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An Efficacy and Safety Study to Compare Fentanyl Ionsys and Routine Care With Intravenous (IV) Morphine Patient-controlled Analgesia (PCA) in Participants Who Have Undergone Elective Major Abdominal or Orthopedic Surgery

This study has been terminated.
(Product class one recall)

Sponsor:
Janssen-Cilag Ltd.

Information provided by (Responsible Party):
Janssen-Cilag Ltd.

ClinicalTrials.gov Identifier:
NCT00766506

First received: October 3, 2008
Last updated: March 14, 2013
Last verified: March 2013
History of Changes

Results First Received: January 21, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Pain, Postoperative
Interventions:	Device: Fentanyl IONSYS Device: Morphine IV PCA

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
No text entered.

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS [a device which uses an electric current to move drug through the skin into the blood]), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Participant Flow: Overall Study

	Fentanyl IONSYS	Morphine IV PCA
STARTED	**58**	**50**
COMPLETED	**53**	**48**

NOT COMPLETED	**5**	**2**
Use rescue medication after 3 hours	**3**	**0**
Unspecified	**2**	**2**

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
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.
Total	Total of all reporting groups

Baseline Measures

	Fentanyl IONSYS	Morphine IV PCA	Total
Overall Participants [units: participants]	**58**	**50**	**108**
Age [units: Years] Mean (Standard Deviation)	**58.4 (12.1)**	**58.9 (11.8)**	**58.7 (11.9)**
Gender [units: Participants]			
Female	**33**	**33**	**66**
Male	**25**	**17**	**42**

Outcome Measures

Hide All Outcome Measures

1. Primary: Participant's Evaluation of Mean Ability to Mobilize After Surgery [Time Frame: Hour 72 or early study withdrawal]

Measure Type	Primary
Measure Title	Participant's Evaluation of Mean Ability to Mobilize After Surgery
Measure Description	The ability to mobilize was assessed through a combined analysis of participant's responses to the following 3 questions: 1-Because of the system/device, I had to be careful when I used my hands; 2-The system/device made it difficult for me to adjust my position in bed; 3-The system/device interfered with my ability to get out of bed and walk around. All 3 items were scored on a 6-point Likert scale, ranging from "not at all" (score 0) to "a very great deal" (score 5). Total ability to mobilize was assessed as average of 3 scores which range from 0 (best mobility) to 5 (worst mobility).
Time Frame	Hour 72 or early study withdrawal
Safety Issue	No

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.
The intention-to-treat (ITT) population included all participants randomly assigned to study treatment and used the study medication at least

once, and who had at least 1 efficacy measure after system application or device enablement (0 hours).

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Measured Values

	Fentanyl IONSYS	Morphine IV PCA
Overall Participants [units: participants]	**58**	**50**
Participant's Evaluation of Mean Ability to Mobilize After Surgery [units: Units on scale] Mean (Standard Deviation)	**0.02 (0.101)**	**2.26 (1.146)**

Statistical Analysis 1 for Participant's Evaluation of Mean Ability to Mobilize After Surgery

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	<0.001
Least square mean difference [4]	-2.23
95% Confidence Interval	-2.55 to -1.91

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	P-value was calculated from analysis of covariance (ANCOVA), with centre, surgery type and treatment included as covariates in the analysis.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	Least square mean difference = Least square mean value for Fentanyl IONSYS group minus Least square mean value for Morphine IV PCA group

2. Secondary: Pain Intensity Numerical Rating Scale (NRS) [Time Frame: Baseline, Hour 1, 2, 3, 4, 5, 6, 8, 12, 24, 48, 72, study treatment discontinuation or withdrawal, and when participant was fit for discharge (FFD) (assessed up to 91 hours)]

