DEVELOPING MEANINGFUL ENDPOINTS FOR PAIN CLINICAL TRIALS

THE EUROPEAN PERSPECTIVE WITH EMPHASIS ON NEUROPATHIC PAIN

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Declaration of interest

Type of activity	
Research Support/P.I.	Dolorisk European Study
Employee	
Consultant	
Major Stockholder	
Honoraria	Aptynix, Ipsen, Pfizer, Lilly, Grunenthal, Novartis, Sanofi MSD, MSD, Air Liquide
Scientific Advisory Board	Aptynix, Grunenthal, Sanofi MSD

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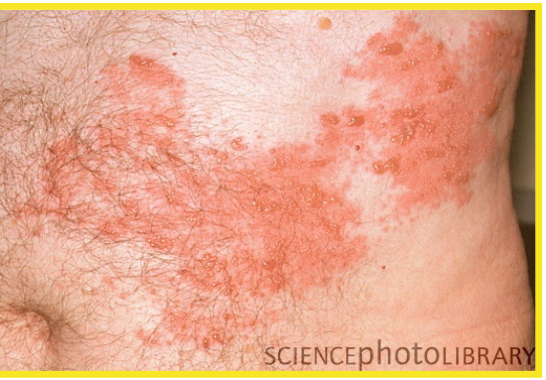
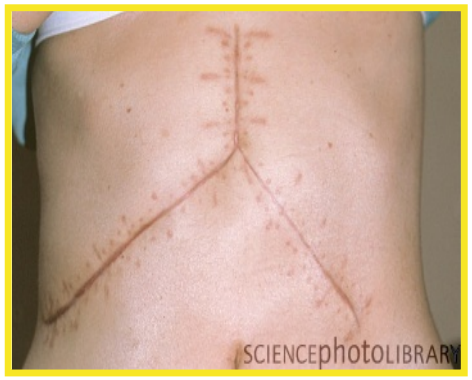
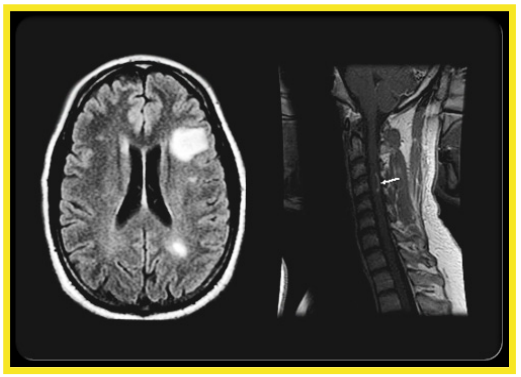
Neuropathic pain (NP): a multi-aetiology pain



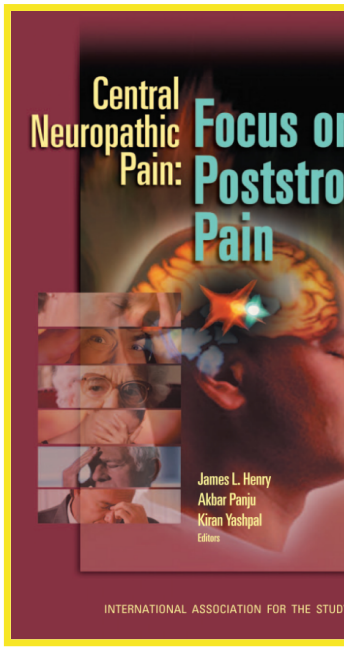
Herpes zoster



Surgery



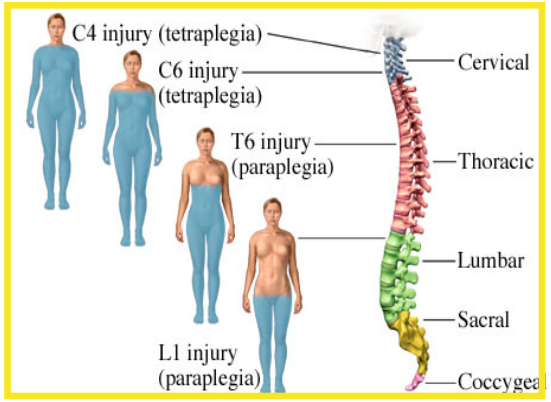
Multiple sclerosis



Stroke

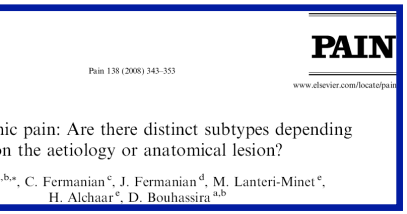
Diabetic polyneuropathy

Discal herniation



Spinal cord injury

Neuropathic pain : a multi-multidimensional pain syndrome


PAIN

Pain 138 (2008) 343-353

www.elsevier.com/locate/pain

ic pain: Are there distinct subtypes depending
n the aetiology or anatomical lesion?

C. Fermanian [c], J. Fermanian [d], M. Lanteri-Minet [e],
H. Alchaar [e], D. Bouhassira [a,b]

Similar neuropathic symptoms accross neuropathic pain conditions (n = 482)
Confirmed by multivariate analyses

	PHN	Diabetes	PPN	Nerve trauma	Radicu-lopathy	Trig. N	Spinal trauma	MS	Syrinx	Stroke
	n=49	n=35	n=53	n=110	n=43	n=18	n=25	n=32	n=40	n=31
Burning pain	89.8	62.8	58.5	51.1	65.1	16.7	76	56.2	75	74.2
Deep pain	28.5	68.6	62.3	58	51.2	22.2	74	62.5	60	64.5
Paroxysmal pain	63.2	62.8	62.3	66.3	72	89.9	72	65.6	65	58
Evoked pain	91.9	51.5	64.1	76	44.2	61.1	70	75	62.5	74
Paresthesia	30	82.9	84.9	86	81.4	33	80	84.4	87.5	83.9

Treatment (and therapeutic recommendations)
should not necessarily be driven by the aetiology of neuropathic pain

Neuropathic pain : European Medicines Agency (EMA) guidelines for approval

- EMA approvals have been granted for peripheral or central neuropathic pain
- To justify an general indication for the treatment of neuropathic pain, efficacy needs to be demonstrated in central and peripheral neuropathic pain (e.g. diabetic painful neuropathy, postherpetic neuralgia, but also other neuropathic pain conditions such as small fiber neuropathy, HIV neuropathy…)
- Efficacy should be shown in two or more models of peripheral neuropathic pain ; data in a single model of central neuropathic pain could be sufficient in this situation to support broad indicaiton (eg stroke, spinal cord injury pain)
- In Europe drugs approved for « neuropathic pain » include :

- Pregabalin (peripheral and central neuropathic pain)
- Gabapentin (peripheral neuropathic pain)
- Amitriptyline, clomipramine and imipramine (peripheral neuropathic pain or neuropathic pain)
- Carbamazepine (neuropathic pain)
- Capsaicin high concentration patches (peripheral neuropathic pain)

Medicines Agency, 15 december 2016

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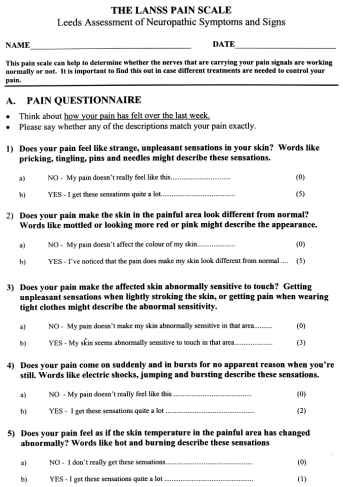
- Clinical endpoints for neuropathic pain clinical trials

Defining neuropathic pain in clinical trials : screening questionnaires

LANSS



THE LANSS PAIN SCALE
Leeds Assessment of Neuropathic Symptoms and Signs

NAME_____ DATE_____

This pain scale can help to determine whether the nerves that are carrying your pain signals are working normally or not. It is important to find this out in case different treatments are needed to control your pain.

