Trial record **1 of 1** for: 204503

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Exploratory Study to Investigate Cognition Function and Mobility in Individuals With Pain

ClinicalTrials.gov Identifier: NCT02974114

Recruitment Status : Terminated
First Posted : November 28, 2016
Results First Posted : August 28, 2018
Last Update Posted : August 28, 2018

Sponsor:
GlaxoSmithKline

Information provided by (Responsible Party):
GlaxoSmithKline

Study Type	Interventional
Study Design	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Triple (Participant, Investigator, Outcomes Assessor); Primary Purpose: Other
Condition	Pain
Interventions	Drug: Paracetamol and caffeine Drug: Paracetamol Other: Placebo
Enrollment	21

Participant Flow

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Recruitment Details	All participants were recruited at a single center from the United Kingdom.
Pre-assignment Details	A Total of 54 participants were screened, out of which 21 participants were randomized to the study, 5 participants were screening failure, 1 participant withdrew consent and 27 participants were not randomized due to other reasons (not specified).

Arm/Group Title	Paracetamol and Caffeine	Paracetamol	Placebo
Arm/Group Description	All the participants in this arm received test product (containing 500 milligram [mg] of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets orally once with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets orally once with 200

	200 milliliters (mL) of water.		mL of water.
Period Title: **Overall Study**			
Started	6	7	8
Completed	6	6	6
Not Completed	0	1	2
Reason Not Completed			
Other (Not specified)	0	1	2

Baseline Characteristics

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Arm/Group Title	Paracetamol and Caffeine	Paracetamol	Placebo	Total
Arm/Group Description	All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets orally once with 200 mL of water.	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets orally once with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets orally once with 200 mL of water.	Total of all reporting groups
Overall Number of Baseline Participants	6	7	8	21
Baseline Analysis Population Description	[Not Specified]			
Age, Continuous				

Mean (Standard Deviation) Unit of measure: Years					
	Number Analyzed	6 participants	7 participants	8 participants	21 participants
		27.8 (4.83)	30.0 (9.45)	40.0 (15.87)	33.2 (12.31)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: Participants					
	Number Analyzed	6 participants	7 participants	8 participants	21 participants
	Female	4 66.7%	5 71.4%	5 62.5%	14 66.7%
	Male	2 33.3%	2 28.6%	3 37.5%	7 33.3%
Race (NIH/OMB) Measure Type: Count					

of Participants Unit of measure: Participants							
	Number Analyzed	6 participants		7 participants		8 participants		21 participants	
	American Indian or Alaska Native	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	Asian	2	33.3%	2	28.6%	1	12.5%	5	23.8%
	Native Hawaiian or Other Pacific Islander	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	Black or African American	1	16.7%	0	0.0%	2	25.0%	3	14.3%
	White	3	50.0%	5	71.4%	4	50.0%	12	57.1%
	More than one race	0	0.0%	0	0.0%	1	12.5%	1	4.8%
	Unknown or Not Reported	0	0.0%	0	0.0%	0	0.0%	0	0.0%

Outcome Measures

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1. Primary Outcome

Title	Change From Pain Free State (Day 3) in Error Adjusted Simple Reaction Time (SRT) in the Pain State (Day 2)

▼ Description	Error adjusted SRT was one of the main outcomes of the Axon Sports Priming Application. The Axon Sports Priming Application is a computerized test performed on a tablet device that measures cognitive performance, namely psychomotor speed. Axon sports test assessment included 1. Pain-state assessment performed at Visit 2 (Day 2 pre-treatment assessment and post-treatment assessment 1hour [hr] ± 15 minutes [mins] post-dosing) and 2. Pain-free assessment performed at Visit 3 (Day 3).
Time Frame	At Day 2 (pre and post-treatment) and Day 3 of the study

▼ Outcome Measure Data

▼ Analysis Population Description
Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in the mITT population.

