Interview

Betaferon® and Pregnancy
Issue 1/2019

INTERVIEW WITH PROFESSOR DR. KERSTIN HELLWIG

Pregnancy and Betaferon®:

An expert's perspective

Find out more in the interview with
Professor Dr. Kerstin Hellwig inside this issue.

EDITORIAL

The typical multiple sclerosis (MS) patient is a woman of childbearing age. Therefore, not surprisingly, pregnancy is a major concern for many MS patients and they expect proactive counseling from their neurologist before, during and after the pregnancy.

In this series of articles we present the viewpoints of MS experts from around the world on the practical management of pregnancy and pregnancy-related topics for patients with MS. In this issue, Professor Dr. Kerstin Hellwig from Germany, highlights recommendations from published academic guidelines as well as the outcomes of pregnancies exposed to Betaferon® from the Bayer Pharmacovigilance Database.

Patrick Salonis
Bayer U.S. LLC,
Global and US Brand Director, Betaferon®

More interviews to be published soon!

Interview with Professor Dr. Kerstin Hellwig

Pregnancy and Betaferon®: An expert's perspective

Why is pregnancy a relevant topic in MS?

MS is a disease where 2/3 of the affected people are women. The diagnosis is usually made between the age of 20 and 40. That means the diagnosis is mostly made during the years when you plan a family.

Your research allowed you to gain insights into many aspects around MS and pregnancy. In your view, are MS patients able to become pregnant? What should a women with MS particularly consider when she wants to become pregnant / to have a child?

Most women with MS who want to have children can and should have children. It is advisable to arrange a timely agreement with the neurologist on how to proceed with MS treatment before pregnancy. Like healthy women, women with MS should already take folic acid in their planning phase.

How long does it take a MS patient to conceive if a pregnancy is intended?

That is not sure. Our old data from 12 years ago show that it takes about 4 months.[1] As far as I know there isn't any new data yet. However, it should be noted that time to conception also is, among other factors, age-dependent, ie the older the woman, the longer it takes to conceive.

What are the official recommendations from academic guidelines and what is the common practice in Germany with regards to therapy continuation and pregnancy?

That depends on the therapy. The recently published ECTRIMS/EAN guideline recommends physicians to consider using interferon beta or glatiramer acetate until pregnancy is confirmed, if there is a high risk of disease reactivation. The German Competence Network Multiple Sclerosis (KKNMS) refers to increasing clinical experience suggesting that the continuation of interferon beta therapy until pregnancy is generally without issues.

Do babies have a lower birth weight and length whose mother was exposed to interferon beta before or during early pregnancy compared with babies whose mother was unexposed?

The Nordic cohort study, using health care register data from Sweden and Finland (2005-2014), compared pregnancy outcomes of women with MS being exposed to interferon beta within 6 months prior to the last menstrual period and / or up to the end of the pregnancy and of women with MS without dispensed MS disease modifying drugs. Recently presented data of this Nordic study suggests that exposure to interferon-beta during pregnancy does not influence birth weight, birth height, or head circumference.[2,3]

At ECTRIMS 2018, you presented the outcomes of the pregnancy cases of the Bayer Pharmacovigilance Database for Betaferon®. Could you please shortly explain this dataset and summarize the core findings?

More than 1300 women who took Betaferon® as they were getting pregnant gave birth to babies from which 90 percent were healthy. The risk for complications as malformations, stillbirths and miscarriages which can also occur in healthy women who do not take any medication was not increased. This cohort provides an important additional contribution in the counselling of MS patients that want to become pregnant.[4]

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When should MS patients start therapy again after delivery?

That depends on several factors: Do they want to breastfeed? How was the disease activity before and during the pregnancy? With a high disease activity during the pregnancy women should abstain from breast-feeding and instead should consider to start treatment early after birth. It is different for patients with mild MS as interferon beta can be used during breastfeeding. Even though information is limited on the excretion of interferon beta in the human milk it is assumed that levels would be negligible and no harmful effects on the breastfed infant are anticipated.

PROFESSOR DR. KERSTIN HELLWIG

Professor Dr. Kerstin Hellwig is a senior consultant in the Department of Neurology, St. Josef Hospital, Ruhr University, Bochum, Germany specialized in MS and neuroimmunology. She is one of the vice chairs of the department of neurology and leads the neurological outpatient clinic.

Her scientific interest is mainly clinical with a special interest in the field of MS and family planning. Since 2006, she has initiated and maintained the German-speaking MS and pregnancy registry (DMSKW). She published multiple peer-reviewed manuscripts, in particular about MS and pregnancy.

[1] Hellwig K., personal survey [2] Hellwig K et al., Poster P1753, ECTRIMS 2018, Berlin (Germany) [3] Burkill S et al., Poster 766, ICPE 2019, Philadelphia (USA)
[4] Hellwig K et al., Poster P1771, ECTRIMS 2018, Berlin (Germany)

Bayer AG

Betaferon®
(Refer to full SmPC before prescribing.)

