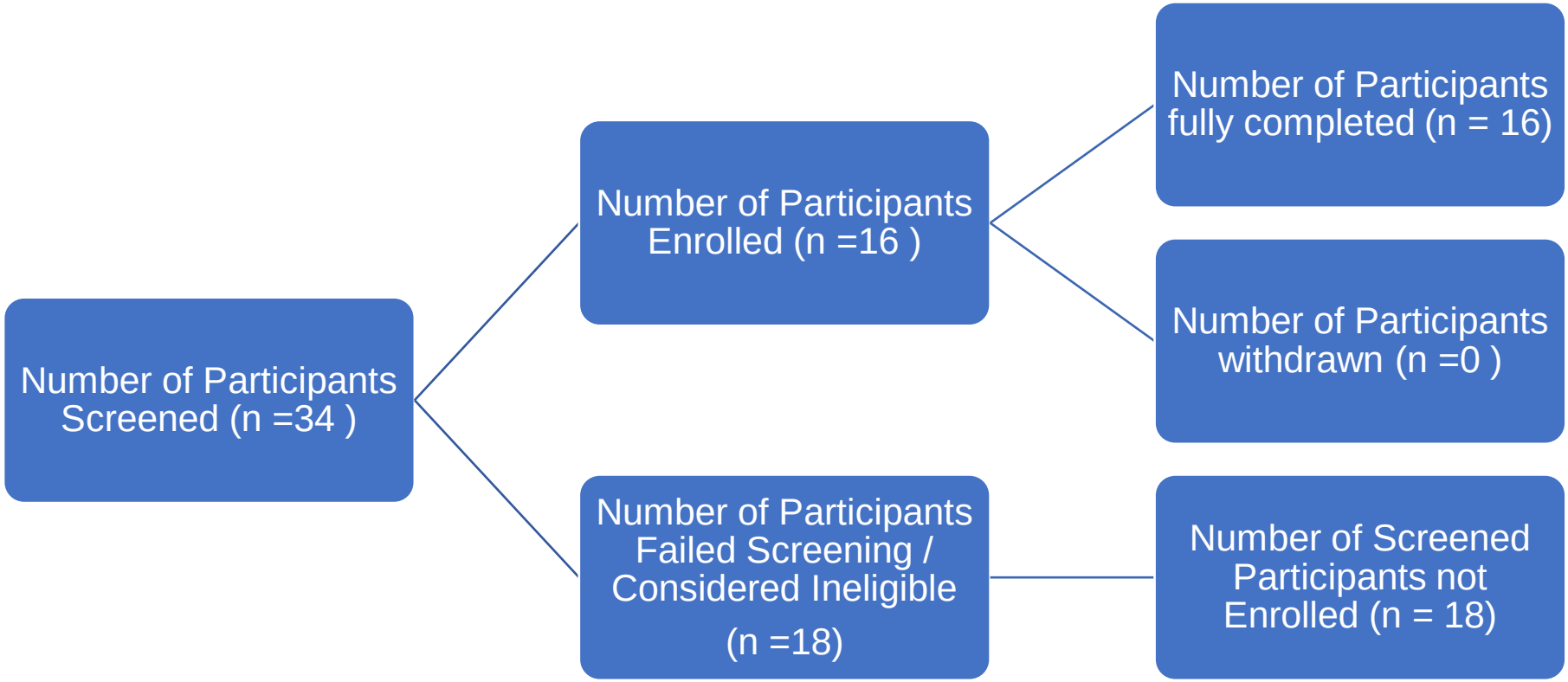
Participant Flow



Baseline Characteristics

Table 1: Summary of Subject Demographics and Baseline Data (Safety Analysis Set)

