Do Environmental Parameters Influence the Prediction of the Placebo Response ?

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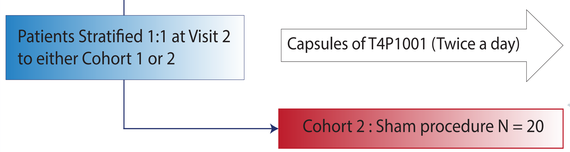
Introduction & Objectives

- It has been shown that the social environment and the investigator behavior might influence patient's response to a treatment. This mays contribute to the placebo effect observed in RCT's.
- To evaluate the influence of the conditions of drug administration on patient response to a treatment, we have conducted a single center, 4 weeks pain clinical trial in peripheral neuropathic patients (PNP), receiving placebo as add-on therapy, and have compared the decrease of APS observed following diferent contexts of administration.

Methods

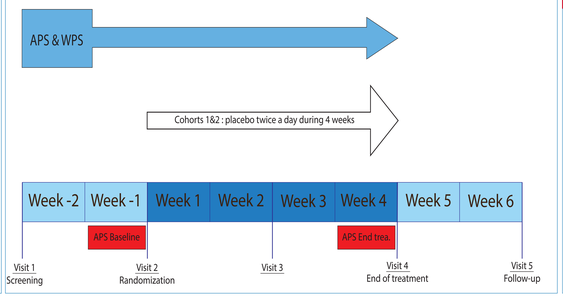
- **Single centre, randomized patient-blind study**
  - Placebo treatment b.i.d for 4 weeks as add-on therapy;
  - Placebo presented as new investigational drug named T4P1001.
- **Patients main criteria for inclusion**:
  - Chronic PNP diagnosed since at least 6 months (traumatic event, surgical procedure (excluding limb amputation), radiculopathy, post-herpetic or post-zoster neuralgia, diabetic polyneuropathy);
  - Males or females; at least 18 years of age;
  - Body weight greater than 40 kg and less than 120 kg; BMI between 19-31 kg/m^2 inclusive;
  - DN4 score ≥ 4.
- **41 patients randomized and stratified (based on personality traits) into 2 arms :**
  - Placebo-reinforcing or;
  - Sham procedure.
- **Investigator was blind to Re-inforcement/Sham procedure**
- **Patients main criteria for exclusion**:
  - 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.
- **Psychological and Pain Evaluations**
  - Big Five Inventory questionnaire, NEO Personality Inventory Revised, Belief in a Just World, Revised Life Orientation Test, Multidimensional Iowa Suggestibility Scale, Multidimentional Health Locus of Control Scale, Hospital Anxiety and Depression Scale, Expectation questionnaire, Pain Compliance Questionnaire, Average Pain Score, Worst Pain Score, Brief Pain Inventory short form, Investigator Global Assessment of Changes, Patient Global Assessment of Changes, DN4 questionnaire.

Treatment Arms

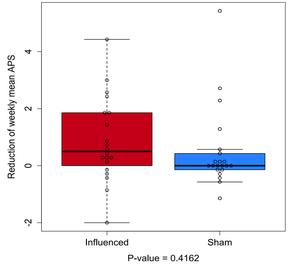


- Positive social observational learning :
  Video with emphasis on **positive information about investigational drug**. Complete heat pain procedure/test demonstrated.
- Pain conditioning :
  Visits 2 and 3 : 1 hour post study drug administration with ***lower heat pain stimuli*** compared to the baseline one.
  Visit 4 : same stimuli as at baseline.
- Sham procedure :
  Neutral social observational learning : video with neutral information on investigational drug and ***partial*** heat pain procedure demonstrated.
  All heat pain stimuli were the same (baseline and post treatment).

Neuropathic Patient Study Design



Difference Between Re-Inforced and Sham Group Placebo Response



APS Endpoints		Placebo Responder	Placebo Non-Responder	All
N		12 (29.3%)	29 (70.7%)	41 (100%)
APS Week -1		5.2	5.3	5.3
APS Week 4		2.7	5.4	4.6
Reduction	Mean	-48.2%	1.3%	-13.2%
	P-Value	<0.001	0.487	0.003

Placebo Responder arbitrary defined as patient having 20% APS Reduction

APS Endpoints		Re-inforced	Sham	All
N		20 (48.8%)	21 (51.2%)	41 (100%)
APS Week -1		5.2	5.4	5.3
APS Week 4		4.3	4.9	4.6
Reduction	Mean	-0.9	-0.5	-0.7
	P-Value	0.0167	0.127	0.00469

P-Value : 0.4162

Conclusion

- APS decreased by more than 20% in about 30% of the patients.
- No statistical difference between the Sham and Placebo re-inforced group suggesting that :
  The effect of context administration on placebo response was not significant and seemed marginal compared to the individual variations.
- Those results advocate for a better characterization of the individual placebo response in clinical trials :
  Such stratification could help to prevent distribution heterogeneity of «high placebo responders».

Disclosure

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

Dominique Demolle : Employee, Shareholder - Tools4Patient
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