INUS Neuro-Urology News

The Periodical of the International Neuro-Urology Society

Volume 4 • Issue 1 • February 2025 • neuro-uro.org

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Interview with the Expert

Mirabegron in Neurogenic Lower Urinary Tract Dysfunction

Dr. Blayne Welk (CA)
Professor
Western University, London, Ontario, Canada
Interviewed by Dr. Glenn Werneburg (US), Editor NUN

For this Issue of Neuro-Urology News, I had the opportunity for discussion with Prof. Blayne Welk. Dr. Welk is Professor of Surgery and Urologist at Western University in London, Ontario, Canada. He is the recipience of numerous grants and has published more than 200 peer-reviewed publications. He is a global expert in the field of functional urology. He currently serves as the Vice President of INUS, and the President of the Neurogenic Bladder Research Group. Amongst many impactful investigations, he has recently led a randomized-controlled clinical trial of the role of beta-3 agonist medication in neurogenic lower urinary tract dysfunction. Subsequently, his group performed a meta-analysis in this area, which was published in Neurourology & Urodynamics last year. Our discussion focuses on this work.

GW: What is known about beta 3 agonists in NLUTD?

BW: Initially a lot of the evidence for the use of beta-3 agonists in patients with spinal cord injury or multiple sclerosis came from small case series and pre-post treatment studies. These results were promising – there did not seem to be any significant adverse effects. Initial review articles examining mirabegron in NLUTD concluded that compliance and maximal systematic capacity were often improved. The magnitude of change for the urodynamic variables was often similar to people using OAB anticholinergics.

GW: What was the impetus for your study?

BW: There is considerable interest in avoiding some of the anticholinergic side effects in people with NLUTD. I find patients frequently experience constipation and dry mouth, and often ask about the potential association with cognitive dysfunction. For many patients they don't realize they're having side effects from some of the OAB anticholinergics until they try stopping them for a period of time. Given the advantages in the beta-3 agonist side effect profile that were seen in the overactive bladder population, I had an immediate interest in assessing their efficacy in patients with NLUTD in a randomized clinical trial.

Both myself and Professor Krhut conducted very similar randomized controlled trials in people with multiple sclerosis or spinal cord injury. Because of the similarities, I felt they were well suited to this type of meta-analysis. (continued on Page 2).

INUS Calendar

INUS Lecture at the European Academy of Neurology (EAN) Congress
Helsinki, Finland
June 21-24, 2025

INUS Lecture at the Italian Society of Urodynamics (SIUD)
Bologna, Italy
June 26-28, 2025

INUS Annual Congress 2026
Yogyakarta, Indonesia
January 22-24, 2026

GW: How did you choose the outcomes of maximum cystometric capacity and the patient change in perception of bladder condition?

BW: Both of these outcomes were included in the two randomized controlled studies that we analyzed. They are nice outcomes because they cover both a valid and reliable urodynamic assessment of bladder physiology and a patient-relevant assessment of the overall effectiveness of the medication on bladder function.

GW: Describe the design of the current study. What is an Individual Participant Data Meta-analysis and how does it differ from other meta-analyses? What was your hypothesis?

BW: An Individual Participant Data Meta-Analysis (IPDMA) involves directly analyzing raw data from each participant across multiple studies rather than aggregating summary statistics like overall odds ratios. This approach offers several key advantages. By pooling participant-level data, IPDMA increases statistical power. It also allows for standardized analyses, ensuring consistent data handling and outcome definitions across studies, which improves reliability. Access to original data enables better data quality through error correction and variable harmonization. Additionally, it facilitates more accurate subgroup analyses, and avoids ecological bias wherein relationships observed at the group level may not hold for individuals. These strengths make IPDMA the gold standard for meta-analyses, providing more nuanced and trustworthy findings. However, its resource-intensive and logistically-complex nature often limits its use compared to traditional meta-analyses. Our hypothesis was that mirabegron would lead to significant improvements in the measured outcomes compared to placebo.

GW: What were the main findings of the current study? What are its implications?

