

EULAR STUDY GROUP ON THERAPEUTIC DRUG MONITORING OF BIOLOGICS

Study group leader: Prof. John Isaacs

Therapeutic drug monitoring (TDM) of biologics is a potentially important development in the management of patients with a variety of rheumatic conditions. It refers explicitly to the measurement of circulating drug concentrations (drug levels), and anti-drug antibodies, in patients receiving biologic drugs. There is an increasing literature on this subject, suggesting that the use of TDM can both improve patient management and be cost-effective. Indeed, some data suggest that the implementation of TDM may lead to cost savings, by facilitating the tapering and sometimes cessation of biologic therapy.

Nonetheless, there are still many important questions that need to be resolved with regard to this technology:

- Is TDM likely to be truly cost-effective? To date there has not been a formal controlled trial that compares usual management (including drug tapering and biologic class switching) with management guided by TDM. Trials are being planned, which will provide important information.
- If implemented, should TDM apply to all patients, or only a subgroup? Cost savings are most likely in patients in disease remission but TDM may also be useful in patients in whom the effects of therapy are waning (reactive TDM). What about patients with adverse reactions – can TDM help here?
- Related to the above point, how frequently should TDM take place, particularly if routinely implemented (proactive TDM)?
- If proactive TDM is advocated, should this routinely include drug levels and anti-drug antibodies or just drug levels, with anti-drug antibody measurements when drug levels are found to be low?
- How important is it that 'trough' rather than random drug levels are measured? The former is straightforward when biologics are infused but less convenient, for patients and their clinical team, when the drug is administered at home. If trough levels are important, how can this best be assimilated into overall management?
- Is there benefit to be gained from performing TDM when switching between originator drugs and biosimilars, or between biosimilars?
- Who should interpret the results of TDM testing? Is a simple algorithmic approach adequate or is deeper interpretation likely to be needed? How much delay is acceptable in routine practice, between blood draw and consequent change to patient management?
- What can we learn from other specialties? In some countries, gastroenterologists are already routinely using TDM.
- Which is the preferred technology for TDM? A number of technologies exist, including ELISA, radioimmunoassay, electro-chemiluminescent assay (ECLISA), etc. For measurement of anti-drug antibodies some assays are subject to interference by free drug, others are not. Similarly, some measure total anti-drug antibodies, others measure only unbound anti-drug antibodies. Which assays support clinical efficacy?
- Given the potential complexity of these measurements, how much education is required for physicians requesting these tests, how should this be provided, and by whom?

The purpose of this EULAR Study Group is to debate the above questions, and others that emerge.

Below you will find a list of the founding members of the proposed group but we welcome, and anticipate, additional membership. Patients are very welcomed as well as the patient perspectives are very important.

UK

- John Isaacs, Institute Director, Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne
- Martin Perry, NHS Greater Glasgow & Clyde, Glasgow
- Meghna Jani, Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal Research, University of Manchester, Manchester
- Patrick Kiely, St George's University Hospitals, London
- Meryll Blake, Newcastle upon Tyne (patient voice)
- Neil McCarthy, Newcastle upon Tyne (patient voice)
- Lisa Tait, Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne

SPAIN

- Dora Pascual, Salcedo, IdiPaz, Madrid
- Chamaida Plasencia Rodriguez, University Hospital, La Paz, Madrid
- Alejandro Balsa, University Hospital La Paz, Madrid
- Loreto Carmona, InMusc, Madrid
- Borja Hernandez-Breijo, La Paz University Hospital & IdiPaz, Madrid

FRANCE

- Denis Mulleman, University of Tours
- Guillaume Le Mélédo, University of Tours
- Philippe Goupille, University of Tours

THE NETHERLANDS

- Gertjan Wolbink, READE/Sanquin, Amsterdam
- Theo Rispens, IP Research, Sanquin, Amsterdam
- Annick de Vries, Bioanalysis, Sanquin, Amsterdam
- Merel L'Ami, Reade, Amsterdam
- Jill Ruwaard, Reade, Amsterdam
- Charlotte Krieckaert, Reade, Amsterdam
- Zohra Layegh, Reade, Amsterdam
- Elsemieke Hackenitz, Sanquin, Amsterdam
- Dieneke Schonenberg, Emma Children's Hospital/ UMC Amsterdam
- Merlijn van den Berg, Emma Children's Hospital/ UMC Amsterdam

NORWAY

- Silje W. Syversen, Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo
- Nils Bolstad, Dept of Medical Biochemistry, Oslo University Hospital, Radiumhospitalet
- Guro Lovik Goll, Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo
- Johanna Gehin, Dept of Medical Biochemistry, Oslo University Hospital, Radiumhospitalet
- Tore Kristian Kvien, Dept Rheumatology, Diakonhjemmet Hospital, Oslo