Measure Type	Secondary
Measure Title	Pain Intensity Numerical Rating Scale (NRS)
Measure Description	Pain intensity NRS measured pain intensity experienced by the participant on a scale, 0 to 10, where 0 means no pain and 10 mean the worst possible pain. Participant's pain intensity was assessed by asking following question to the participant: on a scale 0 to 10 where 0 means no pain, and 10 means the worst possible pain, rate the pain that you have now.
Time Frame	Baseline, Hour 1, 2, 3, 4, 5, 6, 8, 12, 24, 48, 72, study treatment discontinuation or withdrawal, and when participant was fit for discharge (FFD) (assessed up to 91 hours)
Safety Issue	No

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.
The ITT population included all participants randomly assigned to study treatment and used the study medication at least once, and who had at least 1 efficacy measure after system application or device enablement (0 hours). Here 'n' signifies those participants evaluable for this measure at the specified time point for each arm group, respectively.

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Measured Values

	Fentanyl IONSYS	**Morphine IV PCA**
Overall Participants [units: participants]	**58**	**50**
Pain Intensity Numerical Rating Scale (NRS) [units: Unit on Scale] Mean (Standard Deviation)		
Baseline (n = 58, 49)	**1.2 (1.76)**	**1.3 (1.84)**
Hour 1 (n = 58, 48)	**1.6 (2.36)**	**1.5 (2.09)**
Hour 2 (n = 57, 49)	**2.2 (2.51)**	**2.1 (2.30)**
Hour 3 (n = 57, 48)	**2.7 (2.28)**	**2.2 (2.16)**
Hour 4 (n = 57, 47)	**2.9 (2.20)**	**2.9 (2.68)**
Hour 5 (n = 58, 46)	**3.1 (2.25)**	**2.5 (2.19)**
Hour 6 (n = 55, 46)	**3.1 (2.12)**	**2.5 (2.24)**
Hour 8 (n = 54, 44)	**3.0 (1.86)**	**2.3 (2.33)**
Hour 12 (n = 48, 40)	**2.5 (2.03)**	**1.8 (1.91)**
Hour 24 (n = 52, 34)	**1.5 (1.69)**	**1.9 (1.85)**
Hour 48 (n = 13, 6)	**0.6 (0.96)**	**1.5 (1.05)**
Hour 72 (n = 3, 2)	**0.7 (1.15)**	**0.5 (0.71)**
Study discontinuation or withdrawal (n = 53, 50)	**1.8 (2.66)**	**1.6 (1.78)**
FFD (n = 44, 38)	**0.6 (1.06)**	**1.3 (1.62)**

Statistical Analysis 1 for Pain Intensity Numerical Rating Scale (NRS)

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.219

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	At Hour 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	P-value was calculated from ANCOVA, with centre, surgery type and treatment included as covariates in the analysis.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Pain Intensity Numerical Rating Scale (NRS)

Groups [1]	All groups
Method [2]	ANCOVA

P Value [3]	0.299

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	At Hour 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	P-value was calculated from ANCOVA, with centre, surgery type and treatment included as covariates in the analysis.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Pain Intensity Numerical Rating Scale (NRS)

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.136

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	At study discontinuation or withdrawal
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	P-value was calculated from ANCOVA, with centre, surgery type and treatment included as covariates in the analysis.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

3. Secondary: Nurse Ease of Care (EOC) Questionnaire Score [Time Frame: When participant was fit for discharge (FFD) (assessed up to 91 hours)]

Measure Type	Secondary
Measure Title	Nurse Ease of Care (EOC) Questionnaire Score
Measure Description	Nurse EOC questionnaire had 22 items and covered 3 aspects of care delivery associated with acute care pain management systems: time, bothersome and satisfaction. Items were scored on a 6-point Likert scale, ranging from 'not at all' (Score 0) to 'a very great deal' (score 5). The total score was calculated as the mean of the non-missing items for all the questions.
Time Frame	When participant was fit for discharge (FFD) (assessed up to 91 hours)
Safety Issue	No

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.
The ITT population included all participants randomly assigned to study treatment and used the study medication at least once, and who had at least 1 efficacy measure after system application or device enablement (0 hours).

