ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 06/06/2014

The Pharmacokinetics of Anagrelide in Elderly and Young Patients With Essential Thrombocythaemia (ET)

This study has been completed.

Sponsor:	Shire
Collaborators:	
Information provided by:	Shire
ClinicalTrials.gov Identifier:	NCT00413634

Purpose

Age related differences in response to a drug could arise from variation in pharmacokinetic (PK) and/or pharmacodynamic (PD) profiles between age groups. Whilst the efficacy and safety profile of anagrelide is well established through a well-documented clinical trial programme in patients of all ages, no formal studies have been carried out to investigate whether the PK profile of anagrelide and its metabolites is altered with age.

This study is designed to allow comparisons to be made in terms of pharmacokinetics of anagrelide and its metabolites between elderly (≥ 65 years) and young (18-50 years) ET patients

Condition	Intervention	Phase
Essential Thrombocythaemia	Drug: anagrelide hydrochloride	Phase 2

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Non-Randomized, Pharmacokinetics/Dynamics Study
Official Title: A Phase II, Open-label, Multicentre, Pharmacokinetic, Pharmacodynamic and Safety Study of Anagrelide Hydrochloride in Young (18-50 Years) and Elderly (≥ 65 Years) Patients With Essential Thrombocythaemia.

Further study details as provided by Shire:

Primary Outcome Measure:

- Maximum Plasma Concentration (Cmax) of Agrylin [Time Frame: over 1 day] [Designated as safety issue: Yes]

- Time of Maximum Plasma Concentration (Tmax) of Agrylin [Time Frame: over 1 day] [Designated as safety issue: Yes]
- Area Under the Steady-state Plasma Concentration-time Curve (AUC) of Agrylin [Time Frame: over 1 day] [Designated as safety issue: Yes]
- Terminal Half-life (T 1/2) of Agrylin [Time Frame: over 1 day] [Designated as safety issue: Yes]
- Total Clearance (CL/F) of Agrylin [Time Frame: over 1 day] [Designated as safety issue: Yes]
- Volume of Distribution (Vz/F) of Agrylin [Time Frame: over 1 day] [Designated as safety issue: Yes]
- Cmax of Active Metabolite [Time Frame: over 1 day] [Designated as safety issue: Yes]
  An active metabolite has therapeutic activity similar to the parent compound and must be considered in therapeutic pharmacokinetics.
- Tmax of Active Metabolite [Time Frame: over 1 day] [Designated as safety issue: Yes]
- AUC of Active Metabolite [Time Frame: over 1 day] [Designated as safety issue: Yes]
- T 1/2 of Active Metabolite [Time Frame: over 1 day] [Designated as safety issue: Yes]
- CL/F of Active Metabolite [Time Frame: over 1 day] [Designated as safety issue: Yes]
- Vz/F of Active Metabolite [Time Frame: over 1 day] [Designated as safety issue: Yes]

Secondary Outcome Measures:

- Platelet Count [Time Frame: over 1 day] [Designated as safety issue: Yes]
  Platelet counts in patients with ET receiving Agrylin
- Heart Rate [Time Frame: over 1 day] [Designated as safety issue: Yes]
  Heart rates in patients with ET receiving Agrylin
- Systolic Blood Pressure [Time Frame: over 1 day] [Designated as safety issue: Yes]
  Systolic blood pressures in patients with ET receiving Agrylin
- Diastolic Blood Pressure [Time Frame: over 1 day] [Designated as safety issue: Yes]
  Diastolic blood pressures in patients with ET receiving Agrylin

Enrollment: 24
Study Start Date: August 2006
Primary Completion Date: January 2008
Study Completion Date: March 2008

Arms	Assigned Interventions
Experimental: 1	Drug: anagrelide hydrochloride Anagrelide hydrochloride 0.5 mg per capsule; patients will be stable on an anagrelide treatment regimen and will take capsules from their own prescription except on the PK day when the patient specific anagrelide dose will be administered from a controlled study specific supply.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Young patients aged 18-50 years inclusive or Elderly patients aged 65 years and over
- Patients must have a confirmed diagnosis of ET.
- Currently receiving anagrelide hydrochloride at a stable maintenance dose < 5 mg/day for at least 4 weeks.

Exclusion Criteria:

- Diagnosis of any other myeloproliferative disorder.
- Current use of tobacco in any form (e.g. smoking or chewing)
- Treatment with any known enzyme altering agents (barbiturates, phenothiazines, cimetidine etc.) within 30 days prior to or during the study.
- Patients for whom use of another cytoreductive agent in addition to anagrelide is considered necessary for control of platelet count.

