Trial record **1 of 1** for: F1J-EW-HMGQ

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A Study in Painful Diabetic Neuropathy (COMBO-DN)

ClinicalTrials.gov Identifier: NCT01089556

Recruitment Status : Completed
First Posted : March 18, 2010
Results First Posted : December 4, 2012
Last Update Posted : January 24, 2013

Sponsor:
Eli Lilly and Company

Collaborator:
Boehringer Ingelheim

Information provided by (Responsible Party):
Eli Lilly and Company

Study Details | Tabular View | Study Results | Disclaimer

How to Read a Study Record

Study Type:	Interventional

Study Design:	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Diabetic Neuropathy, Painful
Interventions:	Drug: Duloxetine Drug: Pregabalin Drug: Placebo

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
The study consisted of 4 study periods (SP): 2 weeks screening and washout (SP I), 8 weeks initial treatment (SP II), 8 weeks intensive treatment (SP III), 2 weeks tapering (SP IV). Participants who did not achieve good pain control during SP II (<30% improvement) were considered non-responders and continued in the study and entered SP III.

Reporting Groups

	Description
Duloxetine (SP II)	Duloxetine 30 milligram (mg) daily for Week 1 and 60 mg daily for Weeks 2-8 in Study Period II (SP II).
Pregabalin (SP II)	Pregabalin 150 mg daily for Week 1 and 300 mg daily for Weeks 2-8 in Study Period II.
Duloxetine (SP III)	Duloxetine 90 mg daily for Week 9 and 120 mg daily for Weeks 10-16 in Study Period III (SP III).

DLX + PGB (SP III)	Duloxetine (DLX) 60 mg plus Pregabalin (PGB) 150 mg daily for Week 9 and Duloxetine 60 mg plus Pregabalin 300 mg daily for Weeks 10-16 in Study Period III.
PGB + DLX (SP III)	Pregabalin (PGB) 300 mg plus Duloxetine (DLX) 30 mg daily for Week 9 and Pregabalin 300 mg plus Duloxetine 60 mg daily for Weeks 10-16 in Study Period III.
Pregabalin (SP III)	Pregabalin 450 mg daily for Week 9 and Pregabalin 600 mg daily for Weeks 10-16 in Study Period III.

Participant Flow for 2 periods

Period 1: Study Period II (Weeks 1-8)

	Duloxetine (SP II)	Pregabalin (SP II)	Duloxetine (SP III)	DLX + PGB (SP III)	PGB + DLX (SP III)	Pregabalin (SP III)
STARTED	404	407	0	0	0	0
Safety Population	401 [1]	403 [1]	0	0	0	0
Non-responders Who Completed SPII	158	205	0	0	0	0
COMPLETED	333	333	0	0	0	0
NOT COMPLETED	71	74	0	0	0	0
Adverse Event	35	39	0	0	0	0
Entry Criteria Not Met	12	8	0	0	0	0
Lack of Efficacy	1	2	0	0	0	0
Lost to Follow-up	0	3	0	0	0	0
Physician Decision	4	0	0	0	0	0

Protocol Violation	4	4	0	0	0	0
Withdrawal by Subject	12	14	0	0	0	0
Not received any study drug	3	4	0	0	0	0

[1] Received at least 1 dose of study drug.

Period 2: Study Period III (Weeks 9-16)

	Duloxetine (SP II)	Pregabalin (SP II)	Duloxetine (SP III)	DLX + PGB (SP III)	PGB + DLX (SP III)	Pregabalin (SP III)
STARTED	0	0	74 [1]	75 [2]	95 [1]	99 [3]
Efficacy and Safety Population	0	0	73 [4]	75 [4]	94 [4]	97 [4]
COMPLETED	0	0	60	66	83	92
NOT COMPLETED	0	0	14	9	12	7
Adverse Event	0	0	4	2	4	3
Entry Criteria Not Met	0	0	1	1	1	1
Lack of Efficacy	0	0	0	2	1	0
Lost to Follow-up	0	0	1	0	0	0
Protocol Violation	0	0	1	1	1	0
Satisfactory Response	0	0	4	3	4	1
Withdrawal by Subject	0	0	3	0	1	2

