

WORKING GROUP REPORT

2016

Idiopathic Nephrotic Syndrome

Marina Vivarelli - Georges Deschênes

Members

Since the start of the WG in September 2013, 50 members from different European countries have joined the group. The steering committee includes Licia Perruzzi, Johan VandeWalle, Carmine Pecoraro, Sevgi Mir and Georges Deschenes, past coordinator until 2015.

Enquiries

Study#1: the treatment of the first flare. Coordinated by Georges Deschênes (Nov 2013 to Jan 2014). 25 members participated to the study and returned the questionnaire. Results: the cumulative dose that ranged from 2240 mg/m² to 4245 mg/m². and the duration ranged from 8 to 24 weeks. Other results showed that a/ 18/25 protocols include several steps of tapering before withdrawal (more or less as the French protocol); b/ 13/25 teams are using prednisone and 12/25 are using prednisolone; c/ 18/25 are limiting the dose up to 60mg/d meaning that patients over 1m² (30 KgBW) are receiving less than the expected cumulative dose; d/16/24 are using an IV-MP test in case of steroid resistance. Patients with a first flare were uniformly treated in UK, Germany, Denmark & France

Study#2: Steroid resistancy. Coordinated by Licia Peruzzi (Jan 2014 to Mar 2014). 15 members from 11 countries participated to the study and returned the questionnaire. Results: Most centers define steroid resistance after 6 weeks and MP pulses, add CyA or Tac and wait for at least 6 months for response. 50% proteinuria reduction is considered partial response together with sAlb increase. In most centers, MMF is added if partial response on top on other drugs after at least 6 months. Two centers carried out plasma exchange or immunoadsorption associated with B cell depletion in multiresistant forms, based on the involvement of B cells and immunoglobulins in the mechanism of the disease.

Study#3: Rituximab. Coordinated by Georges Deschênes (Dec 2014 to Mar 2015). rituximab is widely used in european countries. more than 350 patients has been treated by this set of 23 teams (22 answers + robert-debré); paris, roma and london totalized more than 200 (may be 300) patients. Most of the patient treated had SDNS previously treated with MMF and/or CNI; more marginally some has been treated only for poor compliance to treatment, long duration of the disease, drugs toxicity, and complications of the nephrotic syndrome. A handful of patients have also been treated for SRNS, generally without effect. Rituximab has been declared as the last line of treatment of SDNS by 3 (may be 4) teams but others have clearly used it as a first line in SDNS; the treatment is not refunded in 2 countries, thus clearly limiting indications. The conclusion is that retrospective studies have been convincing enough to treat hundred of patients far prior the release of the first study bringing a formal evidence of efficiency.

Study#4: Vaccinations. Coordinated by Marina Vivarelli. Nephrotic syndrome, both in itself and due to concomitant immunosuppression, determines an impaired response to vaccinations, and reduced levels of total IgGs during flares. There are very disparate attitudes towards vaccinations and the risk of disease flares. Moreover, the increasing use of rituximab with its effect on B cell depletion may affect immune competence and response to vaccinations. Therefore, the ESPN Working Group has 3 aims:

1) A questionnaire on vaccinations: what members advise their patients to do regarding vaccinations and the risk of relapse, if in their experience relapse happens or not, if they routinely check for specific

antibodies and have ever noted any abnormalities both at onset and further on with concomitant immunosuppression.

2) An expanded questionnaire on rituximab, doses, frequency, B cell reconstitution, concomitant immunosuppression, side effects.

3) A prospective project of assessing total serum IgG, IgA and IgM in patients with INS at onset, during immunosuppression and before and after rituximab infusion.

Basic research

2 teams from the Nephrotic syndrome WG have declared an activity in the field of basic research:

M Vivarelli [Roma (Bambino Gesù)]: Role of B cells in the Idiopathic Nephrotic Syndrome

A Jamin [Paris (Robert-Debré)]: Role of Immunoglobulin & free light chains in the Idiopathic Nephrotic Syndrome.

Collaboration with Patients Association

A text of popularization on the Idiopathic Nephrotic Syndrome written by Elena Levchenko and Moin Saleem has been translated from English to 11 national languages that have been posted on the website of Nephceurope, the European patient association for nephrotic syndrome (June 2014)

Registry of trials

Several trials coordinated by a member of the Nephrotic Syndrome WG have been registered on the website of the Nephrotic Syndrome WG:

PREDNOS (Birmingham United Kingdom) comparing 2 prednisolone regimens for the first flare (recruitment completed)

NEPHROMYCY (Paris France): Cyclophosphamide Versus Mycophenolate Mofetil for the Treatment of Steroid-dependent Nephrotic Syndrome in Children (recruitment completed, results expected in 2015)

NEPHRUTIX Limoges France): Efficacy of Rituximab for the Treatment of Calcineurin Inhibitors Dependent Nephrotic Syndrome during Childhood (recruitment completed, results released in 2015)

Steroid Treatment of Idiopathic Nephrotic Syndrome (Bologne, Italy): assess the benefits and potential adverse effects of a prolonged initial corticosteroid regimen, for the treatment of the initial episode. (Currently recruiting)

INTENT study (Heidelberg Germany) Initial treatment of idiopathic nephrotic syndrome in children with mycophenolate mofetil vs. prednisone (recruitment in course)

NEPHROVIR-2 (Paris France) Factors of Steroid Dependency in Idiopathic Nephrotic Syndrome (Recruitment completed, analysis in progress)

NEPHROVIR-3 (Paris France) Efficiency of Levamisole in association with Prednisone in the treatment of the first flare (In preparation)

Meetings

The 1st meeting of the Nephrotic Syndrome WG has been held in Porto during the ESPN meeting. Program: brief presentation of each participant in the group (a "tour de table"); research work (ESPN grant applications) m vivarelli: rituximab and Ig; a jamin - g deschenes: light chains and podocytes; jc davin Psychological stress and relapses of nephrotic syndrome; collaboration with the US midwest group on NS; unformal discussion: others questionnaires- what is your aim in the group and for the group - how to work altogether.

The 2nd meeting of the Idiopathic Nephrotic syndrome was held in Brussels during the ESPN meeting of 2015.

2016 no meeting scheduled due to concomitant ESPN – IPNA meeting

The 3rd meeting of the ESPN Working Group will be scheduled during the ESPN Meeting in Glasgow September 2017.

Projects for 2016

Compiling results of the survey on vaccinations, coordinating the study on immunoglobulins and on response to Rituximab.

Publications

The first paper resulting from an ESPN INS Working Group survey has been finalized and submitted:

“Childhood idiopathic nephrotic syndrome - Variability of treatment in European centers”

Georges Deschênes, Marina Vivarelli & Licia Peruzzi, On behalf of the ESPN Working Group on Idiopathic Nephrotic Syndrome