Contacts and Locations

Locations

Spain
- Hospitl Del Mar
  - Barcelona, Barcelona, Spain

Sweden
- Quintiles Hermelinen
  - Sandviksgatan, Lulea, Sweden
- Quintiles AB Phase I Unit
  - Strandbodgatan, Uppsala, Sweden
- Uppsala Akademiska Sjukhus
  - Uppsala, Uppsala, Sweden, 75185

United Kingdom
- Belfast City Hospital
  - Belfast, Belfast, United Kingdom

Investigators

Principal Investigator:	Carlos Besses Raebel	Spain

More Information

FDA-approved Label
http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020333s015lbl.pdf

Synopsis of Study Results
http://www.clinicalstudyresults.org/documents/company-study_8912_0.pdf

FDA Recall Information
http://www.fda.gov/opacom/7alerts.html

Responsible Party: Shire (Timothy Whitaker, M.D.)
Study ID Numbers: SPD422-203
2004-004058-20 [EudraCT Number]
Health Authority: United Kingdom: Medicines and Healthcare Products Regulatory Agency
Germany: Federal Institute for Drugs and Medical Devices
Sweden: Medical Products Agency
Spain: Ministry of Health

Study Results

Participant Flow

Recruitment Details	Patients were between 18-50 years (young) and 65 or older (elderly) with a diagnosis of essential thrombocythemia (ET) and receiving a stable dose of anagrelide <=5mg/day for at least 4 weeks.
Pre-Assignment Details	The study comprised four phases: Screening (patients take their normal regimen of anagrelide), a run-in period (patients divided their normal anagrelide daily dose equally into two daily doses), Pharmacokinetics (PK) sampling day (patients take normal morning dose), and follow-up (patients were contacted by phone 30 days after PK visit).

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Overall Study

	Agrylin (Young)	Agrylin (Elderly)
Started	12	12
Completed	12	12
Not Completed	0	0

Baseline Characteristics

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Baseline Measures

	Agrylin (Young)	Agrylin (Elderly)	Total
Number of Participants	12	12	24
Age, Categorical [units: participants]			
<=18 years	0	0	0.0
Between 18 and 65 years	12	0	12.0
>=65 years	0	12	12.0
Age, Continuous [units: years] Mean (Standard Deviation)	39.2 (8.4)	69.2 (3.0)	54.2 (16.5)
Gender, Male/Female [units: participants]			
Female	9	8	17.0
Male	3	4	7.0
Region of Enrollment [units: participants]			
Germany	5	10	15.0
United Kingdom	2	1	3.0
Spain	1	1	2.0
Sweden	2	0	2.0
Serbia	2	0	2.0

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Maximum Plasma Concentration (Cmax) of Agrylin
Measure Description	
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description

PK population (defined as all patients with post-dose drug concentration data)

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Maximum Plasma Concentration (Cmax) of Agrylin [units: ng/ml] Geometric Mean (Standard Deviation)	2.66 (0.99)	3.63 (1.44)

Statistical Analysis 1 for Maximum Plasma Concentration (Cmax) of Agrylin

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.092
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

2. Primary Outcome Measure:

Measure Title	Time of Maximum Plasma Concentration (Tmax) of Agrylin
Measure Description	
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
PK population

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Time of Maximum Plasma Concentration (Tmax) of Agrylin [units: hours] Geometric Mean (Standard Deviation)	1.11 (0.39)	1.14 (0.91)

Statistical Analysis 1 for Time of Maximum Plasma Concentration (Tmax) of Agrylin

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.857
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

3. Primary Outcome Measure:

Measure Title	Area Under the Steady-state Plasma Concentration-time Curve (AUC) of Agrylin
Measure Description	
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
PK population

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Area Under the Steady-state Plasma Concentration-time Curve (AUC) of Agrylin [units: ng.h/ml] Geometric Mean (Standard Deviation)	6.4 (2.4)	10.3 (4.0)

Statistical Analysis 1 for Area Under the Steady-state Plasma Concentration-time Curve (AUC) of Agrylin

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.013
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

4. Primary Outcome Measure:

Measure Title	Terminal Half-life (T 1/2) of Agrylin
Measure Description	
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
PK population

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Terminal Half-life (T 1/2) of Agrylin [units: hours] Geometric Mean (Standard Deviation)	1.3 (0.4)	1.4 (0.3)

