Biomarker methods to enable stratification of patient populations in clinical trials for neuropathic pain

Jan Vollert, Imperial College London
22 & 23 October 2018 • IMI Scientific Symposium • Brussels, Belgium
Neuropathic pain as a treatment challenge

How can we increase probability of success in NeP development programs?

- In the general population, 5-8% suffer treatment demanding NeP. Today label indications in NeP are based on etiologies, which are the cause of the neuropathy, not the cause of the pain linked to neuropathy.
- Drugs are developed from targets – but treatments are based on signs and symptoms. There is a lack of regulatory validated clinical biomarkers, linking signs and symptoms to pathophenotypes.
- Validating existing phenotype biomarker patterns as specific for NeP, across etiologies, would help overcoming this gap.
- One of them is Quantitative Sensory Testing (QST) – will use this as an example of what we achieved in the project.
Peripheral neuropathic pain: a mechanism-related organizing principle based on sensory profiles

Ralf Baron¹⁺, Christoph Maier², Nadine Attal², Andreas Binder³, Didier Bouhassira², David Cruccu⁴, Nanna B. Finnerup¹, Maija Haapala², Per Hansson¹, Philipp Hüllemann², Troels S. Jensen¹, Rainer Freynhagen⁵, Jeffrey D. Kennedy, Walter Magerl⁶, Tina Mainka², Maren Reimer³, Andrew S.C. Rice⁶, Marta Segerdahl²,², Jordi Serra⁷, Sören Sindrup⁶, Claudia Sommer⁶, Thomas Tölle, Jan Völlert⁷,³, Rolf-Detlef Treede⁷,³, on behalf of the German Neuropathic Pain Research Network (DFNS), and the EUROPAIN, and NEUROPAIN consortia

The effect of oxcarbazepine in peripheral neuropathic pain depends on pain phenotype: A randomized, double-blind, placebo-controlled study.

The number needed to treat for 50% pain relief:
- Total sample: 6.9
- Non-irritable nociceptor: 13
- Irritable nociceptor: 3.9

Change in total pain (NRS 0-10) over 6 weeks for non-irritable and irritable nociceptors.
QST is adequate for determining specific sensory phenotypes of patients in exploratory trials on neuropathic pain. Further work on NE, μNG and CCM is required before they can be implemented in Phase III clinical trials and clinical practice. It is agreed that the identification and quantification of abnormal activity with μNG can be used as a reliable correlate of spontaneous pain and it could be used for stratification purposes in phase II studies. CCM was acknowledged to confirm a small fiber neuropathy diagnosis in diabetes, but needs further confirmation in other small fiber neuropathy etiologies for extended use.

Pathophysiologically mechanisms of neuropathic pain: comparison of sensory phenotypes in patients and human surrogate pain models

Jan Vollert, Walter Mager, Ralf Baron, Andreas Binder, Elena K. Enax-Krumova, Gerd Geisslinger, Janne Gierthmühlen, Florian Henrich, Philipp Hüllemann, Thomas Klein, Jörn Lötsch, Christoph Maier, Bruno Oertel, Sigrid Schuh-Hofer, Thomas R. Tölle, Rolf-Detlef Treede

Stratifying patients with peripheral neuropathic pain based on sensory profiles: algorithm and sample size recommendations


Sensory profiling in animal models of neuropathic pain: a call for back-translation

Andrew S. C. Rice, Nanna B. Finnerup, Harriet I. Kemp, Gillian L. Currie, Ralf Baron