Parameter	Statistic	Cohort 1: 200 µg IPP-201101 (N=8)	Cohort 2: 800 µg IPP-201101 (N=8)	Overall (N=16)
Age (Yrs)	n	8	8	16
	Mean	41.5	42.1	41.8
	SD	8.57	11.89	10.01
Height (M)	n	8	8	16
	Mean	1.794	1.774	1.784
	SD	0.0560	0.0396	0.0480
Weight (Kg)	n	8	8	16
	Mean	89.39	83.70	86.54
	SD	7.672	7.226	7.776
BMI (Kg/M^2)	n	8	8	16
	Mean	27.80	26.68	27.24
	SD	2.321	2.850	2.577
Ethnicity:				
Not Hispanic Or Latino	n (%)	8 (100.0)	8 (100.0)	16 (100.0)
Hispanic Or Latino	n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Not Reported	n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Unknown	n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Race:				
Caucasian	n (%)	8 (100.0)	6 (75.0)	14 (87.5)
Other	n (%)	0 (0.0)	2 (25.0)	2 (12.5)
Gender:				
Male	n (%)	8 (100.0)	8 (100.0)	16 (100.0)

Treatment:

Cohort 1: Treatment period 1 a single s.c. dose of 200 µg IPP-201101

Cohort 2: Treatment period 1 a single s.c. dose of 800 µg IPP-201101. Treatment period 2 a single i.v. dose of 800 µg IPP-201101

Percentages calculated from the number of subjects in the safety set within a cohort.

BMI = body mass index, i.v. = intravenous, s.c. = subcutaneous

Outcome Measures – Primary Objectives

Table 2: Summary of Derived IPP 201101 PK Parameters (PK Set)

Treatment	Summary Statistic	C_{max} (pg/mL)	t_{max} (min)	C_0 (pg/mL)	λz (l/min)	$t_{1/2}$ (min)	AUC_{0-t} (min*pg/ml)	AUC_{0-inf} (min*pg/ml)	$AUC_{\%extrap.}$ (%)	CL/F (L/h)	CL (L/h)	Vz/F (L)	Vz (L)	F
200 µg s.c. IPP-201101 (N=8)	N	8	8	NC	NC	NC	5	NC	NC	NC	NC	NC	NC	NC
	Mean	29.7	3.75	NC	NC	NC	285	NC	NC	NC	NC	NC	NC	NC
	Geo. Mean	32.8	5.74	NC	NC	NC	137	NC	NC	NC	NC	NC	NC	NC
	SD	46.7	3.54	NC	NC	NC	324	NC	NC	NC	NC	NC	NC	NC
	CV%	157.5	94.3	NC	NC	NC	113.8	NC	NC	NC	NC	NC	NC	NC
	Min	0.00	0.00	NC	NC	NC	35.6	NC	NC	NC	NC	NC	NC	NC
	Median	16.4	5.00	NC	NC	NC	74.6	NC	NC	NC	NC	NC	NC	NC
	Max	140	10.0	NC	NC	NC	716	NC	NC	NC	NC	NC	NC	NC
800 µg s.c. IPP-201101 (N=8)	N	8	8	NC	6	6	8	6	6	6	NC	6	NC	6
	Mean	113	9.38	NC	0.0926	8.21	1840	2420	12.3	26000	NC	4680	NC	0.0176
	Geo. Mean	98.2	8.23	NC	0.0885	7.83	1520	2100	10.0	22900	NC	4310	NC	0.0128
	SD	66.1	4.96	NC	0.0296	2.82	1350	1500	8.53	14200	NC	2160	NC	0.0134
	CV%	58.6	52.9	NC	31.9	34.3	73.0	62.0	69.6	54.8	NC	46.2	NC	75.9
	Min	45.7	5.00	NC	0.0548	5.16	693	939	4.65	9160	NC	2790	NC	0.00339
	Median	95.7	7.50	NC	0.0935	7.48	1450	2090	9.10	23500	NC	4150	NC	0.0151
	Max	245	15.0	NC	0.134	12.7	4790	5240	25.2	51100	NC	8320	NC	0.0343
800 µg i.v. IPP-201101 (N=8)	N	8	8	8	8	8	8	8	8	NC	8	NC	8	N/A
	Mean	19100	2.13	188000	0.0228	34.7	181000	181000	0.592	NC	405	NC	347	N/A
	Geo. Mean	16100	2.10	122000	0.0215	32.2	142000	143000	0.453	NC	335	NC	259	N/A
	SD	13800	0.354	207000	0.00737	16.4	151000	151000	0.405	NC	245	NC	241	N/A
	CV%	72.3	16.6	110.0	32.2	47.1	83.6	83.2	68.3	NC	60.6	NC	69.3	N/A
	Min	7940	2.00	36900	0.00977	22.0	57600	58100	0.115	NC	92.0	NC	56.2	N/A
	Median	16600	2.00	114000	0.0248	28.0	134000	135000	0.563	NC	362	NC	323	N/A
	Max	51200	3.00	657000	0.0315	71.0	521000	522000	1.26	NC	826	NC	727	N/A