Statistical Analysis 1 for Terminal Half-life (T 1/2) of Agrylin

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.378
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

5. Primary Outcome Measure:

Measure Title	Total Clearance (CL/F) of Agrylin
Measure Description	
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
PK population

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Total Clearance (CL/F) of Agrylin [units: L/h] Geometric Mean (Standard Deviation)	156 (73)	97 (70)

Statistical Analysis 1 for Total Clearance (CL/F) of Agrylin

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.013
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

6. Primary Outcome Measure:

Measure Title	Volume of Distribution (Vz/F) of Agrylin
Measure Description	
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
PK population

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Volume of Distribution (Vz/F) of Agrylin [units: L] Geometric Mean (Standard Deviation)	286 (125)	195 (137)

Statistical Analysis 1 for Volume of Distribution (Vz/F) of Agrylin

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.035
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

7. Primary Outcome Measure:

Measure Title	Cmax of Active Metabolite
Measure Description	An active metabolite has therapeutic activity similar to the parent compound and must be considered in therapeutic pharmacokinetics.
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
PK population

Reporting Groups

	Description
Agrylin (Young)	Active metabolite of Agrylin (BCH24426) in ages 18-50
Agrylin (Elderly)	Active metabolite of Agrylin (BCH24426) in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Cmax of Active Metabolite [units: ng/ml] Geometric Mean (Standard Deviation)	7.26 (3.74)	4.19 (3.47)

Statistical Analysis 1 for Cmax of Active Metabolite

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.023
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

8. Primary Outcome Measure:

Measure Title	Tmax of Active Metabolite
Measure Description	
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
PK population

Reporting Groups

	Description
Agrylin (Young)	Active metabolite of Agrylin (BCH24426) in ages 18-50
Agrylin (Elderly)	Active metabolite of Agrylin (BCH24426) in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Tmax of Active Metabolite [units: hours] Geometric Mean (Standard Deviation)	0.92 (0.26)	1.04 (0.99)

Statistical Analysis 1 for Tmax of Active Metabolite

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.557
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

9. Primary Outcome Measure:

Measure Title	AUC of Active Metabolite
Measure Description	
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
PK population

Reporting Groups

	Description
Agrylin (Young)	Active metabolite of Agrylin (BCH24426) in ages 18-50
Agrylin (Elderly)	Active metabolite of Agrylin (BCH24426) in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
AUC of Active Metabolite [units: ng.h/ml] Geometric Mean (Standard Deviation)	27.6 (10.9)	17.4 (14.8)

Statistical Analysis 1 for AUC of Active Metabolite

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.027
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

10. Primary Outcome Measure:

Measure Title	T 1/2 of Active Metabolite
Measure Description	
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
PK population

Reporting Groups

	Description
Agrylin (Young)	Active metabolite of Agrylin (BCH24426) in ages 18-50
Agrylin (Elderly)	Active metabolite of Agrylin (BCH24426) in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
T 1/2 of Active Metabolite [units: hours] Geometric Mean (Standard Deviation)	2.7 (0.5)	3.5 (1.1)

Statistical Analysis 1 for T 1/2 of Active Metabolite

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.007
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

11. Primary Outcome Measure:

Measure Title	CL/F of Active Metabolite
Measure Description	
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
PK population

Reporting Groups

	Description
Agrylin (Young)	Active metabolite of Agrylin (BCH24426) in ages 18-50
Agrylin (Elderly)	Active metabolite of Agrylin (BCH24426) in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
CL/F of Active Metabolite [units: L/h] Geometric Mean (Standard Deviation)	36 (16)	57 (27)

Statistical Analysis 1 for CL/F of Active Metabolite

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.027
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

12. Primary Outcome Measure:

Measure Title	Vz/F of Active Metabolite
Measure Description	
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
PK population

Reporting Groups

	Description
Agrylin (Young)	Active metabolite of Agrylin (BCH24426) in ages 18-50
Agrylin (Elderly)	Active metabolite of Agrylin (BCH24426) in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Vz/F of Active Metabolite [units: L] Geometric Mean (Standard Deviation)	139 (86)	277 (203)

Statistical Analysis 1 for Vz/F of Active Metabolite

Statistical Analysis Overview	Comparison Groups	Agrylin (Young), Agrylin (Elderly)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.011
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

13. Secondary Outcome Measure:

Measure Title	Platelet Count
Measure Description	Platelet counts in patients with ET receiving Agrylin
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description

Safety population (defined as all patients who received study treatment)