A. PAIN QUESTIONNAIRE

- Think about how your pain has felt over the last week.
- Please say whether any of the descriptions match your pain exactly.

1) Does your pain feel like strange, unpleasant sensations in your skin? Words like pricking, tingling, pins and needles might describe these sensations.

a) NO - My pain doesn't really feel like this..... (0)
b) YES - I get these sensations quite a lot..... (5)

2) Does your pain make the skin in the painful area look different from normal? Words like mottled or looking more red or pink might describe the appearance.

a) NO - My pain doesn't affect the colour of my skin..... (0)
b) YES - I've noticed that the pain does make my skin look different from normal .... (5)

3) Does your pain make the affected skin abnormally sensitive to touch? Getting unpleasant sensations when lightly stroking the skin, or getting pain when wearing tight clothes might describe the abnormal sensitivity.

a) NO - My pain doesn't make my skin abnormally sensitive in that area..... (0)
b) YES - My skin seems abnormally sensitive to touch in that area..... (3)

4) Does your pain come on suddenly and in bursts for no apparent reason when you're still. Words like electric shocks, jumping and bursting describe these sensations.

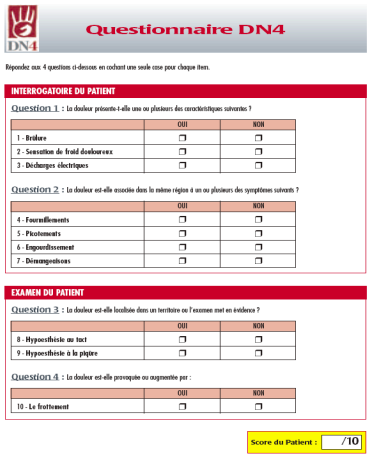
a) NO - My pain doesn't really feel like this ..... (0)
b) YES - I get these sensations quite a lot ..... (2)

5) Does your pain feel as if the skin temperature in the painful area has changed abnormally? Words like hot and burning describe these sensations

a) NO - I don't really get these sensations..... (0)
b) YES - I get these sensations quite a lot ..... (1)

Bennett et al Pain 2001

DN4



Questionnaire DN4

Répondez aux 4 questions ci-dessous en cochant une seule case pour chaque item.

INTERROGATOIRE DU PATIENT

Question 1 : La douleur présente-t-elle une ou plusieurs des caractéristiques suivantes ?

	OUI	NON
1 - Brûlure	❒	❒
2 - Sensation de froid douloureux	❒	❒
3 - Décharges électriques	❒	❒

Question 2 : La douleur est-elle associée dans la même région à un ou plusieurs des symptômes suivants ?

	OUI	NON
4 - Fourmillements	❒	❒
5 - Picotements	❒	❒
6 - Engourdissement	❒	❒
7 - Démangeaisons	❒	❒

EXAMEN DU PATIENT

Question 3 : La douleur est-elle localisée dans un territoire ou l'examen met en évidence ?

	OUI	NON
8 - Hypoesthésie au tact	❒	❒
9 - Hypoesthésie à la piqûre	❒	❒

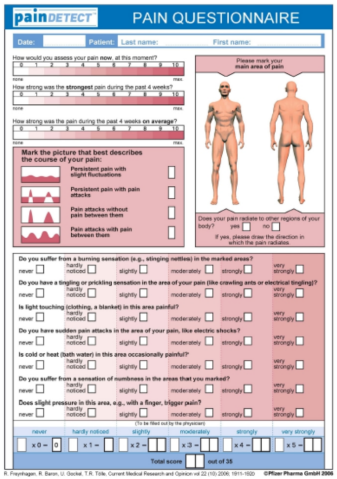
Question 4 : La douleur est-elle provoquée ou augmentée par :

	OUI	NON
10 - Le frottement	❒	❒

Score du Patient : /10

Bouhassira et al Pain 2005

PainDETECT



painDETECT PAIN QUESTIONNAIRE

Date: Patient: Last name: First name:

How would you assess your pain now, at this moment?
How strong was the strongest pain during the past 4 weeks?
How strong was the pain during the past 4 weeks on average?
none max.

Please mark your main area of pain

Mark the picture that best describes the course of your pain:
- Persistent pain with slight fluctuations
- Persistent pain with pain attacks
- Pain attacks without pain between them
- Pain attacks with pain between them

Does your pain radiate to other regions of your body? yes no
If yes, please draw the direction in which the pain radiates

Do you suffer from a burning sensation (e.g., stinging nettles) in the marked areas?
Do you have a tingling or prickling sensation in the area of your pain (like crawling ants or electrical tingling)?
Is light touching (clothing, a blanket) in this area painful?
Do you have sudden pain attacks in the area of your pain, like electric shocks?
Is cold or heat (bath water) in this area occasionally painful?
Do you suffer from a sensation of numbness in the areas that you marked?
Does slight pressure in this area, e.g., with a finger, trigger pain?
never | hardly noticed | slightly | moderately | strongly | very strongly

(To be filled out by the physician)
never | hardly noticed | slightly | moderately | strongly | very strongly
x 0 = 0 | x 1 = | x 2 = | x 3 = | x 4 = | x 5 =
Total score out of 35

R. Freynhagen, R. Baron, U. Gockel, T.R. Tölle, Current Medical Research and Opinion vol 22 (10) 2006: 1911-1920 ©Pfizer Pharma GmbH 2006