BW: Our IPDMA included 98 patients from the two trials of Welk et al. and Krhut et al. Mirabegron was associated with a significant improvement in maximum cystometric capacity (+41 mL, $p = 0.04$) and in the patient perception of change in bladder condition (−0.8, $p < 0.01$) compared to placebo. Secondary outcomes including peak neurogenic detrusor overactivity pressure (−20 cm H2O, $p < 0.01$), incontinence-QOL score (+12, $p < 0.01$), and 24 h pad weights (−79 g, $p = 0.04$) also improved significantly compared to placebo. Exploratory analyses found similar improvements in people with multiple sclerosis and spinal cord injury (SCI); some outcomes improved to a greater degree among people within complete SCI, or SCIs that were below T7. Our IPDMA confirmed a very good safety profile for mirabegron, with a low number of adverse effects.

GW: What were the limitations of the study? What are the next steps?

BW: Differences in patient populations and study protocols where present between the two RCTs, although these are unlikely to significantly impact results and are also present in study-level meta-analyses. Despite a larger sample size than the individual studies, it still remains relatively small. The efficacy of mirabegron may be underestimated, as many participants had prior anticholinergic use, possibly representing a more severe bladder phenotype. The findings are most applicable to individuals with multiple sclerosis and SCI, though population-specific studies are recommended for other cases of NLUTD.

GW: Can you suspect that other beta-3 agonists such as vibegron and solabegron might have similar results?

BW: At this point, I think it is likely that other beta-3 agonists would have a similar effect in NLUTD, just as many of the OAB anticholinergics have not been specifically studied in NLUTD despite being commonly used in this population. However, further work would be needed to prove this.

GW: Is there any concern regarding mirabegron's hemodynamic effects in the context of individuals at risk for autonomic dysreflexia?

BW: At this point there is no evidence of a negative effect of mirabegron in the general population in terms of risk of patient relevant outcomes from increased heart rate/blood pressure (such as arrythmia, heart attack, stroke or death), and in the two randomised trials in the IPDMA, a single patient with a C6 SCI had palpitations which may have been related to mirabegron, and this resolved with discontinuation of the treatment.

GW: What advice do you have for junior INUS members interested in embarking on a career as a surgeon-scientist with a neuro-urological focus?

BW: There are a lot of interesting and important unanswered questions in neuro-urology. The challenges include securing funding, recruiting enough patients, and eventual acceptance in a urologic journal, many of which tend not to prioritize neuro-urology . I would recommend junior members start off with a focused question that ideally would impact practice, and try to come up with the most realistic study that could answer it. Mentorship is important, and INUS provides a great venue to seek out research partners (Professor Krhut and myself first discussed this idea at an INUS meeting). The meetings provide a place to interact with experienced neuro-urologists to gauge interest and impact of research questions.

Further Reading:

Welk, B., Krhut, J., & Sýkora, R. (2024). An individual participant meta-analysis of mirabegron in multiple sclerosis and spinal cord injury. Neurourology and Urodynamics, 43(4), 803-810.

Welk, B., Hickling, D., McKibbon, M., Radomski, S., & Ethans, K. (2018). A pilot randomized-controlled trial of the urodynamic efficacy of mirabegron for patients with neurogenic lower urinary tract dysfunction. Neurourology and urodynamics, 37(8), 2810-2817.

Krhut, J., Borovička, V., Bílková, K., Sýkora, R., Míka, D., Mokriš, J., & Zachoval, R. (2018). Efficacy and safety of mirabegron for the treatment of neurogenic detrusor overactivity—prospective, randomized, double-blind, placebo-controlled study. Neurourology and urodynamics, 37(7), 2226-2233.

INUS Congress 2025: Recap

The 10th Anniversary meeting of the International Neuro-Urology Society

Congress Recap

Dr. Glenn Werneburg (US)
Editor, Neuro-Urology News
INUS Early Career Officer

The 10th Annual Congress of the International Neuro-Urology Society (INUS) took place from January 16-18, 2025, in the town of Zermatt, Switzerland. This Congress marked a decade of excellence in neuro-urology. The milestone event brought together top researchers, clinicians, and professionals from around the world, united by the shared mission of advancing neuro-urological science and patient care.

Nestled at the foot of the Matterhorn mountain, Zermatt was a superb setting for the Congress. The snow-covered peaks, crisp alpine air, and Swiss ambiance inspired deep scientific conversation and collaborative efforts. As the birthplace of the International Neuro-Urology Society, returning to Switzerland for this special anniversary underscored the society's commitment to its roots and future growth.