[1] Of those who completed SPII, 10 non-responders did not enter SPIII, while 4 responders entered SPIII

[2] Of those who completed SPII, 6 non-responders did not enter SPIII, while 3 responders entered SPIII

[3] Of those who completed SPII, 6 non-responders did not enter SPIII, while 1 responders entered SPIII

[4] Received ≥1 dose study drug, had Week 8 and at least 1 assessment during Weeks 9-16 (SPIII)

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Duloxetine	Duloxetine 30 milligram (mg) daily for Week 1 and 60 mg daily for Weeks 2-8 in Study Period II.
Pregabalin	Pregabalin 150 mg daily for Week 1 and 300 mg daily for Weeks 2-8 in Study Period II.
Total	Total of all reporting groups

Baseline Measures

	Duloxetine	**Pregabalin**	**Total**
Overall Participants Analyzed [Units: Participants]	**401**	**403**	**804**
	61.5 (10.62)	**61.9 (10.95)**	**61.7 (10.78)**

Age [Units: Years] Mean (Standard Deviation)			
Gender [Units: Participants]			
Female	**182**	**174**	**356**
Male	**219**	**229**	**448**
Race (NIH/OMB) [Units: Participants]			
American Indian or Alaska Native	**37**	**36**	**73**
Asian	**34**	**34**	**68**
Native Hawaiian or Other Pacific Islander	**1**	**0**	**1**
Black or African American	**2**	**2**	**4**
White	**324**	**328**	**652**
More than one race	**0**	**0**	**0**
Unknown or Not Reported	**3**	**3**	**6**
Region of Enrollment [Units: Participants]			
Greece	**16**	**12**	**28**
Spain	**6**	**8**	**14**
Turkey	**5**	**7**	**12**
United Kingdom	**31**	**31**	**62**
Italy	**16**	**18**	**34**
France	**22**	**24**	**46**
Mexico	**75**	**71**	**146**
Canada	**19**	**19**	**38**
Poland	**56**	**57**	**113**
Croatia	**27**	**29**	**56**
Australia	**27**	**22**	**49**
Netherlands	**5**	**4**	**9**

Germany	**52**	**54**	**106**
Korea, Republic of	**31**	**32**	**63**
Sweden	**13**	**15**	**28**
Clinical Global Impressions of Severity Scale (CGI-S) [1] [Units: Units on a scale] Mean (Standard Deviation)	**4.0 (1.07)**	**4.0 (1.09)**	**4.0 (1.08)**

[1] The clinician recorded how ill the participant was at the time of assessment, in relation to the clinician's total experience with this participant population. Scores range from 1 (normal, not at all ill) to 7 (among the most extremely ill participants). One participant in Duloxetine group and 2 participants in Pregabalin group had missing data and were not included in the calculation of mean and standard deviation (SD).

Patient Global Impressions of Severity Scale (PGI-S) [1] [Units: Units on a scale] Mean (Standard Deviation)	**3.4 (1.42)**	**3.4 (1.41)**	**3.4 (1.42)**

[1] Measures participant's perception of severity of illness at the time of assessment. Scores range from 1 (normal, not at all ill) to 7 (extremely ill).

Brief Pain Inventory (BPI) Severity: Average Pain Score [1] [Units: Units on a scale] Mean (Standard Deviation)	**6.0 (1.55)**	**6.0 (1.57)**	**6.0 (1.56)**

[1] A self-reported scale that measures the severity of pain based on the average pain experienced over the past 24-hours. The severity scores range from 0 (no pain) to 10 (pain as severe as you can imagine). Two participants in Pregabalin group had missing data and were not included in the calculation of mean and SD.