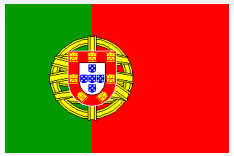
Freynhagen et al Curr Med Res Op 2006

et al Lancet Neurol 2018

DN4 : translations et revalidations in multiple languages


English


Spanish


Portughese


Dutch


Greek


Swedish


Turkish


Arabic


Farsi


Amharic


Hindi


Korean

Afrikaans for South Africa	Estonian for Estonia	Malayalam for India	Sotho for South Africa
Arabic for Israel	Filipino for the Philippines	Mandarin for China	Spanish for Argentina
Belarusian for Belarus	Finnish for Finland	Mandarin for Malaysia	Spanish for Chile
Bengali for India	French for Belgium	Mandarin for Singapore	Spanish for Colombia
Bulgarian for Bulgaria	French for Canada	Marathi for India	Spanish for Mexico
Cebuano for the Philippines	French for Switzerland	Norwegian for Norway	Spanish for Peru
Croatian for Croatia	Georgian for Georgia	Polish for Poland	Spanish for Puerto Rico
Czech for Czech Republic	German for Austria	Portuguese for Brazil	Spanish for Spain
Danish for Denmark	German for Germany	Portuguese for Portugal	Spanish for the USA
Dutch for Belgium (Flemish)	Greek for Greece	Punjabi for India	Swedish for Finland
Dutch for the Netherlands	Gujarati for India	Romanian for Romania	Swedish for Sweden
English for Australia	Hebrew for Israel	Russian for Belarus	Tamil for India
English for Canada	Hindi for India	Russian for Estonia	Tamil for Malaysia
English for India	Hungarian for Hungary	Russian for Israel	Telugu for India
English for Malaysia	Italian for Italy	Russian for Latvia	Thai for Thailand
English for New Zealand	Kannada for India	Russian for Lithuania	Turkish for Turkey
English for Singapore	Korean for Korea	Russian for Russia	Ukrainian for Ukraine
English for South Africa	Latvian for Latvia	Russian for Ukraine	Urdu for India
English for the Philippines	Lithuanian for Lithuania	Serbian for Serbia	Xhosa for South Africa
English for the UK	Malay for Malaysia	Slovak for Slovakia	Zulu for South Africa
English for the USA	Malay for Singapore	Slovenian for Slovenia	

t al Lancet Neurol 2018

EMA recommendations to establish patient populations (NP) in clinical trials

- Patients pain at baseline should be categorized according to relative contributions of nociceptive and neuropathic components

- Screening questionnaires (e.g. LANSS, PainDETECT, DN4) may help to identify patients with a neuropathic component

Medicines Agency, 15 december 2016

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Primary and secondary endpoints for pain clinical trials : the current situation

- In the large majority of clinical trials of pain, the primary endpoint is an unidimensional measure of self-reported **average pain intensity over the past 24 hours:**

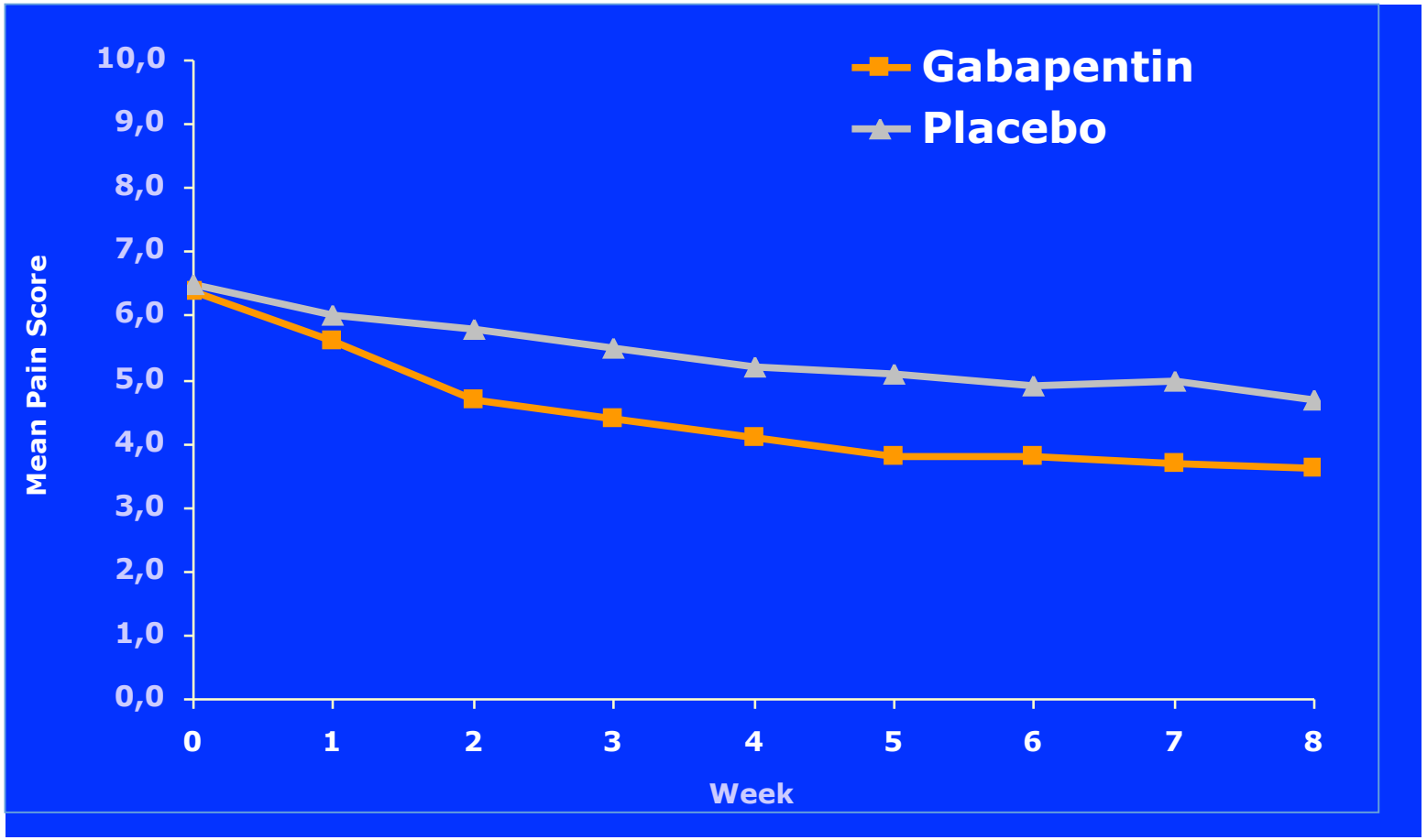
- Numerical Rating Scale for Pain Intensity (NRS-PI)
- VAS for pain intensity

- Secondary outcomes generally include :

- Additional unidimensional measures of pain intensity (e.g. pain intensity as its worst on NRS, categorical measures)
- Multidimensional questionnaires (e.g. MgGill Pain Questionnaires)
- Measure of pain relief (0-100 % pain relief)
- Measures of quality of life, sleep, psychological comorbidities, function
- Global measures of improvement : PGIC/CGIC