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Measured Values

	Fentanyl IONSYS	**Morphine IV PCA**

Overall Participants [units: participants]	**58**	**50**
Nurse Ease of Care (EOC) Questionnaire Score [units: Units on scale] Least Squares Mean (95% Confidence Interval)	**0.28** **(0.07 to 0.49)**	**0.80** **(0.55 to 1.05)**

Statistical Analysis 1 for Nurse Ease of Care (EOC) Questionnaire Score

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	<0.001
Least square mean difference [4]	-0.52
95% Confidence Interval	-0.74 to -0.30

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	P-value was calculated from ANCOVA, with centre, surgery type and treatment included as covariates in the analysis.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	Least square mean difference = Least square mean value for Fentanyl IONSYS group minus Least square mean value for Morphine IV PCA group

4. Secondary: Number of Participants With Patient Global Assessment (PGA) of Method of Pain Control [Time Frame: Hour 72 or early study withdrawal]

Measure Type	Secondary
Measure Title	Number of Participants With Patient Global Assessment (PGA) of Method of Pain Control
Measure Description	The assessment consist of a categorical evaluation (poor, fair, good or excellent) of the method of pain control by asking following question from the participant: “Overall, would you rate this PCA (participant controlled analgesia) method of pain control as being poor, fair, good, or excellent?”
Time Frame	Hour 72 or early study withdrawal
Safety Issue	No

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.
The ITT population included all participants randomly assigned to study treatment and used the study medication at least once, and who had at least 1 efficacy measure after system application or device enablement (0 hours). Here 'N' (number of participants analyzed) signifies those participants evaluable for this measure.

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician’s discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Measured Values

	Fentanyl IONSYS	Morphine IV PCA
Overall Participants [units: participants]	**58**	**49**
Number of Participants With Patient Global Assessment (PGA) of Method of Pain Control [units: Participants]		
Poor	**5**	**1**
Fair	**1**	**6**
Good	**21**	**23**
Excellent	**31**	**19**

Statistical Analysis 1 for Number of Participants With Patient Global Assessment (PGA) of Method of Pain Control

Groups [1]	All groups
Method [2]	Mantel Haenszel
P Value [3]	0.131
Odds Ratio (OR) [4]	1.81
95% Confidence Interval	0.84 to 3.92

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	P-value was calculated from a Mantel-Haenszel Chi-Squared test.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

5. Secondary: Time to Fit For Discharge (FFD) [Time Frame: When participant was FFD (assessed up to 91 hours)]

Measure Type	Secondary
Measure Title	Time to Fit For Discharge (FFD)
Measure Description	Participants were assessed for fulfilling the following FFD criteria: 1- Retaining fluids and food; 2- Passing urine without the aid of a catheter; 3- Bowel sounds and/or opening; 4- Cardiovascular stability; 5- Respiratory stability; 6- No post-operative wound complications; 7- Pain adequately controlled with oral analgesia only; 8- Adequately mobile according to locally acceptable standards for mobility for surgery type and pre-operative expectations. The FFD criteria were answered on a “Yes” or “No” basis. When all criteria were answered as Yes, participant was considered to be FFD.
Time Frame	When participant was FFD (assessed up to 91 hours)
Safety Issue	No

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.
The ITT population included all participants randomly assigned to study treatment and used the study medication at least once, and who had at least 1 efficacy measure after system application or device enablement (0 hours).