Neuropathic Pain Symptom Inventory (NPSI) [1] [Units: Units on a scale] Mean (Standard Deviation)	**47.3 (19.16)**	**47.7 (20.46)**	**47.5 (19.81)**

[1] The NPSI is a 12-item self-administered questionnaire to assess 5 different dimensions of neuropathic pain: superficial spontaneous burning pain, deep spontaneous pressing pain, paroxysmal pain, evoked pains, and paresthesias/dysesthesias. Questionnaire generates a

score in each of the relevant dimensions and a total score of 0-100. Higher score indicates a greater intensity of pain. Two participants in Duloxetine group and 6 participants in Pregabalin group had missing data and were not included in the calculation of mean and SD.

Hospital Anxiety and Depression Scale (HADS) - Anxiety Subscale Score [1] [Units: Units on a scale] Mean (Standard Deviation)	**6.8 (4.31)**	**6.6 (4.32)**	**6.7 (4.31)**

[1] A 14-item questionnaire with 2 subscales: anxiety and depression. Each item is rated on a 4-point scale (0-3), giving maximum scores of 21 for anxiety and for depression. Scores of 11 or more on either subscale are considered to be a significant case of psychological morbidity, while scores of 8-10 represent 'borderline' and 0-7, 'normal.' Three participants in both Duloxetine group and Pregabalin group had missing data and were not included in the calculation of mean and SD.

Hospital Anxiety and Depression Scale (HADS) - Depression Subscale Score [1] [Units: Units on a scale] Mean (Standard Deviation)	**5.5 (4.19)**	**5.5 (3.88)**	**5.5 (4.04)**

[1] A 14-item questionnaire with 2 subscales: anxiety and depression. Each item is rated on a 4-point scale (0-3), giving maximum scores of 21 for anxiety and for depression. Scores of 11 or more on either subscale are considered to be a significant case of psychological morbidity, while scores of 8-10 represent 'borderline' and 0-7, 'normal.' Two participants in Duloxetine group and 1 participant in Pregabalin group had missing data and were not included in the calculation of mean and SD.

Sheehan Disability Scale (SDS) [1] [Units: Units on a scale] Mean (Standard Deviation)	**13.3 (7.47)**	**13.3 (7.59)**	**13.3 (7.52)**

[1] The SDS is completed by the participants and is used to assess the effect of their symptoms on work (Item 1), social (Item 2) and family life (Item 3). Each item is measured on a 0 (not at all) to 10 (extremely) point scale with higher values indicating greater disruption. Total scores is the sum of the 3 items and range from 0-30 with higher values indicating greater disruption in the participant's work/social/family life. There were 118 participants in

Duloxetine group and 128 participants in Pregabalin group who had missing data and were not included in the calculation of mean and SD.

Average number of hours worked for pay per week [1] [Units: Hours] Mean (Standard Deviation)	**39.5 (20.33)**	**41.4 (16.36)**	**40.4 (18.47)**

[1] Data presented are average number of hours worked for pay per week during last 8 weeks prior to entering Study Period II. There were 275 participants in Duloxetine group and 281 participants in Pregabalin group who had missing data and were not included in the calculation of mean and SD.

Number of days of work/school missed [1] [Units: Days] Mean (Standard Deviation)	**2.3 (7.98)**	**1.3 (4.69)**	**1.8 (6.56)**

[1] Data presented are the number of days of work/school missed due to diabetic peripheral neuropathic pain (DPNP) during the last 8 weeks prior to entering Study Period II. There were 278 participants in Duloxetine group and 281 participants in Pregabalin group who had missing data and were not included in the calculation of mean and SD.

Number of days hospitalized [1] [Units: Days] Mean (Standard Deviation)	**0.0 (0.45)**	**0.1 (0.67)**	**0.1 (0.57)**

[1] Data presented are the number of days hospitalized due to DPNP during the last 8 weeks prior to entering Study Period II. There were 21 participants in Duloxetine group and 23 participants in Pregabalin group who had missing data and were not included in the calculation of mean and SD.