PACT RECOMMENDATIONS chaired by RH Dworkin since 2005

Example of a pivotal trial in neuropathic pain using NRS-PI as primary outcome



a et al JAMA 1998

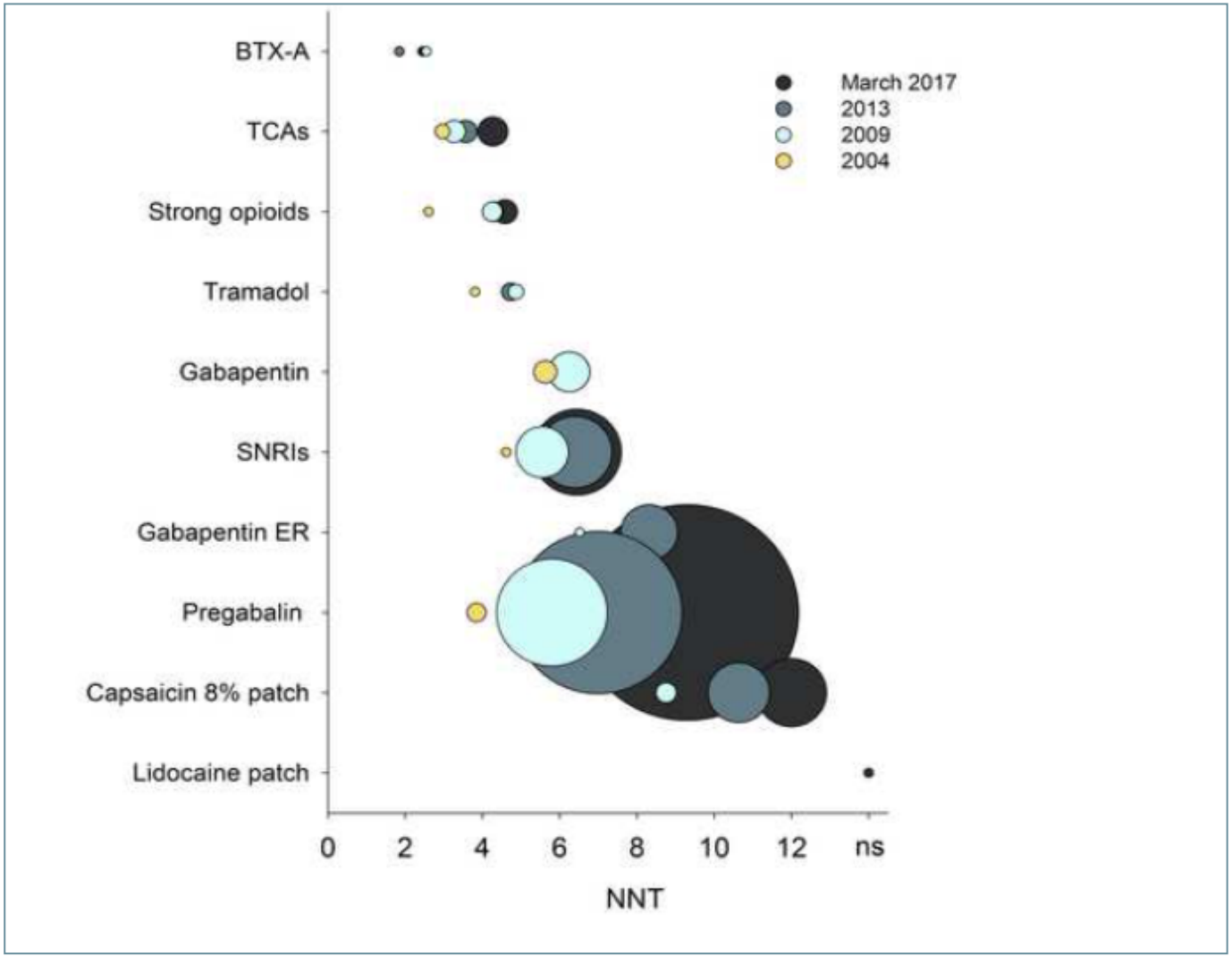
Recent meta-analysis based on Numbers Needed to Treat for 50 % pain relief in neuropathic pain

earch Paper

AIN

uropathic pain clinical trials: factors associated h decreases in estimated drug efficacy

B. Finnerup[a,b,*], Simon Haroutounian[c], Ralf Baron[d], Robert H. Dworkin[e,f,g], Ian Gilron[h], Maija Haanpaa[i], S. Jensen[a,b], Peter R. Kamerman[j,k], Ewan McNicol[l,m], Andrew Moore[n], Srinivasa N. Raja[o], . Andersen[p], Emily S. Sena[q], Blair H. Smith[r], Andrew S.C. Rice[s], Nadine Attal[t]



Heterogeneity of responses to therapy in neuropathic pain clinical trials

This has led multiple experts since 1998 (CJ Woolf) to recommend a « personalized » mechanism-based approach for the treatment of neuropathic pain


European Journal of Pain 15 (2011) 441–443

Contents lists available at ScienceDirect

European Journal of Pain

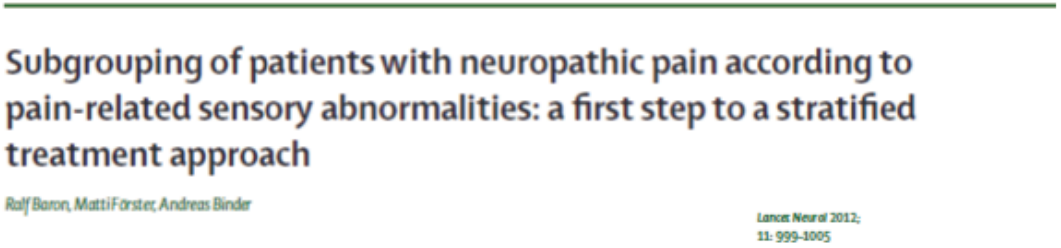
journal homepage: www.EuropeanJournalPain.com

ELSEVIER

Editorial

Assessing symptom profiles in neuropathic pain clinical trials: Can it improve outcome?

Attal, Bouhassira, Baron, Dostrovsky et al


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

Lancet Neurol 2012; 11: 999–1005


Reappraising neuropathic pain in humans —how symptoms help disclose mechanisms

Andrea Truini, Luis García-Larrea and Giorgio Cruccu

NATURE REVIEWS | NEUROLOGY VOLUME 9 | OCTOBER 2013

One underlying hypothesis is that self-reported symptoms are surrogates of mechanisms

Symptoms

Q1. Does your pain feel like burning?

No burning	0	1	2	3	4	5	6	7	8	9	10	Worst burning imaginable

Q2. Does your pain feel like squeezing?