Arm/Group Title	Paracetamol and Caffeine	Paracetamol	Placebo
▼ Arm/Group Description:	All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with 200 mL of water.
Overall Number of Participants Analyzed	6	7	7
Median (Full Range)			

Unit of Measure: milliseconds (msec)				
Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	5 participants
		0.05 (0.0 to 0.2)	0.07 (0.0 to 0.8)	0.06 (0.0 to 0.2)

Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	5 participants
		0.04 (0.0 to 0.4)	0.01 (0.0 to 0.3)	0.00 (-0.2 to 0.1)

2. Primary Outcome

Title	Change From Pain-free State (Day 3) in Reaction Time in the Pain State (Day 2)
▼ Description	The reaction time of five-choice reaction time task (provided by Cambridge Cognition) was measured. In five-choice reaction time task, all the participants hold down a button at the bottom of the screen till a yellow spot appears in one of the five circles at the top of the screen. Participants then released the button and touch inside of the circle where the yellow spot appeared as quickly as they can. The median duration, between the onset of the stimulus and the release of the button, was recorded as reaction time. Calculated for correct, assessed trials where the stimulus appeared in any one of five locations.
Time Frame	At Day 2 (pre and post-treatment) and Day 3 of the study

▼ Outcome Measure Data

▼ Analysis Population Description

Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in the mITT population.

	Arm/Group Title	Paracetamol and Caffeine	Paracetamol	Placebo

▼ Arm/Group Description:		All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with 200 mL of water.
Overall Number of Participants Analyzed		6	7	7
Median (Full Range) Unit of Measure: msec				
Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	5 participants
		2.00 (-17.5 to 36.0)	-1.75 (-41.0 to 170.5)	-1.00 (-6.5 to 18.5)
Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	5 participants
		25.75 (-11.5 to 83.5)	12.50 (-65.5 to 26.0)	-8.00 (-28.0 to 24.5)

3. Primary Outcome

Title	Change From Pain-free State (Day 3) in Number of One Touch Stockings (OTS) of Cambridge Assessment Problems (on Which the First Box Choice Made Was Correct) in the Pain State (Day 2)

▼ Description	OTS was a measure of executive function and takes approximately 10 minutes to complete. The participant was shown two displays containing three coloured balls. The displays were presented in such a way that they can easily be perceived as stacks of coloured balls held in stockings or socks suspended from a beam. There was a row of numbered boxes along the bottom of the screen. The test administrator first demonstrated to the participant how to use the balls in the lower display to copy the pattern in the upper display, and completed one demonstration problem, where the solution requires one move. The participant then completed three further problems, one each of two moves, three moves, and four moves. Next, the participant was shown further problems, and participants worked out in their head how many moves the solutions to these problems required, and then touch the appropriate box at the bottom of the screen to indicate their response.
Time Frame	At Day 2 (pre and post treatment) and Day 3 of the study

▼ Outcome Measure Data

▼ Analysis Population Description

Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in the mITT population.

Arm/Group Title	Paracetamol and Caffeine	Paracetamol	Placebo
▼ Arm/Group Description:	All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 mL	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2

		at once orally with 200 mL of water.	of water.	tablets at once orally with 200 mL of water.
Overall Number of Participants Analyzed		6	7	7

Mean (Standard Deviation) Unit of Measure: OTS of correct first box choice				
Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	5 participants
		-2.67 (3.077)	0.00 (1.095)	-0.20 (1.789)
Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	5 participants
		-1.83 (1.941)	2.17 (1.835)	-1.40 (2.702)

4. Primary Outcome

Title	Change From Pain-free State (Day 3) in Attention Switching Task (AST) Congruency Cost in the Pain State (Day 2)
▼ Description	AST was a measure of executive attention. The test displayed an arrow which can appear on either side of the screen and can point in either direction. Each trial displayed a cue at the top of the screen that indicates whether to press the right or left button. Some trials displayed congruent stimuli (e.g. arrow on the right side of the screen pointing to the right) whereas other trials display incongruent stimuli which require a higher cognitive demand (e.g. arrow on the right side of the screen pointing to the left). The AST congruency cost was the difference between the median latencies of response (from stimulus appearance to button press) on the trials that were congruent versus the trials that were incongruent. It was calculated by subtracting the median of congruent from incongruent latency. A positive score indicated response was faster on congruent trials and a negative score indicated response was faster on incongruent trials.
Time Frame	At Day 2 (pre and post treatment) and Day 3 of the study

▼ Outcome Measure Data

▼ Analysis Population Description

Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in

the mITT population.

