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

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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.

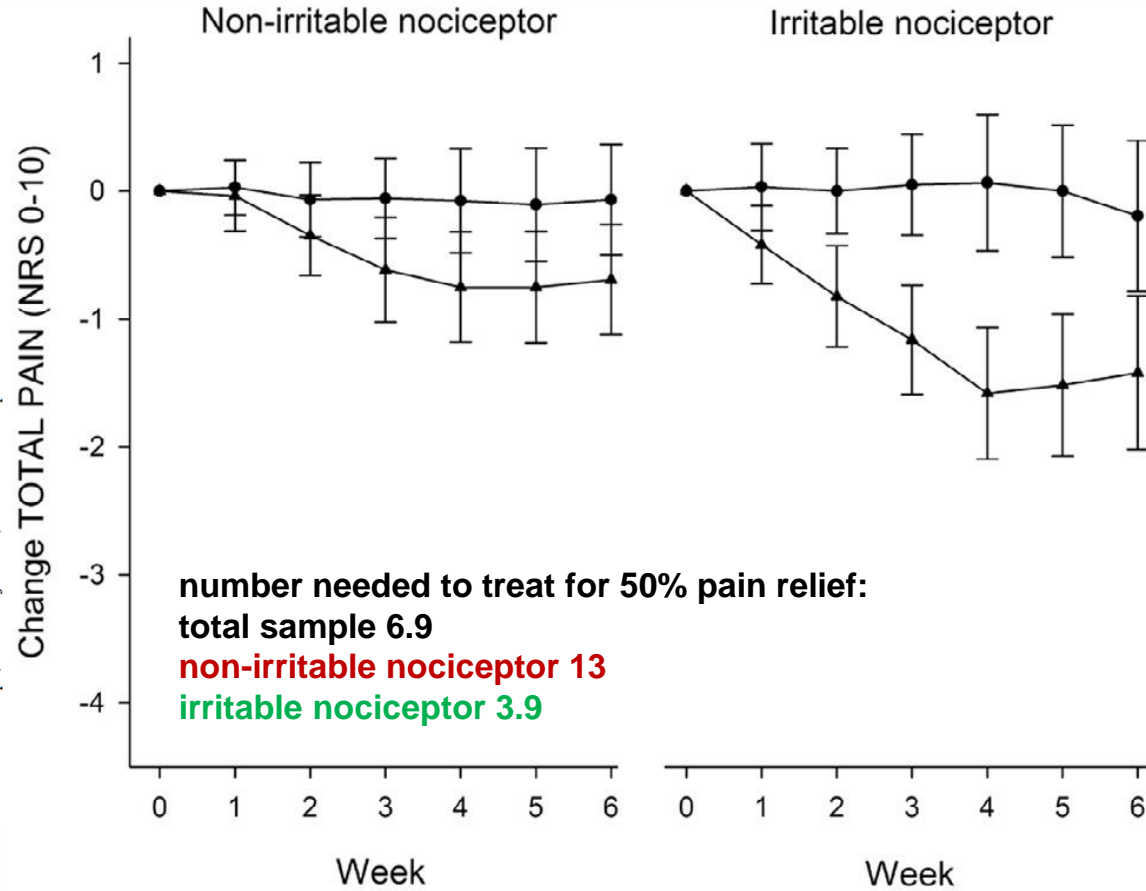
Peripheral neuropathic pain: a mechanism-related organizing principle based on sensory profiles

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

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EMA/CHMP/970057/2011. Guideline on the clinical development of medicinal products intended for the treatment of pain.

- **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.

Hyperexcitable C Nociceptors in Fibromyalgia

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Use of Corneal Confocal Microscopy to Evaluate Small Nerve Fibers in Patients With Human Immunodeficiency Virus

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Subgrouping of patients with neuropathic pain according to pain-related sensory abnormalities: a first step to a stratified treatment approach

Ralf Baron, Matti Förster, Andreas Binder

THE LANCET Neurology

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

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

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

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