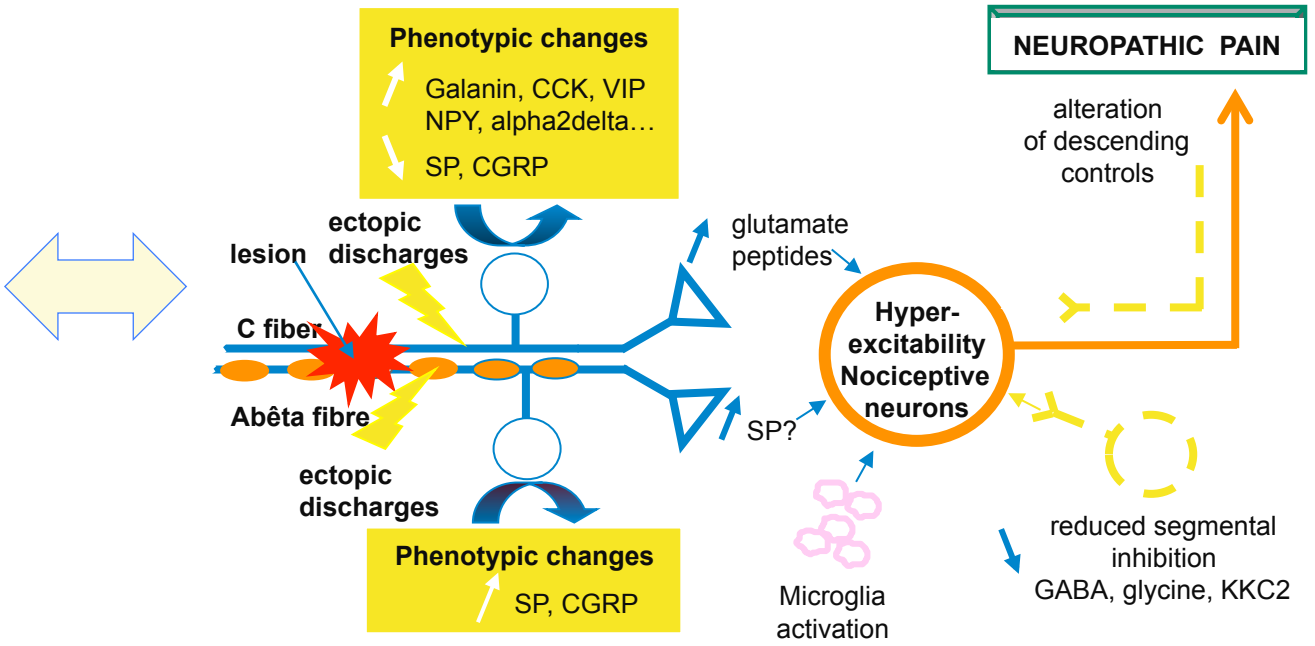
No squeezing	0	1	2	3	4	5	6	7	8	9	10	Worst squeezing imaginable

Q3. Does your pain feel like pressure?

No pressure	0	1	2	3	4	5	6	7	8	9	10	Worst pressure imaginable

Q4. *During the past 24 h*, your spontaneous pain has been present:
Select *the response* that best describes your case

Permanently	/_/
Between 8 and 12 h	/_/
Between 4 and 7 h	/_/
Between 1 and 3 h	/_/
Less than 1 h	/_/



et al Lancet Neurol 2018 ; Baron et al Lancet Neurol 2012 ; Attal and Bouhassira Pain 2019

One way to better assess sensory phenotypes in clinical trials is the use of multidimensional pain quality questionnaires

Neuropathic Pain Scale
(NPS)
Galer & Jensen, Neurology, 1997

Neuropathic Pain
Symptom Inventory
(NPSI)
Bouhassira et al, Pain 2004

SF McGill 2
Dworkin et al Pain 2009

Pain Quality Assessment Scale
Jensen et al J Pain 2006

l et al Lancet Neurol 2018

PAIN

Pain 108 (2004) 248–257

www.elsevier.com/locate/pain

ment and validation of the Neuropathic Pain Symptom Inventory

nassira[a,b,*], Nadine Attal[a,b], Jacques Fermanian[c], Haiel Alchaar[d], Michèle Gautron[a,b], nne Masquelier[e], Sylvie Rostaing[f], Michel Lanteri-Minet[d], Elisabeth Collin[g], Jacques Grisart[e], François Boureau[f]

ERM E-332, Centre d'Evaluation et de Traitement de la Douleur, Hôpital Ambroise Paré, Boulogne-Billancourt, France
[b]Université Versailles Saint-Quentin, Versailles, France
[c]Service de Biostatistique, Hôpital Necker, Paris, France
[d]Hôpital Pasteur, Nice, France
[e]Cliniques Universitaires Saint-Luc, Brussels, Belgium
[f]Hôpital Saint-Antoine, Paris, France

Afrikaans for South Africa	Finnish for Finland*	Malay for Singapore	Spanish for Chile*
Armenian for Armenia	French for Belgium*	Malayalam for India	Spanish for Colombia
Bengali for India*	French for Canada	Mandarin for Hong Kong	Spanish for Costa Rica
Bulgarian for Bulgaria*	French for Switzerland	Mandarin for Malaysia	Spanish for Mexico*
Chinese for Hong Kong	Georgian for Georgia*	Mandarin for Singapore	Spanish for Panama
Chinese for Malaysia	German for Austria*	Chinese for Taiwan	Spanish for Peru*
Chinese for Singapore	German for Germany*	Marathi for India	Spanish for Spain*
Chinese for Taiwan	German for Switzerland	Norwegian for Norway*	Spanish for Venezuela
Chinese for Taiwan	Greek for Greece	Polish for Poland*	Spanish for the USA
Croatian for Croatia*	Gujarati for India*	Portuguese for Brazil	Swedish for Finland
Czech for Czech Republic	Hindi for India	Portuguese for Portugal	Swedish for Sweden*
Danish for Denmark*	Hungarian for Hungary*	Punjabi for India	Tagalog for the Philippines
Dutch for Belgium (Flemish)*	Indonesian for Indonesia	Romanian for Romania*	Tamil for India
Dutch for the Netherlands*	Italian for Italy	Russian for Latvia	Telugu for India
English for Australia*	Japanese for Japan*	Russian for Russia	Thai for Thailand
English for Canada	Kannada for India	Russian for Ukraine	Turkish for Turkey
English for India*	Korean for Korea	Serbian for Serbia*	Ukrainian for Ukraine
English for South Africa	Latvian for Latvia	Slovak for Slovakia*	Urdu for India
English for the UK*	Lithuanian for Lithuania	Slovenian for Slovenia*	Urdu for Pakistan
English for the USA	Malay for Malaysia	Spanish for Argentina	

al Lancet Neurol 2018

What is the potential added value of pain quality questionnaires in clinical trials of neuropathic pain ?

- They may indicate selective effects of therapy on pain subtypes
- They may identify predictors of the response to therapy, which is one step towards individualized pain management