Treatment: Cohort 1: Treatment period 1 a single s.c. dose of 200 µg IPP-201101; Cohort 2: Treatment period 1 a single s.c. dose of 800 µg IPP-201101. Treatment period 2 a single i.v. dose of 800 µg IPP-201101. LLOQ = 10.00 pg/mL. For the purposes of PK parameter calculation, BLQ values were set to zero.
BLQ = below the limit of quantification, i.v. = intravenous, LLOQ = lower limit of quantification, N/A = not applicable, NC = not calculated, PK = pharmacokinetic, s.c. = subcutaneous

Table 3: Summary of Statistical Analysis of Absolute Bioavailability of Derived Plasma IPP 201101 PK Data (PK Set)

Parameter	Number in Comparison	Geometric LSMeans (95% CI)	Geometric LSMean Ratio (%) (90% CI) [Within-Subject CV%]	
		800 µg s.c. IPP-201101 (N=8)	800 µg i.v. IPP-201101 (N=8)	800 µg s.c. IPP-201101 / 800 µg i.v. IPP-201101
C_{max} (pg/mL)	8	98.2 (63.7 - 152)	16100 (10400 - 24900)	0.609 (0.373 - 0.996) [55.6]
AUC_{0-t} (min*pg/mL)	8	1520 (881 - 2610)	142000 (82700 - 245000)	1.065 (0.576 - 1.969) [72.3]

Treatment: Cohort 2: Treatment period 1 a single s.c. dose of 800 µg IPP-201101. Treatment period 2 a single i.v. dose of 800 µg IPP-201101.
Results obtained using an ANOVA with fixed effects for treatment and subject.
ANOVA = analysis of variance, i.v. = intravenous, s.c. = subcutaneous

Note: no urine PK data are presented in this summary as all urine concentration values measured were below the level of quantification and therefore no data are available.

Outcome Measures – Secondary Objectives

Laboratory Safety Data

Biochemistry profiles (alanine transaminase, albumin, alkaline phosphatase, aspartate transaminase, bicarbonate, total bilirubin, calcium, chloride, c reactive protein, creatine kinase, creatinine, glucose (random), gamma glutamyl transferase, potassium, total protein, sodium and urea) were measured at set timepoints throughout the study. There were no clinically significant biochemistry results during the study. There were no dose or dose administration route related changes/trends in any biochemistry parameters, with similar values observed for 200 µg and 800 µg IPP 201101 administered s.c. and 800 µg administered i.v.

Haematology profiles (haemoglobin, haematocrit, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, platelet count, red blood cell count, red blood cell distribution width, white blood cell count and differential [absolute and % neutrophils, lymphocytes, monocytes, eosinophils, and basophils]) were measured at set timepoints throughout the study. There were no clinically significant haematology results during the study. There were no dose or dose administration route related changes/trends in any haematology parameters, with similar values observed for 200 µg and 800 µg IPP 201101 administered s.c. and 800 µg administered i.v.

Urinalysis profiles (bilirubin, blood, glucose, ketones [or ketone bodies], leukocytes, nitrite, pH, protein, specific gravity, and urobilinogen) were measured at set timepoints throughout the study. There were no clinically significant urinalysis results during the study.

Vital Signs

Vital signs (semi supine systolic/diastolic blood pressure, heart rate, oral body temperature) were measured at set timepoints during the study. There were no clinically significant vital sign results during the study. There were no dose or dose administration route related changes/trends in any vital sign parameters, with similar values observed for 200 µg and 800 µg IPP 201101 administered s.c. and 800 µg administered i.v.

