Baseline Pain Measurements as Predictors of the Placebo Response in Patients with Neuropathic Pain

Authors : *Samuel Branders, PhD; Fréderic Clermont, PhD; Chantal Gossuin, PharrmD; Dominique Demolle, PhD; Alvaro Pereira, PhD.*
Affiliations : *Tools4Patient SA, Gosselies, Belgium.*

Introduction

The characterization of the Individual Placebo Response (IPR) is an important challenge.

Baseline pain measurements are predictors of the placebo analgesia response.

What are their real impact on clinical trial results?

Methodology

88 Peripheral Neuropathic Pain (PNP) patients from two similar pain studies:

Randomized, patient-blind studies;
Placebo treatment b.i.d for 4 weeks as add-on therapy;
Placebo presented as new investigational drug named T4P1001.

Pain evaluation:

Average Pain score
Worst Pain score
Brief Pain Inventory (Severity and Interference)

Combined Pain score:

Scaled average of all baseline pain measurements.

Patients

Main inclusion criteria:

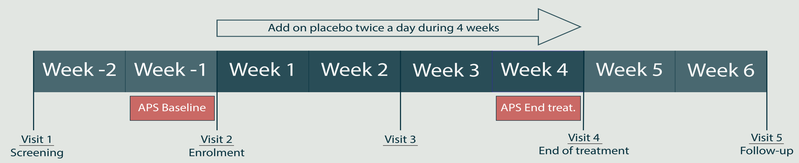
Chronic PNP diagnosed since at least 6 months (traumatic event, surgical procedure (excluding limb amputation), radiculopathy, post-herpetic or post-zoster neuralgia, diabetic polyneuropathy);

4≤ APS ≤8.

Main exclusion criteria:

Neuropathic pain due to trigeminal neuralgia, central pain, complex regional pain syndrome and phantom limb pain;
Patient changed his/her « regular therapy » in the last 4 months.

Study Design



Tables & Figures

Evolution of Average Pain Score (fig. 1)

Average Pain Score		Study 1 N=30	Study 2 N=58	All N=88
APS Week -1	Mean	5.28	5.45	5.39
APS Week 4	Mean	4.32	5.11	4.84
APS reduction	Mean	- 0.95	- 0.34	- 0.55
	[Min/Max]	[-5.43/1.14]	[-5.57/3.43]	[-5.57/3.43]
	P-Value	0.002**	0.166	0.005**

Correlation of Baseline Pain Measures (fig. 2)

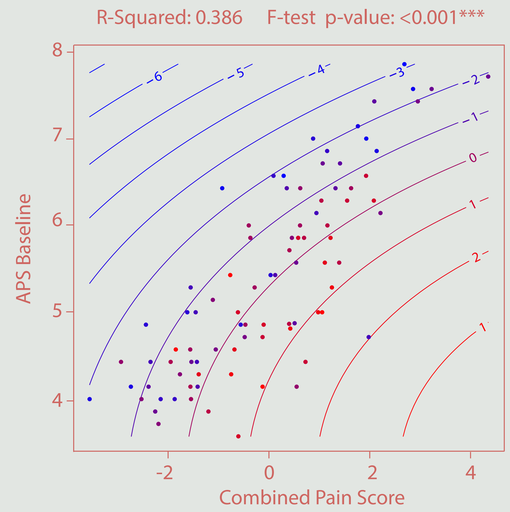
	WPS	BPI-Sever	BPI-Interf	Combined Pain Score
APS	66.3%***	58.1%***	32.9%**	81.2%***
WPS		67.4%***	42.8%***	87.6%***
BPI-Sever			48.3%***	86.1%***
BPI-Interf				65.9%***

p-value : *<0.05; **0.01; ***<0,001.

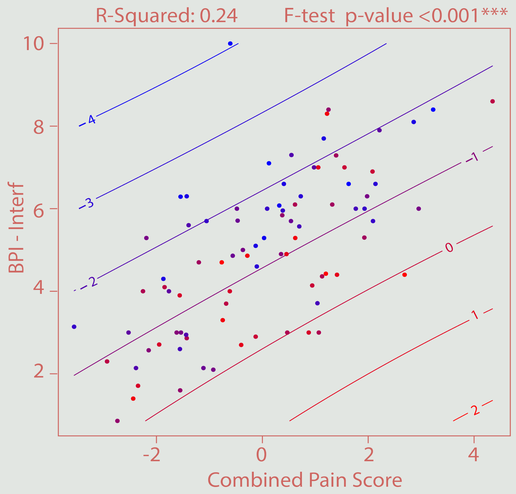
Correlation between Combined Pain Score and Placebo Response (fig. 3)

Placebo Response in change from baseline of	Combined Pain Score	
	Correlation	P-value
APS	3.5%	0.749
BPI-Sever	-1.2%	0.909
BPI-Interf	1.3%	0.907

(fig. 4a)



(fig. 4b)



Visualisation of the placebo response (Fig4a APS reduction, Fig4b BPI interference reduction) as a function of its corresponding baseline pain measure and combined pain score using Bayesian statistics (contour plot).
Each dot represents a patient with colour corresponding to its observed pain evolution (from blue for placebo-responders to red for non-responders).

Results & Conclusion

The average pain score decrease significantly after 4 weeks of placebo administration (fig. 1)

Baseline pain measures are correlated with each other (fig. 2);

Baseline pain measurements are correlated with the placebo response;

The combined pain score is correlated with all baseline pain ...(fig. 2)
... but is **not directly correlated with the placebo response** (fig.3).

The combined pain score can be used to identify overestimated baseline pain score(s).
This information may contribute to the placebo response prediction (fig. 4).