Blood pressure (BP) [1] [Units: Millimeter of mercury (mm Hg)] Mean (Standard Deviation)			
Systolic BP	**135.0 (16.27)**	**134.3 (15.62)**	**134.7 (15.94)**
Diastolic BP	**77.6 (10.04)**	**76.7 (9.43)**	**77.1 (9.74)**

[1] One participant in both Duloxetine group and Pregabalin group had missing data and were not included in the calculation of mean and SD.

Pulse rate [1] [Units: Beats per minute (bpm)] Mean (Standard Deviation)	**76.0 (10.81)**	**75.6 (11.05)**	**75.8 (10.92)**

[1] Three participants in Duloxetine group and 1 participant in Pregabalin group had missing data and were not included in the calculation of mean and SD.

Outcome Measures

Show All Outcome Measures

1. **Primary: Change From Week 8 to Week 16 Endpoint in 24 Hour Average Pain Item Score on the Brief Pain Inventory (BPI) Modified Short Form [Time Frame: Week 8, Week 16]**

   Show Outcome Measure 1

2. **Secondary: Mean Change From Week 8 to Week 16 Endpoint in Items of the Brief Pain Inventory (BPI) Modified Short Form Worst Pain Score [Time Frame: Week 8, Week 16]**

   Show Outcome Measure 2

3. **Secondary: Percentage of Participants With a Reduction of Greater Than or Equal to 30% on Brief Pain Inventory (BPI) Modified Short Form 24-Hour Average Pain Item Score at Week 16 Endpoint [Time Frame: Week 8 through Week 16]**

   Show Outcome Measure 3

4. **Secondary: Percentage of Participants With a Reduction of Greater Than or Equal to 50% on Brief Pain Inventory (BPI) Modified Short Form 24-Hour Average Pain Item Score at Week 16 Endpoint [Time Frame: Week 8 through Week 16]**

   Show Outcome Measure 4

5. **Secondary: Percentage of Participants With a Decrease of Greater Than or Equal to 2 Points on Brief Pain Inventory (BPI) Modified Short Form 24-Hour Average**

Pain Item Score at Week 16 Endpoint [Time Frame: Week 8 through Week 16]

Show Outcome Measure 5

6. **Secondary: Clinical Global Impression of Improvement (CGI-I) at Week 16 Endpoint [Time Frame: Week 16]**

Show Outcome Measure 6

7. **Secondary: Mean Change From Week 8 to Week 16 Endpoint on the Neuropathic Pain Symptom Inventory (NPSI) Questionnaire [Time Frame: Week 8, Week 16]**

Show Outcome Measure 7

8. **Secondary: Mean Change From Week 8 to Week 16 Endpoint in Sheehan Disability Scale (SDS) [Time Frame: Week 8, Week 16]**

Show Outcome Measure 8

9. **Secondary: Mean Change From Week 8 to Week 16 Endpoint in Hospital Anxiety and Depression Scale (HADS) [Time Frame: Week 8, Week 16]**

Show Outcome Measure 9

10. **Secondary: Resource Utilization (Number of Days Hospitalized, Number of Days of Sick Leave) Week 8 Through Week 16 [Time Frame: Week 8 through Week 16]**

Show Outcome Measure 10

11. **Secondary: Patient Global Impression of Improvement (PGI-I) Score at Week 16 Endpoint [Time Frame: Week 16]**

Show Outcome Measure 11

12. **Secondary: Mean Change in Blood Pressure (BP) From Week 8 to Week 16 Endpoint [Time Frame: Week 8, Week 16]**

Show Outcome Measure 12

13. **Secondary: Mean Change in Heart Rate From Week 8 to Week 16 Endpoint [Time Frame: Week 8, Week 16]**

Show Outcome Measure 13

14. Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) Between Week 8 and Week 16 Endpoint [Time Frame: Week 8 through Week 16]

Show Outcome Measure 14

15. Secondary: Number of Participants Who Discontinued From Study Between Week 8 and Week 16 Endpoint [Time Frame: Week 8 through Week 16]