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per

	hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Measured Values

	Fentanyl IONSYS	Morphine IV PCA
Overall Participants [units: participants]	**58**	**50**
Time to Fit For Discharge (FFD) [units: Hours] Median (95% Confidence Interval)	**70.08** **(65.50 to 72.25)**	**71.21** **(67.42 to 90.77)**

Statistical Analysis 1 for Time to Fit For Discharge (FFD)

Groups [1]	All groups
Method [2]	Log Rank
P Value [3]	0.342

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	P-value was calculated from a log-rank test stratified for surgery type.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

6. Secondary: Number of Participants Who Require Rescue Medication [Time Frame: Baseline up to Hour 3]

Measure Type	Secondary
Measure Title	Number of Participants Who Require Rescue Medication
Measure Description	Rescue medication was defined as a fast-acting medication given besides the study drug that could alleviate pain quickly, but the effects were not long lasting. Morphine was given intravenously as rescue medication for all participants randomly assigned to either treatment group.
Time Frame	Baseline up to Hour 3
Safety Issue	No

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.
The ITT population included all participants randomly assigned to study treatment and used the study medication at least once, and who had at least 1 efficacy measure after system application or device enablement (0 hours).

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Measured Values

	Fentanyl IONSYS	Morphine IV PCA
Overall Participants [units: participants]	**58**	**50**
Number of Participants Who Require Rescue Medication [units: Participants]	**10**	**2**

Statistical Analysis 1 for Number of Participants Who Require Rescue Medication

Groups [1]	All groups
Method [2]	Chi-squared
P Value [3]	0.029
Odds Ratio (OR) [4]	5.00
95% Confidence Interval	1.04 to 24.03

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

7. Secondary: Number of Participants Who Require Concomitant Antiemetic Medication [Time Frame: Baseline up to end of study treatment (Hour 72)]

Measure Type	Secondary
Measure Title	Number of Participants Who Require Concomitant Antiemetic Medication
Measure Description	Antiemetic medicines are the drugs which prevent vomiting.
Time Frame	Baseline up to end of study treatment (Hour 72)
Safety Issue	No

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.
The ITT population included all participants randomly assigned to study treatment and used the study medication at least once, and who had at least 1 efficacy measure after system application or device enablement (0 hours).

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Measured Values

	Fentanyl IONSYS	Morphine IV PCA
Overall Participants [units: participants]	**58**	**50**
Number of Participants Who Require Concomitant Antiemetic Medication [units: Participants]		
Dexamethasone	**1**	**0**
Cyclizine	**19**	**20**
Metoclopramide	**0**	**3**
Domperidone	**1**	**0**
Ondansetron	**11**	**12**
Granisetron	**2**	**2**
Mentha X Piperita	**0**	**1**

No statistical analysis provided for Number of Participants Who Require Concomitant Antiemetic Medication

8. Secondary: Number of Participants Who Require Concomitant Non-opioid Analgesics [Time Frame: Baseline up to end of study treatment (Hour 72)]

Measure Type	Secondary
Measure Title	Number of Participants Who Require Concomitant Non-opioid Analgesics
Measure Description	Non-opioid analgesics are non morphine like medications used to get relieve from pain.
Time Frame	Baseline up to end of study treatment (Hour 72)
Safety Issue	No

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.
The ITT population included all participants randomly assigned to study treatment and used the study medication at least once, and who had at least 1 efficacy measure after system application or device enablement (0 hours).

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Measured Values

	Fentanyl IONSYS	Morphine IV PCA
Overall Participants [units: participants]	**58**	**50**
Number of Participants Who Require Concomitant Non-opioid Analgesics [units: Participants]		
Paracetamol	**39**	**28**
NSAID's	**31**	**20**

Statistical Analysis 1 for Number of Participants Who Require Concomitant Non-opioid Analgesics

Groups [1]	All groups
Method [2]	Chi-squared
P Value [3]	0.230

Odds Ratio (OR) [4]	1.61
95% Confidence Interval	0.74 to 3.53

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Paracetamol: P-value was calculated using Chi-squared test.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Number of Participants Who Require Concomitant Non-opioid Analgesics

Groups [1]	All groups
Method [2]	Chi-squared
P Value [3]	0.163
Odds Ratio (OR) [4]	1.72
95% Confidence Interval	0.80 to 3.70

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	NSAID's: P-value was calculated using Chi-squared test.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