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Platelet Count [units: x 1,000,000,000/L] Mean (Standard Deviation)		
Baseline	488.8 (167.4)	548.5 (278.7)
2 hours post-dose	487.9 (168.1)	539.2 (258.6)
12 hours post-dose	473.2 (146.0)	540.3 (263.6)

14. Secondary Outcome Measure:

Measure Title	Heart Rate
Measure Description	Heart rates in patients with ET receiving Agrylin
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description

Safety population

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Heart Rate [units: beats/min] Mean (Standard Deviation)		
Baseline	74.0 (9.6)	70.3 (8.4)
0.5 hours post-dose	72.4 (8.9)	77.7 (13.5)
1 hour post-dose	75.8 (5.5)	80.6 (11.7)
1.5 hours post-dose	78.1 (7.7)	82.7 (12.9)
2 hours post-dose	74.3 (7.0)	81.2 (13.8)
4 hours post-dose	75.0 (5.5)	74.7 (13.7)
6 hours post-dose	75.9 (8.6)	76.9 (11.4)
8 hours post-dose	75.5 (6.7)	76.3 (10.1)
12 hours post-dose	73.2 (6.0)	71.9 (8.1)

15. Secondary Outcome Measure:

Measure Title	Systolic Blood Pressure
Measure Description	Systolic blood pressures in patients with ET receiving Agrylin
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description

Safety population

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Systolic Blood Pressure [units: mmHg] Mean (Standard Deviation)		
Baseline	122.2 (9.6)	154.3 (19.6)
0.5 hours post-dose	122.7 (12.9)	145.2 (20.3)
1.0 hours post-dose	121.8 (11.7)	143.7 (21.8)
1.5 hours post-dose	122.3 (11.6)	140.1 (17.7)
2 hours post-dose	121.3 (12.3)	139.9 (19.8)
4 hours post-dose	122.2 (13.6)	133.7 (18.1)
6 hours post-dose	120.2 (16.1)	141.8 (19.5)
8 hours post-dose	123.6 (14.5)	136.3 (24.3)
12 hours post-dose	124.7 (13.6)	159.8 (28.6)

16. Secondary Outcome Measure:

Measure Title	Diastolic Blood Pressure
Measure Description	Diastolic blood pressures in patients with ET receiving Agrylin
Time Frame	over 1 day
Safety Issue?	Yes

Analysis Population Description
Safety population

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Measured Values

	Agrylin (Young)	Agrylin (Elderly)
Number of Participants Analyzed	12	12
Diastolic Blood Pressure [units: mmHg] Mean (Standard Deviation)		
Baseline	76.9 (7.5)	81.4 (10.3)
0.5 hours post-dose	74.8 (7.3)	75.2 (9.9)
1 hour post-dose	72.4 (6.6)	72.6 (7.5)
1.5 hours post-dose	72.8 (6.7)	71.6 (9.5)
2 hours post-dose	71.3 (7.9)	72.8 (7.1)
4 hours post-dose	76.2 (6.0)	73.0 (9.5)
6 hours post-dose	73.4 (10.0)	71.3 (7.6)
8 hours post-dose	76.3 (6.2)	75.0 (11.3)
12 hours post-dose	76.3 (9.1)	84.2 (12.4)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Agrylin (Young)	Anagrelide hydrochloride in ages 18-50 years
Agrylin (Elderly)	Anagrelide hydrochloride in ages 65 and older

Serious Adverse Events

	Agrylin (Young)		Agrylin (Elderly)	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	0/12 (0%)		0/12 (0%)	

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Agrylin (Young)		Agrylin (Elderly)	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	3/12 (25%)		0/12 (0%)	
Infections and infestations				
Nasopharyngitis *	1/12 (8.33%)	1	0/12 (0%)	0
Urinary tract infection *	1/12 (8.33%)	1	0/12 (0%)	0
Nervous system disorders				
Headache *	1/12 (8.33%)	1	0/12 (0%)	0
Respiratory, thoracic and mediastinal disorders				
Epistaxis *	1/12 (8.33%)	1	0/12 (0%)	0

* Indicates events were collected by non-systematic methods.

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

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

If a multicenter publication is not submitted within twelve (12) months after conclusion, abandonment or termination of the Study at all sites, or after Sponsor confirms there shall be no multicenter Study publication, the Institution and/or such Principal Investigator may publish the results from the Institution site individually.

Results Point of Contact:

Name/Official Title: Timothy Whitaker, M.D.
Organization: Shire

Phone:
Email: twhitaker@shire.com