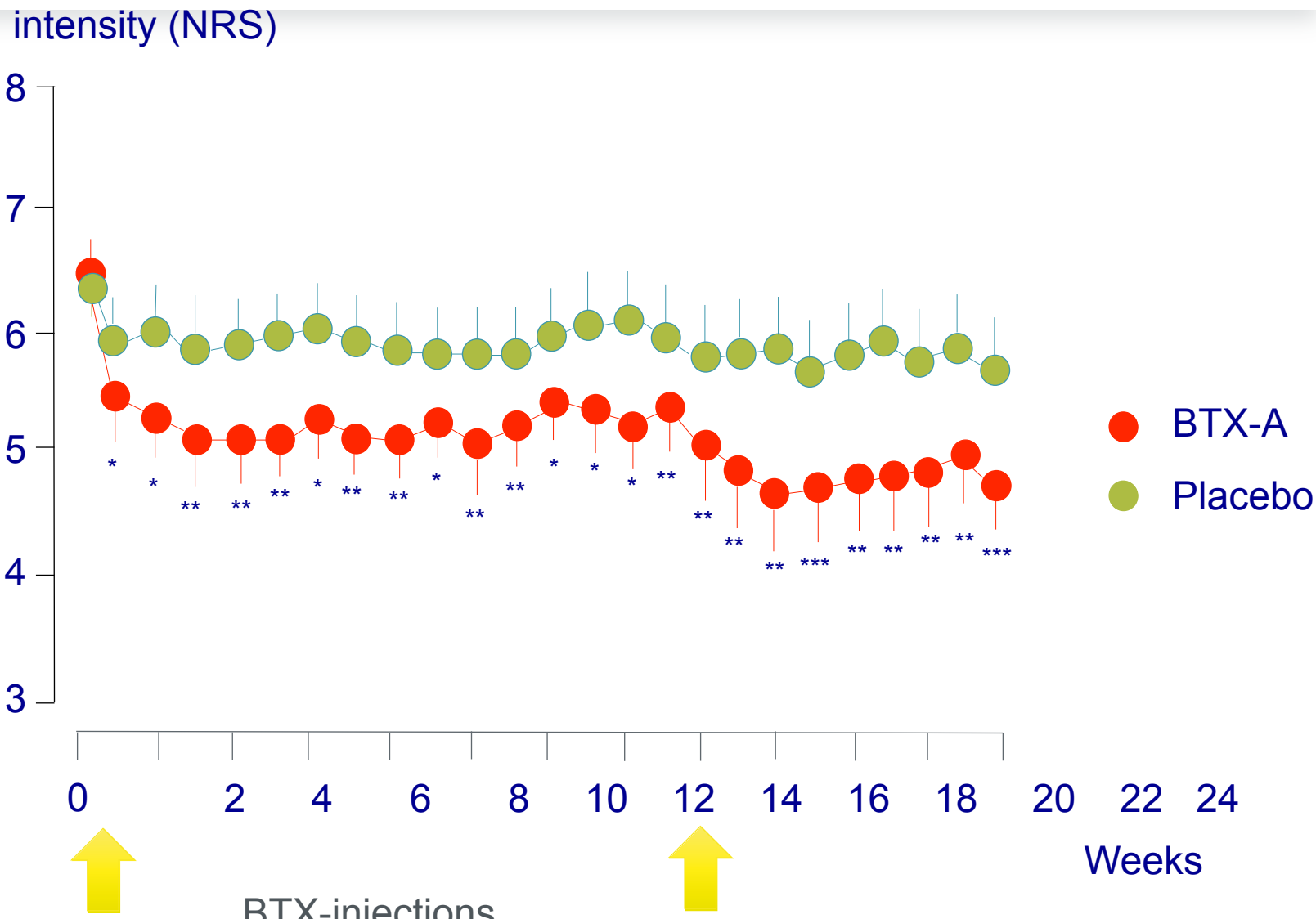
l et al Lancet Neurol 2018

The example of botulinum toxin A

icacy of repeated injections of botulinum
pheral neuropathic pain (BOTNEP):
double-blind, placebo-controlled trial

Frédéric Adam, Danièle Ranoux, Manoel J Teixeira, Ricardo Galhardoni, Irina Raicher, Nurcan Üçeyler,

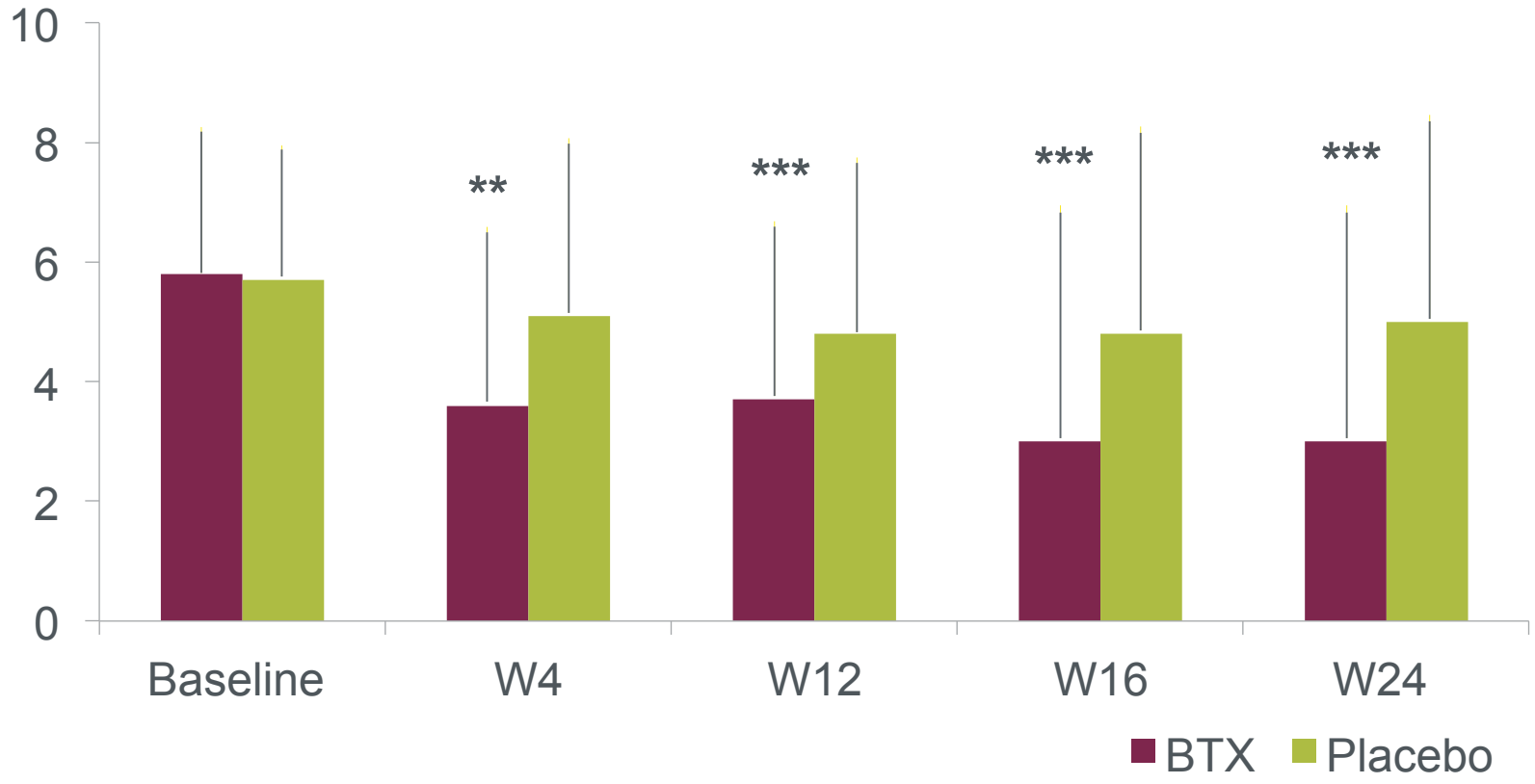
Lancet Neurol 2016



al Lancet Neurol 2016

Preferential effect on selective pain subtypes using the NPSI

NRS (0-10) **Robust effects of botulinum toxin A (BTX-A) on paroxysmal pain (NPSI)**



W = week

al Lancet Neurol 2016

Positive effects on pain subtypes in one negative clinical trial

PAIN® 154 (2013) 761–767

PAIN®

www.elsevier.com/locate/pain

zed, double-blind, placebo-controlled trial of a chemokine receptor 2 tagonist in posttraumatic neuralgia

mäki[a,*], Nadine Attal[b,c], Bror Jonzon[a], Flemming W. Bach[d], Karin Huizar[a]
fe[e], Britta Eriksson[a], Marcin Janecki[f], Andrei Danilov[g], Didier Bouhassira[b,c],
423 PTN Study Group