9. Other Pre-specified: Time to Actual Discharge [Time Frame: When participant was actually discharged from ward care (assessed up to 258.5 hours)]

Measure Type	Other Pre-specified
Measure Title	Time to Actual Discharge
Measure Description	The time from baseline to the time at which the participant was actually discharged from ward care was recorded as time to actual discharge.
Time Frame	When participant was actually discharged from ward care (assessed up to 258.5 hours)
Safety Issue	No

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.
The ITT population included all participants randomly assigned to study treatment and used the study medication at least once, and who had at least 1 efficacy measure after system application or device enablement (0 hours).

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per

	hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Measured Values

	Fentanyl IONSYS	Morphine IV PCA
Overall Participants [units: participants]	**58**	**50**
Time to Actual Discharge [units: Hours] Median (95% Confidence Interval)	**91.44** **(75.33 to 96.50)**	**94.61** **(76.77 to 96.08)**

Statistical Analysis 1 for Time to Actual Discharge

Groups [1]	All groups
Method [2]	Log Rank
P Value [3]	0.836

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	P-value was calculated from a log-rank test stratified for surgery type.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

10. Other Pre-specified: Number of Participants Facing Technical Failure of the Device [Time Frame: Baseline up to end of study treatment (Hour 72)]

Measure Type	Other Pre-specified
Measure Title	Number of Participants Facing Technical Failure of the Device
Measure Description	Technical failure was defined as malfunctioning or failure of device to work appropriately.
Time Frame	Baseline up to end of study treatment (Hour 72)
Safety Issue	Yes

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.
Safety population included all participants randomly assigned to study treatment and who used either of the study treatment at least once.

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Measured Values

	Fentanyl IONSYS	Morphine IV PCA

Overall Participants [units: participants]	**58**	**50**
Number of Participants Facing Technical Failure of the Device [units: Participants]	**1**	**1**

No statistical analysis provided for Number of Participants Facing Technical Failure of the Device

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	From the time a signed informed consent form was obtained until the participant was discharged from ward care
Additional Description	No text entered.

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Serious Adverse Events

	Fentanyl IONSYS	**Morphine IV PCA**
Total, serious adverse events		
# participants affected / at risk	**1/58 (1.72%)**	**2/50 (4.00%)**
Infections and infestations		
Wound infection * 1		
# participants affected / at risk	**1/58 (1.72%)**	**1/50 (2.00%)**
Injury, poisoning and procedural complications		
Femur fracture * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
Respiratory, thoracic and mediastinal disorders		
Pulmonary embolism * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
Vascular disorders		
Haematoma * 1		
# participants affected / at risk	**1/58 (1.72%)**	**0/50 (0.00%)**

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA version 11.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	From the time a signed informed consent form was obtained until the participant was discharged from ward care
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	0

Reporting Groups

	Description
Fentanyl IONSYS	Fentanyl 40 microgram (mcg) per 10 minutes up to a maximum of 240 mcg (6 doses each of 10 minutes duration) per hour but not more than a maximum of 3.2 milligram (80 doses) within 24 hour from an Iontophoretic Transdermal System (IONSYS), applied on the intact, non-irritated skin on the chest or upper arm. Duration of study treatment was 72 hours.
Morphine IV PCA	Morphine sulphate solution administered intravenously (directly into the vein) by a patient-controlled analgesia (PCA) pump using set bolus doses with a fixed lock out period as per physician's discretion (maximum total dose of 20 milligram per 2 hours) for 72 hours.