Arm/Group Title		Paracetamol and Caffeine	Paracetamol	Placebo
▼ Arm/Group Description:		All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with 200 mL of water.
Overall Number of Participants Analyzed		6	7	7
Median (Full Range) Unit of Measure: msec				
Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	5 participants
		-3.25 (-44.5 to 46.5)	46.25 (-22.5 to 99.5)	2.50 (-4.0 to 113.5)
Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	5 participants
		-8.25 (-44.0 to 43.5)	23.00 (-5.0 to 104.0)	22.50 (-171.5 to 113.5)

5. Primary Outcome

Title	Change From Pain-free State (Day 3) in Spatial Working Memory (SWM) Between Errors in the Pain State (Day 2)

▼ Description	SWM task was a measure of working memory. The task involved number of coloured squares (boxes) being shown on the screen. The aim of this test was to find one blue token in the boxes shown to the participants by process of elimination and used these to fill up an empty column on the right-hand side of the screen. The number of boxes gradually increased up to a maximum of eight boxes to search and the colour and position of the boxes changed from trial to trial. SWM between errors was defined as times the participant revisited a box in which a token has previously been found. This was calculated for trials of four, six and eight tokens.
Time Frame	At Day 2 (pre and post treatment) and Day 3 of the study

▼ Outcome Measure Data

▼ Analysis Population Description
Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in the mITT population.

Arm/Group Title	Paracetamol and Caffeine	Paracetamol	Placebo
▼ Arm/Group Description:	All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with 200 mL of water.
Overall Number of Participants Analyzed	6	7	7

Mean (Standard Deviation) Unit of Measure: SWM between errors				
Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	5 participants
		-9.33 (18.747)	25.17 (29.075)	13.80 (23.994)
Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	5 participants
		4.83 (22.248)	13.50 (23.193)	-9.80 (32.920)

6. Primary Outcome

Title	Change From Pain-free State (Day 3) in Rapid Visual Information Processing A Prime (RVPA) in the Pain State (Day 2)
▼ Description	RVP task was measures of attention. A white box appeared in the centre of the computer screen, inside which digits, from 2 to 9, appeared in a pseudo-random order, at the rate of 100 digits per minute. Participants were requested to detect target sequences of digits (for example, 2-4-6, 3-5-7, 4-6-8) and to register responses using the press pad. The RVPA (A prime) was the signal detection measure of sensitivity to the target, regardless of response tendency (the expected range will be 0.00 to 1.00; bad to good). RVP metric was a measure of how good the subject was at detecting target sequences.
Time Frame	At Day 2 (pre and post treatment) and Day 3 of the study

▼ Outcome Measure Data

▼ Analysis Population Description

Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in the mITT population.

	Arm/Group Title	Paracetamol and Caffeine	Paracetamol	Placebo

▼ Arm/Group Description:		All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with 200 mL of water.
Overall Number of Participants Analyzed		6	7	7
Median (Full Range) Unit of Measure: msec				
Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	4 participants
		-0.04 (-0.1 to 0.0)	0.00 (0.0 to 0.0)	-0.03 (-0.1 to 0.0)
Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	4 participants
		-0.02 (-0.1 to 0.0)	-0.01 (-0.1 to 0.0)	0.00 (0.0 to 0.0)

7. Secondary Outcome

Title	Change From Pain-free State (Day 3) in Grip Force in Pain State (Day 2)
▼ Description	This task was a measure of grip strength. The participant held the dynamometer in their dominant hand and the arm was swung from above the head to by the side of the body. If the dominant arm or hand was painful then the non-dominant hand was used. The participant was instructed to assert maximum effort during the squeezing motion and maintain it for about 4 seconds using a metronome. Participant conducted the

	movement 4-times (1 practice effort and 3 test efforts) and there was a 1-minute recovery period between each effort.
Time Frame	At Day 2 (pre and post-treatment) and Day 3 of the study

▼ Outcome Measure Data

▼ Analysis Population Description

Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in the mITT population.

Arm/Group Title		Paracetamol and Caffeine	Paracetamol	Placebo
▼ Arm/Group Description:		All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with 200 mL of water.
Overall Number of Participants Analyzed		6	7	7
Mean (Standard Deviation) Unit of Measure: Kilogram (Kg)				
Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	5 participants
		-1.98 (5.505)	-3.87 (3.792)	-1.70 (3.533)
Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	5 participants
		0.68 (2.384)	-2.80 (3.059)	-0.46 (1.365)

8. Secondary Outcome

Title	Change From Pain-free State (Day 3) in Time to Standing in Pain State (Day 2)

▼ Description	Time to standing provides a simple assessment of physical mobility. From a seated position with arms crossed so that the right hand is placed on the left shoulder and the left hand on the right shoulder, participants stood to a fully erect stature in as short a time as possible. Time to standing recorded which was measured using a stopwatch. Participants conducted the same movement 3-times continuously as a practice effort and 5-times continuously as a test effort at each visit. There was a 1-minute rest between the practice and test effort.
Time Frame	At Day 2 (pre and post treatment) and Day 3 of the study

▼ Outcome Measure Data

▼ Analysis Population Description

Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in the mITT population.