Engaging Workshops: Exploring Innovations and Best Practices

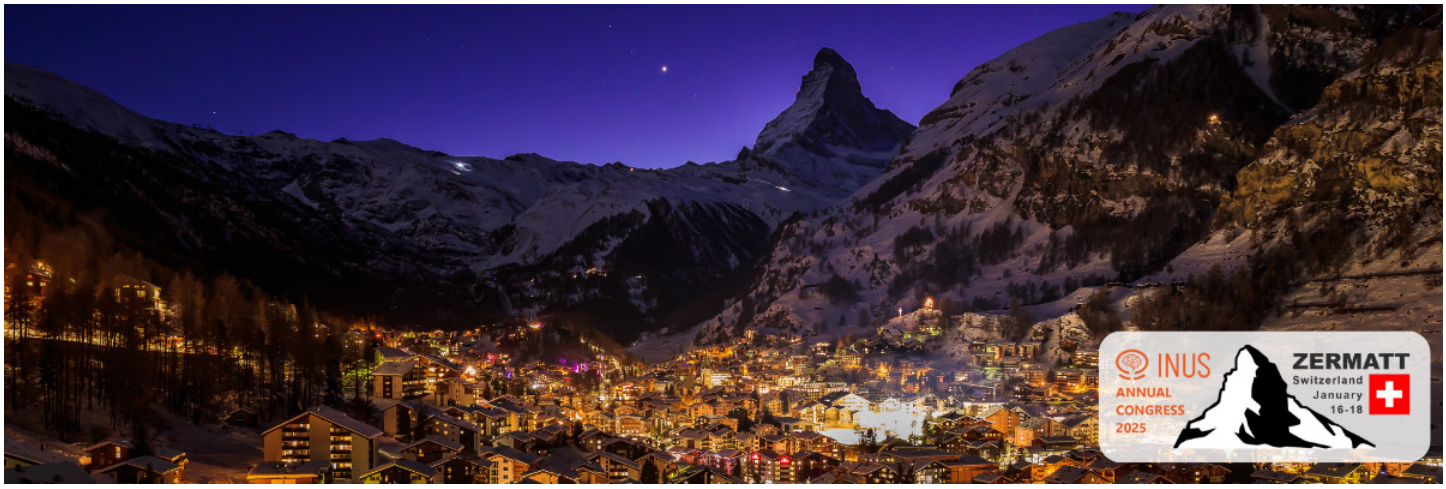
The Congress opened with a series of specialized workshops, designed to provide hands-on learning experiences and discussions surrounding the latest advancements in neuro-urology.

Urodynamics and Urodynamics for Nurses
Led by Drs. Stefania Musco, Lorenz Leitner, Sarah Baumann, Helmut Madersbacher, Mehri Mehrad, and Sivilaikul Sonthidetch, these workshops focused on the standardization of urodynamic assessments, practical skills in equipment handling, and the interpretation of findings. A dedicated session for nurses emphasized their crucial role in neurogenic bladder management.

Innovations from the Lab: Shaping the Future of Neuro-Urology
This forward-thinking workshop, chaired by Drs. Célia Cruz and Andrea Sartori, explored the latest breakthroughs in tissue remodeling, neural control mechanisms, and emerging therapies for neuro-urological disorders. Sessions included animal models, molecular insights, and spinal cord stimulation techniques, laying the groundwork for future research collaborations.

Neuromodulation: From Concept to Clinical Practice
With Drs. Bertil Blok and Marcio Averbeck at the helm, this workshop provided an in-depth look at both non-invasive and invasive neuromodulation techniques, including sacral nerve modulation and percutaneous tibial nerve stimulation. Attendees participated in hands-on training, reinforcing their theoretical knowledge.

Microbiome & Phages in Neuro-Urology
Led by Drs. Shawna McCallin and Lorenz Leitner, this workshop addressed the emerging role of the urinary microbiome in neuro-urological health, including discussions on bacteriophage therapy, antibiotic resistance, and novel treatment pathways. (continued on Page 4).



Neuroscience
Led by Drs. Claire Hentzen and Jalesh Panicker, this session discussed the neural control of continence and micturition. Amongst other exciting areas of interest, discussions centered on the intersection between cardiovascular and urogenital function, with an eye toward understanding correlations between the two and developing practical clinical assessment tools.

Nightmare Cases in Neuro-Urology
This engaging session, chaired by Drs. Blayne Welk and Ulrich Mehnert, examined complex clinical cases, providing invaluable insights into managing challenging patient scenarios through expert panel discussions.