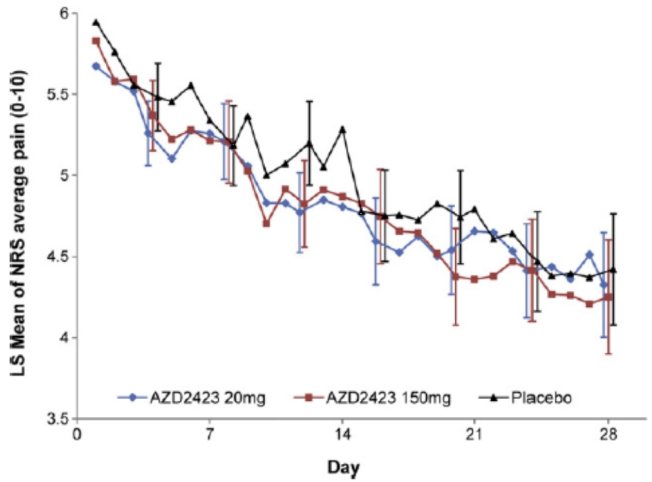


Fig. 3. Mean daily pain scores during treatment. LS means and 80% confidence intervals of daily NRS–Average Pain scores from days 1 to 28 in AZD2423 and placebo groups (mITT analysis set). Confidence intervals are shown every 4 days.

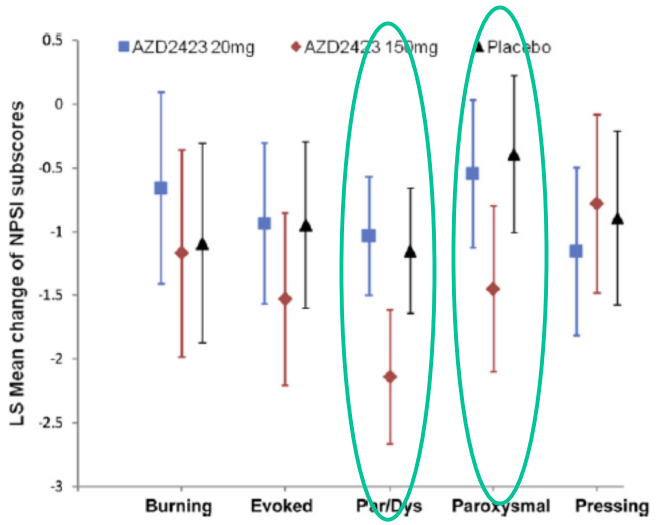


Fig. 4. Change in NPSI subscores from baseline to end of treatment. LS mean NPSI change and 80% confidence intervals from treatment day 1 to 29 in AZD2423 and placebo groups (mITT analysis set).

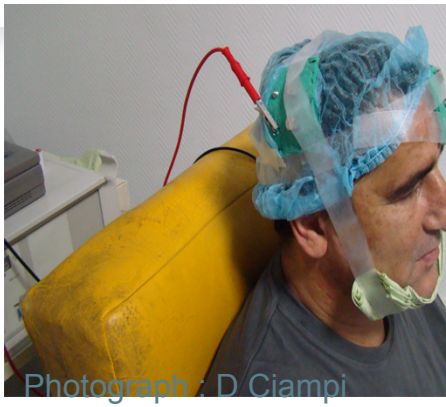
so Attal et al Lancet Neurol 2018 ; Edwards et al IMMPACT recommendations Pain 2016

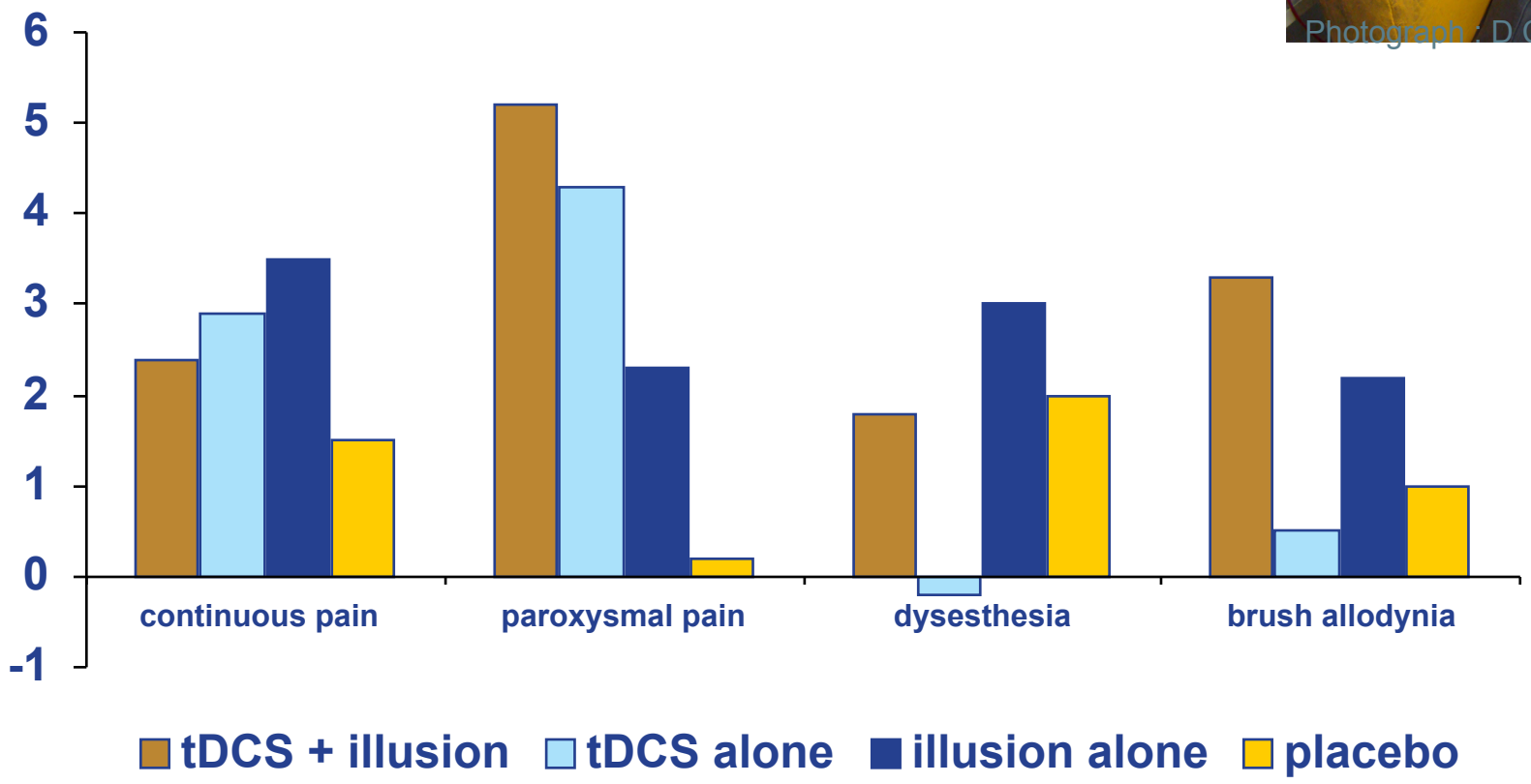
Effects of brain neurostimulation on selective pain symptoms

Brain 2010: 133: 2565–2577 | 2565

ness of transcranial direct current
on and visual illusion on neuropathic
pinal cord injury

ler,[1] Hatice Kumru,[1] Raul Pelayo,[1] Joan Vidal,[1] Josep Maria Tormos,[1]
avier Navarro[3] and Alvaro Pascual-Leone[1,2]





What is the potential added value of pain quality questionnaires in clinical trials of neuropathic pain ?