Other Adverse Events

	Fentanyl IONSYS	Morphine IV PCA
Total, other (not including serious) adverse events		
# participants affected / at risk	**40/58 (68.97%)**	**38/50 (76.00%)**
Blood and lymphatic system disorders		
Anaemia * 1		
# participants affected / at risk	**4/58 (6.90%)**	**2/50 (4.00%)**
Cardiac disorders		
Bradycardia * 1		
# participants affected / at risk	**4/58 (6.90%)**	**5/50 (10.00%)**
Sinus tachycardia * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
Tachycardia * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
Gastrointestinal disorders		
Nausea * 1		
# participants affected / at risk	**19/58 (32.76%)**	**13/50 (26.00%)**
Vomiting * 1		
# participants affected / at risk	**4/58 (6.90%)**	**6/50 (12.00%)**
Constipation * 1		
# participants affected / at risk	**5/58 (8.62%)**	**4/50 (8.00%)**
Dyspepsia * 1		
# participants affected / at risk	**2/58 (3.45%)**	**5/50 (10.00%)**
Diarrhoea * 1		
# participants affected / at risk	**2/58 (3.45%)**	**2/50 (4.00%)**
Abdominal discomfort * 1		
# participants affected / at risk	**2/58 (3.45%)**	**0/50 (0.00%)**
Abdominal distension * 1		
# participants affected / at risk	**0/58 (0.00%)**	**2/50 (4.00%)**
Haematemesis * 1		
# participants affected / at risk	**1/58 (1.72%)**	**1/50 (2.00%)**
Abdominal pain * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
Faeces discoloured * 1		
# participants affected / at risk	**1/58 (1.72%)**	**0/50 (0.00%)**
Gastrooesophageal reflux disease * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
Reflux gastritis * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
General disorders		
Pyrexia * 1		
# participants affected / at risk	**5/58 (8.62%)**	**4/50 (8.00%)**
Application site erythema * 1		
# participants affected / at risk	**5/58 (8.62%)**	**0/50 (0.00%)**
Pain * 1		
# participants affected / at risk	**5/58 (8.62%)**	**0/50 (0.00%)**

Application site vesicles * 1		
# participants affected / at risk	2/58 (3.45%)	0/50 (0.00%)
Catheter Site pain * 1		
# participants affected / at risk	1/58 (1.72%)	0/50 (0.00%)
Chest discomfort * 1		
# participants affected / at risk	1/58 (1.72%)	0/50 (0.00%)
Inflammation of wound * 1		
# participants affected / at risk	0/58 (0.00%)	1/50 (2.00%)
Infections and infestations		
Urinary tract infection * 1		
# participants affected / at risk	1/58 (1.72%)	1/50 (2.00%)
Cellulitis * 1		
# participants affected / at risk	1/58 (1.72%)	0/50 (0.00%)
Infection * 1		
# participants affected / at risk	1/58 (1.72%)	0/50 (0.00%)
Lower respiratory tract infection * 1		
# participants affected / at risk	0/58 (0.00%)	1/50 (2.00%)
Oral candidiasis * 1		
# participants affected / at risk	1/58 (1.72%)	0/50 (0.00%)
Injury, poisoning and procedural complications		
Wound secretion * 1		
# participants affected / at risk	1/58 (1.72%)	2/50 (4.00%)
Procedural hypotension * 1		
# participants affected / at risk	1/58 (1.72%)	1/50 (2.00%)
Bladder injury * 1		
# participants affected / at risk	0/58 (0.00%)	1/50 (2.00%)
Contusion * 1		
# participants affected / at risk	1/58 (1.72%)	0/50 (0.00%)
Investigations		
Haemoglobin decreased * 1		
# participants affected / at risk	4/58 (6.90%)	4/50 (8.00%)
Electrocardiogram abnormal * 1		
# participants affected / at risk	0/58 (0.00%)	1/50 (2.00%)
Metabolism and nutrition disorders		
Dehydration * 1		
# participants affected / at risk	0/58 (0.00%)	1/50 (2.00%)
Musculoskeletal and connective tissue disorders		
Back pain * 1		
# participants affected / at risk	1/58 (1.72%)	1/50 (2.00%)
Joint effusion * 1		
# participants affected / at risk	0/58 (0.00%)	1/50 (2.00%)
Nervous system disorders		
Dizziness * 1		
# participants affected / at risk	4/58 (6.90%)	6/50 (12.00%)
Syncope vasovagal * 1		
# participants affected / at risk	3/58 (5.17%)	1/50 (2.00%)
Loss of consciousness * 1		
# participants affected / at risk	0/58 (0.00%)	2/50 (4.00%)
Somnolence * 1		
# participants affected / at risk	1/58 (1.72%)	1/50 (2.00%)
Psychiatric disorders		
Anxiety * 1		
# participants affected / at risk	1/58 (1.72%)	0/50 (0.00%)