Physical Examination

Physical examinations (ear/nose/throat, ophthalmological, dermatological, cardiovascular, respiratory, gastrointestinal, central nervous system, lymph nodes and musculoskeletal and other) were performed at set timepoints during the study. There were no clinically significant physical examination findings.

12 Lead ECG

12 lead ECGs (heart rate, PR interval, QRS width, QT interval and QTcF interval) were performed at set timepoints during the study. There were no clinically significant 12 lead ECG results during the study. There were no dose or dose administration route related changes/trends in any 12 lead ECG parameters, with similar values observed for 200 µg and 800 µg IPP 201101 administered s.c. and 800 µg administered i.v.

Injection Site Reaction Assessment

Injection site reaction (pain, tenderness, erythema/redness, induration/swelling) assessments were performed at set timepoints during the study. There was 1 injection site reaction of pain 1 h post i.v. administration of 800 µg IP 201101 reported as an AE. There were no other injection site reactions reported during the study.

Adverse Events

A total of 3 TEAEs were reported by 3 (18.8%) subjects during the study. The majority were mild and unrelated to IMP. One (1) subject reported an almost definitely related event (mild, transient, injection site pain) following i.v. administration of 800 µg IPP-201101, but there were no other TEAEs of note and no subject reported any injection site reactions following s.c. administration of IPP-201101. There were no dose or dose administration route-related trends in AEs observed for *200 µg and 800 µg* IPP-201101 administered s.c. and 800 µg IPP-201101 administered i.v.

Table 4: Overall Summary of TEAEs by Severity and Relationship (Safety Set)

	Cohort 1	Cohort 2		
	200 µg s.c. IPP-201101 (N=8)	**800 µg s.c. IPP-201101 (N=8)**	**800 µg i.v. IPP-201101 (N=8)**	**Overall (N=16)**
Number of TEAEs	1	1	1	3
Number (%) of subjects reporting at least one:				
TEAE	1 (12.5)	1 (12.5)	1 (12.5)	3 (18.8)
Serious TEAE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TEAE Leading to Withdrawal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TEAE Leading to Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Number (%) of subjects with TEAE by severity:				
Mild	1 (12.5)	0 (0.0)	1 (12.5)	2 (12.5)
Moderate	0 (0.0)	1 (12.5)	0 (0.0)	1 (6.3)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Number (%) of subjects with TEAE by relationship to study drug:				
Almost Definite	0 (0.0)	0 (0.0)	1 (12.5)	1 (6.3)
Probable	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Possible	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Cohort 1	Cohort 2		
	200 µg s.c. IPP-201101 (N=8)	800 µg s.c. IPP-201101 (N=8)	800 µg i.v. IPP-201101 (N=8)	Overall (N=16)
Unlikely	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unrelated	1 (12.5)	1 (12.5)	0 (0.0)	2 (12.5)
N/A	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Treatment:

Cohort 1: Treatment period 1 a single s.c. dose of 200µg IPP-201101

Cohort 2: Treatment period 1 a single s.c. dose of 800µg IPP-201101. Treatment period 2 a single i.v. dose of 800µg IPP-201101

Percentages calculated from the number of subjects in the Safety Set within a treatment group.

i.v. = intravenous, N/A = not applicable, s.c. = subcutaneous, TEAE(s) = treatment emergent adverse event(s)

Table 5: TEAEs in each Treatment Group by System Organ Class and Preferred Term (Safety Set)

SYSTEM ORGAN CLASS Preferred Term	Number of Events / Number (%) of Subjects			
	Cohort 1	Cohort 2		
	200 µg s.c. IPP-201101 (N=8)	800 µg s.c. IPP-201101 (N=8)	800 µg i.v. IPP-201101 (N=8)	Overall (N=16)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Injection site pain	0/ 0 (0.0)	0/ 0 (0.0)	1/ 1 (12.5)	1/ 1 (6.3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS				
Post-traumatic neck syndrome	1/ 1 (12.5)	0/ 0 (0.0)	0/ 0 (0.0)	1/ 1 (6.3)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
Back pain	0/ 0 (0.0)	1/ 1 (12.5)	0/ 0 (0.0)	1/ 1 (6.3)