In addition to the workshops, a Guidelines Working Group session brought together a global group of leading experts to discuss the existing clinical practice guidelines in neuro-urology, and gaps in such guidelines due to insufficient scientific evidence. The meeting focused on identification of the gaps and development of suitable methodology to address them. The meeting marked the commencement of an approximately year-long effort to develop a series of Delphi-consensus statements aimed to address the gaps and to provide pragmatic guidance in resource-limited settings.

Scientific Sessions: Elevating Neuro-Urology to New Heights

Beyond the workshops, the Congress delivered an exceptional lineup of scientific sessions, debates, and panel discussions on key topics shaping the future of neuro-urology.

The opening lecture, presented by Prof. Helmut Madersbacher, traced the history of INUS, setting the stage for in-depth discussions on cutting-edge research and best practices. Notable panel discussions included: Upper Urinary Tract Risk Stratification and Follow-Up, Role of Pelvic Floor Physiotherapy for Neurological Patients, Interface Between Mental Health Disorders and Lower Urinary Tract Symptoms (LUTS); and Understanding the Complex Interplay of Bladder, Bowel, and Sexual Function.

A highlight of the Congress was The Future in Neuro-Urology session, where 5 finalists presented their neuro-urologic research. They competed for the prestigious Swiss Continence Foundation (SCF) Award. The competition, judged by the jury panel of Drs. Célia Cruz, Martina Liechti, Jalesh Panicker, John Stoffel, and Glenn Werneburg, showcased the next generation of neuro-urology pioneers. Dr. Andrea Sartori, post-doctoral research fellow at Beth Israel Deaconess Medical Center/ Harvard Medical School was the 2025 winner of the Swiss Continence Foundation Award (Photo). His presentation was entitled "Molecular characterization of the spinal circuitries controlling lower urinary tract function". We look forward to including more about Dr. Sartori and this work in a subsequent Neuro-Urology News issue.

The final day of the Congress featured expert-led sessions on the latest developments in surgical techniques, catheter use, and urinary tract infections in neuro-urological patients. Highlights included: Surgical Management of Urinary Incontinence: From Open to Nano, Catheter Use: Curse or Blessing?, and UTIs in Neuro-Urological Patients: Definition, Epidemiology, and Prophylaxis.

As the 10th INUS Congress drew to a close, Prof. Thomas Kessler, INUS President, delivered closing remarks, emphasizing the importance of continued collaboration and innovation in neuro-urology. Attendees came away from the Congress with new knowledge and skills, but also inspiration and motivation to advance patient care and research in this dynamic field.

The Annual Congress Dinner at Mont Cervin Palace provided a perfect conclusion to a remarkable event, with the presentation of the Swiss Continence Foundation Award and celebrations in a stunning winter setting.

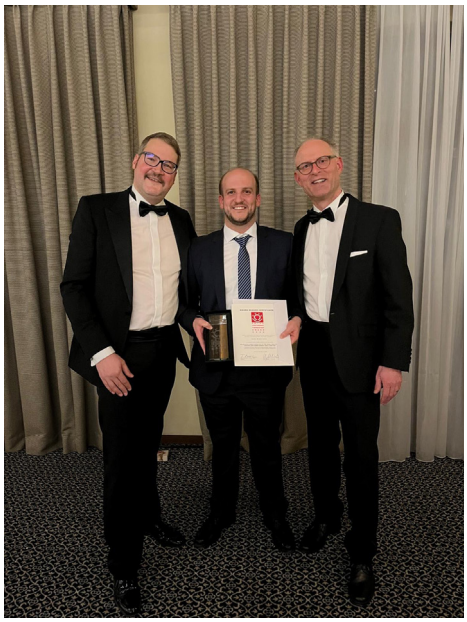


Photo: Dr. Ulrich Mehnert (left) and Dr. Thomas Kessler (right) presenting the Swiss Continence Foundation Award to Dr. Andrea Sartori (center).

See You at INUS 2026!
With a successful 10th anniversary Congress now behind us, the INUS community looks forward to its next gathering in 2026, continuing the tradition of excellence, innovation, and collaboration that defines the society. The 2026 Annual Congress will take place in the beautiful location of Yogyakarta, Indonesia, which, according to the New York Times last month, "might be the center of the universe." We look forward to welcoming you all next year to an exceptional Congress in a remarkable location.

Stay connected with INUS for updates and details on the next edition at www.neuro-uro.org.

INUS Congress 2025: Zermatt