Hallucination * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
Insomnia * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
Sleep disorder * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
Renal and urinary disorders		
Urinary retention * 1		
# participants affected / at risk	**1/58 (1.72%)**	**4/50 (8.00%)**
Haematuria * 1		
# participants affected / at risk	**1/58 (1.72%)**	**0/50 (0.00%)**
Reproductive system and breast disorders		
Vaginal haemorrhage * 1		
# participants affected / at risk	**1/58 (1.72%)**	**0/50 (0.00%)**
Respiratory, thoracic and mediastinal disorders		
Respiratory depression * 1		
# participants affected / at risk	**1/58 (1.72%)**	**3/50 (6.00%)**
Hypoxia * 1		
# participants affected / at risk	**0/58 (0.00%)**	**2/50 (4.00%)**
Epistaxis * 1		
# participants affected / at risk	**1/58 (1.72%)**	**0/50 (0.00%)**
Nasal discomfort * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
Pharyngolaryngeal pain * 1		
# participants affected / at risk	**0/58 (0.00%)**	**1/50 (2.00%)**
Skin and subcutaneous tissue disorders		
Pruritus * 1		
# participants affected / at risk	**1/58 (1.72%)**	**3/50 (6.00%)**
Drug eruption * 1		
# participants affected / at risk	**1/58 (1.72%)**	**1/50 (2.00%)**
Erythema * 1		
# participants affected / at risk	**1/58 (1.72%)**	**0/50 (0.00%)**
Rash * 1		
# participants affected / at risk	**1/58 (1.72%)**	**0/50 (0.00%)**
Surgical and medical procedures		
Perioperative analgesia * 1		
# participants affected / at risk	**1/58 (1.72%)**	**0/50 (0.00%)**
Spinal anaesthesia * 1		
# participants affected / at risk	**1/58 (1.72%)**	**0/50 (0.00%)**
Vascular disorders		
Hypotension * 1		
# participants affected / at risk	**14/58 (24.14%)**	**13/50 (26.00%)**
Hypertension * 1		
# participants affected / at risk	**3/58 (5.17%)**	**1/50 (2.00%)**
Haematoma * 1		
# participants affected / at risk	**1/58 (1.72%)**	**1/50 (2.00%)**
Orthostatic hypotension * 1		
# participants affected / at risk	**1/58 (1.72%)**	**1/50 (2.00%)**
Wound haemorrhage * 1		
# participants affected / at risk	**1/58 (1.72%)**	**0/50 (0.00%)**

* Events were collected by non-systematic assessment

1 Term from vocabulary, MedDRA version 11.0

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
Study was temporarily stopped due to an issue with a batch of drug outside the study and later permanently stopped.

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:

- [x] 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:

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Organization: Janssen-Cilag Ltd. 50-100 Holmers Farm Way, High Wycombe , BUCKS, UK, HP12 4EG
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Responsible Party:	Janssen-Cilag Ltd.
ClinicalTrials.gov Identifier:	NCT00766506 History of Changes
Other Study ID Numbers:	CR015211 **FENHYDPAI4012** 2008-000529-20
Study First Received:	October 3, 2008
Results First Received:	January 21, 2013
Last Updated:	March 14, 2013
Health Authority:	United Kingdom: Medicines and Healthcare Products Regulatory Agency Great Britain: Medicines and Healthcare Products Regulatory Agency

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