Composition: *Active ingredient:* Recombinant interferon beta-1b 250 microgram (8.0 million IU) per ml when reconstituted. Betaferon contains 300 microgram (9.6 million IU) of recombinant interferon beta-1b per vial. *Excipients:* Human albumin, Mannitol. **Indications:** Betaferon is indicated for the treatment of patients with a single demyelinating event with an active inflammatory process, if it is severe enough to warrant treatment with intravenous corticosteroids, if alternative diagnoses have been excluded, and if they are determined to be at high risk of developing clinically definite MS, patients with relapsing-remitting MS and two or more relapses within the last two years and patients with secondary progressive MS with active disease, evidenced by relapses. **Contraindications:** Patients with a history of hypersensitivity to natural or recombinant interferon beta, human albumin or any of the excipients. Patients with current severe depression and/or suicidal ideation. Patients with decompensated liver disease. **Special warnings / Precautions:** The administration of cytokines to patients with a pre-existing monoclonal gammopathy has been associated with the development of systemic capillary leak syndrome with shock-like symptoms and fatal outcome. • In rare cases, pancreatitis was observed with Betaferon use, often associated with hypertriglyceridaemia. • Betaferon should be administered with caution to patients with previous or current depressive disorders, in particular to those with antecedents of suicidal ideation. Patients should be advised to immediately report symptoms of depression and/or suicidal ideation to their prescribing physician. Patients exhibiting depression should be monitored closely during therapy with Betaferon and treated appropriately. Cessation of therapy with Betaferon should be considered. Betaferon should be administered with caution to patients with a history of seizures, particularly if their epilepsy is not adequately controlled with anti-epileptics. This product contains human albumin and hence carries the risk for transmission of viral diseases. A risk for transmission of Creutzfeld-Jacob disease cannot be excluded. • Thyroid function tests are recommended regularly in patients with a history of thyroid dysfunction or as clinically indicated. Complete blood and differential white blood cell counts, platelet counts, and blood chemistries, including liver function tests (e.g. AST (SGOT), ALT (SGPT) and γ-GT), are recommended prior to initiation and at regular intervals during Betaferon therapy. Patients with anaemia, thrombocytopenia and/ or leukopenia may require more intensive monitoring. • Severe hepatic injury, including cases of hepatic failure, has been reported rarely in patients taking Betaferon. The most serious events often occurred in patients exposed to other drugs or substances associated with hepatotoxicity or with comorbidity. Patients should be monitored for signs of hepatic injury. Withdrawal of Betaferon should be considered if serum transaminases levels increase significantly or are associated with clinical symptoms. • Caution should be used and close monitoring considered with severe renal failure. • Cases of nephrotic syndrome with different underlying nephropathies including collapsing focal segmental glomerulosclerosis, minimal change disease, membranoproliferative glomerulonephritis and membranous glomerulopathy have been reported, at various time points, during treatment with interferon-beta products and may occur after several years of treatment. Periodic monitoring of early symptoms and prompt treatment is required; and discontinuation of treatment with Betaferon should be considered, especially in patients at higher risk of renal disease. Caution is required in patients with pre-existing cardiac disorders. Patients with pre-existing significant cardiac disease should be monitored for worsening of their cardiac condition, particularly during initiation of treatment with Betaferon. While Betaferon does not have known direct-acting cardiotoxicity, flu-like symptoms may prove stressful to pre-existing heart disease. Rare cases of cardiomyopathy have been reported: If this occurs and a relationship to Betaferon is suspected, treatment should be discontinued. • Cases of thrombotic microangiopathy (TMA), manifested as thrombotic thrombocytopenic purpura or haemolytic uraemic syndrome have been reported with interferon-beta products. Events were reported at various time points during treatment and may occur several weeks to several years after starting treatment with interferon-beta. If TMA is diagnosed, prompt treatment is required and immediate discontinuation of Betaferon is recommended.
• Serious hypersensitivity reactions may occur. If reactions are severe, Betaferon should be discontinued and appropriate medical intervention instituted. • Injection site necrosis has been reported in patients using Betaferon. It can be extensive and may result in scar formation. If the patient experiences any break in the skin, the patient should be advised to consult with his/her physician before continuing Betaferon injections. If the patient has multiple lesions Betaferon should be discontinued until healing. **Undesirable effects:** At the beginning of treatment adverse reactions are common but in general they subside with further treatment. The most frequently observed adverse reactions are a flu-like symptom complex and injection site reactions. Dose titration is recommended at the start of treatment in order to increase tolerability to Betaferon. Flu-like symptoms may be reduced by administration of non-steroidal anti-inflammatory drugs. The incidence of injection site reactions may be reduced by the use of an autoinjector. **Undesirable effects which were significantly associated with Betaferon treatment in clinical trials:** *Very common:* lymphocyte count decreased, absolute neutrophil count decreased, white blood cell count decreased, headache, abdominal pain, alanine aminotransferase increased, rash, hypertonia, myalgia, injection site reaction, flu-like symptoms, fever, asthenia, chills; *Common:* abnormal vision, palpitation, hypertension, dyspnoea, vomiting, aspartate aminotransferase increased, menstrual disorder, injection site necrosis, chest pain, sweating, malaise. **Undesirable effects identified during post-marketing surveillance:** *Very common:* arthralgia; *Common:* anaemia, hypothyroidism, blood bilirubin increased, weight increased, weight decreased, confusional state, tachycardia, urticaria, pruritus, alopecia, menorrhagia; *Uncommon:* thrombocytopenia, blood triglycerides increased, suicide attempt, emotional lability, convulsion, hepatitis, skin discolouration, nephrotic syndrome, glomerulosclerosis; *Rare:* thrombotic microangiopathy including thrombotic thrombocytopenic purpura/ haemolytic uraemic syndrome, anaphylactic reactions, hyperthyroidism, thyroid disorders, anorexia, cardiomyopathy, bronchospasm, pancreatitis, hepatic injury, hepatic failure. *Frequency not known:* capillary leak syndrome in pre-existing monoclonal gammopathy, drug-induced lupus erythematosus, pulmonary arterial hypertension.

Please refer to the Summary of Product Characteristics for further information.
On prescription only.
Marketing Authorisation Holder: Bayer AG, 51368 Leverkusen, Germany.
Date of issue of Marketing Authorisation valid throughout the EU: 30.11.1995.
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