- They may indicate selective effects of therapy on pain subtypes
- **They may identify predictors of the response to therapy**

l et al Lancet Neurol 2018 ; Bouhassira et al Pain 2020, in press

Posthoc analyses of clinical trials based on the NPSI questionnaire suggest enhanced drug efficacy in patients with specific clinical phenotypes

Fulranumab for treatment of diabetic peripheral neuropathic pain
A randomized controlled trial

Safety and efficacy of repeated injections of botulinum toxin A in peripheral neuropathic pain (BOTNEP): a randomised, double-blind, placebo-controlled trial

Nadine Attal, Daniel C de Andrade, Frédéric Adam, Danièle Ranoux, Manoel J Teixeira, Ricardo Galhardoni, Irina Raicher, Nurcan Üçeyler, Claudia Sommer, Didier Bouhassira

Neuropathic pain phenotyping as a predictor of treatment response in painful diabetic neuropathy: Data from the randomized, double-blind, COMBO-DN study

Didier Bouhassira[a], Stefan Wilhelm[b,*], Alexander Schacht[c], Serge Perrot[d], Eva Kosek[e], Giorgio Cruccu[f], Rainer Freynhagen[g], Solomon Tesfaye[h], Alberto Lledó[i], Ernest Choy[j], Paolo Marchettini[k], Juan Antonio Micó[l], Michael Spaeth[m], Vladimir Skljarevski[n], Thomas Tölle[o]

Pain relief with lidocaine 5% patch in localized peripheral neuropathic pain in relation to pain phenotype: a randomised, double-blind, and placebo-controlled, phenotype panel study

Dyveke T. Demant[a], Karen Lund[b], Nanna B. Finnerup[b], Jan Vollert[c], Christoph Maier[c], Märtha S. Segerdahl[d,e], Troels S. Jensen[b], Søren H. Sindrup[a,*]

The Journal of Pain, Vol 18, No 1 (January), 2017: pp 42-53
Available online at www.jpain.org and www.sciencedirect.com

Capsaicin 8% Patch in Painful Diabetic Peripheral Neuropathy: A Randomized, Double-Blind, Placebo-Controlled Study

David M. Simpson,[*] Jessica Robinson-Papp,[*] Joanna Van,[†] Malcolm Stoker,[‡] Hélène Jacobs,[‡] Robert J. Snijder,[‡] Diederik S. Schregardus,[‡,§] Stephen K. Long,[‡,¶] Bruno Lambourg,[‖] and Nathaniel Katz[**,††]

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

Dyveke T. Demant[a], Karen Lund[b], Jan Vollert[c], Christoph Maier[c], Märtha Segerdahl[d,e], Nanna B. Finnerup[b], Troels S. Jensen[b], Søren H. Sindrup[a,*]

a et al Nat Dis. Primers 2017; Attal and Bouhassira Pain 2019; Bouhassira and Attal Neuroscience 2016

It should also be possible to predict the response to therapy on individual basis based on questionnaires

- A stratification algorithm based on the NPSI has recently been developed and validated
- It has shown good sensitivity to predict the response to the efficacy of some drugs (eg botulinum toxin A)
- It may be used in future clinical trials to predict the response to other therapy

sira, Banders, Attal et al Stratification of patients based on the neuropathic pain symptom inventory (NPSI) : development and validation of a orithm. Pain 2020, in press

Primary efficacy endpoints for NP clinical trials : the EMA recommendations

- Measurement with a unidimensional or multidimensional assessment questionnaire validated for the model
- Pain intensity is still the key measure of an analgesic drug and should always be reported
- The main shortcomings of the single item pain rating scales is that they do not cover the whole range of pain qualities
- Therefore multidimensional outcome measures are recommended to be used in addition and may reveal differential effects on treatments on different pain components

an Medicines Agency, 15 december 2016

IMI PAIN CARE : A European initiative

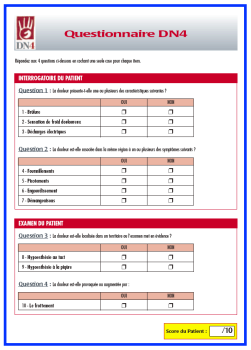
IMI-PainCare

Improving the care of patients suffering from acute or chronic pain

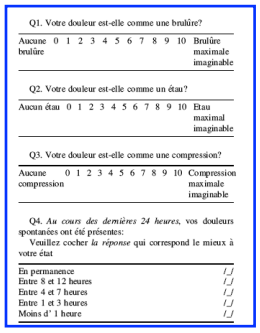
14 countries
40 participants

One goal is patient reported outcomes to improve management of chronic pain

DN4



NPSI



Bouhassira, Terkia Medkour, Marie Pechard,

Measures of global pain assessment should not be forgotten in clinical trials of NP

Two recent placebo controlled randomized clinical trials tend to suggest that PGIC might be more sensitive to treatment that pain intensity and quality in neuropathic pain

- TRANSNEP : « efficacy of rTMS of the motor or prefrontal cortex for neuropathic pain » (supported by PHRC, France) *(submitted)*
- PROTOTOP: « efficacy of nitrous oxide in neuropathic pain » (supported by Air Liquide, France) [1]

Bouhassira et al Safety and efficacy of an equimolar mixture of oxygen and nitrous oxide (EMONO): a randomized controlled al in patients with peripheral neuropathic pain. Pain. 2020 Oct 9.

Which primary endpoints for neuropathic pain in clinical trials ? Some personal suggestions for research

The choice of the **primary endpoint** should probably depend on the targeted mechanism of action of the treatment

- If the treatment has a very selective and narrow mechanism of action (for example Nav1.7 antagonist…), a multidimensional questionnaire might be preferred to a unidimensional NRS for pain intensity
- If the treatment is expected to have a broad effect on pain (for example psychotherapy, rTMS, antidepressants) a more global scale to assess pain or improvement might be preferred (e.g. NRS-PI, PGIC, % pain relief…)

Key messages

- Use of multiple efficacy endpoints for pain clinical trials in neuropathic pain seem mandatory
- The choice of the primary endpoint in neuropathic pain clinical trials might be based on the presumed mechanism of action of the treatment and the patient population
- The prospect of personalized pain medicine is a step forward torwards promising pain management strategies and should be increasingly implemented in exploratory clinical trials

Thank you for your attention