update PARE's 2015 position.

Biological therapies are enormous cost factors for the healthcare system and biological therapies have to be affordable, what is seen as difficult in various countries. But an optimal quality healthcare is enormously important for the individual patient (e.g. fewer sick days, less hospitalisation, less disabilities), prevents early retirement and thus saves costs and contributes to a country's economic and social system.

If so-called naïve patients should take a biologic, the less expensive biosimilar can be used, as long as there are no contraindications, the patient has been informed and the decision is based on a shared decision between rheumatologist and patient.

But transitioning users from an originator to a biosimilar is very controversial and seen critically by PARE's patient organisations. The talk will cover the changing views concerning extrapolation, one-time switch, multiple therapy switches, registries and the relevance of the application form for patients.

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Don't delay, connect today!

SP0027 DON'T DELAY, CONNECT TODAY – IMPLEMENTATION OF THE EULAR CAMPAIGN IN ROMANIA

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Background 22% of the population in Europe currently has, or had experienced "long-term muscle, bone and joint problems".¹ Early referral to a rheumatologist for appropriate diagnosis and treatment prevent structural damage, disability and decrease mortality.²

Objectives: To launch a patient oriented campaign in Romania in order to increase awareness of rheumatic musculoskeletal diseases (RMDs) – early

recognition of symptoms, ways of breaking down the barriers that delay early diagnosis. Also to educate the general public that rheumatic diseases may occur at any age and severe affect both children and young people.

The long term goal of the campaign is to decrease the number of people with disabilities, work loss or early retirement as well as the health care costs.

Methods: The launch event of the campaign will be attended by patients, rheumatologists, GPs, HPs, media and also national and local authorities.

A coordinated media plan will consist of pre-launch teasers, appropriate broad-casting of the event and post-event reminders as well as educational flyers/materials with the slogan "Don't delay, Connect today", handed out in shopping centres and other crowded areas.

Online posts on the www.reumatism.ro website and the dedicated FB page will stimulate communication and mutual support among patients as well as spread information on RMDs to the general public.

Results: Up to 100 participants are expected to attend the launching event and get direct/live benefit from the information on early diagnosis and early treatment.

Over 50% of the Romanian population will audience the campaign messages covered by 50 media articles (in Romanian) and over 10 000 people will receive e-messages (online and Facebook impressions/engagement). This coordinated media plan will stimulate communication and mutual support among people with RMDs.

Conclusions: The implementation of the EULAR campaign in Romania "Don't delay, Connect today" aims an early referral to the rheumatologist for diagnosis and treatment and for a normal quality of life of patients with inflammatory rheumatic diseases. The campaign will have a communication peak around the launching event. Until the end of the year an on-going media and online communication strategy will be implemented.

REFERENCES:

- [1] Health in the European Union Eurobarometer Special Report 272, September 2007.
- [2] Emery P, Breedveld FC, Dougados M, et al, Early referral recommendation for newly diagnosed rheumatoid arthritis: evidence based development of a clinical guide, *ARD* 2002.

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Burning bones

SP0028

EFFECTS OF INFLAMMATION ON BONE IN INFLAMMATORY ARTHRITIS

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Research in my laboratory is devoted to the study of the pathogenesis of rheumatoid arthritis (RA), with a particular interest in the fundamental mechanisms of bone and cartilage destruction. Key research findings include the identification of osteoclasts as the cell type responsible for bone destruction in RA, and receptor activator of NF- κ B ligand (RANKL) as the critical cytokine produced by cells within RA synovial tissues that promotes osteoclastogenesis. More recently, we have identified the inhibitory effects of synovial inflammation on bone formation in RA, and focused on the effects of inflammation in inhibiting the Wnt signalling pathway, resulting in the impairment of osteoblast function. We have also studied the mechanisms that prevent healing of bone erosions in RA, and will discuss a completed clinical trial that addresses the question of erosion healing. Mechanisms of bone loss in RA will be contrasted to mechanisms of bone formation in spondyloarthritis. Finally, we have identified specific pathways in the innate immune system that regulate bone remodelling in the setting of inflammation, and these appear to be directly relevant to inflammatory arthritis. This lecture will thus cover what we have learned about basic mechanisms, and will discuss the clinical implications of this work for the practicing physician.

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SP0029

FINE STRUCTURE ANALYSIS TO DETECT BONE PORES

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The blood supply is essential for the many functions of bones. The bone marrow as well as blood cells generated within are particularly dependent on a functional circulation. Despite this fact there is a remarkable logical gap in our understanding of a closed circulatory loop in long bones. We have discovered a previously unknown type of blood vessels in long bones of mice that forms an intense connexion of bone marrow with the external circulation outside of the bone. These blood vessels transport the majority of blood into and out of bones and hence constitute an essential structural component of bone physiology. I will present a detailed characterisation of these vessels and also show evidence for similar structures in man.

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Delay in treatment and the role of health professionals

SP0030

REASONS FOR DELAY IN HELP SEEKING AT THE ONSET OF SYMPTOMS

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Early intervention following the onset of chronic illnesses such as rheumatoid arthritis, lupus and Sjogren's syndrome can improve disease prognosis, reduce illness related disability and improve patient quality of life. Therefore, it is vital that the time between symptom onset and treatment is short, however, many patients experience long delays. The period of time between an individual's first detection of a bodily change and the first consultation with a healthcare professional is known as patient delay, while the time between first consultation and been referred to a rheumatologist for treatment is known as healthcare professional delay.

Patient delay can be attributed to a range of barrier to consultation, these include contextual barriers (e.g. geographical location, financial barriers and availability of health services), individual barriers (e.g. demographic characteristics and health literacy) the nature of symptom onset (e.g. intermittent symptoms or the experience of a symptoms commonly associated with many conditions such as fatigue) and psychological barriers (e.g. perceptions of illness, the normalising symptoms interpretation of symptoms and fear and worries about wasting the doctor's time). Many interventions to reduce patient delay focus on educating the public about the typical symptoms associated with a specific illnesses in the hope that greater awareness will lead to better recognition of early symptoms. These interventions are based on the premise that the general public may hold misrepresentative stereotypes of what it is like to experience an illness or may even have no stereotypical belief (also known as a prototypical belief) to compare their current symptoms to. There is very little evidence about the evolution of early symptoms over time and how patients appraise these early symptoms and then decide to seek help. Furthermore, the non-specific nature of early symptoms for many rheumatological conditions can also be a significant barrier to patients recognising that symptoms are indicative of a chronic illness. For example, patients may attribute symptoms to stress, ageing or a temporary condition and actively choose not to seek help. Therefore, we must explore patients beliefs about symptom experience and not just focus on their beliefs about specific illnesses. Understanding early symptom presentation and the way that early symptoms are interpreted by patient is important for the development of robust help seeking interventions. However, interventions to promote prompt help-seeking based on symptom presentation must also take in to account for contextual, individual and psychological barriers which may interact with individual perceptions of early symptoms.

Understanding the factors which lead to patient delays and healthcare professional delays across rheumatological conditions can ensure that interventions to reduce delay are developed using a robust evidence base. Evidence based interventions such be multifaceted and may include the development of public health information (e.g posters, tv campaigns etc), the development of robust online information and challenging mis-information online, addressing health inequalities which may lead to delay (e.g. increasing the accessibility of health services and promoting health literacy in hard-to-reach communities) and developing educational information for healthcare professionals.

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