Show Outcome Measure 15

16. Other Pre-specified: Mean Change From Baseline to Week 8 Endpoint in 24 Hour Average Pain Item Score on the Brief Pain Inventory (BPI) Modified Short Form [Time Frame: Baseline, Week 8]

Show Outcome Measure 16

17. Other Pre-specified: Percentage of Participants With a Reduction of Greater Than or Equal to 30% on Brief Pain Inventory (BPI) Modified Short Form 24-Hour Average Pain Item Score at Week 8 Endpoint [Time Frame: Baseline through Week 8]

Show Outcome Measure 17

18. Other Pre-specified: Percentage of Participants With a Reduction of Greater Than or Equal to 50% on Brief Pain Inventory (BPI) Modified Short Form 24-Hour Average Pain Item Score at Week 8 Endpoint [Time Frame: Baseline through Week 8]

Show Outcome Measure 18

19. Other Pre-specified: Percentage of Participants With a Decrease of Greater Than or Equal to 2 Points on Brief Pain Inventory (BPI) Modified Short Form 24-Hour Average Pain Item Score at Week 8 Endpoint [Time Frame: Baseline through Week 8]

Show Outcome Measure 19

20. Other Pre-specified: Clinical Global Impression of Improvement (CGI-I) at Week 8 Endpoint [Time Frame: Week 8]

Show Outcome Measure 20

21. **Other Pre-specified: Mean Change From Baseline to Week 8 Endpoint on the Neuropathic Pain Symptom Inventory (NPSI) Questionnaire [Time Frame: Baseline, Week 8]**

Show Outcome Measure 21

22. **Other Pre-specified: Mean Change From Baseline to Week 8 Endpoint in Sheehan Disability Scale (SDS) [Time Frame: Baseline, Week 8]**

Show Outcome Measure 22

23. **Other Pre-specified: Mean Change From Baseline to Week 8 Endpoint in Hospital Anxiety and Depression Scale (HADS) [Time Frame: Baseline, Week 8]**

Show Outcome Measure 23

24. **Other Pre-specified: Resource Utilization (Number of Days Hospitalized, Number of Days of Sick Leave) Baseline Through Week 8 [Time Frame: Baseline through Week 8]**

Show Outcome Measure 24

25. **Other Pre-specified: Average Number of Hours Worked for Pay Per Week Baseline Through Week 8 [Time Frame: Baseline through Week 8]**

Show Outcome Measure 25

26. **Other Pre-specified: Average Number of Hours Worked for Pay Per Week Week 8 Through Week 16 [Time Frame: Week 8 through Week 16]**

Show Outcome Measure 26

27. **Other Pre-specified: Patient Global Impression of Improvement (PGI-I) Score at Week 8 Endpoint [Time Frame: Week 8]**

Show Outcome Measure 27

28. **Other Pre-specified: Mean Change in Blood Pressure (BP) From Baseline to Week 8 Endpoint [Time Frame: Baseline, Week 8]**

Show Outcome Measure 28

29. Other Pre-specified: Mean Change in Heart Rate From Baseline to Week 8 Endpoint [Time Frame: Baseline, Week 8]

Show Outcome Measure 29

30. Other Pre-specified: Number of Participants With Treatment Emergent Adverse Events (TEAE) Between Baseline and Week 8 Endpoint [Time Frame: Baseline through Week 8]

Show Outcome Measure 30

31. Other Pre-specified: Number of Participants Who Discontinued From Study Between Baseline and Week 8 Endpoint [Time Frame: Baseline through Week 8]

Show Outcome Measure 31

Serious Adverse Events

Show Serious Adverse Events

Other Adverse Events

Show Other Adverse Events

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☑ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Results Point of Contact:

Name/Title: Chief Medical Officer
Organization: Eli Lilly and Company
phone: 800-545-5979

Responsible Party:	Eli Lilly and Company
ClinicalTrials.gov Identifier:	NCT01089556 History of Changes
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