Arm/Group Title	Paracetamol and Caffeine	Paracetamol	Placebo
▼ Arm/Group Description:	All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with 200 mL of water.
Overall Number of Participants Analyzed	6	7	7
Median (Full Range)			

Unit of Measure: Seconds				
Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	5 participants
		0.10 (-0.4 to 0.2)	0.13 (-0.2 to 0.3)	0.09 (0.0 to 0.3)

Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	5 participants
		-0.01 (-0.2 to 0.5)	-0.08 (-0.3 to 0.4)	0.04 (-0.2 to 0.6)

9. Secondary Outcome

Title	Change From Pain-free State (Day 3) in Ground Reaction Force (GRF) in Pain State (Day 2)
▼ Description	From a seated position with arms crossed so that the right hand is placed on the left shoulder and the left hand on the right shoulder, participants stood to a fully erect stature in as short a time as possible. Participants conducted the same movement 3-times continuously as a practice effort and 5-times continuously as a test effort at each visit. There was a 1-minute rest between the practice and test effort. GRF was measured during the movement analyzed using a force plate interfaced with a computer.
Time Frame	At Day 2 (pre and post treatment) and Day 3 of the study

▼ Outcome Measure Data

▼ Analysis Population Description

Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in the mITT population.

Arm/Group Title	Paracetamol and Caffeine	Paracetamol	Placebo
▼ Arm/Group Description:	All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of	All the participants in this arm received test product (containing 500 mg of paracetamol). All the	All the participants in this arm received reference product (placebo to match Paracetamol 665mg

		paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL of water.	paracetamol). All the participants took 2 tablets at once orally with 200 mL of water.	Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with 200 mL of water.
Overall Number of Participants Analyzed		6	7	7
Mean (Standard Deviation) Unit of Measure: Newtons				
Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	5 participants
		3.35 (11.781)	-19.80 (43.788)	3.75 (11.214)
Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	5 participants
		4.21 (8.295)	-13.85 (47.387)	3.08 (12.064)

10. Secondary Outcome

Title	Change From Pain-free State (Day 3) in Contact Phase in Pain State (Day 2)
▼ Description	Participants performed a walking assessment in comfortable walking shoes to measure gait parameter contact phase. An athletic movement analysis system (Optojump, Microgate) was utilized which set up over a 15 meters (m) length of track with only the 5-10m section measured and analysed. Participants were instructed to walk the 15m length a minimum of 6 times (3 practice and a minimum of 3 test walks) always entering the 15m length with the same foot first. The foot (left or right) entering the 5-10m section first was recorded by visual assessment of the Optojump operator for the test walks. Test walks were repeated until there were 3 walks in which the participants have entered the 5-10m section with the same foot first.
Time Frame	At Day 2 (pre and post treatment) and Day 3 of the study

▼ Outcome Measure Data

▼ Analysis Population Description
Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study

treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in the mITT population.

Arm/Group Title		Paracetamol and Caffeine	Paracetamol	Placebo
▼ Arm/Group Description:		All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with 200 mL of water.
Overall Number of Participants Analyzed		6	7	7
Median (Full Range) Unit of Measure: Seconds				
Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	5 participants
		0.03 (0.0 to 0.1)	0.03 (0.0 to 0.1)	0.00 (0.0 to 0.0)
Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	5 participants
		0.03 (-0.0 to 0.1)	0.02 (-0.0 to 0.1)	0.01 (-0.02 to 0.03)

11. Secondary Outcome

Title	Change From Pain-free State (Day 3) in Stride Length in Pain State (Day 2)
▼ Description	Participants performed a walking assessment in comfortable walking shoes to measure gait parameter stride length. An athletic movement analysis system (Optojump, Microgate) was utilized which set up over a 15 meters (m) length of track with only the 5-10m section measured and analysed. Participants were instructed to walk the 15m length a minimum of 6 times (3 practice and a minimum of 3 test walks) always entering the

	15m length with the same foot first. The foot (left or right) entering the 5-10m section first was recorded by visual assessment of the Optojump operator for the test walks. Test walks were repeated until there were 3 walks in which the participants have entered the 5-10m section with the same foot first.
Time Frame	At Day 2 (pre and post treatment) and Day 3 of the study

▼ Outcome Measure Data

▼ Analysis Population Description

Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in the mITT population.

Arm/Group Title		Paracetamol and Caffeine	Paracetamol	Placebo
▼ Arm/Group Description:		All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with 200 mL of water.
Overall Number of Participants Analyzed		6	7	7
Mean (Standard Deviation) Unit of Measure: Centimeter				
Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	5 participants
		-0.06 (0.098)	-0.08 (0.123)	-0.02 (0.038)
Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	5 participants
		-0.04 (0.084)	-0.06 (0.116)	-0.04 (0.037)

12. Secondary Outcome

Title	Change From Pain-free State (Day 3) in Walking Speed in Pain State (Day 2)

▼ Description	Participants performed a walking assessment in comfortable walking shoes to measure gait parameter walking speed over 5-10m for each foot. An athletic movement analysis system (Optojump, Microgate) was utilized which set up over a 15 meters (m) length of track with only the 5-10m section measured and analysed. Participants were instructed to walk the 15m length a minimum of 6 times (3 practice and a minimum of 3 test walks) always entering the 15m length with the same foot first. The foot (left or right) entering the 5-10m section first was recorded by visual assessment of the Optojump operator for the test walks. Test walks were repeated until there were 3 walks in which the participants have entered the 5-10m section with the same foot first.
Time Frame	At Day 2 (pre and post-treatment) and Day 3

▼ Outcome Measure Data

▼ Analysis Population Description
Modified Intent-to-Treat (mITT, N=20) Population: All the participants who were randomized, received at least one dose of the study treatment and had at least one post-baseline assessment without any violation of study inclusion-exclusion criteria were included in the mITT population.

Arm/Group Title	Paracetamol and Caffeine	Paracetamol	Placebo
▼ Arm/Group Description:	All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 milliliters (mL) of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with

	of water.		200 milliliters (mL) of water.
Overall Number of Participants Analyzed	6	7	7
Mean (Standard Deviation) Unit of Measure: meters/second			

Change from pain-free state at Day 2 pre-treatment	Number Analyzed	6 participants	6 participants	5 participants
		-0.11 (0.112)	-0.10 (0.180)	-0.02 (0.052)
Change from pain-free state at Day2 post-treatment	Number Analyzed	6 participants	6 participants	5 participants
		-0.10 (0.105)	-0.07 (0.157)	-0.03 (0.043)

Adverse Events

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Time Frame	Up to 61 days
Adverse Event Reporting Description	[Not Specified]

Arm/Group Title	Paracetamol and Caffeine	Paracetamol	Placebo
▼ Arm/Group Description	All the participants in this arm received test product (containing 500 mg of paracetamol and 65 mg of caffeine). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received test product (containing 500 mg of paracetamol). All the participants took 2 tablets at once orally with 200 mL of water.	All the participants in this arm received reference product (placebo to match Paracetamol 665mg sustained release tablets). All the participants took 2 tablets at once orally with 200 mL of water.

All-Cause Mortality

	Paracetamol and Caffeine	Paracetamol	Placebo
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	0/6 (0.00%)	0/7 (0.00%)	0/8 (0.00%)

Serious Adverse Events

	Paracetamol and Caffeine	Paracetamol	Placebo
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	0/6 (0.00%)	0/7 (0.00%)	0/8 (0.00%)

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	1%

	Paracetamol and Caffeine	Paracetamol	Placebo
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	0/6 (0.00%)	1/7 (14.29%)	2/8 (25.00%)
Gastrointestinal disorders			
Gastrooesophageal reflux disease †	0/6 (0.00%)	0/7 (0.00%)	1/8 (12.50%)
Metabolism and nutrition disorders			
Hypercholesterolaemia †	0/6 (0.00%)	0/7 (0.00%)	1/8 (12.50%)
Respiratory, thoracic and mediastinal disorders			
Pharyngeal erythema †	0/6 (0.00%)	1/7 (14.29%)	0/8 (0.00%)

† Indicates events were collected by systematic assessment

Limitations and Caveats

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Limitations and Caveats

The study was terminated early due to breaches of GCP guidelines observed during a GSKCH internal audit. The minimum requirement of 8 subjects per strata was not met because of early termination so some exploratory analyses were not conducted.

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.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Results Point of Contact

Name/Title:	GSK Response Center
Organization:	GlaxoSmithKline
Phone:	866-435-7343
EMail:	GSKClinicalSupportHD@gsk.com

Responsible Party:	GlaxoSmithKline
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